Cross-Dehydrogenative Couplings

International Edition: DOI: 10.1002/anie.201612190
German Edition: DOI: 10.1002/ange.201612190

Cs_2CO_3-Catalyzed Aerobic Oxidative Cross-Dehydrogenative Coupling of Thiols with Phosphonates and Arenes

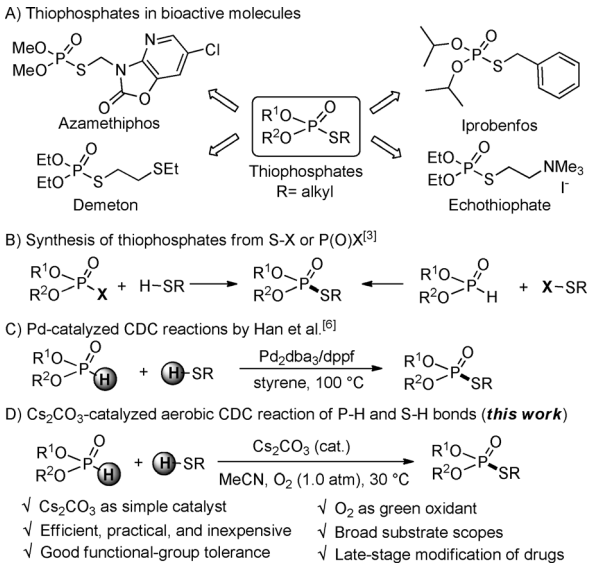
Song Song, Yiqun Zhang, Adeli Yeerlan, Bencong Zhu, Jianzhong Liu, and Ning Jiao**

Dedicated to Professor Qi-Lin Zhou on the occasion of his 60th birthday

Abstract: *An efficient Cs_2CO_3-catalyzed oxidative coupling of thiols with phosphonates and arenes that uses molecular oxygen as the oxidant is described. These reactions provide not only a novel alkali metal salt catalyzed aerobic oxidation, but also an efficient approach to thiophosphates and sulfenylarenes, which are ubiquitously found in pharmaceuticals and pesticides. The reaction proceeds under simple and mild reaction conditions, tolerates a wide range of functional groups, and is applicable to the late-stage synthesis and modification of bioactive molecules.*

The development of efficient, practical, and green oxidation systems for valuable organic transformations has always been a pursuit of organic chemists. Transition-metal catalysts have been widely used in oxidations because of their multivalency. In contrast, although simple alkali-metal salts are inexpensive, of low toxicity, and easily removable, they have rarely been employed as catalysts in oxidative reactions. Thiophosphates, especially *S*-alkyl thiophosphates (R = alkyl, Scheme 1 A), exhibit important bioactivities and are widely used as pharmaceuticals and pesticides.[1] As a result, the development of efficient approaches to thiophosphates has received considerable attention. Aside from Atherton–Todd-type reactions, which proceed in the presence of a strong base with CH_nX_{4-n} (X = Cl, Br, I, F) as the reagent and solvent,[2] syntheses of thiophosphates from prefunctionalized S–X or P(O)X starting materials were developed over the past decades (Scheme 1 B).[3] However, toxic reagents, harsh reaction conditions, narrow substrates scopes, and the employment of air-sensitive reagents have strongly limited the extensive application of these reactions.

Cross-dehydrogenative couplings (CDCs) have attracted much attention because they greatly increase overall reaction efficiencies and improve atom economy.[4] The oxidative CDC of thiols and phosphonates for P–S bond construction is still a challenging task because P–H and S–H bonds are easily oxidized by stoichiometric oxidants.[5] Moreover, these approaches are only suitable for highly active diphenylphosphine oxides[5a,c] or aromatic thiols,[5b,c] and fail for the synthesis of *S*-alkyl thiophosphates. Recently, Han and coworkers developed a novel and significant palladium-catalyzed CDC reaction of thiols and phosphonates for the synthesis of thiophosphates, which featured a broad substrate scope and good functional-group tolerance while stoichiometric amounts of styrene and high reaction temperatures were required for this catalytic process (Scheme 1 C).[6] Despite the significance of these reports, it is highly desirable to develop an efficient approach to thiophosphates with an easily available catalyst, broad substrate scope, high atom economy, and an environmentally friendly oxidant.



Scheme 1. Synthesis and application of thiophosphates.

