THE FUTURE IT'S TODAY

Alexandre Trani - La Mesta

Flow chemistry is certainly the future of chemistry and nowadays, many technologies exist for continuous reactors: static but also stirred reactors. The static reactors – the most common - are often micro-reactors with micro-channels whereas stirred reactors are rather mini-reactors (i.e. millimeter scale). Each of them has advantages and disadvantages but none is universal.

The advantages of stirred mini-reactors are:

- Polyvalent reactors able to work with gas, liquids and solids in suspension (introduced or generated) whereas channels of micro-reactors risk to be blocked.
- Devices designed for industrial applications. The scale-up is facilitated and it's not necessary to multiply the number of reactors to reach industrial flows.
- Mass transfer is very efficient and completely independent of the flows.

On their side, micro-reactors have a very efficient heat transfer and now, with the 3D printing technology, they can be manufactured in one block without risk of leakage. This is a very interesting asset. But, to our knowledge, there are no industrial applications yet.

Following flow chemistry philosophy, we have developed, for example, a phosgene generator combined with a stirred mini-reactor to make continuous phosgenation in a safe way (no phosgene storage, no handling and no transportation). The advantages are mainly:

- Safety: to produce at ton scale with almost no phosgene on the site. Furthermore, due to the size of the equipment (liter unit), the protections are oversized (glovebox, scrubbers) compared to batch reactor (cubic meter unit).
- Quality: phosgene generator is able to produce a pure phosgene with a very small amount of CCl4 (<60ppm) which is very important for pharmaceuticals or cosmetics applications.

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- Reactivity: continuous mode allows a perfect adjustment of the ratio phosgene/raw material compare to batch mode. This is probative when the reagent has two (or more) reactive sites against the phosgene. The final result is low amount of oligomer or by-products compared to batch. A real industrial example to illustrate the above is as follows:

This synthesis in batch (with dimethyl carbonate, phosgene or triphosgene) leads to the formation of a large amount of impurities with the desired product. With the phosgenation continuous unit, reaction is stoichiometric in any point of the vessel avoiding thus oligomers formation. In addition, high mass and heat transfers allow short reaction time (12 seconds) and so, reduce degradation phenomena.

Furthermore, regarding the analytical side, another huge advantage of flow reactors is stability of reaction parameters, reproducibility and robustness of processes. Therefore, parameters monitoring is sufficient to reproduce laboratory process and supply the same quality. But, for a perfect control, real-time analytical tool (e.g. IR analyzer) can be added in order to avoid any quality deviation not detected by the monitoring of reaction parameters. This tool, which should be polyvalent and "easy to use", corresponds to the In-Process-Control performed in batch processes. It cannot replace final analyses.

Moreover, this equipment combined with design of experiments should enable a more efficient process development, faster and so, less expensive than in batch. Thereby, we have from today all keys for the chemistry of future.