A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition Chemie

GDCh

www.angewandte.org

Accepted Article

Title: Silver-catalyzed Oxidative C(sp3)-P Bond Formation via C-C and P-H Bond Cleavages

Authors: Lili Li, Wenbin Huang, Lijin Chen, Jiaxing Dong, Xuebing Ma, and Yungui Peng

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.201704910
Angew. Chem. 10.1002/ange.201704910

Link to VoR: http://dx.doi.org/10.1002/anie.201704910
http://dx.doi.org/10.1002/ange.201704910

WILEY-VCH

10.1002/anie.201704910

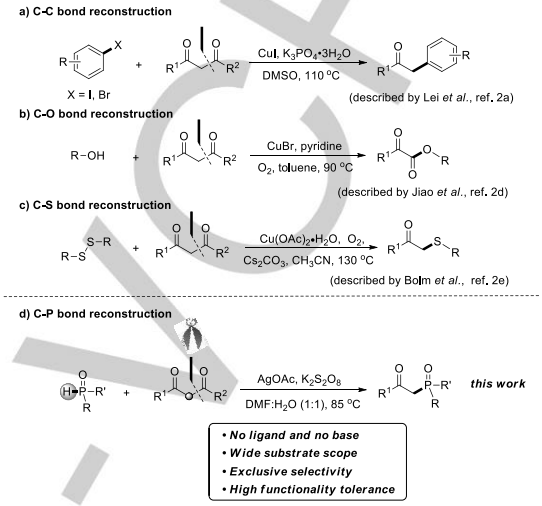
WILEY-VCH

Silver-catalyzed Oxidative C(sp^3)–P Bond Formation via C–C and P–H Bond Cleavages

Lili Li, Wenbin Huang, Lijin Chen, Jiaxing Dong*, Xuebing Ma* and Yungui Peng*

Abstract: A new reaction has been developed for the silver-catalyzed oxidative C(sp^3)–H/P–H cross-coupling of 1,3-dicabonyl compounds with H-phosphonates, followed by a chemo- and regioselective C(sp^3)–C(CO) bond cleavage step to provide heavily functionalized β-ketophosphonates. This novel method exhibits a wide substrate scope, high functional group tolerance and exclusive selectivity, as well as being a readily available reaction system.

Carbon-carbon bonds are the most ubiquitous and fundamental chemical bonds in organic compounds. Compared with transition-metal-catalyzed carbon-carbon bond forming reactions, reactions for the selective cleavage of C–C bonds, especially single bonds, and subsequent formation of new C–X bonds, remains a major challenge to organic synthesis. The difficulties associated with this area have been attributed to two major hurdles, namely (1) the chemo- and regioselective cleavage of a specific C–C single bond in a compound containing many similar chemical bonds; and (2) the thermodynamic stability of the C–C σ-bond. [1] 1,3-Dicarbonyl moieties can be found in a wide range of natural products, pharmaceuticals and functional materials, and can also be used as versatile building blocks in organic synthesis. Recently, several elegant examples of transition-metal-catalyzed C–C bond cleavage and C–X bond reconstruction of 1,3-dicarbonyl compounds have been reported.[2] In 2010, Lei and co-workers reported their seminal work on the formation of α-aryl ketones via the copper-catalyzed cleavage of the C–C σ-bond of a 1,3-diketone, followed by the formation of a new C–C bond with an aryl halide (Scheme1, a).[2a] More recently, Jiao's group uncovered a copper-catalyzed oxidative esterification reaction, which underwent sequential C–C bond breaking and C–O bond reconstruction reactions (Scheme1, b).[2d] Almost simultaneously, Bolm's group reported a copper-catalyzed C–S bond forming reaction, which proceeded via C–C and S–S σ-bond cleavages involving 1,3-dicarbonyl and disulfide substrates (Scheme1, c).[2e] These pioneering reports have demonstrated that the formation of C–X bonds via the transition-metal-catalyzed selective cleavage of the C–C bond of a 1,3-dicarbonyl compound represents a powerful method for target-oriented synthesis of organic molecules. However, despite considerable progress, this area of research is still in its infancy. Reports describing the routine use of this strategy are seldom, and the choice of transition-metal catalyst is limited to copper salts.



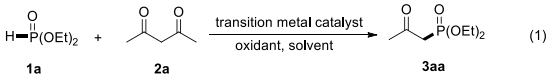
Scheme 1. Representative C–X bond reconstructions via C–C bond cleavage of 1,3-dicarbonyl compounds.

