MS 4A-Promoted Aqueous Phospho-Aldol-Brook Rearrangement Reaction of Isatins

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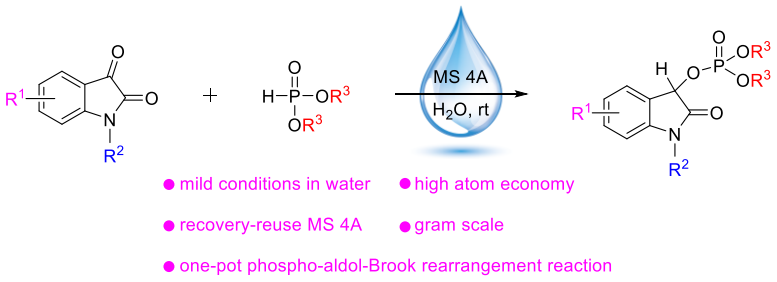
α-Hydroxyphosphonate derivatives have garnered significant attention for their diverse biological activities such as anticancer, antifungal, antibacterial, anti-inflammatory, and antiviral activities. In addition, several studies have reported that α-oxindole-phosphonates could be obtained from α-hydroxyphosphates via the Brook rearrangement reaction in the presence of specific bases. Furthermore, α-oxindole-phosphonates are also useful synthetic intermediates of α-substituted phosphonyl compounds.

Thus, to date, many protocols have been developed for the hydrophosphonation of isatins, but were limited to the use of metal catalysts[1a] or strong bases,[1b] toxic solvents,[1c] heating,[1d] and sonication conditions.[1e] On the other hand, from the perspective of green chemistry, it is considerable to use water rather than organic solvents. However, to the best of our knowledge, there is only one protocol of the hydrophosphonation of isatins in water using β-CD with heating pretreatment that has been reported.[2] Therefore, the hydrophosphonation of isatin with a simpler experimental operation in water is highly desired.

Herein, we present an efficient, simple, environment-friendly, and low-cost protocol for the hydrophosphonation of isatins using inexpensive and non-toxic MS 4A as a recyclable additive in water. Gram-scale recovery/reuse experiments indicated that large-scale synthesis is possible and that MS 4A can be used as a recyclable additive. This protocol can also be used for the reaction of isatin with acetone or acetophenone.[3]



1) a) T. Deng, H. Wang, C. Cai, *Org. Biomol. Chem.*, **2014**, *12*, 5843. b) W. Fang, G. Liu, X. Huang, J. Jia, X. Wang, *Chin. J. Org. Chem.*, **2014**, *34*, 1177. c) A. Kondoh, A. Takei, M. Terada, *Synlett*, **2016**, *27*, 1848. d) X. J. Yang, *Appl. Organomet. Chem.*, **2014**, *28*, 471. e) K. U. M. Rao, G. D. Reddy, C.-M. Chung, *Phosphorus, Sulfur Silicon Relat. Elem.*, **2013**, *188*, 1104. 2) J. Shankar, K. Karnakar, B. Srinivas, Y. V. D. Nageswar, *Tetrahedron Lett.*, **2010**, *51*, 3938. 3) F. Liu, W. Han, T. Oriyama, *Heterocycles*, **2022**, *104*, 159.

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