

R.Reintjens, InnoSyn

E.Steffin, De Dietrich Process Systems

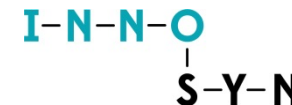
17/03/2020

Cryogenic flow chemistry made easy

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- **Cryogenic Chemistry**
- **Flow Reactor**
- **Pilot Plant - CryoFlowSkid**
- **Summary**

Co-operation



Tomorrow's chemistry. Today.

De Dietrich Process Systems

www.dedietrich.com

more than 335 years

France with 15 subsidiaries worldwide
1200 employees

Know how and equipment

- ROSENMUND® - Filter dryers
- QVF® - Borosilicate glass 3.3
- De Dietrich® - Glass-lined equipment
- Batch reactor technology
- Thermal separation technology
- Plants for corrosive processes

InnoSyn B.V.

www.innosyn.com

3 years but more than 26 years experience

Netherlands
60 employees

Know how and services

- New and improved chemical routes
- Photo chemistry
- Flow chemistry and reactors
- Bio- and Chemo catalysis
- Optimization of reaction processes
- Scale-up of reaction process

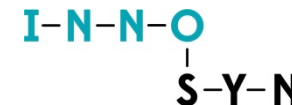
Equipment manufacturing
Engineering,
Project management



Chemical research,
Process design

Complementary competences

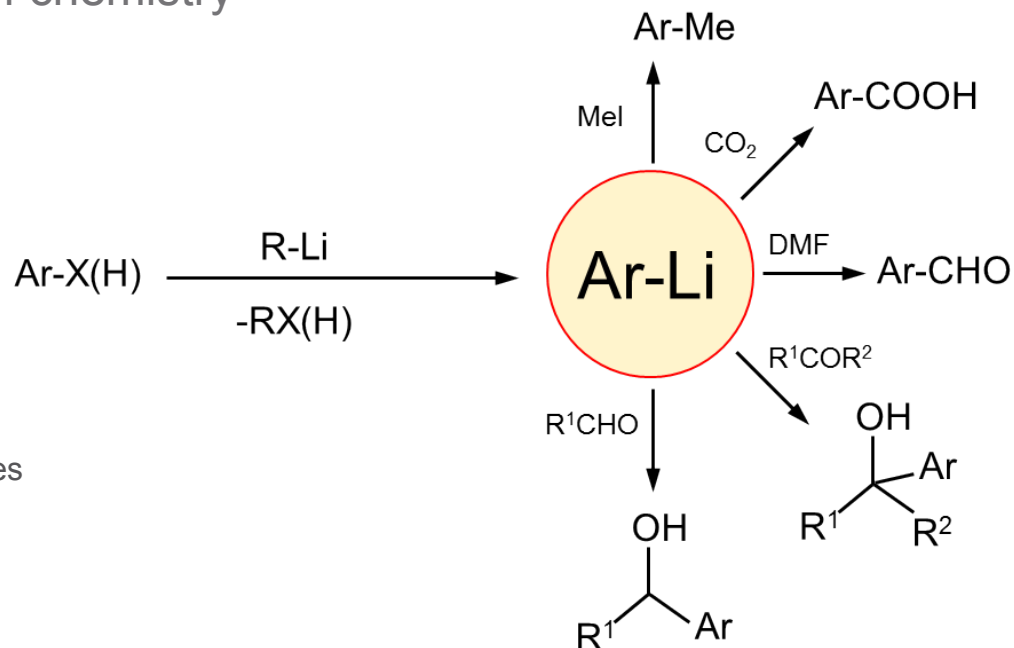
Cryogenic Chemistry



Tomorrow's chemistry. Today.

Syntheses routes at low temperature – commonly down to -100°C

Such as organolithium chemistry



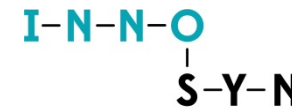
Typicals

- Unstable intermediates
- Exothermic
- Fast

Challenges

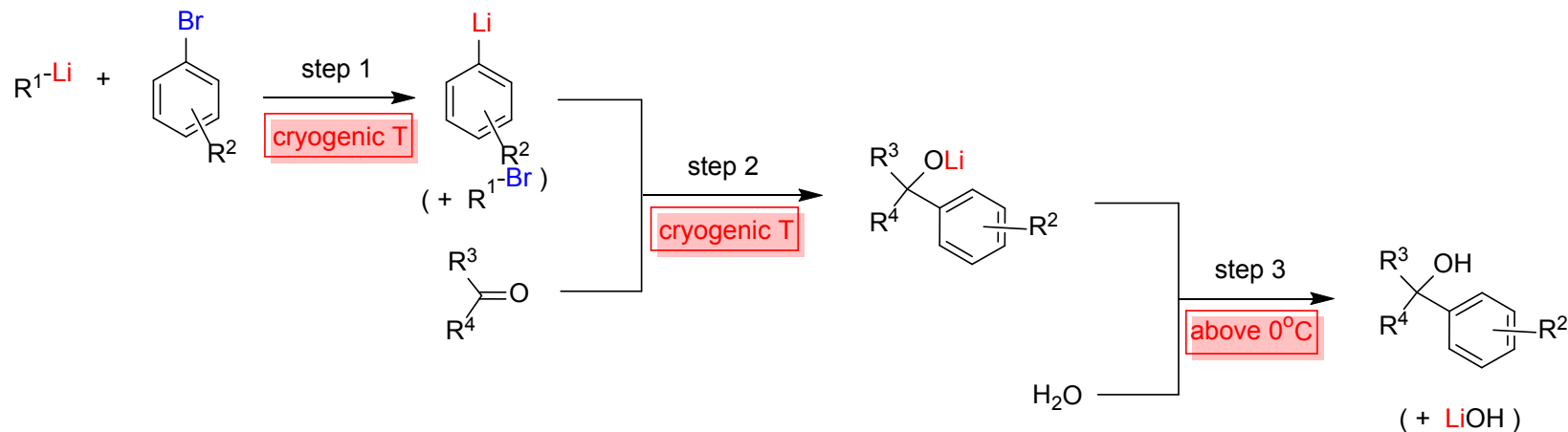
- Degradation of the intermediate
- Production rate limited by cooling capacity
- Costs for low temperature cooling

Organolithium chemistry



Tomorrow's chemistry. Today.

3 Step model reaction as basis for design of the skid



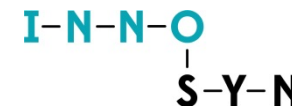
Capacity Range

- 1 – 5 kg/h as 5 m% solution after quench

Objectives

- Pilot plant unit for process development and small production
- Maximum yield at less challenging temperatures
- Fast reliable scale-up
- Small footprint

The impact of processing mode



Tomorrow's chemistry. Today.