On the other hand, silver catalysts have attracted more and more attentions due to their excellent reactivity and impressive selectivity in a variety of organic transformations during the past few decades. [3] Particularly, silver-triggered radical-type reactions, including oxidation, addition, coupling and cyclization have sprung up rapidly, and become the cutting-edge research area in organic chemistry in recent years. [4] However, to the best of our knowledge, no example has been described in literature of silver-catalyzed carbon–heteroatom bond formation via C–C bond activation reaction. Herein, we wish to disclose the development of a novel silver-catalyzed tandem transformation involving an oxidative C(sp^3)–P bond formation,[5] followed by the selective C(sp^3)–C(CO) bond cleavage of a 1,3-dicarbonyl compound with a H-phosphonate. This reaction provided facile access to a series of heavily functionalized β-ketophosphonates,[6] which are omnipresent in a wide range of biologically active molecules, natural products and functional materials. Compounds of this type are also widely employed as synthetic intermediates and metal ligands [7] (Scheme1, d).

Our study commenced with the reaction of diethyl phosphonate (**1a**) with acetylacetone (**2a**) [Eq (1); also see the Supporting Information, Table S1). After judicious evaluation of the reaction parameters, we found that the desired product **3aa** could be obtained in high yield (76%) when 20 mol% AgOAc was used as a catalyst in combination with 2.0 equivalents of $K_2S_2O_8$ as an oxidant in a 1:1 (v/v) mixture of DMF and H_2O at 85 °C over a period of 24 h (Table S1, entry 1). A series of control experiments demonstrated that silver catalysts were indispensable to the success of this transformation (Table S1, entries 2 and 16). Several other silver catalysts were also tested, including $AgNO_3$ and Ag_2SO_4, but both performed poorly (Table S1, entries 3 and 4), whereas palladium and copper (I) salts

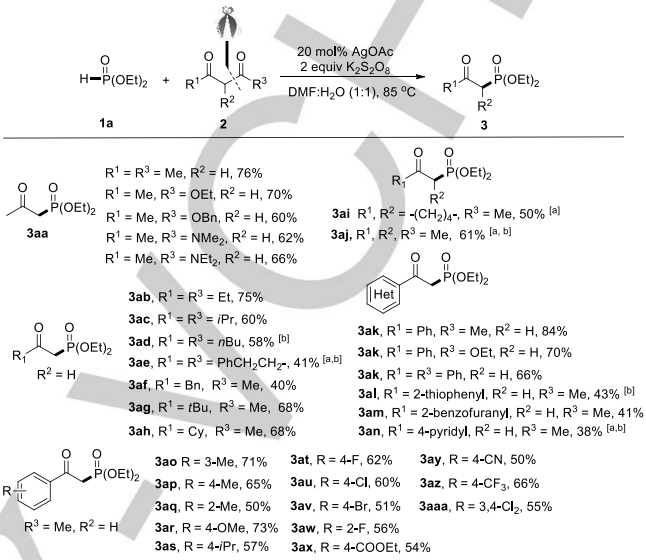
[*] L. Li, W. Huang, L. Chen, Prof. Dr. J. Dong, Prof. Dr. X. Ma and Prof. Dr. Y. Peng
School of Chemistry and Chemical Engineering
Southwest University
2 Tiansheng Road, Beibei, Chongqing 400715 (PR China)
E-mail: jiaxingdong@swu.edu.cn;
zcj123@swu.edu.cn;
pyg@swu.edu.cn.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201xxxxxx.

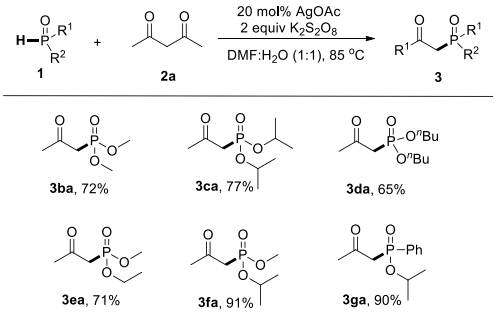


failed to afford any of the desired product (Table S1, entry 2). The choice of oxidant was also found to be critical to the outcome of this transformation (Table S1, entries 5, 6 and 17). For example, some of the most commonly used oxidants in transition-metal-catalyzed reactions, such as $Cu(OAc)_2$, *tert*-butyl peroxide (DTBP), phenyliodine diacetate (PIDA) and oxone, were determined to be completely ineffective for this reaction (Table S1, entry 5). Interestingly, the use of 2.0 equivalents of AgOAc as a dual catalyst and terminal oxidant also afforded the desired product **3aa** in a comparable yield (72%, Table S1, entry 7). It is noteworthy that this reaction also proceeded smoothly in water (Table S1, entry 8), while other mixed-solvents diminished the reaction efficiency to some extent (Table S1, entries 9-11). Increasing or decreasing the temperature of the reaction led to a decrease in the yield (Table S1, entries 12 and 13). Similar small reductions in the yield were also observed when the reaction was conducted under an atmosphere of air or oxygen (Table S1, entries 14 and 15). Decreasing the catalyst loading to 10 mol% resulted in a slight loss in yield (68%, Table S1, entry 18).

