From Batch to Flow - Converting Microwave to Flow Chemistry under High Temperature/Pressure Conditions

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Microwave chemistry has become an extremely popular technique in the scientific community for performing synthetic transformations. One disadvantage of microwave-assisted synthesis, however, is the limited potential for scale-up of the technology due to the comparatively small penetration depth of microwave irradiation (2.45 GHz) into absorbing media. Therefore, translating microwave chemistry to scalable continuous flow possesses is of increasing interest. Herein we describe a series of pharmaceutically relevant organic synthetic transformations that require medium to high reaction temperatures and compare processing under batch microwave conditions to continuous flow processing in different mesofluidic flow reactors capable of reaching high reaction temperatures (350 °C, 200 bar), thus mimicking microwave batch conditions.

After optimizing the general reaction conditions including reaction temperature and time under small scale batch microwave conditions, in most instances a successful translation to a continuous flow process was achieved where the residence time in flow correlates with the reaction time in the batch experiment. In addition to a variety of chemistry examples (including reactions in supercritical solvents), the multistep synthesis of pharmaceutically relevant target compounds will be discussed. This technology allows the process intensification of important synthetic

transformations and eliminates the scale-up problems inherent to microwave synthesis.