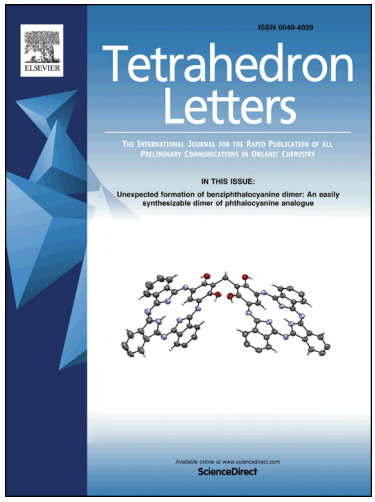


CDI-Promoted Direct Esterification of P(O)-OH Compounds with Phenols

Biquan Xiong, Chenghong Hu, Haotian Li, Congshan Zhou, Pangliang Zhang, Yu Liu, Kewen Tang

PII: S0040-4039(17)30620-2
DOI: http://dx.doi.org/10.1016/j.tetlet.2017.05.036
Reference: TETL 48929

To appear in: *Tetrahedron Letters*

Received Date: 31 March 2017
Revised Date: 10 May 2017
Accepted Date: 12 May 2017

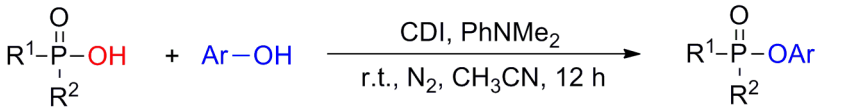
Please cite this article as: Xiong, B., Hu, C., Li, H., Zhou, C., Zhang, P., Liu, Y., Tang, K., CDI-Promoted Direct Esterification of P(O)-OH Compounds with Phenols, *Tetrahedron Letters* (2017), doi: http://dx.doi.org/10.1016/j.tetlet.2017.05.036

Graphical Abstract

CDI-Promoted Direct Esterification of P(O)-OH Compounds with Phenols

Leave this area blank for abstract info.

Biquan Xiong,* Chenghong Hu, Haotian Li, Congshan Zhou, Pangliang Zhang, Yu Liu, Kewen Tang*
Department of Chemistry and Chemical Engineering, Hunan Institute of Science and Technology, Yueyang, 414006, P.R.China.



R^1 = Aryl, alkyl; R^2 = Aryl, alkoxyl;

34 examples, up to 99% yield

Metal free; Excellent functional groups tolerance;

Tetrahedron Letters
journal homepage: www.elsevier.com

CDI-Promoted Direct Esterification of P(O)-OH Compounds with Phenols

Biquan Xiong,* Chenghong Hu, Haotian Li, Congshan Zhou, Pangliang Zhang, Yu Liu, Kewen Tang*

Department of Chemistry and Chemical Engineering, Hunan Institute of Science and Technology, Yueyang, 414006, P.R.China.

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
N,N'-carbonyl diimidazole
Esterification
P(O)-OH compounds
Phenols

ABSTRACT

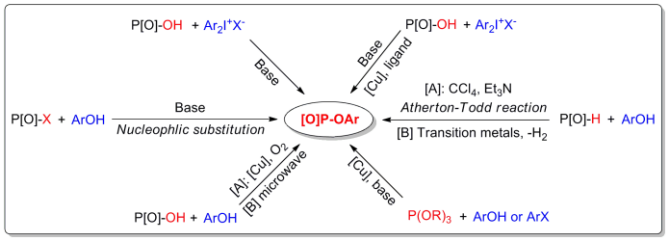
A novel and efficient *N,N'*-carbonyl diimidazole-catalyzed protocol for the direct esterification of P(O)-OH compounds using phenols as efficient esterification reagents is illustrated. It is a simple way to synthesis a broad spectrum of functionalized *O*-aryl phosphinates, phosphonates, and phosphates from basic starting materials with moderate to excellent yields.

