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Highly Enantioselective Organocatalytic Biginelli Reaction
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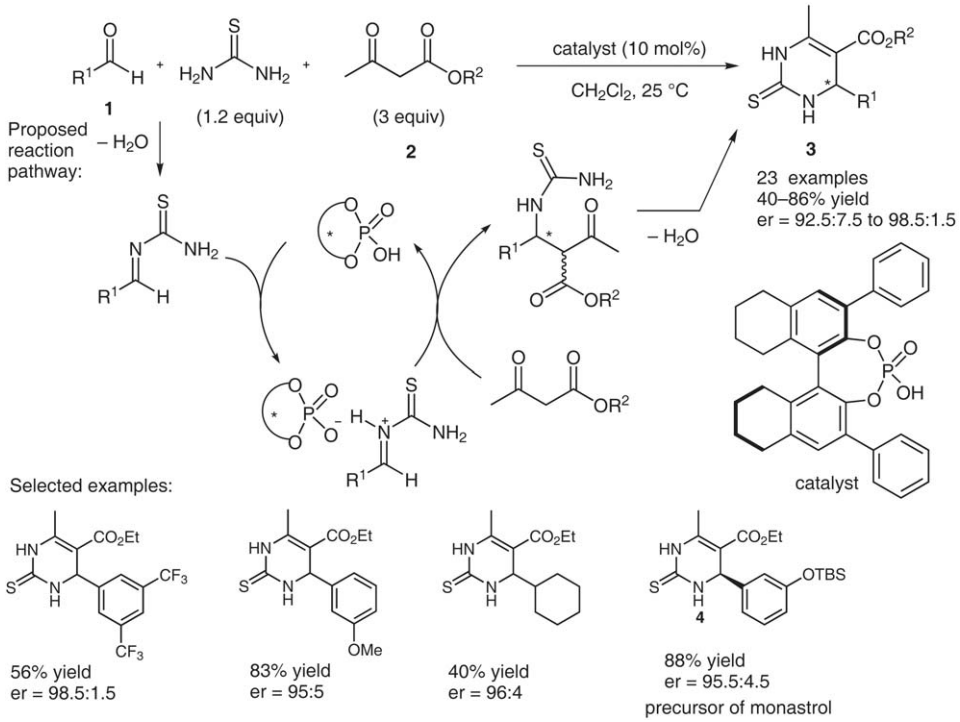
First Organocatalytic Asymmetric Biginelli Reaction



Significance: The first highly enantioselective organocatalytic Biginelli reaction is described. Starting from an aldehyde (**1**), thiourea, and various acetoacetates (**2**), this acid-catalyzed multicomponent reaction furnishes thio-analogues of diversely substituted 3,4-dihydropyrimidin-2-(1*H*)-ones (DHPMs) (**3**), in moderate to good yields and high enantioselectivities. As chiral Brønsted acid organocatalyst the authors employed a binol-derived phosphoric acid. Moreover, three examples of the use of urea instead of thiourea are shown to obtain original DHPMs rather than the thio-analogues. Furthermore, an application in the synthesis of the drug monastrol is reported.

Comment: Multicomponent reactions are of great interest in organic chemistry, since they allow for the rapid and facile access to complex target structures in one step. Moreover, they display an entry to diversity-orientated synthesis, often used in the discovery of new lead compounds in pharmaceutical industry. The heterocyclic Biginelli products are of particular interest since a wide range of dihydropyrimidones exhibits distinct pharmacological properties. To date, only one asymmetric Biginelli reaction with a chiral ytterbium catalyst is known (C. Zhu and co-workers *J. Am. Chem. Soc.* **2005**, *127*, 16386-16387).

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