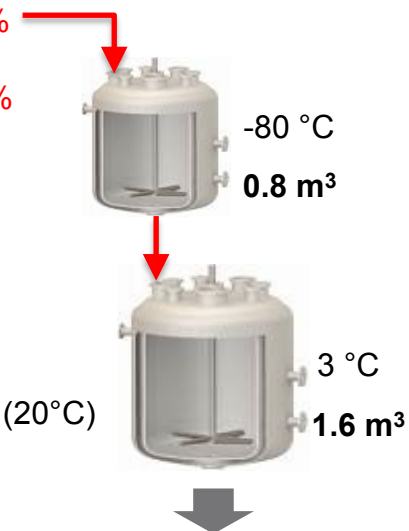
50kg in batch mode

	Mass (kg)	Heat (MJ)	Cooling time (h)	Exposure time (h)
Precool aryl-Br	263	53	3.4	
Dose R-Li	124	106	6.9	6.9
Dose ketone	158	96	6.3	6.3
Total	545	254	16.6	

Productivity 4 kg/m³h (50 kg / 7.06 h / 0.8 m³)

	Batch
Reactor size	800 L
Installation footprint	Large
Exposure time	Hours
Required temperature	-80°C

263 kg Aryl-Br 20m%
124 kg R-Li 24m%
158 kg Ketone 20m%



Aqueous quench
527 kg H₂SO₄ 3m% (20°C)

50 kg product in 1072 kg

Cooling capacity 4 kW

- K 200 W/m²°C heat transfer coefficient

- A 2 m²

- ΔT 10 °C

The impact of processing mode

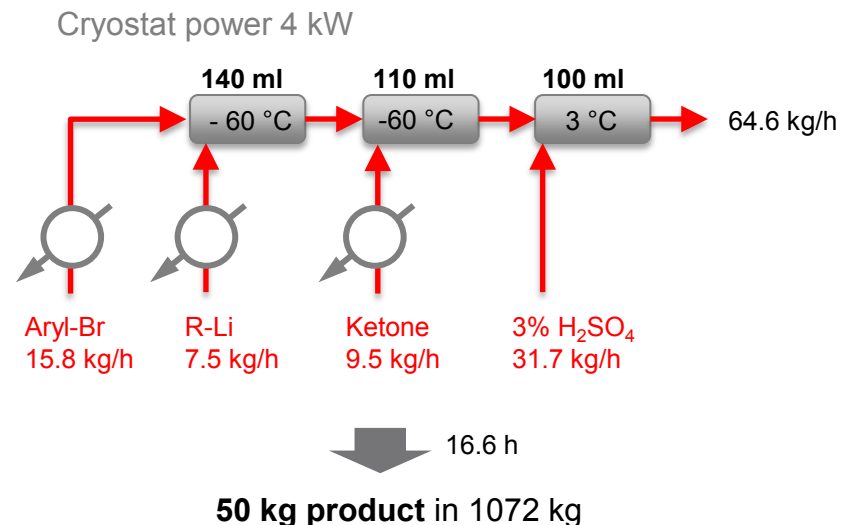


Tomorrow's chemistry. Today.

50kg in continuous mode

	Total flow (kg/h)	Cooling (kW)	Exposure time (s)
Reactor 1	23.3	2.4	18
Reactor 2	32.8	1.5	10
Total		3.9	

Productivity 12000 kg/m³h (50 kg / 16.6 h / 0.25 L)

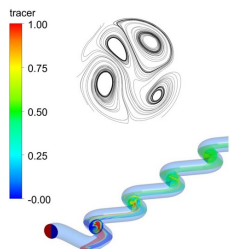


	Batch	Continuous
Reactor size	800 L	0.25 L
Installation footprint	Large	Small
Exposure time	Hours	Seconds
Required temperature	-80°C	-60°C

Flow reactors offer a clear advantage

The Flow Reactor

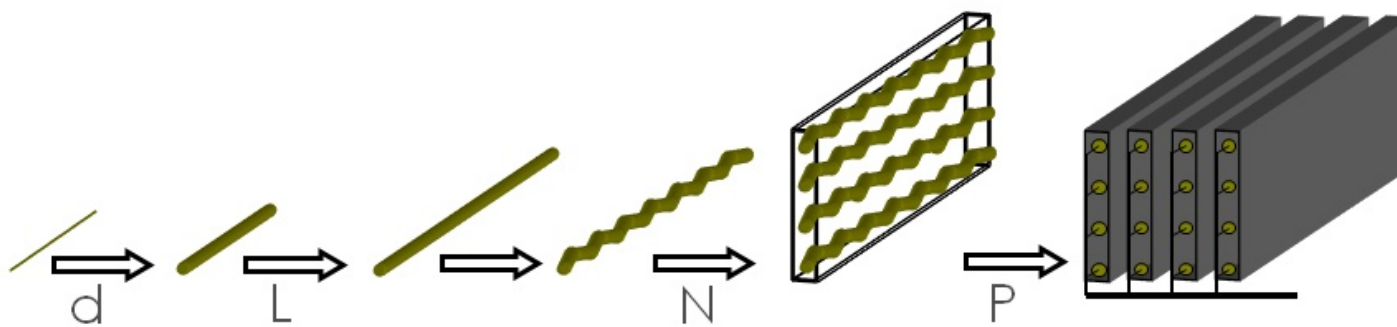
Performance originates from channel geometry and dimension



Performance

Mixing time	0,001 – 0,1 s
Heat transfer coeff.	2000 – 10,000 W/m ² K
Heat transfer area	1000 - 4000 m ² /m ³