1. Introduction

Phosphonic and phosphoric acids are widely existed in natural resources, especially certain phosphoryl esters are important motifs in natural products, pharmacological agents, amino acid analogues, and synthetic precursors. In recent years, due to the wide application of *O*-aryl substituted phosphonic and phosphoric acids derivatives in industrial materials, medicinal chemicals, lubricants, and phosphine ligands, there is a growing interest in these kinds of compounds. [1-7]

For their preparation, orthodox nucleophlic substitution of toxic phosphorus halides with phenols are commonly adopted. The Atherton-Todd reaction of P(O)-H compounds with phenols is also extensively used for the synthesis of the compounds, but the protocol suffers from the low tolerance of functional groups and substrate limitations, as well as the introduction of toxic reagents.[8] In 2014, Feringa *et al* first disclosed the synthesis of mixed alkyl aryl phosphonates using easily available phosphonates with diaryl iodonium triflates over copper catalysts, where the P=O bond coordinates with copper efficiently to activate the phosphonates.[9] In addition, we recently reported the functionalization of P(O)-OH compounds using diaryl iodonium triflates or phenols for the synthesis of *O*-aryl organophosphorus compounds, and where the copper salts and CCl_4 is essential for the reaction of P(O)-OH compounds with phenols.[10]

As an ongoing effort on the activation of P(O)-OH compounds, we studied the direct esterification of P(O)-OH compounds with phenols under mild conditions using *N,N'*-carbonyl diimidazole as the coupling reagent. Herein we report this efficient and simple protocol that is more economical and convenient than those reported in the literature for the synthesis of *O*-aryl organophosphorus compounds without the use of diaryliodonium salts and metal salts. Compared with P(O)-H or P-Cl compounds, P(O)-OH compounds are more air- and/or moisture-stable, and the use of them is more cost-saving and effective.[11-13]



Scheme 1. Methods for the synthesis of P[O]-OAr compounds.

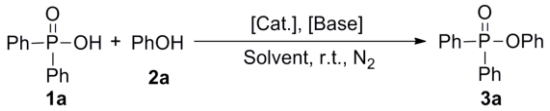
2. Results and Discussion

The reaction of diphenyl phosphinic acid with phenol at room temperature with the assistance of *N,N'*-carbonyl diimidazole (CDI) and Et_3N in THF under N_2 atmosphere gives *O*-phenyl diphenyl phosphinate **3a** in 31% yield (Table 1, entry 1). The introduction of CDI is crucial for the reaction. Then we concentrated on the optimization of reaction conditions. Different solvents (THF, DCM, DCE, DMF, 1,4-dioxane, EtOAc, CH_3CN) were screened for the reaction, and CH_3CN is found to be the best, affording **3a** in 43% yield (Table 1, entries 1-7). Among the coupling reagents tested (CDI (*N,N'*-carbonyl diimidazole), TBTU (*N,N,N',N'*-Tetramethyl-O-(benzotriazol-1-yl) uronium tetrafluoroborate), HATU (1-[bis (dimethyl-lamino) methylene]-1H-1,2,3-triazolo-[4,5-b] pyridinium 3-oxid hexafluoro

phosphate), COMU ((1-cyano-2-ethoxy-2-oxoethylidenaminooxy) dimethyl amino-morpholino-carbenium hexafluorophosphate), BOP ((benzotriazol1yloxy)-tris-(dimethylmino) phosphonium hexafluophosphate)), their efficiency is in the order: CDI > COMU > TBTU > HATU > BOP, and CDI gives the best result (Table 1, entries 8-11).[14] Besides Et_3N, we further tested other bases such as DBU, *N*,*N*-dimethylaniline, *N*,*N*-diethylaniline, and diisopropyl ethyl amine. It is apparent that *N*,*N*-dimethylaniline is the best, and 99% yield of **3a** is obtained at a "diphenyl phosphinic acid:$PhNMe_2$ molar ratio" of 1:1.5 (Table 1, entries 12-16).

Table 1

Optimization of the esterification of **1a** with **2a** [a]



