Integration of Liquid-Liquid Biphasic Flow Alkylation and Continuous Crystallization based on Taylor Vortices

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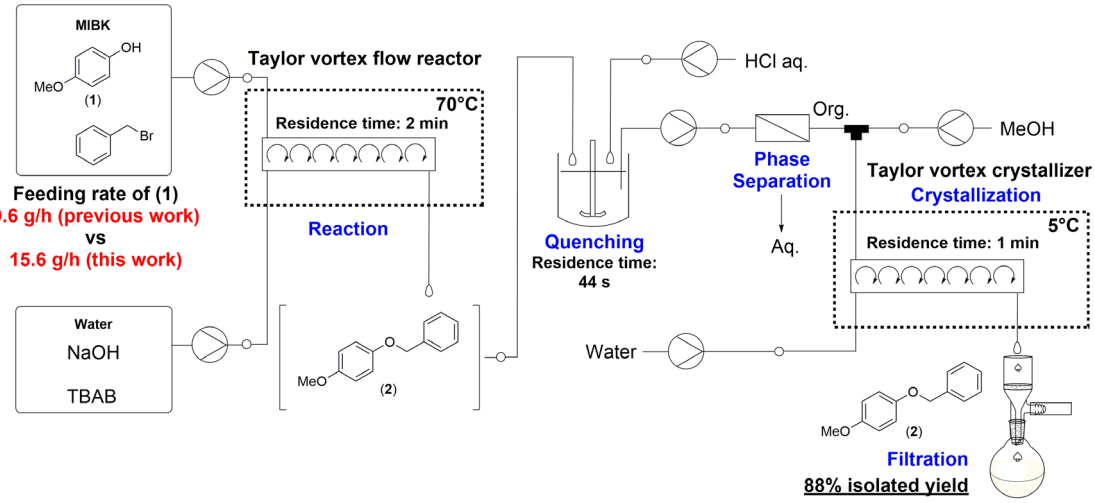
Alkylation under Liquid-liquid biphasic conditions is an attractive synthetic method to avoid the use of hazardous amide solvents and organic bases. However, the heterogeneous reaction system has a drawback to scale-up from the aspect of the mixing efficiency. To overcome this drawback, our previous work has established the methodology for liquid-liquid biphasic flow alkylation using Taylor vortex flow reactor, which is scalable with the high mixing efficiency.[1)] In this presentation, we report the optimization of reaction conditions to improve the productivity of this continuous flow reaction system. Under the optimized conditions, the throughput increased more than twentyfold, and a long-run experiment (4 h) ensured its robustness.

To realize fully continuous manufacturing, we subsequently integrated liquid-liquid biphasic flow alkylation, phase separation, continuous crystallization and filtration. The integrated system avoided the exposure to benzyl bromide with tearing property because of the closed system and successfully provided the alkylated product continuously from the solution of starting material using Taylor vortex flow reactors. Furthermore, the total residence under this integrated system was shortened to less than 5 min, which will contribute to the rapid supply of desired products.



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