Reactor development and scale-up



Channel design

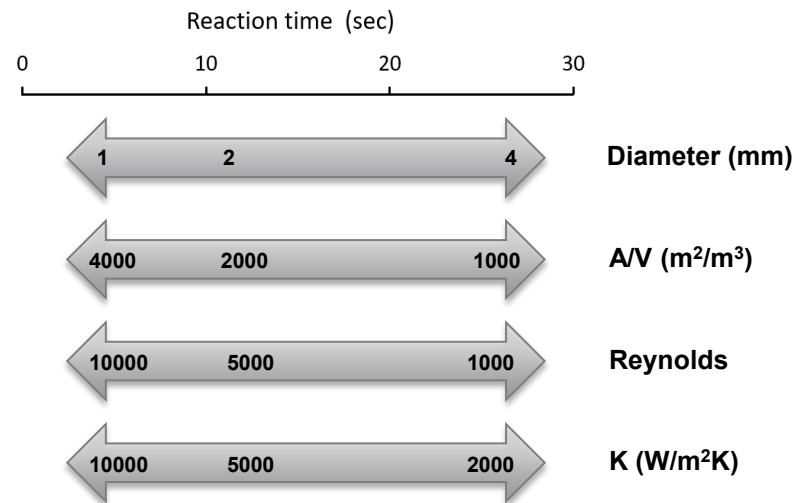
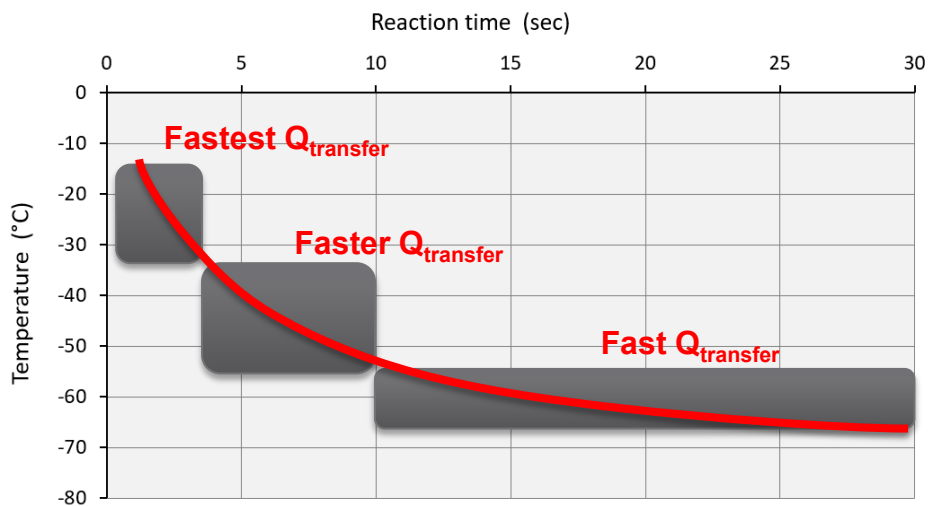
Optimize geometry and volume
vs. heat transfer capability

Numbering-up

Minimize number of parallel
channels and modules

Design the reactor to the needs

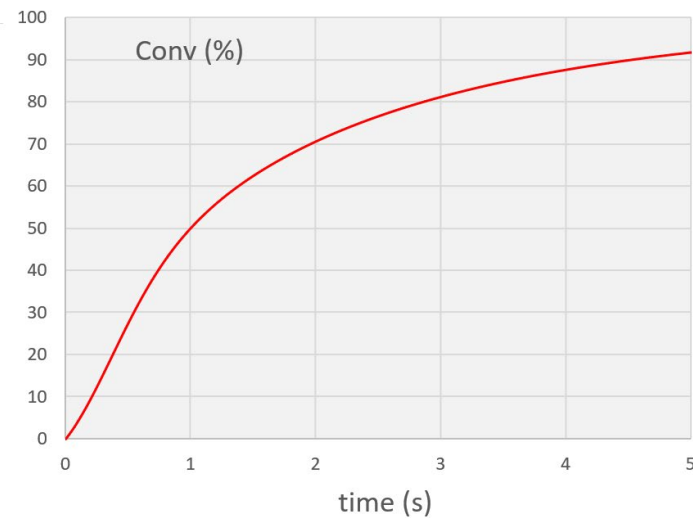
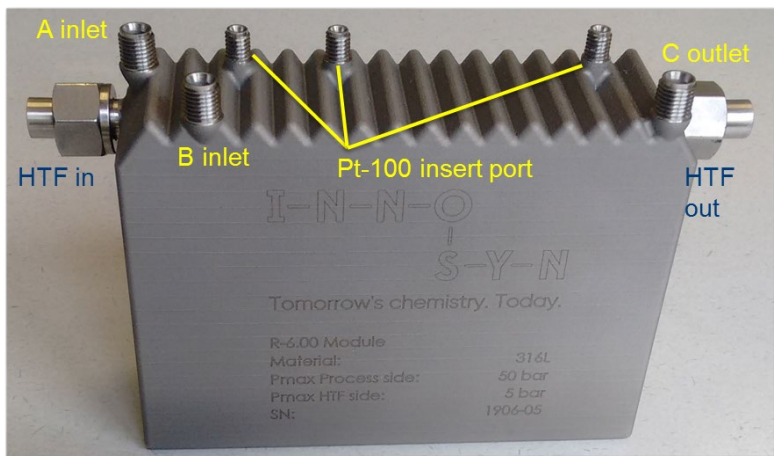
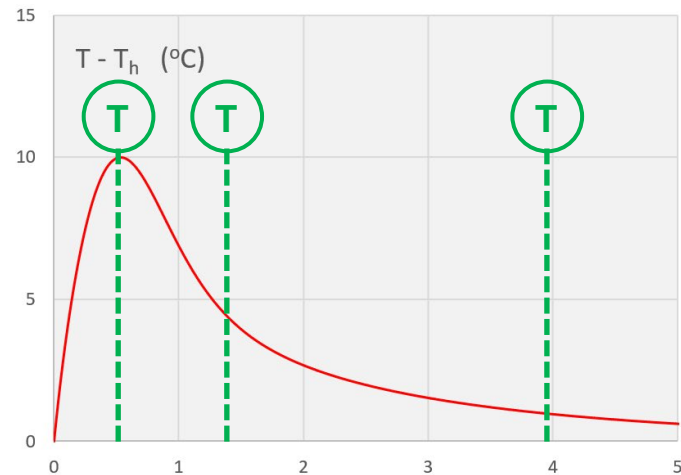
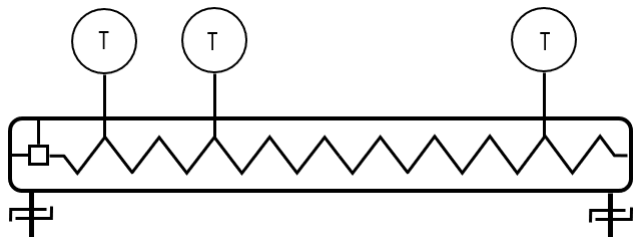
Kinetics can vary significantly



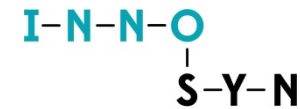
Channel design allows to fit the reactor performance to the needs of the chemistry

