



CrossMark  
click for updates

Cite this: *RSC Adv.*, 2015, 5, 27853

Received 11th March 2015  
Accepted 13th March 2015

DOI: 10.1039/c5ra04136h

www.rsc.org/advances

## A silver-initiated free-radical intermolecular hydrophosphinylation of unactivated alkenes†

Zejiang Li, Fenghua Fan, Zengyan Zhang, Yingxia Xiao, Dong Liu and Zhong-Quan Liu\*

A scalable, operationally easy intermolecular hydrophosphinylation of various unactivated alkenes with H–P(O) compounds *via* an Ag(I)-initiated free radical process was developed. Mechanistic studies including electron-spin-resonance (ESR) and radical clock experiments suggest that atom transfer processes were involved in this system.

As a large class of important and valuable building blocks, organophosphorus compounds are widely applied in the synthesis of pharmaceuticals, agrochemicals and materials.<sup>1</sup> In the past few decades, considerable advances have been made to construct C–P bonds.<sup>2</sup> Among them, one of the most atom-economical and attractive strategies is the direct hydrophosphinylation of alkenes.<sup>3</sup> The free-radical strategies for the addition of a P–H or (O)P–H bond to alkenes represent one of the most important methods to form a C–P bond.<sup>4</sup> Although this radical addition using peroxide,<sup>5</sup> AIBN,<sup>6</sup> Et<sub>3</sub>B,<sup>7</sup> air/nitrogen,<sup>8</sup> and organic dye/photoirradiation<sup>9</sup> *etc.* as the radical initiators has been achieved, more efficient and practical strategies are still highly desirable.

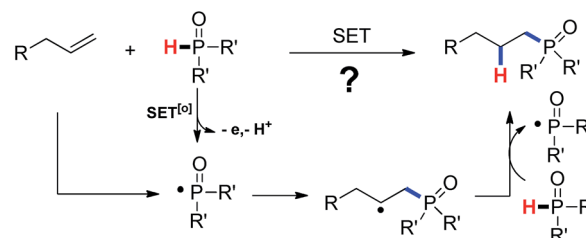
As our continuous investigations on the C–C bond formation *via* free-radical processes,<sup>10</sup> we began to question whether a C–P bond could be formed *via* a single-electron-transfer (SET) process. As demonstrated in Scheme 1, single-electron oxidation of the secondary phosphine oxide followed by a deprotonation would generate a P-centered free radical. Addition of the phosphinyl radical to an olefin followed by hydrogen abstract from the phosphine oxide would lead to the product by hydrophosphinylation of alkene and regenerate the phosphinyl radical. Fortunately, we successfully accomplished an Ag(I)-initiated intermolecular hydrophosphinylation of a wide range of unactivated alkenes with phosphites (Scheme 1).

State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou, Gansu, 730000, P. R. China. E-mail: liuzhq@lzu.edu.cn; Fax: +86 931 8915557; Tel: +86 931 8912500

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c5ra04136h

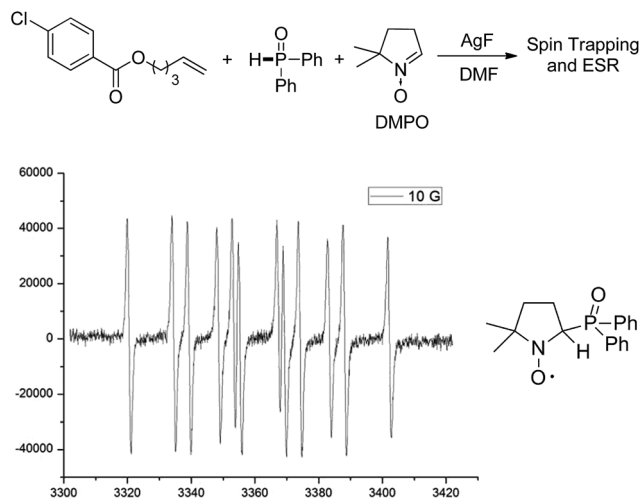
Initially, a series of experiments were carried out to test the hypothesis for hydrophosphinylation of unactivated alkenes with phosphites through a one-electron transfer process. It can be seen from Table 1 that the desired product was isolated in nearly quantitative yield by using catalytic amount of AgF (20 mol%), which was more efficient than other silver salts such as Ag<sub>2</sub>CO<sub>3</sub>, AgNO<sub>3</sub>, and AgOAc *etc.* (Table 1, entries 1–7). Further optimization of the typical reaction conditions indicated that the solvent, concentration as well as the temperature also affected the reaction efficiency (entries 8–12). Furthermore, addition of persulfates such as K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> and (NH<sub>4</sub>)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> could slightly raise the yield of the product (entries 13 and 14).