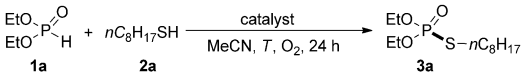
Molecular oxygen (O_2) as the ideal green oxidant is widely applied in organic synthesis.[7] In 2008, Li and Zhao reported a significant Cs_2CO_3/ketone-catalyzed CDC of glycine esters and malonates with stoichiometric $Cu(OAc)_2$ as oxidant.[8] Since then, our group has also developed a Cs_2CO_3-catalyzed hydroxylation of ketones with O_2 as the oxygen source.[9] However, a simple Cs_2CO_3-catalyzed aerobic oxidative CDC with O_2 as the green oxidant has not been realized. Herein, we disclose an efficient and practical approach to thiophosphates starting from thiols and dialkyl phosphates. To the best of our

[*] Dr. S. Song, Y. Zhang, A. Yeerlan, B. Zhu, J. Liu, Prof. N. Jiao
State Key Laboratory of Natural and Biomimetic Drugs
School of Pharmaceutical Sciences, Peking University
Xue Yuan Rd. 38, Beijing 100191 (China)
E-mail: ssong@bjmu.edu.cn
jiaoning@pku.edu.cn
Homepage: http://sklnbd.bjmu.edu.cn/nj
Prof. N. Jiao
State Key Laboratory of Organometallic Chemistry
Chinese Academy of Sciences
Shanghai 200032 (China)
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: http://dx.doi.org/10.1002/anie.201612190.

knowledge, this is the first Cs_2CO_3-catalyzed oxidative coupling without transition-metal assistance. The mild reaction conditions, good functional-group tolerance, and broad S–H, P–H, and C–H scope make this protocol applicable in the late-stage synthesis and modification of bioactive molecules (Scheme 1D).

A preliminary optimization of the reaction conditions was carried out with diethyl phosphonate (**1a**) and octanethiol (**2a**; 1.2 equiv) at 40 °C under O_2 atmosphere (Table 1).

Table 1: Optimization of the reaction conditions.[a]

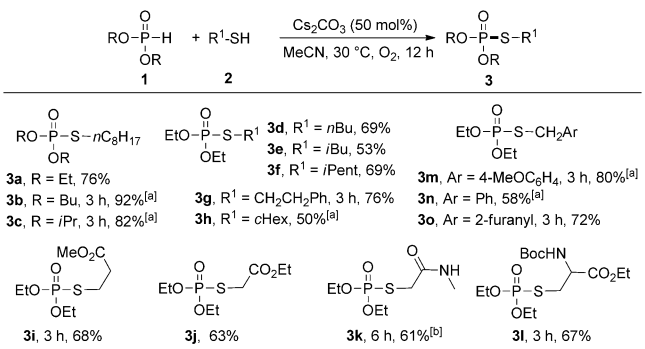


Entry	Catalyst (equiv)	T [°C]	Yield [%][b]
1	Li_2CO_3 (0.1)	40	n.d.
2	Na_2CO_3 (0.1)	40	n.d.
3	K_2CO_3 (0.1)	40	n.d.
4	KO*t*Bu (0.1)	40	trace
5	NaOH (0.1)	40	trace
6	Cs_2CO_3 (0.1)	40	18
7	Cs_2CO_3 (0.5)	40	77
8	Cs_2CO_3 (1.0)	40	76
9	$CsOH·H_2O$ (0.5)	40	37
10	CsOAc (0.5)	40	trace
11	CsOPiv (0.5)	40	15
12	Cs_2CO_3 (0.5)	30	77 (76)
13[c]	Cs_2CO_3 (0.5)	30	7

[a] A solution of **1a** (0.25 mmol), **2a** (0.3 mmol), and catalyst in MeCN (1 mL) was stirred under O_2 atmosphere for 24 h. [b] Yields determined by ^{31}P NMR analysis of the crude reaction mixture using $Ph_3P(O)$ as an internal standard. Yields of isolated products given in parentheses. [c] Under argon atmosphere.