The Flow Reactor – Process Control

Multiple Sensor Ports

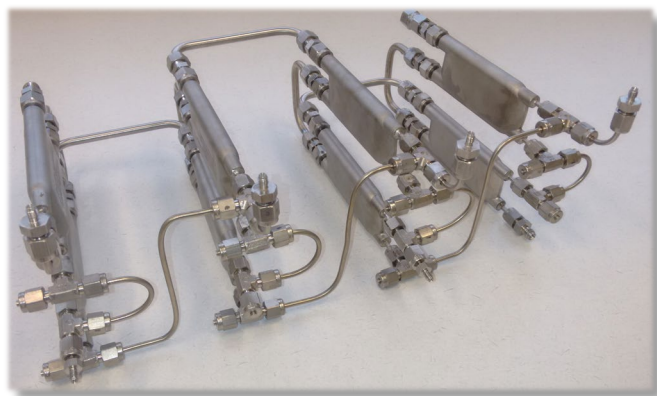
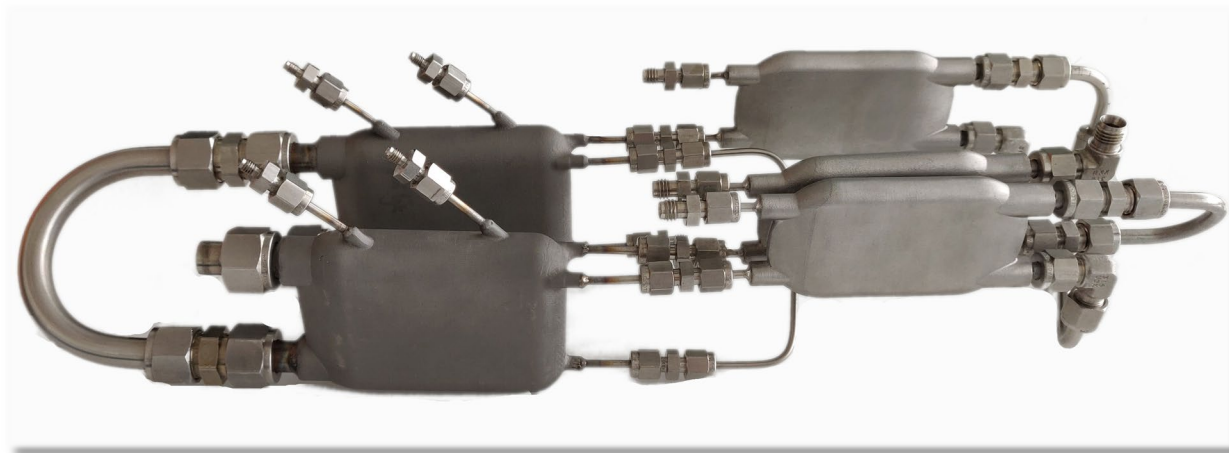


The advantage of modular design



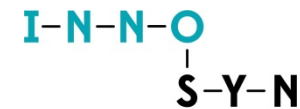
Tomorrow's chemistry. Today.

Modules can vary in size and functionality

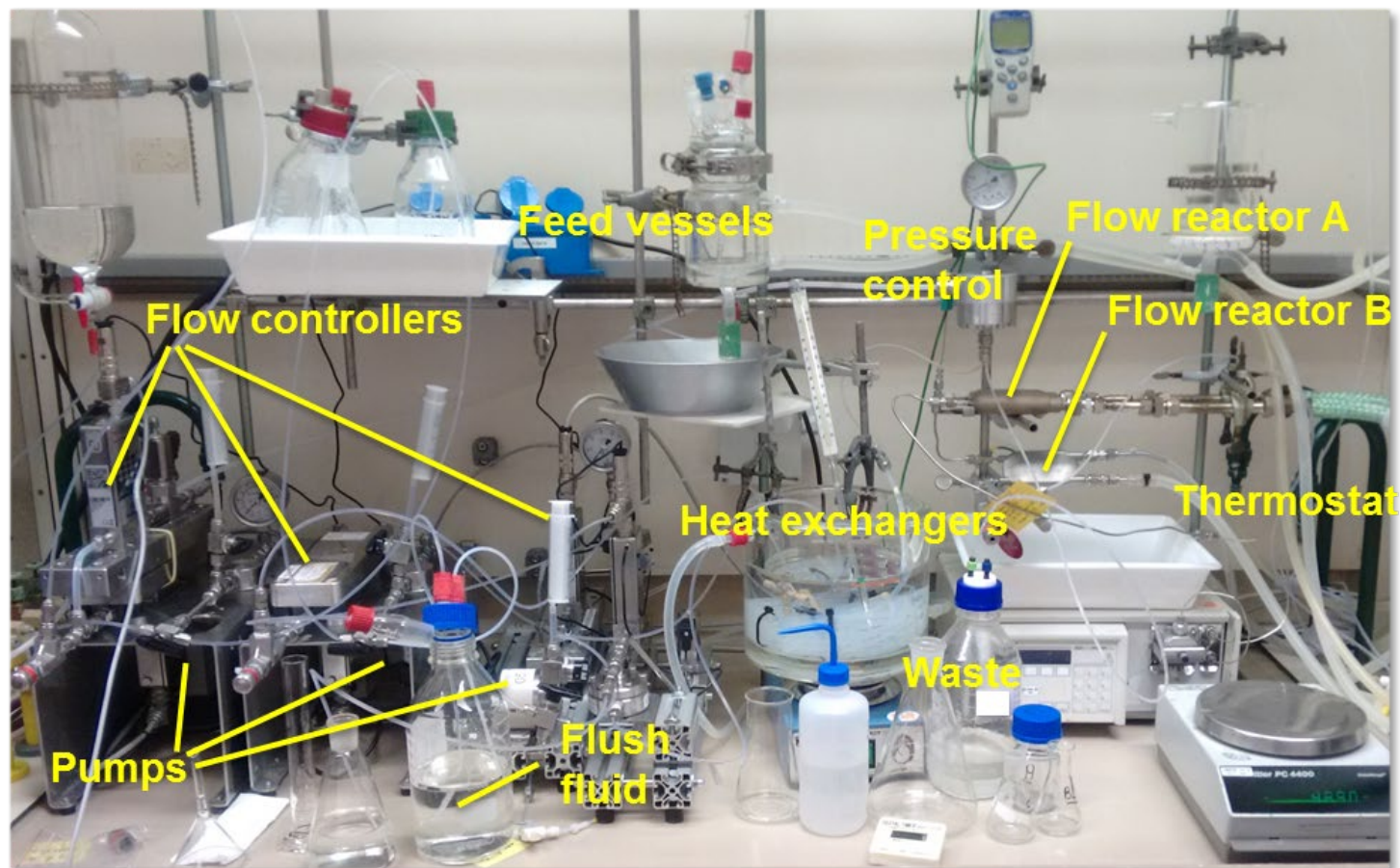


Modular design allows for flexible and fast (re)configuration of the reactor system

Flow reactor set-up in the laboratory



Tomorrow's chemistry. Today.