The substrate scope and functional group tolerance were demonstrated in Scheme 2. A wide range of terminal and internal unactivated alkenes are compatible to this system (entries 1–25). Various functional groups such as ester, halogen, ether, hydroxyl, amide and ketone *etc.* can all be well-survived. It is noteworthy that the free radical addition didn't happen at the internal C=C double bond but the terminal one when 7-(but-3-en-1-yloxy)-2H-chromen-2-one was used as the substrate (entry 13). (*E*)-Oct-2-ene afforded a regio-isomers with the ratio of 1.7/1 (entry 19). 2-Vinylpyridine also gave the corresponding product 25 in high yield. However, styrene and its derivatives are not effective in this system. Notably, *H*-phosphinates and *H*-phosphonates are proven to be effective substrates (entries 26–28). For example, ethyl phenylphosphinate afforded the desired product in 95% yield (entry 26). Addition of the dimethyl



Scheme 1 Free radical hydrophosphinylation of alkene *via* SET.





**Scheme 4** ESR studies. ESR spectrum of a solution of pent-4-en-1-yl 4-chlorobenzoate ( $5.0 \times 10^{-2} \text{ mol L}^{-1}$ ), diphenylphosphine oxide ( $0.2 \text{ mol L}^{-1}$ ), AgF ( $1.0 \times 10^{-2} \text{ mol L}^{-1}$ ), and DMPO ( $6.0 \times 10^{-2} \text{ mol L}^{-1}$ ) in DMF (2 mL),  $110^\circ \text{C}$  for 2.5 h.

Markovnikov addition and scalability make this methodology attractive to organophosphorus synthetic chemistry. Radical clock and ESR studies support the free-radical addition pathway.

## Acknowledgements

This project is supported by the National Science Foundation of China (nos 21272096, 21472080).

