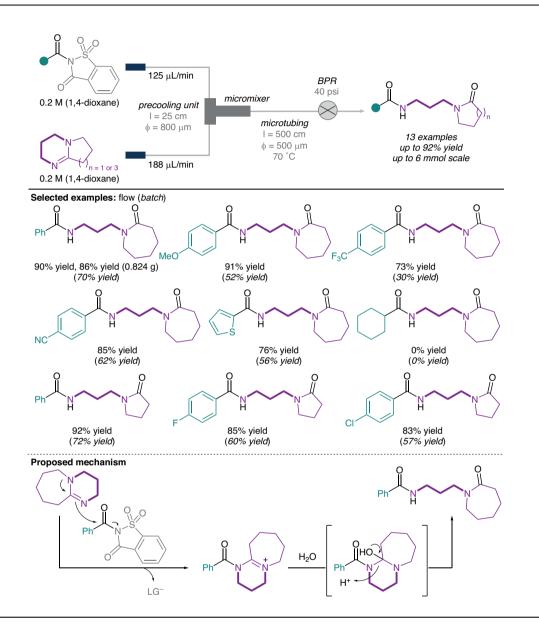
K. GOVINDAN, N.-Q. CHEN, G. VENKATACHALAM, T.-F. LEUNG, W.-Y. LIN* (KAOHSIUNG MEDICAL UNIVERSITY, TAIWAN) Batch vs Continuous-Flow Method to Synthesize *N*-(3-Acylamidopropyl)lactams through N–C Bond Cleavage in Amides with Amidines

Adv. Synth. Catal. 2024, DOI: 10.1002/adsc.202401179

Synthesis of γ - and ϵ -Lactams in Flow



Significance: Lin and colleagues report an efficient reaction of *N*-acyl saccharin with DBU or DBN to produce *N*-(3-acylamidopropyl)lactam derivatives, in both batch and continuous-flow processes. The microreactor employs a T-shaped micromixer and a back-pressure regulator (40 psi). Compared to the batch method, the flow reaction achieves significantly shorter reaction times (8 minutes versus 24 hours), and improved yields in all examples.

Comment: The authors propose that *N*-acyl saccharin reacts with DBU or DBN via a nucleophilic acylation mechanism, which is thermodynamically driven by the departure of the saccharin leaving group and the formation of an iminium ion. They suggest that trace amounts of water, either present in the solvent or introduced during quenching, react with the iminium ion, leading to ring opening and the subsequent formation of the desired product.

SYNFACTS Contributors: Mark Lautens[®], Alexa Torelli Synfacts 2025; 21(02), 219 Published online: 28.01.2025 **DOI:** 10.1055/a-2496-9918; **Reg-No.:** F00225SF

Category

Flow Chemistry

Key words

lactam synthesis flow vs batch N–C bond cleavage