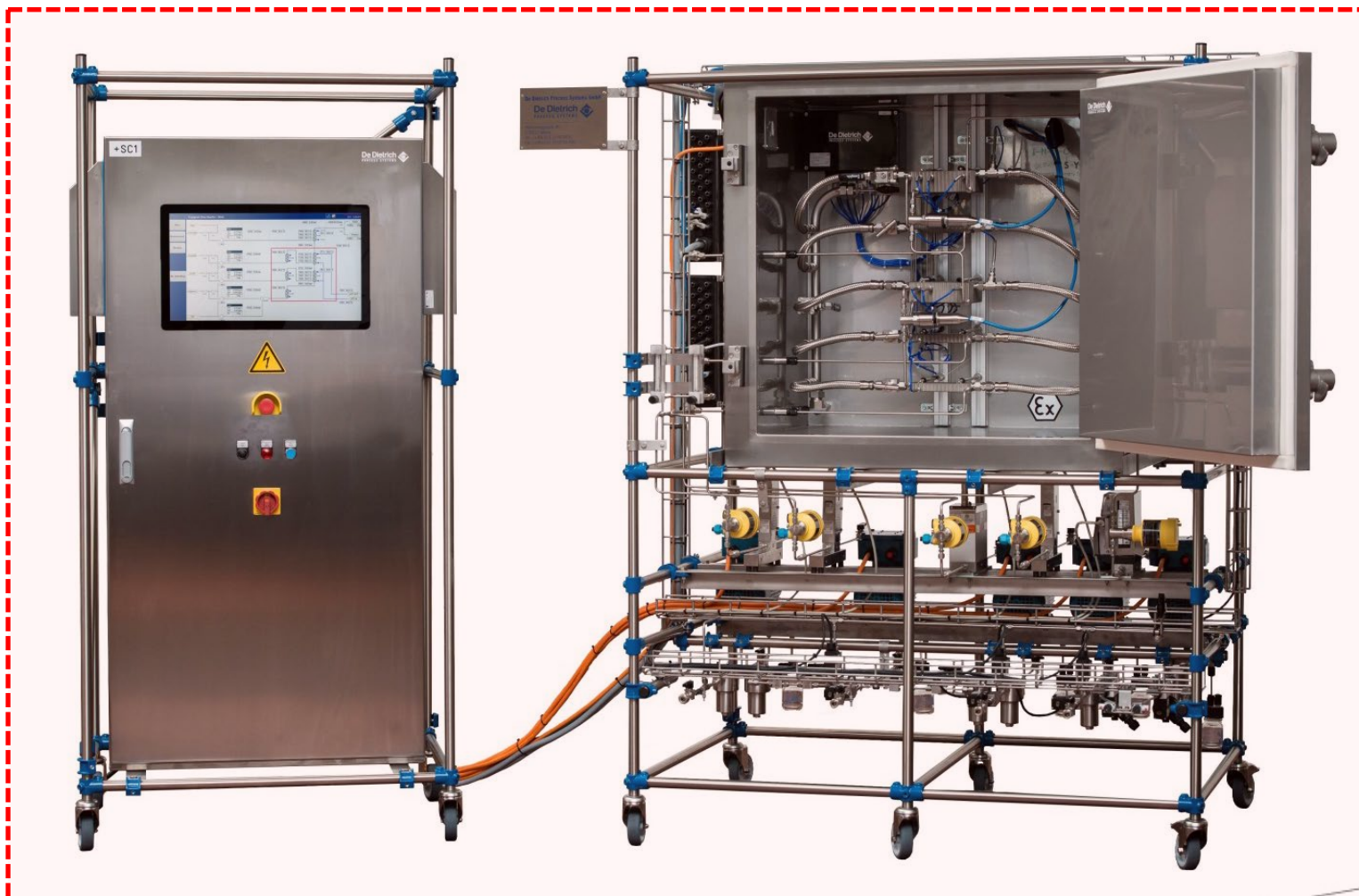


Auxiliary systems introduce quite some complexity

3 Step Pilot Plant

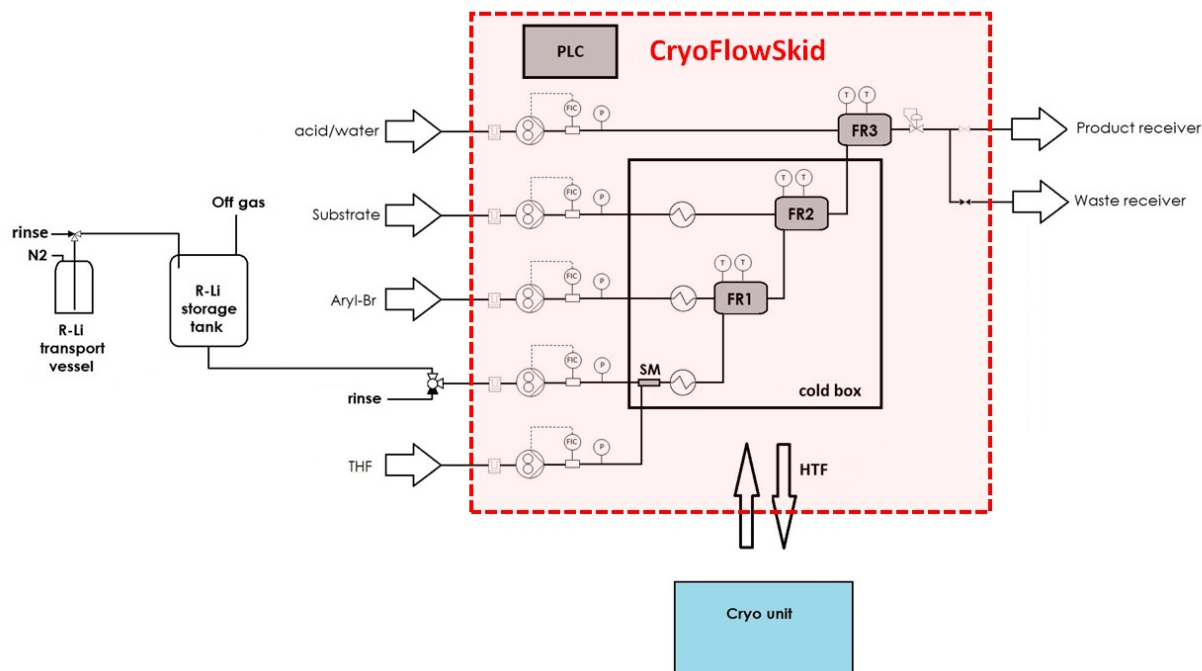
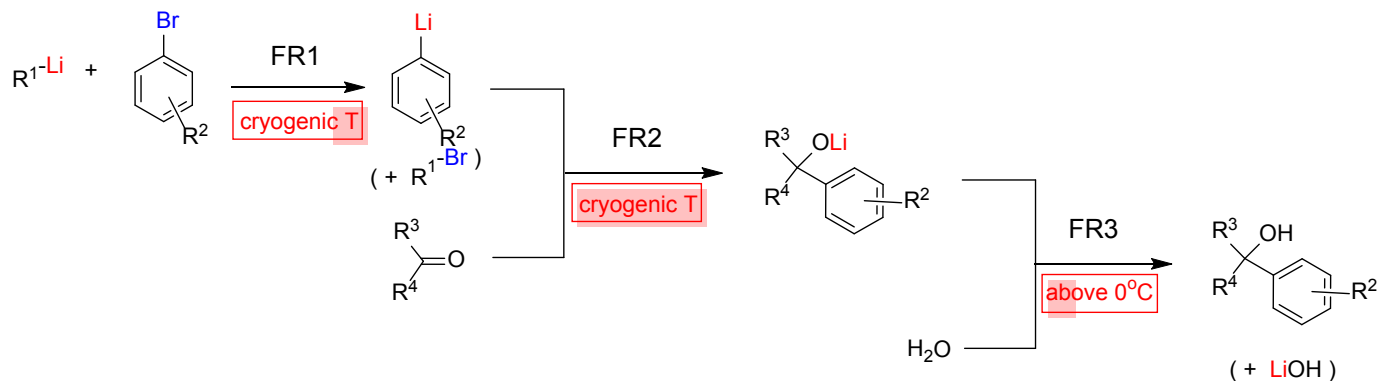
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CryoFlowSkid