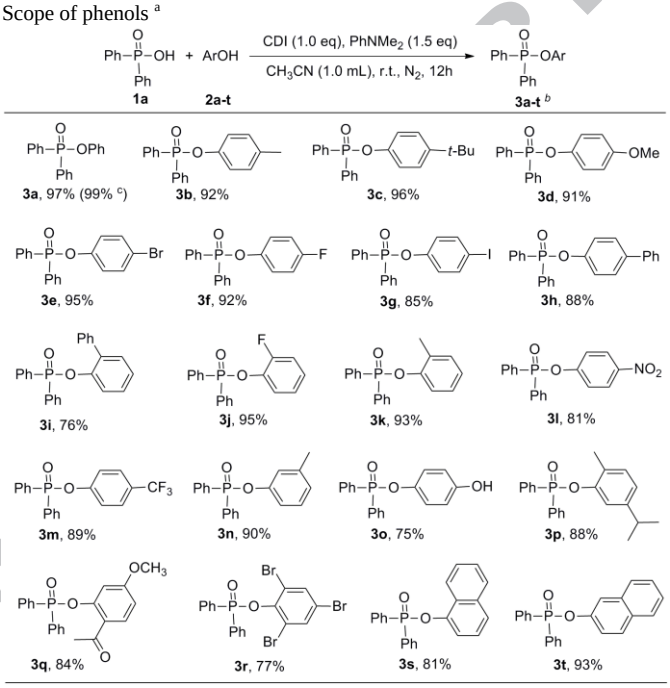
Entry	Coupling reagent (1.0 eq)	Solvent	Base (1.0 eq)	Yield [b]
1	CDI	THF	Et_3N	31%
2	CDI	DCE	Et_3N	11%
3	CDI	DCM	Et_3N	13%
4	CDI	DMF	Et_3N	5%
5	CDI	Dioxane	Et_3N	2%
6	CDI	EtOAc	Et_3N	13%
7	CDI	CH_3CN	Et_3N	43%
8	TBTU	CH_3CN	Et_3N	39%
9	HATU	CH_3CN	Et_3N	33%
10	COMU	CH_3CN	Et_3N	41%
11	BOP	CH_3CN	Et_3N	27%
12	CDI	CH_3CN	DBU	31%
13	CDI	CH_3CN	$PhNMe_2$	71%
14	CDI	CH_3CN	$PhNEt_2$	57%
15	CDI	CH_3CN	DIEA	49%
16	CDI	CH_3CN	$PhNMe_2$	99% [c]
17	-	CH_3CN	$PhNMe_2$	0%
18	-	CH_3CN	$PhNMe_2$	0% [d]

[a] Reactions were carried out with diphenyl phosphinic acid (0.5 mmol), phenol (0.5 mmol) and base (0.5 mmol) in solvent (1.0 mL), under N_2 atmosphere stirred at room temperarure for 12 h. [b] Yield was determined by GC analysis, and decane was used as internal standard. [c] $PhNMe_2$ (1.5 eq). [d] 100 °C, air.

It turned out that the present esterification reaction is generally applicable for the transformation of P(O)-OH compounds to *O*-aryl organophosphorus compounds. As shown in Table 2, phenols such as *p*-cresol, 4-*tert*-butyl phenol, 4-methoxy phenol, 4-bromo phenol, 4-fluoro phenol, 4-iodo phenol and 4-phenyl phenol react efficiently with diphenyl phosphinic acid (**1a**) under the optimized reaction conditions to afford the corresponding products of *O*-aryl phosphoryl compounds **3a-h** in moderate to excellent yields. *Ortho*-substituted phenols such as 2-phenyl phenol, 2-fluoro phenol and 2-methyl phenol are also well tolerated in the reaction, yielding the desired esterification products of **3i-k** in 76-95% yields. In addition, the reactions of **1a** with 4-nitro phenol and 4-trifluoromethyl phenol also afford the desired product in 81% and 89% yields, respectively. As stated above, it is observed that specials phenols (*.e.g.*, hydroquinone, 2-methyl-5-*iso*-propyl phenol, 1-(2-hydroxy-4-methoxyphenyl) ethanone, 2,4,6,-tribromo phenol, 1-naphthol and 2-naphthol) also exhibit high reactivity, generating the corresponding products in 75-93% yields, respectively (Table 2, **3o**-**3t**). When hydroquinone is used as the starting materials, there is not found the generation of the *di*-esterification product. This result is also consistent with the expectation that **3o** bearing an electron-withdrawing group on the aromatic ring should have a lower redox potential than hydroquinone, suggesting that the another hydroxyl of hydroquinone cannot be esterificated by diphenyl phosphinic acid. For most cases, electron-donating groups (Table 2, **3b**-**3d**, **3m**-**3q**) or electron-withdrawing groups (Table 2, **3e**-**3g**, **3j**, **3l**-**3m**, and **3r**) of phenols do not change the yields significantly.