With the optimized conditions in hand, we proceeded to investigate the scope of the 1,3-dicarbnyl compounds (Scheme 2). Pleasingly, our newly developed catalytic system facilitated the phosphonation/C–C bond activation reactions of a wide range of 1,3-dicarbonyl compounds with diethyl phosphonate (**1a**), provided facile access to a series of β-ketophosphonates **3aa–3aaa** in moderate to good yields. Importantly, this transformation was also amenable to β-ketoamides and β-ketoesters, where the C–C bond cleavage occurred exclusively at the amide or ester side of the substrate to afford the desired product **3aa** in good yield (Scheme 2, **3aa**, for β-ketoesters, R^3 = OEt or OBn; for β-ketoamides,[8] R^3 = NMe_2 or NEt_2). These reactions proceeded in a different manner to those reported in the literatures, [2c, 2e] where the C–C bond cleavages usually occur at the ketone side. For unsymmetrical diketones, the C–C bond cleavage proceeded selectively at the less sterically hindered methyl ketone side (Scheme 2, **3af–3ai**, **3ak–3aaa**). Notably, despite considerable steric hindrance, the reaction still proceeded as anticipated when the R^2 position was substituted with an alkyl group (Scheme 2, **3ai**, **3aj**). In addition to aliphatic 1,3-diketones, this reaction was successfully applied to aryl-substituted diketones bearing an electron-donating (Scheme 2, **3ao–3as**) or electron-withdrawing group (Scheme 2, **3at–3aaa**). The positioning of the substituents on the aromatic ring (i.e., *ortho*-, *meta*- or *para*-positions) had very little effect on the outcome of the reaction (Scheme 2, **3ao–3aq**). This transformation also tolerated ester, nitrile, trifluoromethyl, chlorine and bromine groups, all of which are useful for further synthetic transformations. Moreover, heteroaryl-substituted diketones, such as 2-thiophenyl, 2-benzofuranyl and 4-pyridyl 1,3-diketones, could also participate in the tandem reactions, albeit in moderate yields (Scheme 2, **3al–3an**). It is noteworthy that the current catalytic system also exhibited a high level of chemoselectivity. The H-phosphonates reacted with aryl-substituted diketones specifically at the α-position of their two carbonyl groups, without forming any other aromatic $C(sp^2)$–H or $C(sp^3)$–H phosphonation products. In contrast, previously reported phosphonation reactions usually occur at the aromatic ring in the presence of silver [9] or some other transition-metal catalysts. [10]

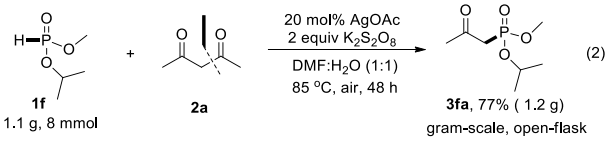


Scheme 2. Scope of 1,3-dicarbonyl compounds. For reaction conditions, see TableS1, entry 1. [a] DME:H_2O (1:1, 1.0 mL). [b] **1a** (0.75 mmol, 3 equiv.), **2** (0.25 mmol).



Scheme 3. Scope of H-phosphonates.

Next, we evaluated the scope of the H-phosphonates (Scheme 3). Gratifyingly, in addition to diethyl phosphonate (**1a**), we found that various H-phosphonates **1b**-**1g** were amenable to this transformation, affording the corresponding β-ketophosphonates **3ba**-**3ga** in good to excellent yields. It is noteworthy that ethyl phenylphosphinate **1g** also reacted as anticipated to give the desired product **3ga** in 90% yield.



10.1002/anie.201704910

As shown in Eq.(2), the gram-scale reaction of **1f** with **2a**, which was conducted using wet solvent without taking any precaution to exclude air or moisture (open-flask), afforded the desired product **3fa** in 77% isolated yield. This reaction highlights the practical utility and robust nature of this transformation.

