

## Catalytic Continuous-flow Synthesis of $\beta$ -Ketoesters Through Roskamp Reactions

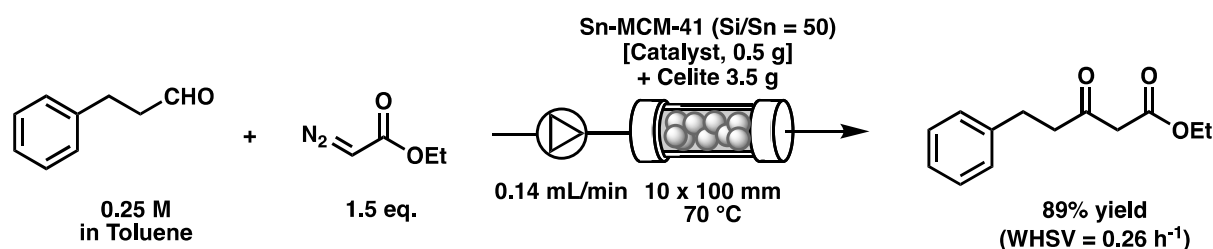
(School of Science<sup>1</sup> and GSC Social Cooperation Laboratory<sup>2</sup>, The Univ. of Tokyo)

○Mohanraj KANDASAMY<sup>1</sup>, Haruro ISHITANI<sup>2</sup>, Shū KOBAYASHI<sup>1, 2</sup>

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$\beta$ -Ketoesters are a potential building block to construct various bioactive heterocycles and API molecules. A typical synthetic method of the compounds is base-mediated Claisen condensation of esters; however, due to low acidity of  $\alpha$ -hydrogen of esters and higher acidity of that in the product  $\beta$ -ketoesters generally require stoichiometric amount of strong bases. The other available strategies to prepare them also require harsh reaction conditions, high catalyst loading and long reaction time.<sup>1,2</sup> To gain maximum advantage for utilization of the target compound as an intermediate in sequential synthesis, development of heterogenous catalytic process and utilization in sequential flow systems are highly demanded.<sup>3</sup>

Herein we present continuous-flow synthesis of  $\beta$ -ketoesters through Roskamp reaction between aldehydes and diazoesters using heterogeneous catalysts. The key features of our protocol are good to excellent yields, safe operation procedure, and broad functional group tolerance. Our investigation for surveying suitable catalysts indicated that silica-based solid acids possessed potential for the use in flow. Further investigations revealed that Sn-planted mesoporous silica (Sn-MCM-41) provided an 89% yield in the flow reaction between 3-phenylpropionaldehyde and ethyl diazoacetate at 0.257 h<sup>-1</sup> of weight hourly space velocity (WHSV). Such the catalytic activity was retained for over three days with keeping the yield on 73-89%. The prepared  $\beta$ -ketoesters were smoothly transformed into coumarin derivatives, vinylidene ketoesters, and 5-pyrazolinones through condensation reactions in sequential flow.



### References

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