## Notes and references

- For reviews, see: (a) *Organic Phosphorus Compounds*, ed. G. M. Kosolapoff and L. Maier, Wiley-Interscience, New York, 1972; (b) A. K. Bhattacharta and G. Thyagarajan, *Chem. Rev.*, 1981, **81**, 415; (c) L. D. Quin, *A Guide to Organophosphorus Chemistry*, Wiley-Interscience, Hoboken, NJ, 2000; (d) C. Giorgio, O. Gianmauro and A. P. Gerard, *Tetrahedron*, 2003, **59**, 9471; (e) W. Tang and X. Zhang, *Chem. Rev.*, 2003, **103**, 3029; (f) D. T. Kolio, *Chemistry and Application of H-Phosphonates*, Elsevier Science, Oxford, 2006; (g) D. E. C. Corbridge, *Phosphorus: Chemistry, Biochemistry and Technology*, CRC Press, London, 6th edn, 2013.
- For selected reviews on C–P bond formation, see: (a) R. Engel and J. I. Cohen, *Synthesis of Carbon–Phosphorus Bonds*, CRC Press, Boca Raton, 2nd edn, 2003; (b) D. K. Wicht and D. S. Glueck, in *Catalytic Heterofunctionalization*, ed. A. Togni and H. Grützmacher, Wiley-VCH, Weinheim, 2001, ch. 5 and references cited therein; (c) O. Delacroix and A.-C. Gaumont, *Curr. Org. Chem.*, 2005, **9**, 1851; (d) A. L. Schwan, *Chem. Soc. Rev.*, 2004, **33**, 218; (e) M. Tanaka, *Top. Curr. Chem.*, 2004, **232**, 25; (f) F. Alonso, I. P. Beletskaya and M. Yus, *Chem. Rev.*, 2004, **104**, 3079; (g) C. Baillie and J. Xiao, *Curr. Org. Chem.*, 2003, **7**, 477.
- For review on hydrophosphinylation, see: L. Coudray and J.-L. Montchamp, *Eur. J. Org. Chem.*, 2008, 3601.
- For reviews on free radical phosphonylation, see: (a) D. Leca, L. Fensterbank, E. Lacôte and M. Malacria, *Chem. Soc. Rev.*, 2005, **34**, 858; (b) S. Marque and P. Tordo, *Top. Curr. Chem.*, 2005, **250**, 43; (c) A. Baralle, A. Baroudi, M. Daniel, L. Fensterbank, J.-P. Goddard, E. Lacote, M.-H. Larraufie, G. Maestri, M. Malacria and C. Ollivier, in *Encyclopedia of Radicals in Chemistry, Biology and Materials*, ed. C. Chatgililoglu and A. Studer, Wiley, Chichester, UK, 2012, pp. 767–816, For selected examples of radical C–P bond formation, see: (d) C. P. Casey, E. L. Paulsen, E. W. Beuttenmueller, B. R. Proft, B. A. Matter and D. R. Powell, *J. Am. Chem. Soc.*, 1999, **121**, 63; (e) L.-B. Han and M. Tanaka, *Chem. Commun.*, 1999, 395; (f) L.-B. Han, F. Mirzaei, C.-Q. Zhao and M. Tanaka, *J. Am. Chem. Soc.*, 2000, **122**, 5407; (g) S. Deprèle and J.-L. Montchamp, *J. Am. Chem. Soc.*, 2002, **124**, 9386; (h) J. R. Moncarz, N. F. Laritcheva and D. S. Glueck, *J. Am. Chem. Soc.*, 2002, **124**, 13356; (i) M. O. Shulyupin, M. A. Kazakova and I. P. Beletskaya, *Org. Lett.*, 2002, **4**, 761; (j) L.-B. Han and C.-Q. Zhao, *J. Org. Chem.*, 2005, **70**, 10121; (k) T. Kagayama, A. Nakano, S. Sakaguchi and Y. Ishii, *Org. Lett.*, 2006, **8**, 407; (l) T. Hirai and L.-B. Han, *J. Am. Chem. Soc.*, 2006, **128**, 7422; (m) X.-J. Mu, J.-P. Zou, Q.-F. Qian and W. Zhang, *Org. Lett.*, 2006, **8**, 5291; (n) X.-Q. Pan, J.-P. Zou, G.-L. Zhang and W. Zhang, *Chem. Commun.*, 2010, **46**, 1721; (o) W. Wei and J.-X. Ji, *Angew. Chem., Int. Ed.*, 2011, **50**, 9097; (p) X.-Q. Pan, L. Wang, J.-P. Zou and W. Zhang, *Chem. Commun.*, 2011, **47**, 7875; (q) Y.-M. Li, M. Sun, H.-L. Wang, Q.-P. Tian and S.-D. Yang, *Angew. Chem., Int. Ed.*, 2013, **52**, 3972; (r) C. Zhang, Z. Li, L. Zhu, L. Yu, Z. Wang and C. Li, *J. Am. Chem. Soc.*, 2013, **135**, 14082; (s) B. Zhang, C. Daniliuc and A. Studer, *Org. Lett.*, 2014, **16**, 250; (t) W. Kong, E. Merino and C. Nevado, *Angew. Chem., Int. Ed.*, 2014, **53**, 5078; (u) Z. Zhao, W. Xue, Y. Gao, G. Tang and Y. Zhao, *Chem.-Asian J.*, 2013, **8**, 713; (v) J. Xu, P. Zhang, X. Li, Y. Gao, J. Wu, G. Tang and Y. Zhao, *Adv. Synth. Catal.*, 2014, **356**, 3331; (w) Y.-R. Chen and W.-L. Duan, *J. Am. Chem. Soc.*, 2013, **135**, 16754; (x) Y. Gao, X. Li, J. Xu, Y. Wu, W. Chen, G. Tang and Y. Zhao, *Chem. Commun.*, 2015, **51**, 1605.
- (a) O. Dubert, A. Gautier, E. Condamine and S. R. Piettre, *Org. Lett.*, 2002, **4**, 359; (b) A. Gautier, G. Garipova, C. Salcedo, S. Balieu and S. R. Piettre, *Angew. Chem., Int. Ed.*, 2004, **43**, 5963.
- (a) E. E. Nifant'ev, R. K. Magdeeva and N. P. Shchepet'eva, *J. Gen. Chem. USSR*, 1980, **50**, 1416; (b) D. S. Karanewsky, M. C. Badia, D. W. Cushman, J. M. DeForrest, T. Dejneka, M. J. Loots, M. G. Perri, E. W. Petrillo and J. R. Powell, *J. Med. Chem.*, 1988, **31**, 204; (c) N. G. Anderson, M. L. Coradetti, J. A. Cronin, M. L. Davies, M. B. Gardineer, A. S. Kotnis, D. A. Lust and V. A. Palaniswamy, *Org. Process Res. Dev.*, 1997, **1**, 315; (d) C. M. Jessop, A. F. Parsons, A. Routledge and D. Irvine, *Tetrahedron Lett.*, 2003, **44**, 479; (e) M. I. Antczak and J.-L. Montchamp, *Synthesis*, 2006, 3080; (f) C. M. Jessop, A. F. Parsons, A. Routledge and D. J. Irvine, *Eur. J. Org. Chem.*, 2006, 1547.

