The application of 2-(trifluoromethyl)pyrrolidine as a catalyst for the reaction of pyruvates and 2,3-diketones in nucleophilic addition to α,β-unsaturated nitroalkenes.

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Biochemical processes within living organisms exploit 2,3-diketones in the synthesis of amino acids. Notably, pyruvate gives rise to alanine, valine, and leucine. The initial decades of the twentieth century marked a period of rapid advancement in organocatalysis, where a diverse array of substrates were subjected to catalytic processes. Despite this, the full potential of 2,3-diketones in chemical synthesis remains underexplored.

This dissertation introduces organocatalytic methodologies for harnessing 2,3-diketones in reactions involving nitroalkenes. It was determined that the catalyst 2-(trifluoromethyl)pyrrolidine facilitates reactions between pyruvate esters, 2,3-diketones, and α,β-unsaturated nitroalkenes bearing various β-substituents. Notably, this catalyst exhibits a unique blend of low basicity and unexpectedly high nucleophilicity, thereby circumventing the enol mechanism typical for reactions involving 2,3-diketone and favoring an enamine mechanism instead.

The dissertation presents twenty-eight case studies illustrating the synthesis of β-substituted γ-nitropyruvate esters from pyruvate esters and nitroalkenes. The resultant compounds were instrumental in obtaining ten distinct 4-substituted proline esters and three precursor molecules for GABA derivatives such as Phenibut, Baclofen, and Pregabalin, which are blockbuster drugs.

Furthermore, the research yielded twenty-two uniquely substituted 4-positioned 2-hydroxy-3-nitrocyclopentanones through a regioselective Michael-Henry domino reaction involving 2,3-diketones and nitroalkenes. The versatility of these compounds was demonstrated through straightforward transformations, including homologation to yield 2-hydroxy-3-nitrocyclohexanones.