Table 2

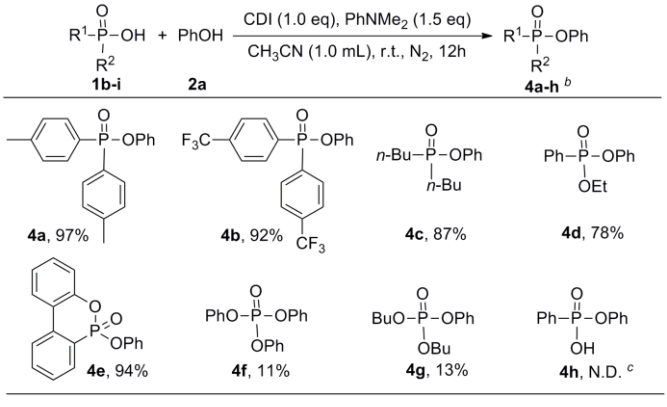
Scope of phenols [a]



[a] Reaction conditions: diphenyl phosphinic acid (0.5 mmol), phenols (0.5 mmol), CDI (0.5 mmol), $PhNMe_2$ (0.75 mmol), CH_3CN (1.0 mL), N_2, room temperature, 12 h. [b] Isolated yields. [c] Yield was determined by GC analysis, and dodecane was used as internal standard.

Table 3

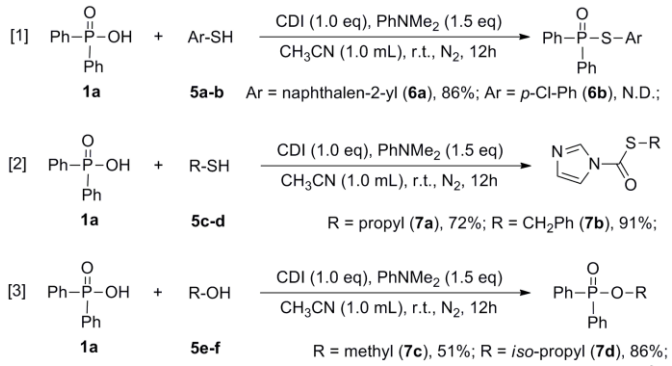
Scope of P(O)-OH compounds [a]



[a] Reaction conditions: P(O)-OH compounds (0.5 mmol), phenol (0.5 mmol), CDI (0.5 mmol), $PhNMe_2$ (0.75 mmol), CH_3CN (1.0 mL), N_2, room temperature, 12 h. [b] Isolated yields. [c] N.D. = Not detected.

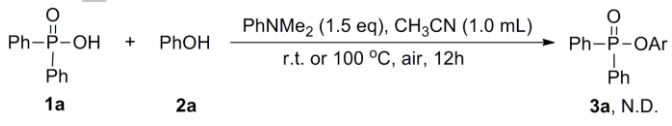
As depicted in Table 3, we investigated a variety of substituted P(O)-OH compounds (**1b**-**1i**) with phenol under the optimized conditions. It is clear that aryl substituted diphenyl phosphinic acids such as *di*-(4-methyl phenyl) phosphinic acid and *di*-(4-trifluoromethyl phenyl) phosphinic acid are also good substrates

for the reaction, and the expected esterification products of **4a** and **4b** are generated in 97% and 92% yields, respectively. In addition, dibutyl phosphinic acid, ethyl hydrogen phenylphosphonate, and 6-hydroxy-6H-dibenzo[c,e][1,2] oxaphosphinine 6-oxide also react with phenol (**2a**) efficiently to give the corresponding *O*-aryl phosphoryl products **4c**-**4e** in 78-94% yields. However, phenyl diphenyl phosphate (**4f**) and phenyl dibutyl phosphonate (**4g**) were generated only in 11% and 13% yields when diphenyl hydrogen phosphate and dibutyl hydrogen phosphate employed. In addition, when phenylphosphonic acid (**1i)** is adopted, there is no detection of the corresponding esterification product. It is maybe ascribe to the great acidity of this type compounds (**1g-i**). So, as described above, the efficiency of P(O)-OH compounds is in the order: $R_2P(O)$-OH > (R)(RO)P(O)-OH >> $(RO)_2P(O)$-OH.



