

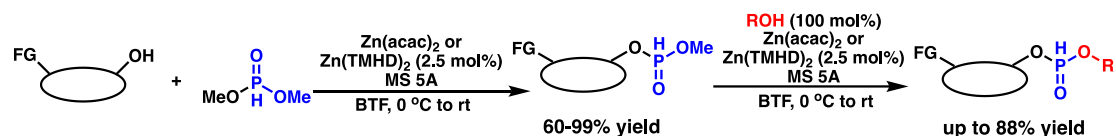
## Zinc-Catalyzed Phosphonylation of Alcohols with Alkyl Phosphites

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Organophosphonate molecules are important functional groups that are found in various kinds of natural products and pharmaceutical agents. They also play a key role in synthesizing oligonucleotides that are short DNA/RNA molecules, which consist of 2'-deoxyrivanucleosides or ribonucleosides joined via phosphodiester linkages. Phosphorylation of alcohols is the most straightforward way to gain organophosphate molecules, but conventional methods have some drawbacks such as requiring stoichiometric amounts of activation reagents that are incompatible with some substrates.<sup>1</sup> Some catalytic phosphorylation reactions have also been reported, but they all require harsh reaction conditions and substrate scopes are rather limited. Most importantly, there has been no effort made to introduce second alcohol to obtain di-substituted phosphates.<sup>2</sup> Therefore, we decided to focus on the phosphonylation of alcohols using a catalytic amount of Lewis acid under mild reaction conditions to access various kinds of phosphates/phosphites/phosphonates and further that allows second introduction of alcohols.

After screening various Lewis acid catalysts, zinc(II) complexes with diketonate units that have square-planar structures were found to be the best catalysts for the reaction, and more sterically hindered Zn complexes showed better activity. Molecular sieves were employed to capture the leaving methanol, and therefore efficiency of the transesterification reaction was increased. The desired reactions proceeded smoothly to afford the products in high yields with wide substrate scope. We also confirmed that a second alcohol could be successfully introduced to obtain a di-substituted phosphite. In this presentation, we will discuss details of the project, focusing on the development of the catalytic systems and reaction mechanism.<sup>3</sup>



- 1) Miller, S. J. *et al. J. Am. Chem. Soc.* **2001**, 123, 10125–10126.
- 2) Ishihara, K. *et al. Angew. Chem., Int. Ed.* **2007**, 46, 1423–1426.
- 3) Kobayashi, S. *et al. Org. Lett.* **2020**, 22, 3171–3175.