

The award-winning project implemented innovative continuous flow process

Application in safer, more stable, higher-yield processes

 High temperature/pressure 	Toxic and/or stinky agents	Sulfonation
 Highly energetic 	 Unstable intermediates 	Esterification
Cryogenic	 Oxidation and/or ozonization 	Halogenation
 Highly reactive and air-sensitive 	 Diazotization 	Reduction

Reactors

Single-tube	 Static mixer 	 Dynamic tubular reactor 	Photo-flow reactor
Multi-tube	Fixed/micropacked bed	Electrochemistry reactor	CSTR



Cryogenic reaction



Comparison	Batch	Flow
Feasibility of scaling up	×	\checkmark
Temperature	-70 to -60°C	-40 to 10 °C
Yield	N/A	84%
Scaling-up risk	High	Low

Completed 260 kg product with 240 mL continuous flow reactor in 30 hours

Diazotization



Comparison	Batch	Flow
Feasibility of scaling up	×	\checkmark
Temperature	N/A	5 to 10 °C
Yield	N/A	80 - 85%
Scaling-up risk	High	Low
Completed 200 kg product with a set of 100 mL continuous flow reactor in 2-3 days		

Nitration

$$\begin{array}{c} \mathsf{R} \\ \mathsf{OHC} \\ \mathsf{OHC} \\ \mathsf{H} \\ \mathsf{H}$$

Comparison	Batch	Flow
Feasibility of scaling up	×	\checkmark
Temperature	20 - 30 °C	30 - 60 °C
Yield	N/A	90 - 93%
Scaling-up risk	High	Low
Automatic leve	Low	High

Over 300 kg of product completed with an integrated continuous tubing reactor

High temperature



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Comparison	Batch	Flow
Feasibility of scaling up	×	\checkmark
Temperature	200 °C	220 - 250 °C
Yield	N/A	>94%
Scaling-up risk	High	Low
Automatic leve	Diphenyl ether (BP: 258 $^\circ\!\!\!C$)	Toluene (BP: 110 [°] C)
Over 100 kg of product completed		

Oxidation



Comparison	Batch	Flow
PMI	15	7
Time	> 4 h	10 min
Yield	88 - 90%	95%
Complexity of work-up	High	Low
Over 100 kg of product completed		

Photocatalytic reaction

 $\begin{bmatrix} R_1 \\ R_2 \end{bmatrix} + \begin{bmatrix} R_3 \\ R_4 \end{bmatrix} \begin{pmatrix} \mathbf{0} \\ \mathbf{K}_1 \end{pmatrix} \begin{pmatrix} \mathbf{h}\mathbf{v} \\ \mathbf{Flow} \end{pmatrix} \begin{pmatrix} R_1 \\ R_2 \end{pmatrix} \begin{pmatrix} R_3 \\ R_4 \end{pmatrix} \begin{pmatrix} \mathbf{0} \\ \mathbf{R}_2 \end{pmatrix} \begin{pmatrix} R_1 \\ R_4 \end{pmatrix} \begin{pmatrix} R_1 \\ R$

Comparison	Batch	Flow
Feasibility of scaling up	×	\checkmark
Time	30 h	40 - 50 min
Light source	Medium pressure mercury lamp	365 nm LED
Scaling-up risk	High	Low
Over 1 MT of product completed		

Electrocatalytic reaction



Entry	General Process	Electrochemical Process
Step	3	1
Yield	45%	67%
PMI	135	73
Cost of Material > 30% cost reduction		
Self-made equipment, Kg scale preparation		

Telescoped flow cases



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End-to-end solution





Continuous Manufacturing GMP Workshop at PharmaBlock Zhejiang

PharmaBlock 03/04