Scheme 2. Scope of nucleophiles.

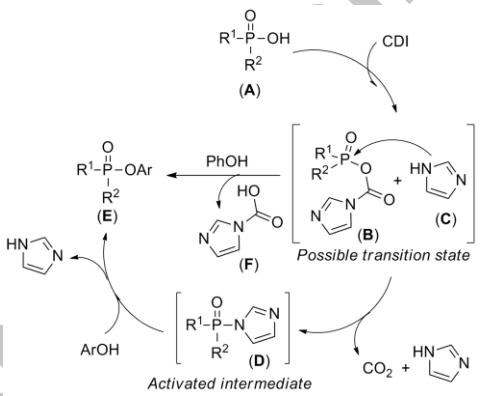
We further expanded the practical application of this method, and *S*-naphthalen-2-yl diphenyl phosphinothioate (**6a**) can be obtained in 86% yield in the reaction of diphenyl phosphinic acid with naphthalene-2-thiol (**5a**) at the optimized reaction conditions. When 4-chloro benzenethiol (**5b**) was adopted, there was not found the desired esterification product (Scheme 2, path 1). Furthermore, aliphatic thiols such as propane-1-thiol (5c) and phenylmethanethiol (5d) were also tested for the reaction. To our surprise, these compounds were also not tolerated in this reaction, while yielded the corresponding 1H-imidazole-1-carbothioates after the reaction. It was obviously that these 1H-imidazole-1-carbothioates lack of the driving force to activate the P(O)-OH compounds to afford the esterification products. Interestingly, when methanol and *iso*-propanol were treated to the reaction, the corresponding products were gained in 51% and 86% yields, respectively.



Scheme 3. Control experiment.

Control experiments for the reaction of diphenyl phosphinic acid with phenol were performed under the standard reaction conditions without the addition of CDI. As depicted in Scheme 3, no matter the reaction conducted in room temperature or heated to 100 °C, there was not found the generation of the desired product after the reaction. So, we deduced that CDI is crucial for the present esterification reaction.

A plausible mechanism for the present esterification of P(O)-OH compounds with phenols is proposed as illustrated in Scheme 3. P(O)-OH compound (**A**) first attacks *N,N'*-carbonyl diimidazole to afford the 1H-imidazole-1-carboxylic phosphoryl anhydride (**B**) and one molecular of 1H-imidazole (**C**). Intermediate **B** could also be attacked directly by phenol to give the esterification product. In the presence of a base, the 1H-imidazole attacks the phosphorus center of intermediate **B** to give the activated intermediate **D**, with the release of H-imidazole and carbon dioxide via the cleavage of P-O bond. Finally, the esterification path is completed via the reaction of activated inermediate **D** with nucleophiles (phenol) with the elimination of one molecular of 1H-imidazole.



Scheme 4. Proposed mechanism.

3. Conclusion

In summary, we developed an highly efficient and convenient method for the direct esterification of P(O)-OH compounds with phenols. The approach avoids the use of metals and air-sensitive reagents, and the reaction can be performed under ambient conditions, making the experimental procedure simple. The synthetic method has high potential for the synthesis of biologically active molecules, catalytic ligands, and organophosphorus compounds.

4. Experimental section

4.1 General information and materials.

All solvents used in reactions were freshly distilled. All other reagents were recrystallized or distilled as necessary. All reactions were performed under an atmosphere of dry nitrogen. ^1H (400 MHz), ^{13}C (100 MHz), and ^{31}P (162 MHz) spectra were recorded on a 400MHz spectrometer in $CDCl_3$. ^1H NMR chemical shifts are reported using TMS as internal standard; ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ as internal standard.

4.2 General procedure.

A mixture of P(O)-OH compounds (0.5 mmol), phenols (0.5 mmol), CDI (0.5 mmol) and $PhNMe_2$ (0.75 mmol) in CH_3CN (1.0 mL) was stirred at room temperature under N_2 atmosphere for 12 h. Removal of the solvent under reduced pressure gave the crude product; pure product was obtained by passing the crude product through a short silica gel column using Hexane/EtOAc (1:1 to 5:1) as eluent .