- 7 (a) S. Deprère and J.-L. Montchamp, *J. Org. Chem.*, 2001, **66**, 6745; (b) Y. Feng and J. K. Coward, *J. Med. Chem.*, 2006, **49**, 770.
- 8 T. Hirai and L.-B. Han, *Org. Lett.*, 2007, **9**, 53.
- 9 (a) W.-J. Yoo and S. Kobayashi, *Green Chem.*, 2013, **15**, 1844; (b) S.-I. Kawaguchi, A. Nomoto, M. Sonoda and A. Ogawa, *Tetrahedron Lett.*, 2009, **50**, 624.
- 10 For our recent contributions on free-radical-initiated C–C bond formation, see: (a) Z.-Q. Liu, L. Sun, J. Wang, J. Han, Y. Zhao and B. Zhou, *Org. Lett.*, 2009, **11**, 1437; (b) Z. Cui, X. Shang, X.-F. Shao and Z.-Q. Liu, *Chem. Sci.*, 2012, **3**, 2853; (c) Z. Li, Z. Cui and Z.-Q. Liu, *Org. Lett.*, 2013, **15**, 406; (d) Z. Li, Y. Zhang, L. Zhang and Z.-Q. Liu, *Org. Lett.*, 2014, **16**, 382; (e) Z. Li, F. Fan, J. Yang and Z.-Q. Liu, *Org. Lett.*, 2014, **16**, 3396; (f) L. Zhang, Z. Li and Z.-Q. Liu, *Org. Lett.*, 2014, **16**, 3688; (g) Z. Hang, Z. Li and Z.-Q. Liu, *Org. Lett.*, 2014, **16**, 3648; (h) Z. Xu, C. Yan and Z.-Q. Liu, *Org. Lett.*, 2014, **16**, 5670; (i) Y. Tian and Z.-Q. Liu, *RSC Adv.*, 2014, **4**, 64855; (j) X.-J. Shang, Z. Li and Z.-Q. Liu, *Tetrahedron Lett.*, 2015, **56**, 233.