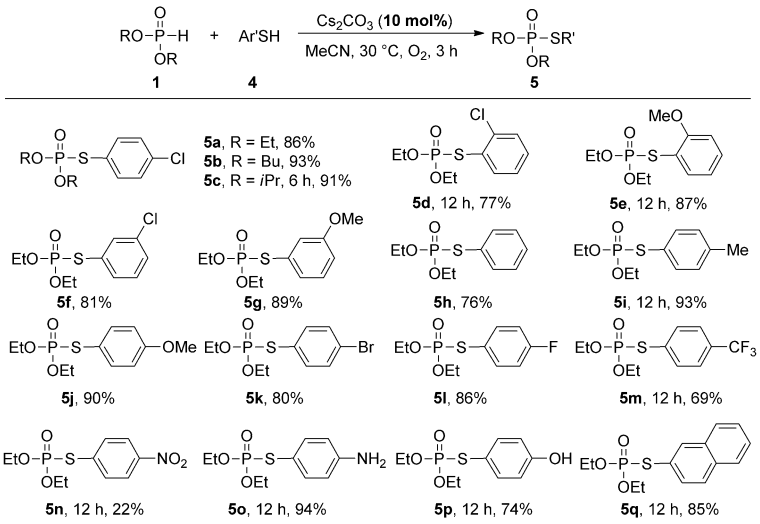
Inspired by Han's significant work[6] and our Cs_2CO_3-catalyzed process,[9] inorganic alkali-metal bases (Li_2CO_3, Na_2CO_3, K_2CO_3, *t*BuOK, and NaOH) were investigated in this reaction, but they failed to catalyze this process (entries 1–5). Other alkali-metal salts and organic bases (NEt_3 and pyridine) also could not catalyze the CDC reaction of **1a** and **2a** (see the Supporting Information). Interestingly, Cs_2CO_3 afforded product **3a** in 18% yield at a catalyst loading of 0.1 equiv (entry 6) whereas **3a** was produced in 77% yield upon addition of 0.5 equiv of Cs_2CO_3 (entry 7). Other cesium salts, such as CsOAc, CsOH, and CsOPiv, did not promote the reaction efficiently (entries 9–11). The CDC reaction of **1a** and **2a** also proceeded well at 30 °C (entry 12). Product **3a** was obtained in only 7% yield when the CDC reaction was conducted in argon atmosphere (entry 13), which indicates that O_2 is essential in this transformation.

We then evaluated the oxidative CDC reaction of phosphonates **1** and aliphatic thiols **2** in the presence of Cs_2CO_3 at 30 °C under O_2 (Scheme 2). Aside from diethyl phosphonate, diisopropyl and dibutyl phosphonate could also be coupled with octanethiol (**2a**) to afford the corresponding products **3b** and **3c** in high yields. Primary thiols reacted smoothly with these phosphonates to afford the products **3a**–**3g** in moderate to good yields. The reaction of cyclohexanethiol and diethyl phosphonate needed a higher reaction temperature to form product **3h** in 50% yield. Ester and amide groups were tolerated by the present Cs_2CO_3/O_2 system. Strikingly, a cysteine derivative was also phosphorylated in 67% yield under the optimized reaction conditions (**3l**). In addition, thiols with benzyl substituents could be easily coupled with diethyl phosphonate at 60 °C. A reactive furan ring was tolerated to afford product **3o** in 72% yield.



Scheme 2. Cs_2CO_3-catalyzed CDC reactions of phosphonates and aliphatic thiols. A solution of **1** (0.25 mmol), **2** (0.3 mmol), and Cs_2CO_3 (0.125 mmol) in MeCN (1 mL) was stirred under O_2 atmosphere. Yields of isolated products are given. [a] At 80 °C. [b] At 60 °C.

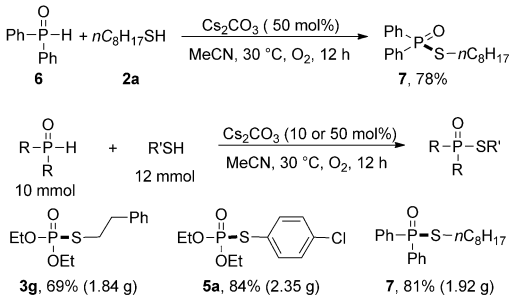
The oxidative CDC reaction of dialkyl phosphonates **1** and aromatic thiols **4** (Scheme 3) provides a direct approach to *S*-aryl thiophosphates, which were used for the construction of pyrophosphate linkages.[10] Cs_2CO_3 was active enough to catalyze these reactions at a loading of only 10 mol% at 30 °C under O_2 atmosphere (Scheme 3). Thiols **4** with different *ortho*, *meta*, and *para* substituents gave the corresponding products in good yields irrespective of the steric bulk of the substituent (**5d**–**5n**). Aromatic thiols bearing Me, MeO, Br, F,



Scheme 3. Cs_2CO_3-catalyzed CDC reactions of phosphonates and aromatic thiols. A solution of **1** (0.25 mmol), **4** (0.3 mmol), and Cs_2CO_3 (0.025 mmol) in MeCN (1 mL) was stirred under O_2 for 3 h. Yields of isolated products are given.