Acknowledgments

This work was supported by National Natural Science Foundation of China (21606080, 21676077, 21476068), Scientific Research Fund of Hunan Provincial Education Department (16B111).

Supplementary Material

Supplementary data associated with this article can be found in the online version.

References and notes

1. (a) Imamoto, T. In *Handbook of Organophosphorus Chemistry*, Engel, R. Eds.; Marcel Dekker: New York, **1992**; (b) Quin, L. D. In *A Guide to Organophosphorus Chemistry*, Wiley-Interscience: New York, **2000**.
2. (a) Bock, T.; Möhwald, H.; Mülhaupt, R. *Macromol. Chem. Phys.* **2007**, *208*, 1324; (b) Kirumakki, S.; Huang, J.; Subbiah, A.; Yao, J.; Rowland, A.; Smith, B.; Mukherjee, A.; Samarajeewa, S.; Clearfield, A. *J. Mater. Chem.* **2009**, *19*, 2593; (c) Kim, D.; Salman, S.; Coropceanu, V.; Padmaperuma, A. B.; Sapochak, L. S.; Kahn, A.; Bredas, J. L. *Chem. Mater.* **2010**, *22*, 247.
3. (a) Pollack, S. J.; Jacobs, J. W.; Schultz, P. G. *Science*. **1986**, *234*, 1570; (b) Janda, K. D.; Schloeder, D.; Benkovic, S. J.; Lerner, R. A. *Science*. **1988**, *241*, 1188.
4. (a) Baumgartner, T.; Réau, R. *Chem. Rev*. **2006**, *106*, 4681; (b) Engel, R. *Chem. Rev*. **1977**, *77*, 349.
5. (a) Williams, N. H.; Harrison, J. M.; Read, R. W.; Black, R. M. *Arch. Toxicol*. **2007**, *81*, 627; (b) Nomura, D. K.; Hudak, C. S.; Ward, A. M.; Burston, J. J.; Issa, R. S.; Fisher, K. J.; Abood, M. E.; Wiley, J. L.; Lichtman, A. H.; Casida, J. E. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5875; (c) Ashani, Y.; Gupta, R. D.; Goldsmith, M.; Silman, I.; Sussman, J. L.; Tawfik, D. S.; Leader, H. *Chem. Biol. Interact.* **2010**, *187*, 362.
6. (a) Spangler, L. A.; Mikolajczyl, M.; Burdge, E. L.; Kielbasinski, P.; Smith, H. C.; Lyzwa, P.; Fisher, J. D.; Omelańczuk, J. *J. Agric. Food Chem.* **1999**, *47*, 318; (b) Kukhar, V. P.; Hudson, H. R. In *Aminophosphonic and Aminopho-sphinic Acids: Chemistry and Biological Activity*; Wiley & Sons: Chichester, U.K., **2000**.
7. (a) Fukuto, T. R.; Metcalf, R. L. *J. Am. Chem. Soc.* **1959**, *81*, 372; (b) Nowlan, C.; Li, Y.; Hermann, J. C.; Evans, T.; Carpenter, J.; Ghanem, E.; Shoichet, B. K.; Raushel, F. M. *J. Am. Chem. Soc.* **2006**, *128*, 15892; (c) Moon, Y.; Moon, Y.; Choi, H.; Hong, S. *Green Chem*, **2017**, *19*, 1007; (d) Botez, L.; De Jong, G. B.; Slootweg, J. C.; Deelman, B.-J. *Eur. J. Org. Chem*, **2017**, *2017*, 434; (e) Xia, M.; Cheng, J. *Tetrahedron Lett.* **2016**, *57*, 4702; (f) Chen, Q.; Zeng, J.; Yan, X.; Huang, Y.; Wen, C.; Liu, X.; Zhang, K. *J. Org. Chem*, **2016**, *81*, 10043.
8. (a) Atherton, F. R.; Openshaw, H. T.; Todd, A. R. *J. Chem. Soc.* **1945**, 660; (b) Atherton, F. R.; Todd, A. R. *J. Chem. Soc.* **1947**, 674; (c) Wang, G.; Shen, R. W.; Xu, Q.; Goto, M.; Zhao, Y.-F.; Han, L.-B. *J. Org. Chem.* **2010**, *75*, 3890.