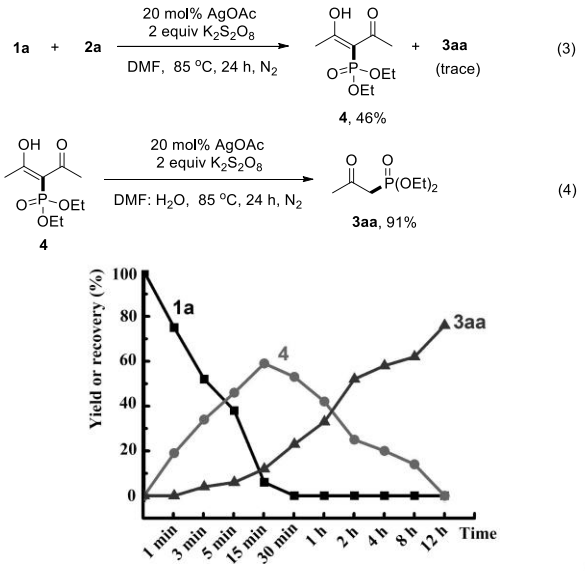
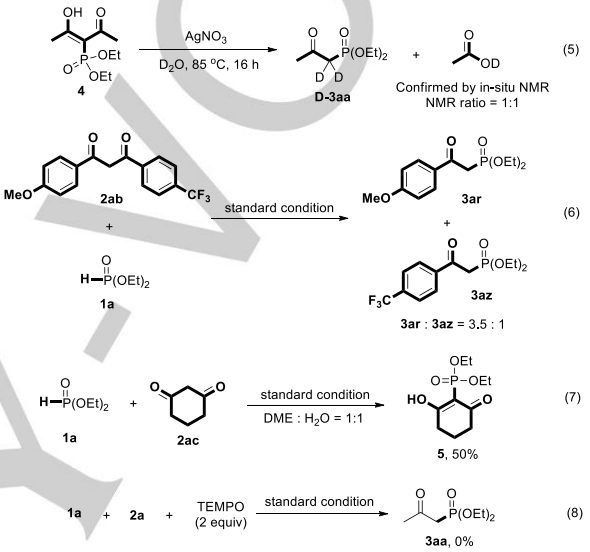
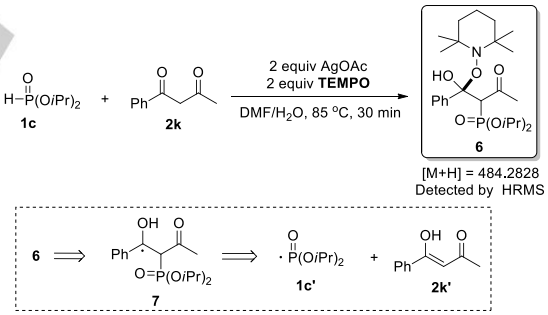


Figure 1. Distribution of substrate **1a** (square), intermediate **4** (dot) and product **3aa** (triangle) with reaction time for the model reaction of **1a** with **2a** under the standard conditions (See SI for details).

To develop some insights into the mechanism of this reaction, we conducted a series of control experiments. When the model reaction of **1a** with **2a** was conducted in anhydrous DMF, we only observed the formation of trace amounts of the target molecule **3aa**, whereas the direct phosphonation product **4** was obtained in 46% yield [Eq.(3)]. Furthermore, isolated **4** could be readily converted to the final product **3aa** under the standard conditions in high yield [Eq.(4)]. Based on these observations and previous reports, [2a, 2e] we envisioned that the reaction of **1a** with **2a** probably proceeded via an oxidative C(sp^3)–H/P–H cross-coupling and a tandem C(sp^3)–C(CO) bond cleavage reaction to provide the desired product **3aa**. To prove our hypothesis, we monitored changes in the levels of the different components of the reaction mixture over time (Figure 1). Not surprisingly, during the first few minutes, the amount of **4** increased steadily, whereas the desired product **3aa** remained at a low concentration. However, as the reaction proceeded, the amount of **3aa** gradually increased, whereas the amount of **4** decreased. These results clearly confirmed our hypothesis that compound **4** was a key intermediate for product **3aa**.

To further clarify the decarbonylated product in the C(sp^3)–C(CO) bond cleavage step, the in-situ NMR study of the crude reaction mixture in Eq. (5) was conducted. After comparison with an authentic sample of HOAc, we confirmed that acetic acid was being formed as a byproduct (see SI for NMR spectra). Furthermore, the intramolecular competitive reaction of unsymmetrical diketone **2ab** with **1a** demonstrated that the C–C bond cleavage was more likely to occur at the more electron-deficient carbonyl center [Eq. (6)]. Taken together, these results convinced us that the nucleophilic attack of H_2O at the carbonyl group of the intermediate would lead to the cleavage of the C(sp^3)–C(CO) bond, leading to the formation of the target molecule along with the carboxylic acid byproduct. However, we found that this nucleophilic attack did not take place in the reaction of **1a** with the cyclic 1,3-diketone **2ac**, probably due to the pronounced steric hindrance of the carbonyl center in compound **5** [Eq. (7)].