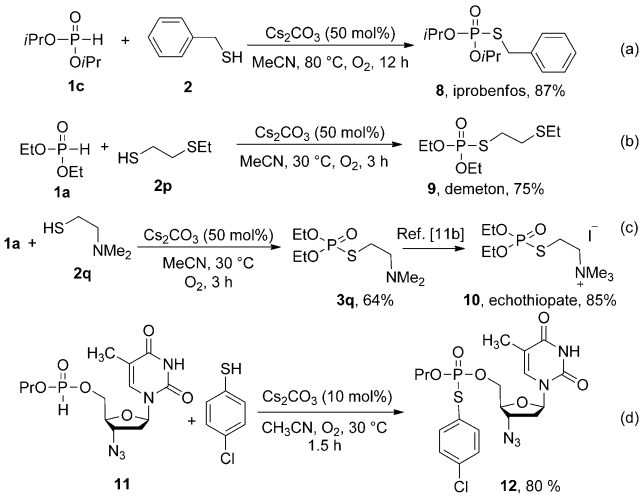
or Cl groups furnished the desired thiophosphates in high yields. Notably, a thiol with an electron-withdrawing CF_3 group was smoothly coupled with **1a** (69% yield, **5m**) whereas a NO_2-substituted thiol afforded product **5n** in 22% yield. Free amine and hydroxy groups, which hardly survive in traditional approaches, were tolerated under these conditions to afford the corresponding products **5o** and **5p** in high yields.

Aside from dialkyl phosphonates, diphenyl phosphine oxide (**6**) could also be coupled with octanethiol (**2a**) to produce **7** in 78% yield (Scheme 4). Furthermore, this Cs_2CO_3-catalyzed oxidative CDC reaction of phosphonates (10 mmol) and thiols (12 mmol) could be performed on gram scale.



Scheme 4. CDC reaction of P–H/S–H bonds on 10 mmol scale.

The present approach for the synthesis of *S*-alkyl thiophosphates features a broad substrate scope, and was also applied in the concise synthesis of several bioactive molecules (Scheme 5). Iprobenfos, a pesticide used against rice blast, could be easily prepared by the CDC reaction of diisopropyl phosphonate (**1c**) and benzyl thiol in 87% yield in the presence of Cs_2CO_3 (Scheme 5a). The synthesis of demeton, which bears a highly reactive ethylthio group that is easily oxidized by oxidants such as *tert*-butyl hydroperoxide[5a] or

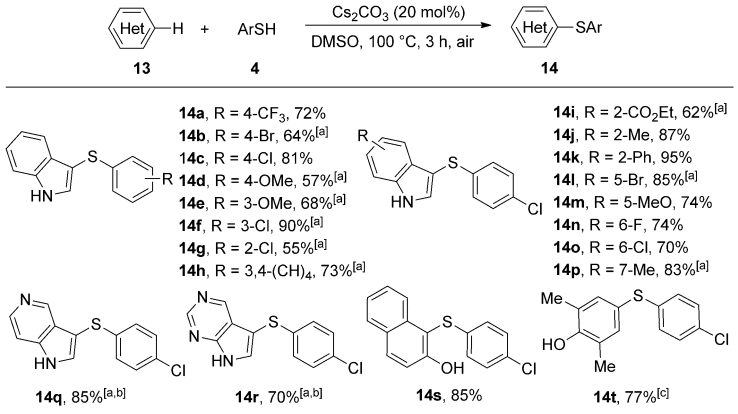


Scheme 5. Application of the Cs_2CO_3-catalyzed CDC reaction for the synthesis of bioactive molecules.

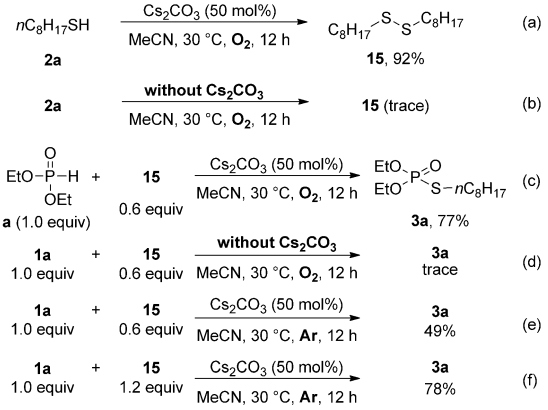
tert-butyl peroxide,[5b] could not be realized by the previously reported oxidative CDC reaction of phosphonate and thiol. Under the present Cs_2CO_3/O_2 conditions, however, the ethylthio-substituted thiol was phosphorylated smoothly to afford demeton in 75% yield (Scheme 5b). The CDC reaction of diethyl phosphonate (**1a**) with commercially available thiol **2q** afforded thiophosphate **3q** in 64% yield, which was easily converted into echothiopate, a drug used for the treatment of glaucoma[11] (Scheme 5c). Compound **11**, a derivative of zidovudine (AZT), which is used for the treatment of AIDS,[12] exhibits attractive bioactivity, and could be coupled with 4-chlorothiophenol to give **12** in 80% yield as amide, double bond, azide, and ester groups are tolerated (Scheme 5d). These experiments (Scheme 5) demonstrate that the Cs_2CO_3/O_2-based CDC reaction of thiols and phosphonates is amenable to the late-stage synthesis and modification of bioactive molecules.