CryoFlowSkid – All Included

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CryoFlowSkid in Place



Cryostat – Cooling Capacity : 5kW at -80°C



3 Step Pilot Plant

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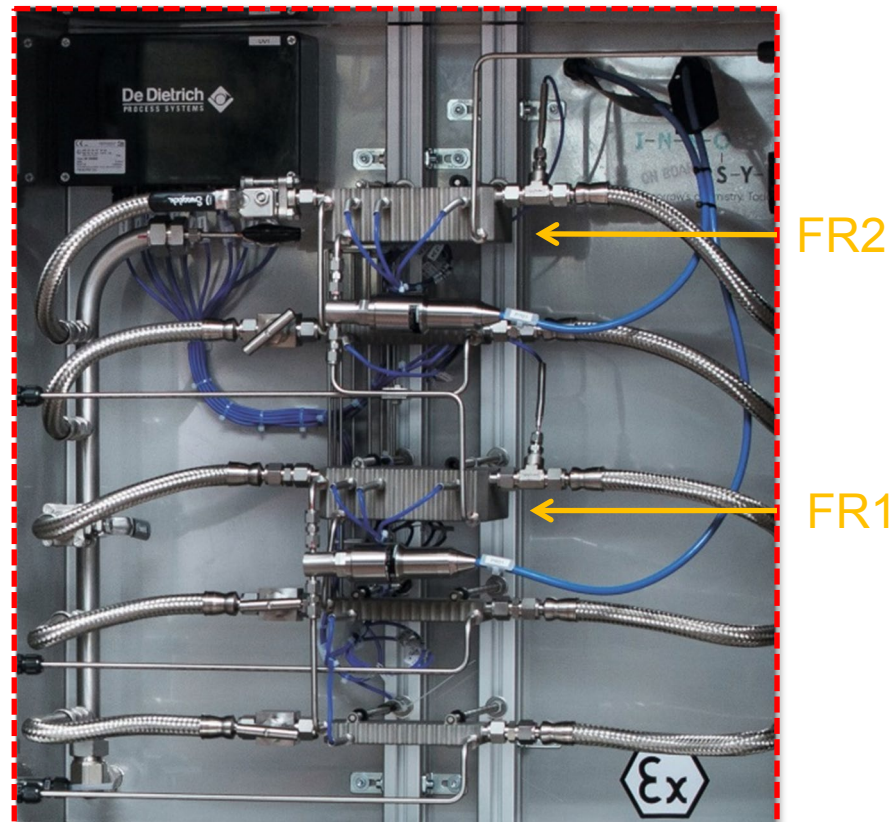
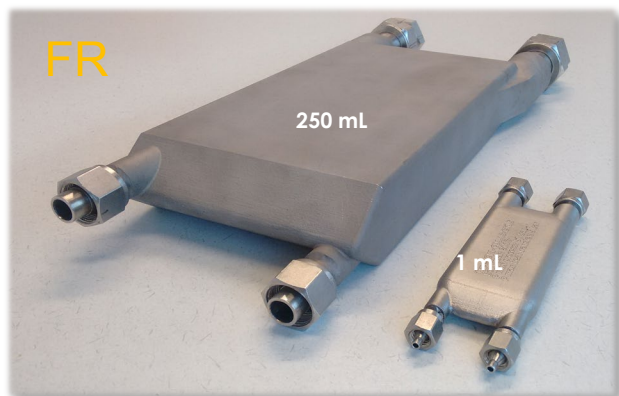
CryoFlowSkid



Flexibility

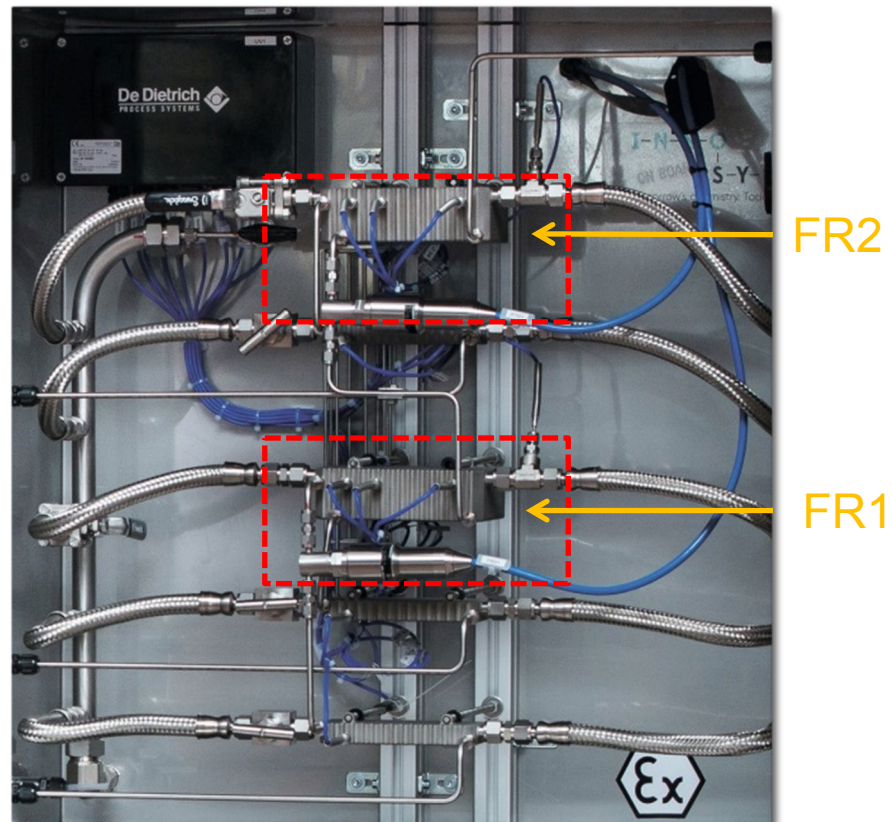
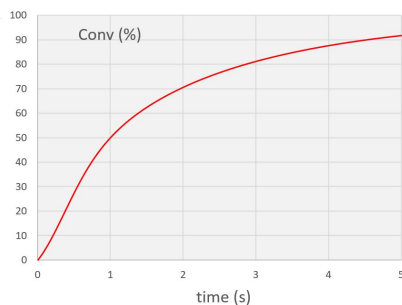
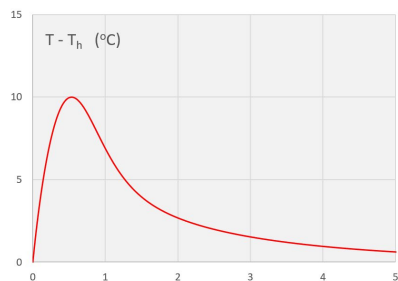
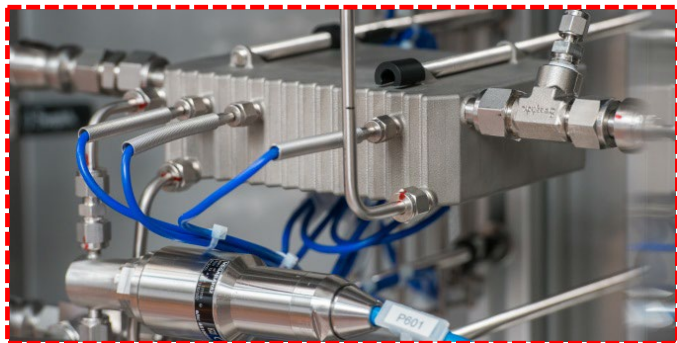
Easy access to adapt reactors and piping