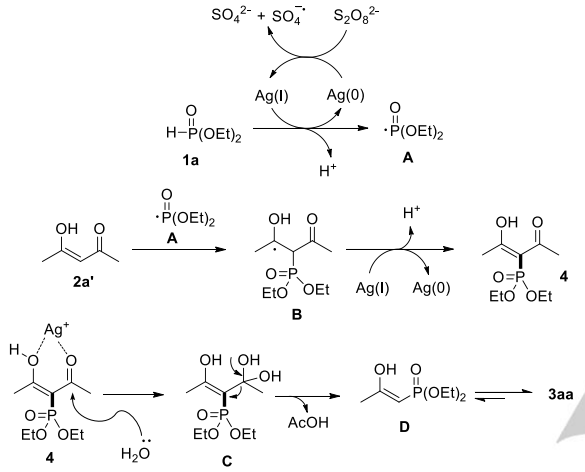




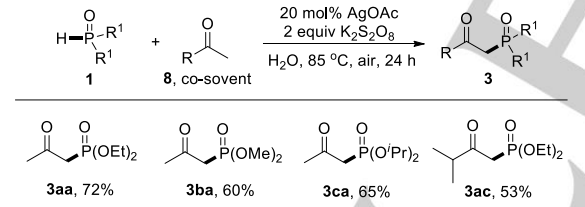
Scheme 4. Trapping and detecting the intermediate.

Although we successfully identified the C(sp^3)–C(CO) bond cleavage step, more efforts are still required to better understand the mechanism of the oxidative C(sp^3)–H/P–H cross-coupling step. The addition of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) completely inhibited the reaction [Eq.(8)], indicating that this transformation may proceed via a radical pathway. Moreover, HRMS analysis of the crude mixture resulting from the reaction of **1c** and **2k** revealed the formation of the adduct **6** (Scheme 4), suggesting that the radical species **7**, probably generated by the radical addition of **1c'** to **2k'**, was the key intermediate in the oxidative C(sp^3)–H/P–H cross-coupling step.

Based on the results described above and literature precedents [2f, 9], a tentative mechanism was proposed in Scheme 5. Diethyl phosphonate (**1a**) was oxidized by Ag^{I} salt to generate the corresponding P-centered radical **A** and Ag^{0}, which would be reoxidized to Ag^{I} by a persulfate anion.[11] The radical addition of intermediate **A** to enolate **2a'** gave intermediate **B**, [12] which would be oxidized to intermediate **4**.[13] Subsequently, the C–C bond cleavage reaction took place immediately after the nucleophilic attack of H_2O to the more electron-deficient carbonyl group to deliver enolate **D**, along with the acetic acid as a byproduct. Finally, enolate **D** rapidly tautomerized to form the more stable product **3aa**.



Scheme 5. Plausible mechanism.



Scheme 6. Silver-catalyzed direct oxidative cross-coupling reactions of H-phosphonates and simple ketones. For details, see supporting information.

It is noteworthy that our newly developed catalytic system could also be applied to the direct C–H/P–H cross-coupling of H-phosphonates and simple aliphatic ketones. We have provided a few representative examples of this reaction in Scheme 6, and detailed results of this transformation will be published in due course.

In summary, we have reported for the first time a silver-catalyzed C(sp^3)–P bond forming reaction consisting of an oxidative C(sp^3)–H/P–H cross-coupling and a tandem C(sp^3)–C(CO) bond cleavage reaction, affording a wide range of functionalized β-ketophosphonates. This reaction was also found to be amenable to β-ketoamides and β-ketoesters, where the C–C bond cleavage reaction occurred specifically at the ester or amide side of the substrate. Notably, this newly developed catalytic system also promoted the oxidative cross-coupling reactions of H-phosphonates and simple aliphatic ketones. Preliminary mechanistic studies revealed that a radical pathway and a nucleophilic attack process may be involved in the C(sp^3)–P bond formation and C(sp^3)–C(CO) bond cleavage steps, respectively. This new method provides an alternative approach to β-ketophosphonate scaffolds and has several key advantages, including (1) simple and readily available catalyst system; (2) base-, ligand- and additive-free; (3) wide substrate scope and good functional group tolerance; and (4) exclusive chemo- and regioselectivity. Further studies aimed at exploring the application of this strategy to other systems are currently underway in our laboratory.

