Enantioselective Michael Addition of Nitrophosphonates to Activated Olefins for Synthesis of Quaternary α-Aminophosphonates

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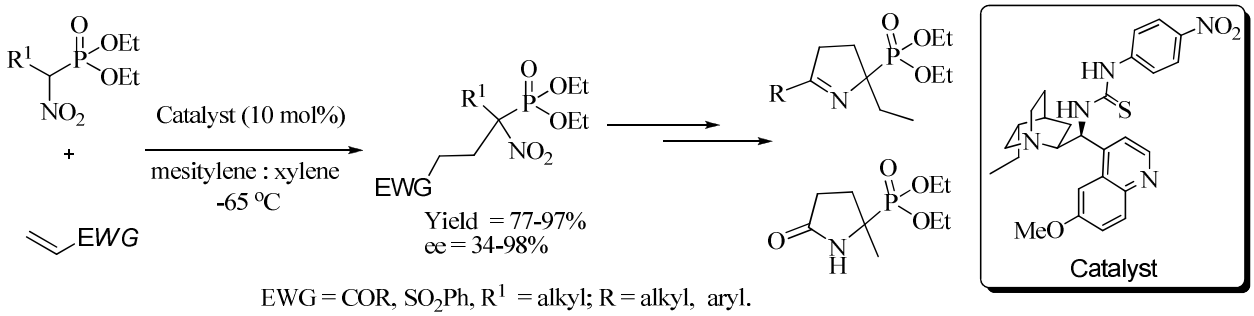
Aminophosphonic acid mimics the tetrahedral transition states of enzyme-mediated peptide bond hydrolysis. Further, the antibacterial, antifungal and anti-HIV properties of α-aminophosphonic acids make them important class of medicinal and pharmaceutical compounds. Their use as organocatalysts and as well as their presence in biologically active natural product K-26 make them attractive synthetic targets.[1] Although various stoichiometric and catalytic methods provide α-aminophosphonic acids with high enantioselectivity, generation of quaternary α-carbon centers via catalytic asymmetric synthesis of α-aminophosphonic acids remains scarcely explored.[2]

Since nitrophosphonates are immediate precursors to aminophophonic acids, our group pursued synthesis of optically active γ-nitrophosphonates and β-nitrophosphonates from nitroalkenes in good yield and enantioselectivity.[3] As a part of our ongoing interest in nitrophosphonate chemistry, we have developed an efficient method for the synthesis of optically active quaternary α-nitrophosphonates by asymmetric Michael addition of dialkyl α-nitrophosphonates to enones[4] and vinyl sulfones. The scope of these asymmetric reactions and transformation of these optically active quaternary α-nitrophosphonates will be discussed.



EWG = COR, SO_2Ph, R^1 = alkyl; R = alkyl, aryl.

References

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