- Various cryogenic chemistries
- Up to 3 Steps
- Printed pre-coolers and reactors to fit
 - Flow rate
 - Kinetic rate
 - Heat production
 - Corrosive media



Process Monitoring

Temperature profile along the flow reactor



Process Monitoring

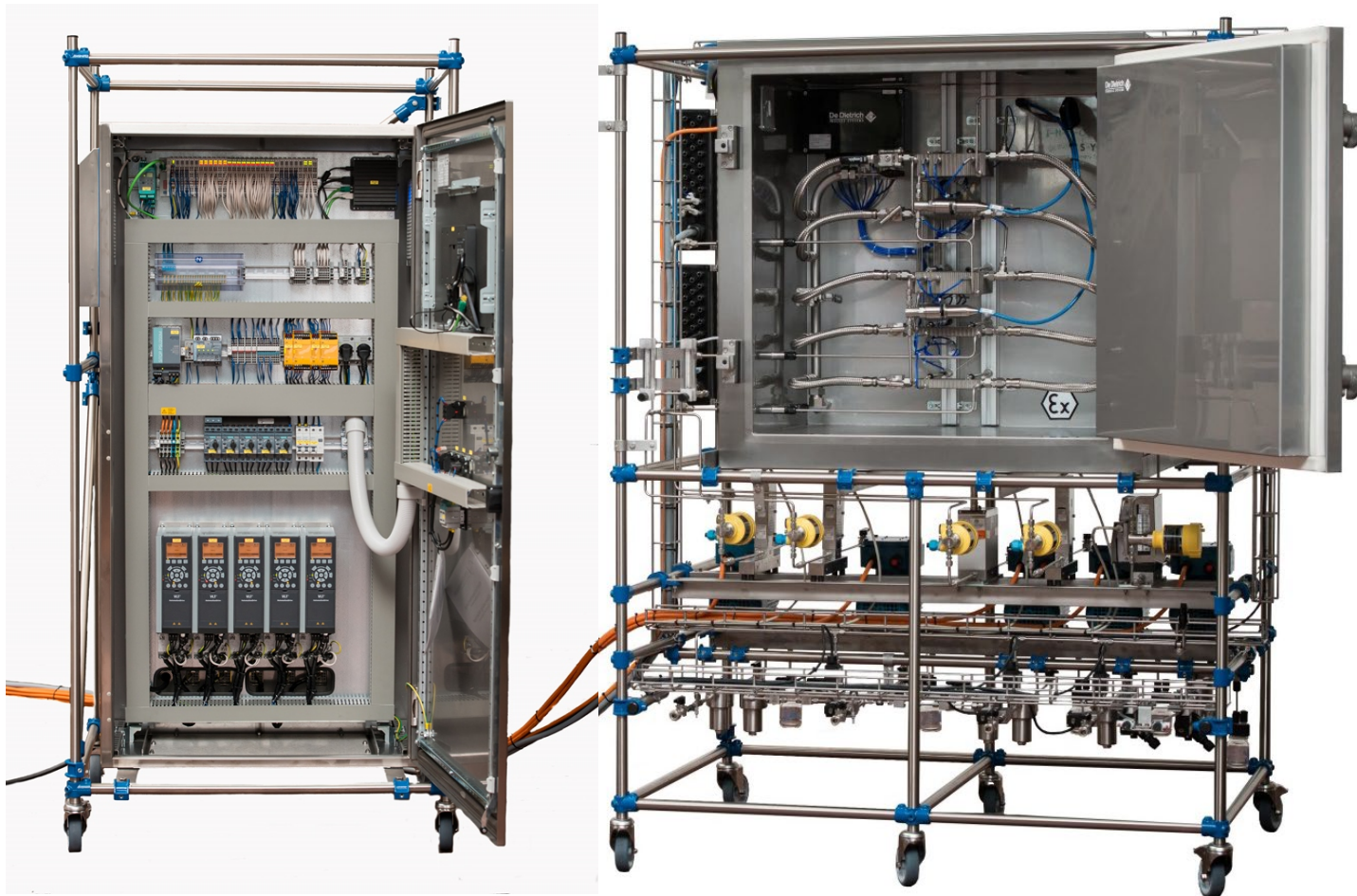
Reliable controls for on-spec process

- Temperature measurements to follow reaction
- Pressure measurement to follow reliable operation
- Coriolis mass flow meters to control the pumps
- Gear type pumps for pulsation free flows
- Process Analytical Technology as per specific project