Aside from P–S bonds, sulfenylarenes bearing C–S bonds are widely used for the treatment of diseases because of their therapeutic value.[13] Such compounds are usually synthesized from prefunctionalized arenes such as aryl halides or aryl boronic acids in transition-metal-catalyzed cross-coupling reactions.[14] Methods for the direct sulfenylation of arenes with sulfenylating agents,[15] such as sulfenyl halides, *N*-thioimides, sulfonium salts, disulfides, quinone mono-*O,S*-acetals, arylsulfonyl chlorides, and sulfonyl hydrazides, have also been developed. Several reports have described oxidative CDC reactions of arenes and thiols;[16] however, harsh reaction conditions, narrow substrates scopes, or the employment of stoichiometric amounts of oxidant have strongly restricted the widely application of these methods. Inspired by the above success in P–S bond construction, we expanded the Cs_2CO_3/O_2 system to C–S bond formation (Scheme 6). In the presence of 20 mol% Cs_2CO_3, the coupling of indole derivatives and thiols proceeded smoothly to afford sulfenylindoles in good to high yields. Thiols bearing various functional groups at the aryl ring, such as CF_3 (**14a**), OMe (**14d**, **14e**), Cl (**14c**, **14f**, **14g**), or Br (**14b**), furnished the desired products in high yields. The substituents on the indole ring have little influence on the sulfenylation. Other arenes, such as azaindoles (**14q**, **14r**), naphthalene (**14s**), and benzene (**14t**), could also be sulfenylated. Importantly, both Cs_2CO_3 and air are indispensable in the present coupling reaction of thiols and arenes (see the Supporting Information).

We conducted detailed control experiments to understand the roles of Cs_2CO_3 and O_2 in this CDC reaction (Scheme 7). Under the standard conditions without the addition of phosphonate, octanethiol (**2a**) is converted into disulfide **15** in high yield (Scheme 7a). Cs_2CO_3 is indispensable in this transformation (Scheme 7b). It is noteworthy that oxidative couplings of thiols and disulfides with O_2 as the oxidant are usually catalyzed by flavoenzyme,[17a] laccase,[17b] heterogeneous gold catalysts,[17c] iron metal–organic frameworks,[17d] eosin Y,[17e] or diaryl tellurides.[17f] Compared to these systems, the present Cs_2CO_3/O_2 system is much more economic, practical, and environmentally friendly. As reported, aryl disulfides can be easily converted into thiophosphates,[3j–l] but AIBN is required for the reaction with aliphatic disulfides.[3m] It is noteworthy that the efficiency of the reaction with

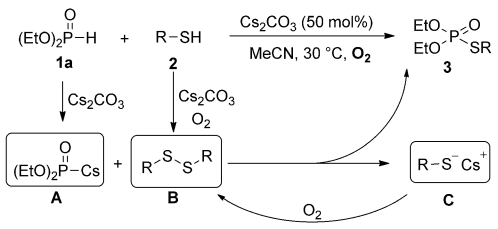


Scheme 6. Cs_2CO_3-catalyzed CDC reaction of arenes and thiols. A solution of **13** (0.25 mmol), **4** (0.3 mmol), and Cs_2CO_3 (0.05 mmol) in DMSO (1 mL) was stirred at 100 °C under air. Yields of isolated products are given. [a] **4** (0.5 mmol) [b] Cs_2CO_3 (0.25 mmol). [c] At 130 °C with **4** (0.375 mmol).



Scheme 7. Mechanistic studies.

aliphatic disulfides **15** in the presence of Cs_2CO_3 and O_2 is very high (Scheme 7c). In contrast, in the absence of Cs_2CO_3, the coupling of **1a** and **15** did not proceed, which indicates the importance of Cs_2CO_3 (Scheme 7d). Moreover, **3a** was obtained in 49% yield when **1a** and **15** (0.6 equiv) were coupled in argon atmosphere in the presence of Cs_2CO_3 (Scheme 7e; 78% yield from 1.2 equiv of **15**, Scheme 7f). These results demonstrate that only half the amount of **15** was coupled with **1a** in the absence of O_2, and the other half could be oxidized to **15** in the presence of O_2 (see Scheme 8).



Scheme 8. Proposed mechanism.

Based on the above preliminary results, a possible mechanism was proposed (Scheme 8). Initially, diethyl phosphonate (**1a**) reacts with Cs_2CO_3 to give intermediate **A** ([$(EtO)_2P(O)Cs$]). Meanwhile, the oxidative coupling of thiol **2** or **4** affords disulfide **B** in the presence of Cs_2CO_3 and O_2. Disulfide **B** is then attacked by intermediate **A** to give thiophosphate **3** and **C** ([RS^-Cs^+]). For the nucleophilic attack between **A** and **B**, Cs_2CO_3 and O_2 are not necessary. Species **C** ([RS^-Cs^+]) is oxidized to disulfide **B** by O_2,[18] thus only 1.2 equivalents of thiol **2** are needed for full conversion of **1a**.

