Continuous-Flow Aldol Condensation of Phenylacetate Derivatives with Formalin for α-Aryl Acrylate Synthesis

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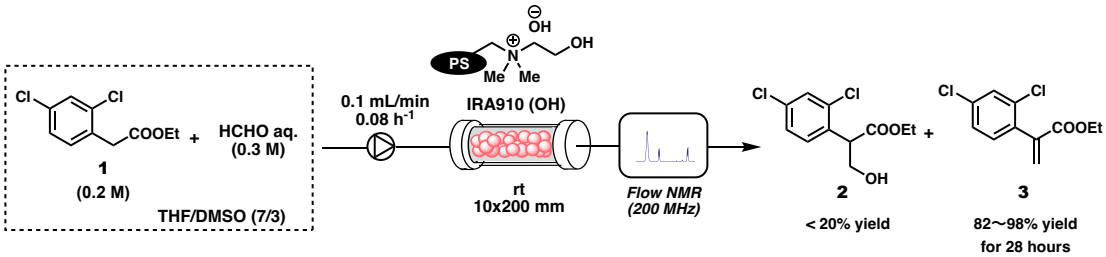
α-Aryl acrylic acid derivatives are important intermediates in the synthesis of polymers and fine chemicals. Their synthesis from the ester and formaldehyde have relied on the catalytic gas-phase reactions or the use of a stoichiometric amount of base,[1,2] and thus condensation under liquid-phase is a desired method for realizing low-energy processes. While it was known that the use of a catalytic amount of base afforded β-hydroxy ester,[3] a continuous-flow system with a catalyst-packed bed reactor will change its reaction outcome to acrylates thanks to the high density of catalyst packed to substrate than the batch system. Through investigations of the reaction conditions, we succeeded in drawing out an efficient catalysis of quaternary ammonium hydroxide resin for the reaction of phenylacetate derivatives **1** with formalin, especially when using DMSO solvent, but at the same time, saponification of the ester proceeded as a side reaction. We then optimized the cation structure and searched for a suitable resin that would effectively catalyze the reaction with suppressing the saponification. As a result, dimethylethanolammonium resin was found to be the optimal for the selective production of the desired acrylate **3** under flow conditions. When this catalyst system was applied for the extended-time reaction, the desired acrylate was obtained with a ratio of 80/20 or more for 28 h under SV = 0.08 h^{-1}. Further extension of the flow operation resulted in lowering the ratio while maintaining the total yield of the condensation products. This change in selectivity was suggested to be related to the total amount of water supplied and produced by the reaction. In addition, a detailed comparison of the reaction kinetic profiles of the batch and the flow system suggested that under the optimal flow conditions, the stepwise mechanism was dominant for the outcome, but that there existed a mechanism for direct formation of acrylate via a pathway separate from the stepwise reaction.



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