ORGANOCATALYTIC HIGHLY ENANTIOSELECTIVE VINYLOGOUS ALDOL REACTION: RAPID ACCESS TO *δ*-QUARTERNARY *α*-HYDROXYPHOSPHONATO-3-ALKYLIDENE-2-OXINDOLES

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Phosphonic acids are generally regarded as the structural and functional analogues of carboxylic acids. As a result, hydroxy-functionalized phosphonic acids and their derivatives are found to display inhibitory activities toward a wide range of enzymes such as renin, HIV protease, thrombin, and various classes of protein tyrosine kinases and phosphatases.[1] Particularly, quaternary *α*-hydroxy phosphonates, one of the important sub group of organic phosphoric compounds attracted numerous attention due to their structural similarity with *α*-hydroxy acids exhibits intriguing biological activities. As a consequent, quaternary *α*-hydroxy phosphonates, in general, were synthesized *via* [12] and addition of carbon nucleophiles to α-ketophosphonates.[3]

Since, from past few years, our group actively working on vinylogous reactions,[4] herein we disclose an efficient enantioselective vinylogous aldol reaction of 3-alkylidene-2-oxindoles to *α*-ketophosphonates by a bifunctional thiourea catalyst derived from cinchona alkaloid. The simultaneous H-bond directing dual activation of vinylogous nucleophile and electrophile afforded *δ*-quaternary *α*-hydroxyphosphonato-3-alkylidene-2-oxindoles in high yield (upto 92%) while obtaining excellent stereocontrol (upto 99% ee).

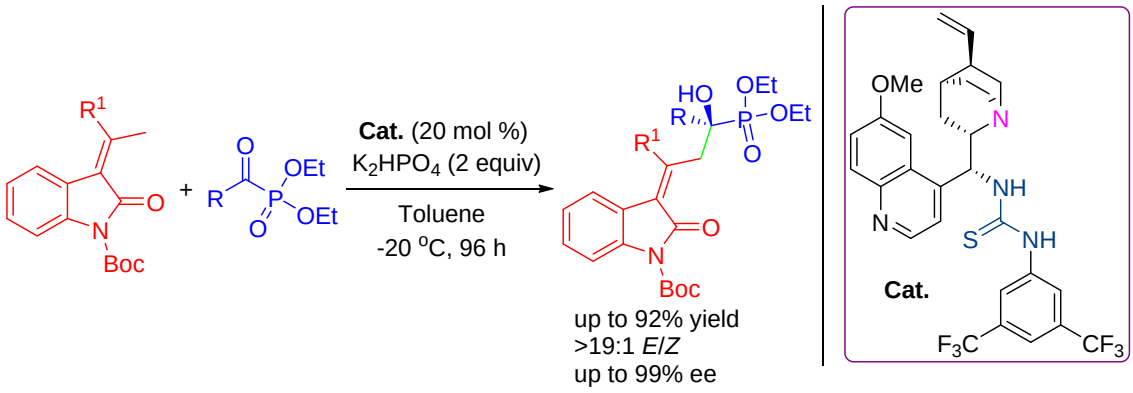

Figure 1.

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