In summary, we have developed a Cs_2CO_3-catalyzed CDC reaction of thiols with phosphonates and arenes for the efficient synthesis of thiophosphates and sulfenylarenes, which are ubiquitous in pharmaceuticals and pesticides. Environmentally friendly molecular oxygen was employed as the oxidant. The simple and mild reaction conditions, good functional-group tolerance, and broad substrate scope make this method applicable in the late-stage synthesis and modification of bioactive molecules.

Acknowledgements

Financial support from the National Basic Research Program of China (973 Program; 2015CB856600), the National Natural Science Foundation of China (21325206, 21632001), the National Young Top-notch Talent Support Program, and Peking University Health Science Center (BMU20150505, BMU20160541) is greatly appreciated.

Conflict of interest

The authors declare no conflict of interest.

Keywords: aerobic oxidation · cesium · cross-dehydrogenative couplings · thiols · thiophosphates

[1] a) L. D. Quin, *A Guide to Organophosphorus Chemistry*, Wiley Interscience, New York, **2000**; b) N. S. Li, J. K. Frederiksen, J. A. Piccirilli, *Acc. Chem. Res.* **2011**, *44*, 1257; c) T. S. Kumar, T. Yang, S. Mishra, C. Cronin, S. Chakraborty, J.-B. Shen, B. T. Liang, K. A. Jacobson, *J. Med. Chem.* **2013**, *56*, 902; d) R. Xie, Q. Zhao, T. Zhang, J. Fang, X. Mei, J. Ning, Y. Tang, *Bioorg. Med. Chem.* **2013**, *21*, 278; e) B. Kaboudin, S. Emadi, A. Hadizadeh, *Bioorg. Chem.* **2009**, *37*, 101; f) J. A. Fraietta, Y. M. Mueller, D. H. Do, V. M. Holmes, M. K. Howett, M. G. Lewis, A. C. Boesteanu, S. S. Alkan, P. D. Katsikis, *Antimicrob. Agents Chemother.* **2010**, *54*, 4064.

[2] a) F. R. Atherton, A. R. Todd, *J. Chem. Soc.* **1947**, 674; b) E. M. Georgiev, J. Kaneti, K. Troev, D. M. Roundhill, *J. Am. Chem. Soc.* **1993**, *115*, 10964; c) S. Li, T. Chen, Y. Saga, L.-B. Han, *RSC Adv.* **2015**, *5*, 71544; d) B. Xiong, Y. Zhou, C. Zhao, M. Goto, S.-F. Yin, L.-B. Han, *Tetrahedron* **2013**, *69*, 9373; e) G. Wang, R.

Shen, Q. Xu, M. Goto, Y. Zhao, L.-B. Han, *J. Org. Chem.* **2010**, *75*, 3890.

[3] a) P. Carta, N. Puljic, C. Robert, A. L. Dhimane, L. Fensterbank, E. Lacote, M. Malacria, *Org. Lett.* **2007**, *9*, 1061; b) P. Carta, N. Puljic, C. Robert, A. L. Dhimane, C. Ollivier, L. Fensterbank, E. Lacote, M. Malacria, *Tetrahedron* **2008**, *64*, 11865; c) M. Arisawa, T. Ono, M. Yamaguchi, *Tetrahedron Lett.* **2005**, *46*, 5669; d) P. Y. Renard, H. Schwebe, P. Vayron, L. Josien, A. Valleix, C. Mioskowski, *Chem. Eur. J.* **2002**, *8*, 2910; e) J. Bai, X. Cui, H. Wang, Y. Wu, *Chem. Commun.* **2014**, *50*, 8860; f) G. Kumaraswamy, R. Raju, *Adv. Synth. Catal.* **2014**, *356*, 2591; g) X. Bi, J. Li, F. Meng, H. Wang, J. Xiao, *Tetrahedron* **2016**, *72*, 706; h) Y.-C. Liu, C.-F. Lee, *Green Chem.* **2014**, *16*, 357; i) R. G. Harvey, H. I. Jacobson, E. V. Jensen, *J. Am. Chem. Soc.* **1963**, *85*, 1623; j) Y.-X. Gao, G. Tang, Y. Cao, Y.-F. Zhao, *Synthesis* **2009**, 1081; k) Y.-J. Ouyang, Y.-Y. Li, N.-B. Li, X.-H. Xu, *Chin. Chem. Lett.* **2013**, *24*, 1103; l) Q. Xu, C.-G. Liang, X. Huang, *Synth. Commun.* **2003**, *33*, 2777; m) W.-M. Wang, L.-J. Liu, L. Yao, F.-J. Meng, Y.-M. Sun, C.-Q. Zhao, Q. Xu, L.-B. Han, *J. Org. Chem.* **2016**, *81*, 6843; n) Y. Moon, Y. Moon, H. Choia, S. Hong, *Green Chem.* **2017**, DOI: 10.1039/c6gc03285k.

