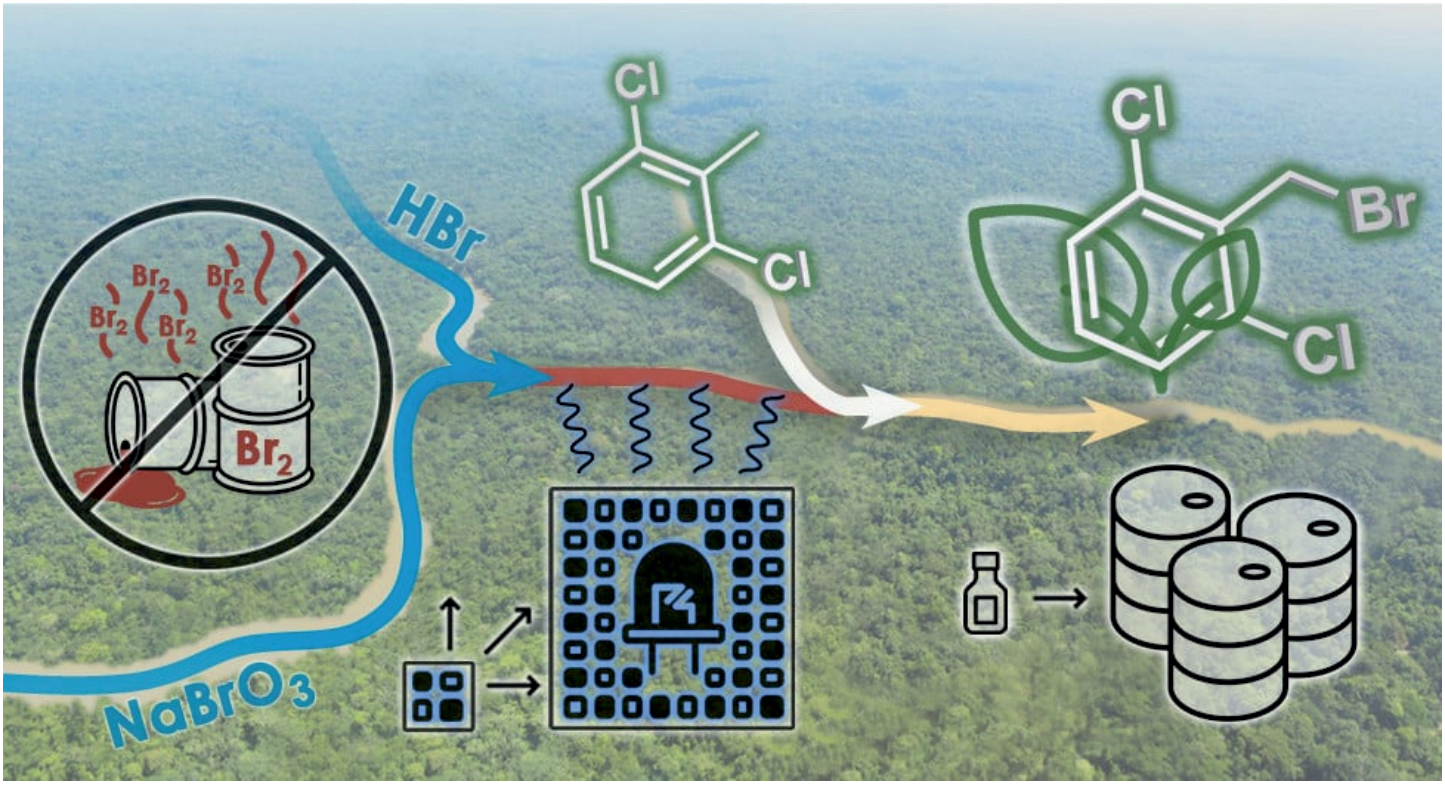
In-Situ Bromine Generation for Photochemical Applications in Continuous Manufacturing

Continuous manufacturing enables options to generate and use hazardous or unstable reagents in a safe manner on manufacturing scale. In this study we present how in-situ generated bromine can be used for a photochemical application. This combines the process intensification of a photochemical reaction with the in-situ generation of the hazardous reagent bromine. The past decade has seen photochemistry become a powerful tool in chemical synthesis. The development of efficient pseudo-monochromatic light sources paves an innovative and efficient way to secure energy supply.

Continuous flow technology has been demonstrated to be a solution to this problem since narrow reaction channels can ensure homogeneous irradiation alongside improved heat transfer and mass transfer (batch-to-conti). Benzyl bromides represent common photo-chemically accessible building blocks in the pharmaceutical and other industries, signifying that their scalable synthesis is of importance to multiple fields. The use of N-bromosuccinimide (NBS) instead is convenient, especially on lab scale since the associated risks are significantly lower and the crystalline solid is easier to handle. The trade-off when using NBS, however, is poorer reactivity, atom economy and solubility.



In a current study that was conducted by the CCFlow and Microinnova teams we can demonstrate a highly intensified process for photochemical benzylic bromination using the chemical generator approach for in-situ bromine formation. A commonly used oxidant is H_2O_2, but there are safety concerns associated with the storage and use of peroxides. Accordingly, we employed $NaBrO_3$, a crystalline solid with a high decomposition temperature of 310 °C, as a safer alternative. By using concentrated hydrobromic acid (one source for both bromide ions and protons), a concentrated sodium bromate solution and no organic solvent (substrate pumped neat), the bromine generator was considerably intensified. Modular plants enable a flexible use of the bromine generator in batch and in continuous applications.