9. Copper-catalyzed *O*-arylation of the dialkyl phosphonates with diaryliodonium salts, see: FanÞanaìs-Mastral, M.; Feringa, B. L. *J. Am. Chem. Soc.* **2014**, *136*, 9894.
10. (a) Xiong, B.; Zeng, K.; Zhang, S.; Zhou, Y.; Au, C.-T.; Yin, S.-F. *Tetrahedron*, **2015**, *71*, 9293. (b) Xiong, B.; Feng, X.; Zhu, L.; Chen, T.; Zhou, Y.; Au, C.-T.; Yin, S.-F. *ACS Catal*. **2015**, *5*, 537.
11. For the activation of P(O)-OH compounds via the P(O)-Cl intermediate, see: (a) Pollart, K. A.; Harwood, H. J. *J. Org. Chem.* **1962**, *27*, 4444; (b) Kasemsuknimit, A.; Satyender, A.; Chavasiri, W.; Jang, D. O. *Bull. Korean Chem. Soc.* **2011**, *32*, 3486; (c) Swamy, K. C. K.; Kumar, N. S. *Acc. Chem. Res.* **2006**, *39*, 324.
12. For reviews of the synthesis of phosphoric acid esters, see: (a) Hayakawa, Y. In *Comprehensive Organic Synthesis*, Trost, B. M.; Fleming, I.; Winterfeldt, E. Eds.; Pergamon, Oxford, **1991**, Vol. 6; (b) Reese, C. B. *Org. Biomol. Chem.* **2005**, *3*, 3851; (c) Keglevich, G.; Kiss, N. Z.; Mucsi, Z.; Körtvélyesi, T. *Org. Biomol. Chem.* **2012**, *10*, 2011; (d) Dumond, Y. R.; Baker, R. L.; Montchamp, J.-L. *Org. Lett.* **2000**, *2*, 3341; (e) Kiss, N. Z.; Ludányi, K.; Drahos, L.; Keglevich, G. *Synth. Commun.* **2009**, *39*, 2392
13. For selected examples for the activation of P(O)-OH compounds, see: (a) Park, Y.; Seo, J.; Park, S.; Yoo, E. J.; Lee, P. H. *Chem. Eur. J.* **2013**, *19*, 16461; (b) Unoh, Y.; Hashimoto, Y.; Takeda, D.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett*. **2013**, *15*, 3258; (c) Park, Y.; Jeon, I.; Shin, S.; Min, J.; Lee, P. H. *J. Org. Chem.* **2013**, *78*, 10209; (d) Peng, A.-Y.; Ding, Y.-X. *J. Am. Chem. Soc.* **2003**, *125*, 15006; (e) Ryu, T.; Kim, J.; Park, Y.; Kim, S.; Lee, P. H. *Org. Lett.* **2013**, *15*, 3986; (f) Sakakura, A.; Katsukawa, M.; Ishihara, K. *Angew. Chem. Int. Ed*. **2007**, *46*, 1423; (g) Sakakura, A.; Katsukawa, M.; Ishihara, K. *Org. Lett.* **2005**, *7*, 1999; (h) Sakakura, A.; Katsukawa, M.; Hayashi, T.; Ishihara, K. *Green Chem.* **2007**, *9*, 1166; (i) Park, C.-H.; Givens, R. S. *J. Am. Chem. Soc.* **1997**, *119*, 2453; (j) Xiong, B.; Ye, Q.; Feng, X.; Zhu, L.; Chen, T.; Zhou, Y.; Au, C.-T.; Yin, S.-F. *Tetrahedron*. **2014**, *70*, 9057; (k) Xiong, B.; Feng, X.; Zhu, L.; Chen, T.; Zhou, Y.; Au, C.-T.; Yin, S.-F. *ACS Catal*. **2015**, *5*, 537.
14. (a) Twibanire, J. K.; Grindley, T. B. *Org. Lett.* **2011**, *13*, 2988; (b) Subiros-Funosas, R.; Khattab, S. N.; Nieto-Rodriguez, L.; El-Faham, A.; Albericio, F. *Aldrichimica Acta*. **2013**, *46*, 21.

Highlights

- Direct esterification reaction of P(O)-OH compounds with phenols is achieved.
- Avoids the use of metals and air-sensitive reagents.
- Reactions can be performed under ambient conditions.