Acknowledgements

This work was supported by grants from the National NSF of China (Nos 21502155) and the Fundamental Research Funds for the Central Universities (SWU114077 and XDJK2015C103).

Conflict of interest

The authors declare no conflict of interest.

Keywords: cross-coupling • C(sp^3)–P bond formation • C–C bond cleavage • 1,3-dicarbonyl compounds • silver

[1] For selected reviews on the transition-metal-catalyzed C–C single bond cleavage, see: a) C.-H. Jun, *Chem. Soc. Rev.* **2004**, *33*, 610-618; b) M. Murakami, T. Matsuda, *Chem. Commun.* **2011**, *47*, 1100-1105; c) T. Seiser, T. Saget, D. N. Tran, N. Cramer, *Angew. Chem.* **2011**, *123*, 7884-7896; *Angew. Chem. Int. Ed.* **2011**, *50*, 7740-7752; d) F. Chen, T. Wang, N. Jiao, *Chem. Rev.* **2014**, *114*, 8613-8661; e) H. Liu, M. Feng, X. Jiang, *Chem. Asian J.* **2014**, *9*, 3360-3389; f) L. Souillart, N. Cramer, *Chem. Rev.* **2015**, *115*, 9410-9464; g) D.-S. Kim, W.-J. Park, C.-H. Jun, *Chem. Rev.* **2017**, DOI: 10.1021/acs.chemrev.6b00554; h) G. Fumagalli, S. Stanton, J. F. Bower, *Chem. Rev.* **2017**, DOI: 10.1021/acs.chemrev.6b00599.

[2] For selected examples, see: a) C. He, S. Guo, L. Huang, A. Lei, *J. Am. Chem. Soc.* **2010**, *132*, 8273-8275; b) L. Huang, K. Cheng, B. Yao, Y. Xie, Y. Zhang, *J. Org. Chem.* **2011**, *76*, 5732–5737; c) J. Ke, C. He, H. Liu, H. Xu, A. Lei, *Chem. Commun.* **2013**, *49*, 6767–6769; d) C. Zhang, P. Feng, N. Jiao, *J. Am. Chem. Soc.* **2013**, *135*, 15257−15262; e) L.-H. Zou, D. L. Priebbenow, L. Wang, J. Mottweiler, C. Bolm, *Adv. Synth. Catal.* **2013**, *355*, 2558–2563; f) X. Sun, P. Li, X. Zhang, L. Wang, *Org. Lett.* **2014**, *16*, 2126−2129; g) Q. Xing, P. Li, H. Lv, R. Lang, C. Xia, F. Li, *Chem. Commun.* **2014**, *50*, 12181-12184; h) S. Wang, Y. Yu, X. Chen, H. Zhu, P. Du, G. Liu, L. Lou, H. Li, W. Wang, *Tetrahedron Letters*, **2015**, *56*, 3093–3096; i) Q. Xing, H. Lv, C. Xia, F. Li, *Chem. Eur. J.* **2015**, *21*, 8591-8596; j) Z. Li, J. Dong, X. Chen, Q. Li, Y. Zhou, S.-F. Yin, *J. Org. Chem.* **2015**, *80*, 9392−9400.

[3] For selected reviews, see: a) M. Naodovic, H. Yamamoto, *Chem. Rev.* **2008**, *108*, 3132-3148; b) J.-M. Weibel, A. Blanc, P. Pale, *Chem. Rev.* **2008**, *108*, 3149-3173; c) M. Álvarez-Corral, M. Muñoz-Dorado, I. Rodríguez-García, *Chem. Rev.* **2008**, *108*, 3174–3198; d) Y. Yamamoto, *Chem. Rev.* **2008**, *108*, 3199-3222; e) G. Fang, X. Bi, *Chem. Soc. Rev.* **2015**, *44*, 8124-8173; f) K. Sekine, T. Yamada, *Chem. Soc. Rev.* **2016**, *45*, 4524-4532; g) Q.-Z. Zheng, N. Jiao, *Chem. Soc. Rev.* **2016**, *45*, 4590-4627.

[4] Quite recently, an elegant review on silver-based radical reactions was published, see: G. Fang, X. Cong, G. Zanoni, Q. Liu, X. Bi, *Adv. Synth. Catal.* **2017**, *359*, 1422–1502.

