Design and Synthesis of Novel Bifunctional Organocatalysts for Enantioselective Rearrangement of α-Acyloxy-β-Keto Sulfides to α-Acyloxy Thioesters

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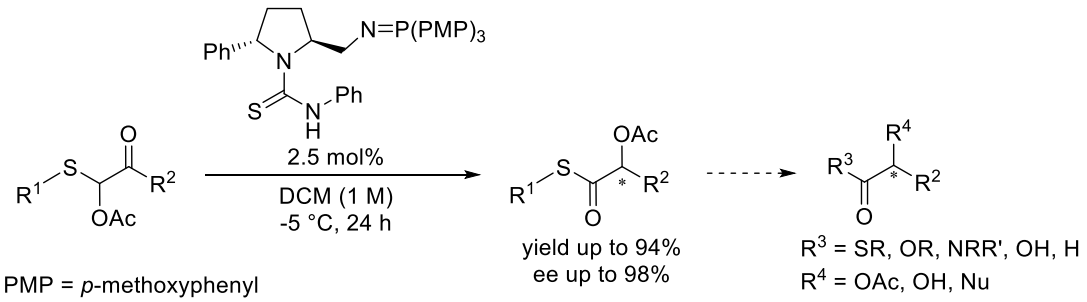
Organocatalysis is a metal-free synthetic methodology established as a highly attractive area in modern organic synthesis and green chemistry because it prevents metal pollution. Applications of organocatalysts have notably made it possible to promote numerous efficient enantioselective reactions giving access to new synthetic routes for natural and non-natural products.[1)] Among them, chiral bifunctional organocatalysts associated with hydrogen-bond donors represent an interesting new class of catalysts. They allow a better asymmetric induction by simultaneous activation of nucleophiles and electrophiles while keeping chiral scaffolds in their proximity.

In this project, we designed new bifunctional organocatalysts bearing an iminophosphorane and a thiourea moiety that function as Brønsted bases and hydrogen-bond donors respectively.[2)] Additionally, L-proline structure was introduced as a rigid chiral source for asymmetric induction. This organocatalyst has been employed for asymmetric rearrangement of α-acyloxy-β-keto sulfides to furnish α-acyloxy thioesters in excellent yields with high enantioselectivities. The starting material formed via a Pummerer rearrangement was deprotonated by the iminophosphorane function. This deprotonation led to the generation of an enolate and allowed its addition to the acetate. Then enantioselective protonation occurred to deliver the final product. This reaction gave up to 94% yield and up to 98% ee of the products in 2.5 mol% catalyst loading. The product underwent plenty of chemical transformations, making it a good molecular platform for forming a variety of compounds with wide applications, such as derivatives of lactic acids used as food additives or cosmetics.



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