[4] a) C.-J. Li, *From C–H to C–C Bonds: Cross-Dehydrogenative-Coupling*, Royal Society of Chemistry, London, **2014**; b) C.-J. Li, *Acc. Chem. Res.* **2009**, *42*, 335; c) S. A. Girard, T. Knauber, C.-J. Li, *Angew. Chem. Int. Ed.* **2014**, *53*, 74; *Angew. Chem.* **2014**, *126*, 76; d) C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3464; e) R. Waterman, *Chem. Soc. Rev.* **2013**, *42*, 5629; f) M. Itazaki, H. Nakazawa, *Top. Organomet. Chem.* **2015**, *50*, 47; g) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215.

[5] a) J. Wang, X. Huang, Z. Ni, S. Wang, J. Wu, Y. Pan, *Green Chem.* **2015**, *17*, 314; b) J. Wang, X. Huang, Z. Ni, S. Wang, Y. Pan, J. Wu, *Tetrahedron* **2015**, *71*, 7853; c) J.-G. Sun, H. Yang, P. Li, B. Zhang, *Org. Lett.* **2016**, *18*, 5114.

[6] Y. Zhu, T. Chen, S. Li, S. Shimada, L.-B. Han, *J. Am. Chem. Soc.* **2016**, *138*, 5825.

[7] a) T. Punniyamurthy, S. Velusamy, J. Iqbal, *Chem. Rev.* **2005**, *105*, 2329; b) S. S. Stahl, *Angew. Chem. Int. Ed.* **2004**, *43*, 3400; *Angew. Chem.* **2004**, *116*, 3480; c) M. S. Sigman, D. R. Jensen, *Acc. Chem. Res.* **2006**, *39*, 221; d) K. M. Gligorich, M. S. Sigman, *Angew. Chem. Int. Ed.* **2006**, *45*, 6612; *Angew. Chem.* **2006**, *118*, 6764; e) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3381; f) W. Wu, H. Jiang, *Acc. Chem. Res.* **2012**, *45*, 1736; g) A. N. Campbell, S. S. Stahl, *Acc. Chem. Res.* **2012**, *45*, 851; h) S. E. Allen, R. R. Walvoord, R. Padilla-Salinas, M. C. Kozlowski, *Chem. Rev.* **2013**, *113*, 6234; i) A. E. Wendlandt, A. M. Suess, S. S. Stahl, *Angew. Chem. Int. Ed.* **2011**, *50*, 11062; *Angew. Chem.* **2011**, *123*, 11256j) C. Liu, D. Liu, A. Lei, *Acc. Chem. Res.* **2014**, *47*, 3459.

[8] L. Zhao, C.-J. Li, *Angew. Chem. Int. Ed.* **2008**, *47*, 7075; *Angew. Chem.* **2008**, *120*, 7183.

[9] Y.-F. Liang, N. Jiao, *Angew. Chem. Int. Ed.* **2014**, *53*, 548; *Angew. Chem.* **2014**, *126*, 558.

[10] a) L.-J. Huang, Y.-Y. Zhao, L. Yuan, J.-M. Min, L.-H. Zhang, *J. Med. Chem.* **2002**, *45*, 5340; b) M. Fukuoka, S. Shuto, N. Minakawa, Y. Ueno, A. Matsuda, *J. Org. Chem.* **2000**, *65*, 5238.

[11] a) B. T. Gabelt, E. A. Hennes, J. L. Seeman, B. Tian, P. L. Kaufman, *Invest. Ophthalmol. Vis. Sci.* **2004**, *45*, 2732; b) L.-E. Tammelin, *Acta Chem. Scand.* **1957**, *11*, 1340.

[12] a) V. M. F. Cardona, A. I. Ayi, A. M. Aubertin, R. Guedj, *Antiviral Res.* **1999**, *42*, 189; b) O. Yurin, A. Kravtchenko, L. Serebrovskaya, E. Golochvastova, N. Burova, E. Voronin, V. Pokrovsky, *AIDS* **1998**, *12*, 240; c) A. Khandazhinskaya, E. Matyugina, E. Shirokova, *Expert Opin. Drug Metab. Toxicol.* **2010**, *6*, 701.