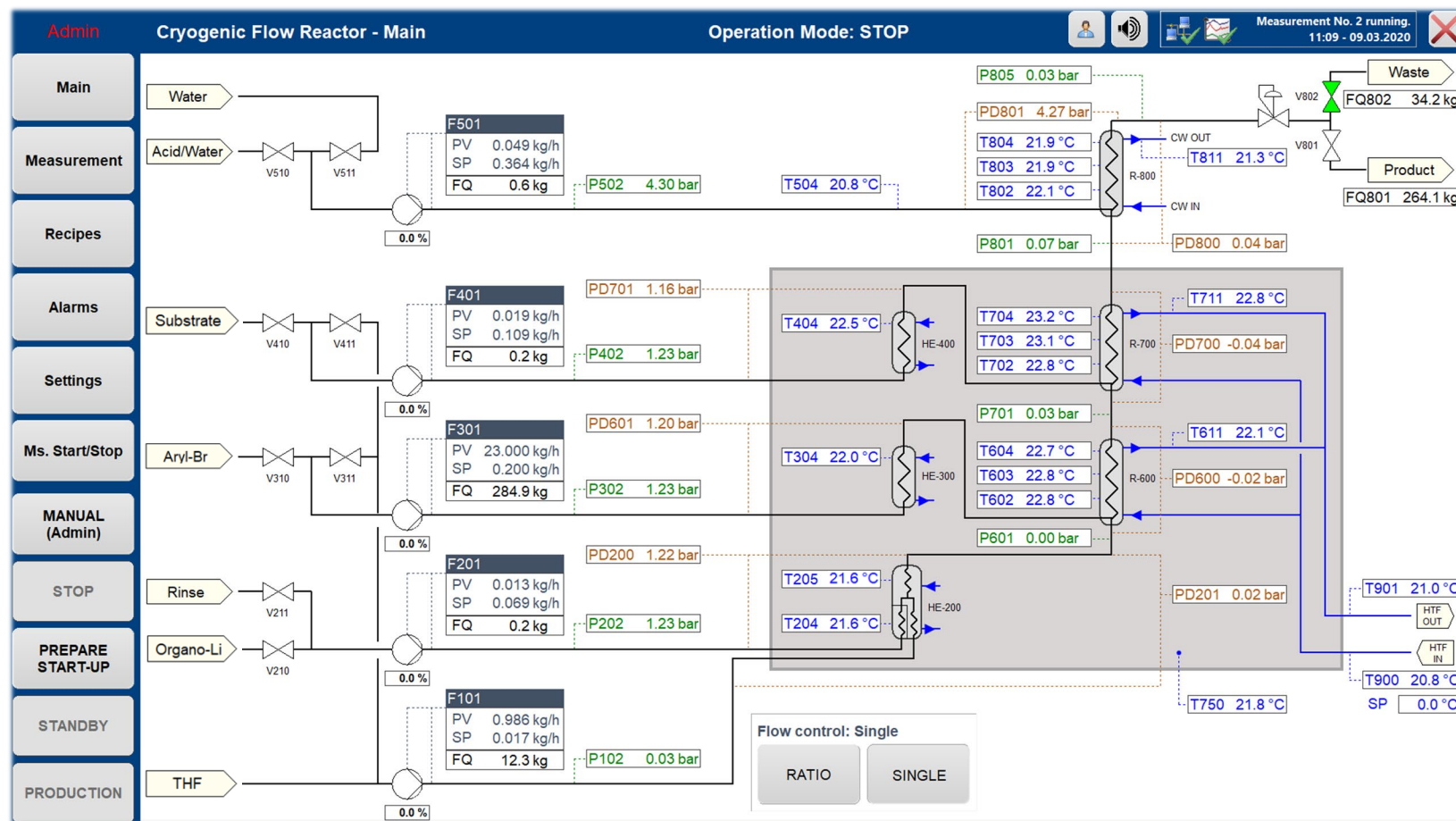
Process Control System

Automation Cabinet incl. soft PLC and HMI fully detachably connected



Process Control System

Comprehensive process control



Process Control System

Automation for unattended safe routine operation

Operational mode	power	cryo	pumps	THF	R-Li	aryl-Br	ketone	outflow
Stop	on	off	off	-	-	-	-	waste
Start-up	on	on	on	on	THF	THF	THF	waste
Stand-by	on	on	on	on	THF	on	on	waste
In operation	on	on	on	on	on	on	on	waste
On-spec	on	on	on	on	on	on	on	product

Flow Chemistry – Cleaning

Difference to batch operation

- Displacing instead of draining
- Construction with low hold-up for fast displacement
- Construction avoiding dead volumes
- Definition of proven rinsing procedures

Flow Chemistry – Clogging

Prevention

- Maximum channel diameter
- Filtration of all liquids
- Solvents have to be dry to avoid precipitation of LiOH
- Observation of fouling by following the pressure drop with pressure sensors
- Rinsing incl. periodical rinsing cycles

Flow Chemistry – Robust Scale-Up

Heat transfer and equipment size

	0.05	0.8	50	6300	Volume (L)
Batch	40	100	400	2000	Diameter (mm)
	100	40	10	2,5	A/V (m ² /m ³)
Flow	0.001	0.01	0.2	2	Volume (L)
	1	1- 2	2	2 - 4	Diameter (mm)
	4000	4000 - 2000	2000	2000 - 1000	A/V (m ² /m ³)

Flow Chemistry – Advantages

Cryogenic flow chemistry is an excellent example

- Smaller volumes in the equipment
 - Safety
 - Footprint and space
- High heat transfer rates
 - Efficiency
 - Productivity
 - Selectivity
 - Less need for deep cooling
 - Robust Scalability

Summary

Cryogenic flow chemistry made easy



CryoFlowSkid



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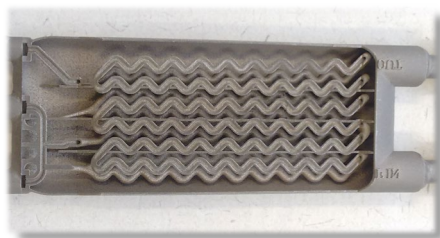
Continuous kg-Production

- Cryogenic reactions
- 3 Steps in 1 system
- Ready for operation
- Fully automated

Plug & Produce & Develop

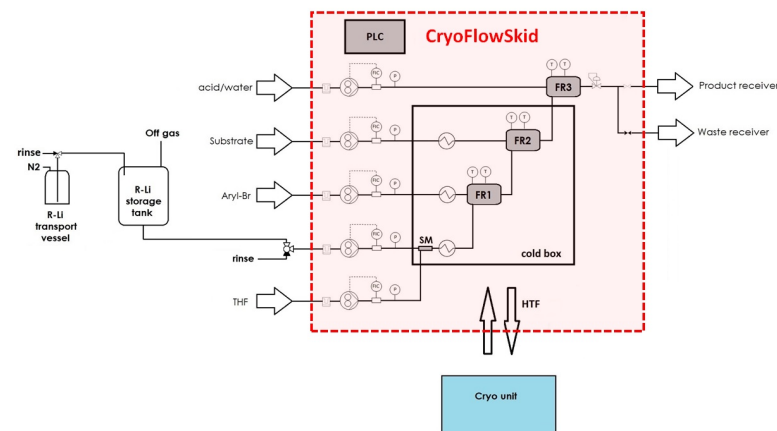
Operating range

- Temperature: -60 to +100 °C
- Pressure: up to 20 barg
- Hydraulic throughput: up to 100 l/h
- Production capacity: up to 5 kg/h



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raf.reintjens@innosyn.com
esteffin@qvf.de

**THANK YOU FOR
YOUR ATTENTION !**