[5] For recent examples of transition-metal-catalyzed oxidative C(sp^3)–P bond formation reactions, see: a) O. Baslé, C.-J. Li, *Chem. Commun.* **2009**, 4124-4126; b) J. Xie, H. Li, Q. Xue, Y. Cheng, C. Zhu, *Adv. Synth. Catal.* **2012**, *354*, 1646-1650; c) J. Ke, Y. Tang, H. Yi, Y. Li, Y. Cheng, C. Liu, A. Lei, *Angew. Chem.* **2015**, *127,* 6704–6707; *Angew. Chem. Int. Ed.* **2015**, *54*, 6604-6607; d) G. Hu, W. Chen, D. Ma, Y. Zhang, P. Xu, Y. Gao, Y. Zhao, *J. Org. Chem.* **2016**, *81*,1704-1711; e) H. Zhi, S. P.-M. Ung, Y. Liu, L. Zhao, C.-J. Li, *Adv. Synth. Catal.* **2016**, *358*, 2553-2557; f) Q. Fu, D. Yi, Z. Zhang, W. Liang, S. Chen, L. Yang, Q. Zhang, J. Ji, W. Wei, *Org. Chem. Front.* **2017**, DOI: 10.1039/c7qo00202e.

[6] For selected examples of transitional-catalyzed-catalyzed reactions about β-ketophosphonate formations, see: a) W. Wei, J.-X. Ji, *Angew. Chem.* **2011**, *123*, 9263–9265; *Angew. Chem. Int. Ed.* **2011**, *50*, 9097–9099; b) X. Li, G. Hu, P. Luo, G. Tang, Y. Gao, P. Xu, Y. Zhao, *Adv. Synth. Catal.* **2012**, *354*, 2427–2432; c) X. Chen, X. Li, X.-L. Chen, L.-B. Qu, J.-Y. Chen, K. Sun, Z.-D. Liu, W.-Z. Bi, Y.-Y. Xia, H.-T. Wu, Y.-F. Zhao, *Chem. Commun.* **2015**, *51*, 3846–3849; d) M. Zhou, M. Chen, Y. Zhou, K. Yang, J. Su, J. Du, Q. Song, *Org. Lett.* **2015**, *17*, 1786–1789; e) P. Zhang, L. Zhang, Y. Gao, J. Xu, H. Fang, G. Tang, Y. Zhao, *Chem. Commun.* **2015**, *51*, 7839-7842; f) N. Yi, R. Wang, H. Zou, W. He, W. Fu, W. He, *J. Org. Chem.* **2015**, *80*, 5023-5029; g) M. Zhou, Y. Zhou, Q. Song, *Chem.–Eur. J.* **2015**, *21*, 10654-10659; h) Y. Zhou, C. Rao, S. Mai, Q. Song, *J. Org. Chem.* **2016**, *81*, 2027—2034.

[7] a) W. S. Wadsworth, W. D. Emmons, *J. Am. Chem. Soc.* **1961**, *83*, 1733-1738; b) F. A. Cotton, R. A. Schunn, *J. Am. Chem. Soc.* **1963**, *85*, 2394-2402; c) D. J. McCabe, E. N. Duesler, R. T. Paine, *Inorg. Chem.* **1985**, *24*, 4626–4629; d) M. Kitamura, M. Tokunaga, R. Noyori, *J. Am. Chem. Soc.* **1995**, *117*, 2931–2932; e) C. Balg, S. P. Blais, S. Bernier, J. Huot, M. Couture, J. Lapointe, R. Chênevert, *Bioorg. Med. Chem.* **2007**, *15*, 295-304; f) S. K. Perumal, S. A. Adediran, R. F. Pratt, *Bioorg. Med. Chem.* **2008**, *16*, 6987–6994; g) G. P. Horsman, D. L. Zechel, *Chem. Rev.* **2017**, *117*, 5704–5783.

[8] When acetoacetamide and N-methyl acetoacetylamide were used as substrates, we only obtained the C(sp^3)–H phosphonation products **9** and **10** in 60% and 48% yields, respectively; and the C–C bond cleavage step didn't occur in these two cases (for details, see SI).

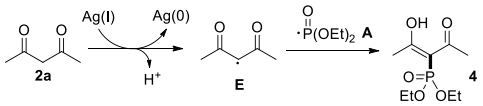
[9] For selected examples, see: a) F. Effenberger, H. Kottmann, *Tetrahedron* **1985**, *41*, 4171–4182; b) C.-B. Xiang, Y.-J. Bian, X.-R. Mao, Z.-Z. Huang, *J. Org. Chem.* **2012**, *77*, 7706-7710; c) X. Mao, X. Ma, S. Zhang, H. Hu, C. Zhu, Y. Cheng, *Eur. J. Org. Chem.* **2013**, 4245-4248; d) Y.-R. Chen, W.-L. Duan. *J. Am. Chem. Soc.* **2013**, *135*, 16754–16757; e) H.-J. Zhang, W. Lin, Z. Wu, W. Ruan, T.-B. Wen, *Chem. Commun.* **2015**, *51*, 3450-3453; f) M. Sun, S. Sun, H. Qiao, F. Yang, Y. Zhu, J. Kang, Y. Wu, Y. Wu, *Org. Chem. Front.* **2016**, *3*, 1646-1650; g) X. Yu, B. Ge, Y. Zhang, X. Wang, D. Wang, *Asian J. Org. Chem.* **2016**, *5*, 1253-1259; also see review 3g and references therein.

