Microscale Chemical Factory

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Miniaturization is invading the world of chemical syntheses. Since typical chemical syntheses take place in several reaction steps with various separation or purification steps in between, microchemistry has almost always been limited to one-step reactions or sequences of reactions requiring no purification between steps.

Researchers at the Massachusetts Institute of Technology (MIT) have now produced an integrated multiple-step microscale production line. As reported in the journal *Angewandte Chemie*, their process includes three reaction steps and two separation processes (one gas–liquid and one liquid–liquid separation). Because it is arranged in a microscale reaction network, it is even possible to configure this process so that related compounds can be simultaneously produced in parallel.

To fully exploit the potential of microscale reaction technology, it is crucial to integrate the necessary separation steps. A team headed by Klavs F. Jensen has recently developed an efficient microfluidic separation technique and has now integrated this concept into a continuously operating, three-step reaction system. Microscale separations are driven by different principles than separations at normal scale, because in microfluidic systems, surface tension forces dominate over gravity.

This is how the microfluidic separation works: A porous separation membrane made of a fluoropolymer is coated with the organic phase of the mixture, which can “sneak through” the fine pores in the membrane. The aqueous phase to be separated off cannot coat the pores that have already been coated by the organic phase, because the two liquids are not miscible; the water can thus not pass through the membrane.

The second separation, a gas–liquid separation, is based on the same principle: In this case, the liquid, which contains the intermediate product, wets the membrane and passes through the pores. Meanwhile, the coated membrane blocks the nitrogen gas that is released during the reaction.

To demonstrate their system, the researchers chose the synthesis of carbamates, compounds that are used as pesticides, among other things, and are important building blocks and reagents in chemical syntheses. The three-step synthesis used to make carbamates (the Curtius Rearrangement) involves intermediate products (azides, isocyanates) that have the potential to be dangerous, since some of these types of compounds pose an explosive or health hazard. The advantage of the microscale reaction system is that these intermediates are formed in situ and are then immediately consumed, so they don't need to be isolated or stored.

If, after the second separation step, the product stream is divided and fed into multiple microreactors, each with a different reagent, a series of different but related carbamates can be produced in parallel.

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