[13] C. D. Funk, *Nat. Rev. Drug Discovery* **2005**, *4*, 664.

[14] I. P. Beletskaya, V. P. Ananikov, *Chem. Rev.* **2011**, *111*, 1596.

[15] a) P. Hamel, *J. Org. Chem.* **2002**, *67*, 2854; b) M. Tudge, M. Tamiya, C. Savarin, G. R. Humphrey, *Org. Lett.* **2006**, *8*, 565; c) S. Jain, K. Shukla, A. Mukhopadhyay, S. N. Suryawanshi, D. S. Bhakuni, *Synth. Commun.* **1990**, *20*, 1315; d) W. Ge, Y. Wei, *Green Chem.* **2012**, *14*, 2066; e) P. Sang, Z. Chen, J. Zou, Y. Zhang, *Green Chem.* **2013**, *15*, 2096; f) S. K. R. Parumala, R. K. Peddinti, *Green Chem.* **2015**, *17*, 4068; g) S. Vásquez-Céspedes, A. Ferry, L. Candish, F. Glorius, *Angew. Chem. Int. Ed.* **2015**, *54*, 5772; *Angew. Chem.* **2015**, *127*, 5864; h) M. Matsugi, K. Murata, K. Gotanda, H. Nambu, G. Anilkumar, K. Matsumoto, Y. Kita, *J. Org. Chem.* **2001**, *66*, 2434; i) Q. Wu, D. Zhao, X. Qin, J. Lan, J. You, *Chem. Commun.* **2011**, *47*, 9188; j) F.-L. Yang, S.-K. Tian, *Angew. Chem. Int. Ed.* **2013**, *52*, 4929; *Angew. Chem.* **2013**, *125*, 5029.

[16] a) J. S. Yadav, B. V. S. Reddy, Y. J. Reddy, K. Praneeth, *Synthesis* **2009**, 1520; b) Y. Maeda, M. Koyabu, T. Nishimura, S. Uemura, *J. Org. Chem.* **2004**, *69*, 7688; c) K. M. Schlosser, A. P. Krasutsky, H. W. Hamilton, J. E. Reed, K. Sexton, *Org. Lett.* **2004**, *6*, 819; d) Y. Liu, Y. Zhang, C. Hu, J. P. Wan, C. Wen, *RSC Adv.* **2014**, *4*, 35528.

[17] a) D. H. Scharf, M. Groll, A. Habel, T. Heinekamp, C. Hertweck, A. A. Brakhage, E. M. Huber, *Angew. Chem. Int. Ed.* **2014**, *53*, 2221; *Angew. Chem.* **2014**, *126*, 2253; b) H. T. Abdel-Mohsen, K. Sudheendran, J. Conrad, U. Beifuss, *Green Chem.* **2013**, *15*, 1490; c) A. Corma, T. Rodenas, M. J. Sabater, *Chem. Sci.* **2012**, *3*, 398; d) A. Dhakshinamoorthy, M. Alvaro, H. Garcia, *Chem. Commun.* **2010**, *46*, 6476; e) A. Talla, B. Driessen, N. J. W. Straathof, L.-G. Milroy, L. Brunsveld, V. Hessel, T. Noel, *Adv. Synth. Catal.* **2015**, *357*, 2180; f) M. Oba, K. Tanaka, K. Nishiyama, W. Ando, *J. Org. Chem.* **2011**, *76*, 4173.

[18] T. J. Wallace, A. Schriesheim, W. Bartok, *J. Org. Chem.* **1963**, *28*, 1311.

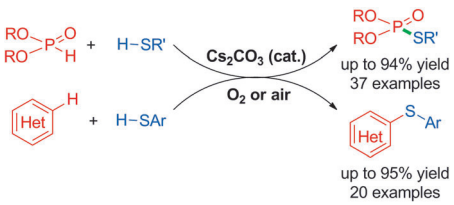
Manuscript received: December 15, 2016
Final Article published: ■■ ■■, ■■■■

Communications

Cross-Dehydrogenative Couplings

S. Song,* Y. Zhang, A. Yeerlan, B. Zhu, J. Liu, N. Jiao* ——— ■■■–■■■

Cs_2CO_3-Catalyzed Aerobic Oxidative Cross-Dehydrogenative Coupling of Thiols with Phosphonates and Arenes



Dehydrogenated: An efficient Cs_2CO_3-catalyzed aerobic cross-dehydrogenative coupling of thiols with phosphonates and arenes enables the synthesis of thiophosphates and sulfenylarenes, which are ubiquitously found in pharmaceuticals and pesticides. This method was also applied for the late-stage functionalization of bioactive molecules.