[10] For palladium catalysts, see: a) Y. Kuninobu, T. Yoshida, K. Takai, *J. Org. Chem.* **2011**, *76,* 7370-7376; b) C.-G. Feng, M. Ye, K.-J. Xiao, S. Li, J.-Q. Yu, *J. Am. Chem. Soc.* **2013**, *135*, 9322-9325; c) G. Hong, D. Mao, S. Wu, L. Wang, *J. Org. Chem.* **2014**, *79,* 10629-10635; for copper catalyst, see: d) S. Wang, R. Guo, G. Wang, S.-Y. Chen X.-Q. Yu, *Chem. Commun.* **2014**, *50*, 12718-12721; for manganese catalysts, see: e) T. Kagayama, A. Nakano, S. Sakaguchi, Y. Ishii, *Org. Lett.* **2006**, *8*, 407-409; f) O. Berger, J.-L. Montchamp, *Chem. Eur. J.* **2014**, *20*, 12385–12388.

[11] In previous reports (see references 9a-9c and 9f), the catalytic cycle of Ag(I)/Ag(II) was usually proposed as following: initially, Ag(I) was believed to be oxidized to Ag(II) by potassium peroxodisulfate. And then, the Ag(II) deprived an electron from **1a** or **2a** to give the corresponding radical species and regenerate the Ag(I). However, in the current reaction system, the catalytic cycle of Ag(I)/Ag(0) seemed more reasonable, because stoichiometric AgOAc could also promote the reaction smoothly in the absence of $K_2S_2O_8$ (Table S1, entry 7), and when the reaction was finished, elemental silver particles were always found at the bottom of the Schlenk test tube (See Figure S1 and S2).

[12] For formation of enolate with transition metal, see: C. He, G. Zhang, J. Ke, H. Zhang, J. T. Miller, A. J. Kropf, A. Lei, *J. Am. Chem. Soc.* **2013**, *135*, 488-493; for a similar mechanism about radical addition to enolate, see: a) Ł. Woźniak, J. J. Murphy, P. Melchiorre, *J. Am. Chem. Soc.* **2015**, *137*, 5678-5681; b) S. Mao, X.-Q. Zhu, Y.-R. Gao, D.-D. Guo, Y.-Q. Wang, *Chem. Eur. J.* **2015**, *21*, 11335-11339.

[13] At this stage, the following possible pathway to intermediate **4** couldn't be completely excluded: oxidation of acetylacetone **2a** by Ag^I gave radical species **E**. Next, selective cross-coupling of two radical species **A** and **E** formed the key intermediate **4**. For similar mechanisms, see: C. Wang, Y. Li, M. Gong, Q. Wu, J. Zhang, J. K. Kim, M. Huang, Y. Wu, *Org. Lett.* **2016**, *18*, 4151−4153; and reference 5c.



10.1002/anie.201704910

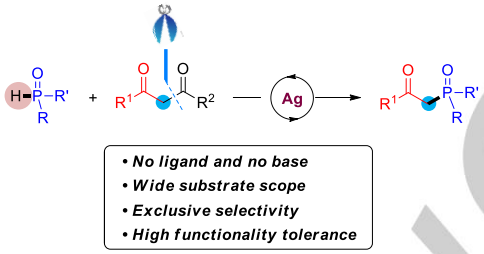
WILEY-VCH

Entry for the Table of Contents (Please choose one layout)

Layout 1:

Tandem transformation

A novel silver-catalyzed transformation involving oxidative C(sp^3)–H/P–H cross-coupling of 1,3-dicabonyl compounds with H-phosphonates and tandem exclusive C(sp^3)–C(CO) bond cleavage has been realized to give heavily functionalized β-ketophosphonate scaffolds.



Lili Li, Wenbin Huang, Lijin Chen, Jiaxing Dong, Xuebing Ma*, Yungui Peng**

Page No. – Page No.

Silver-catalyzed Oxidative C(sp^3)–P Bond Formation via C–C and P–H Bond Cleavages