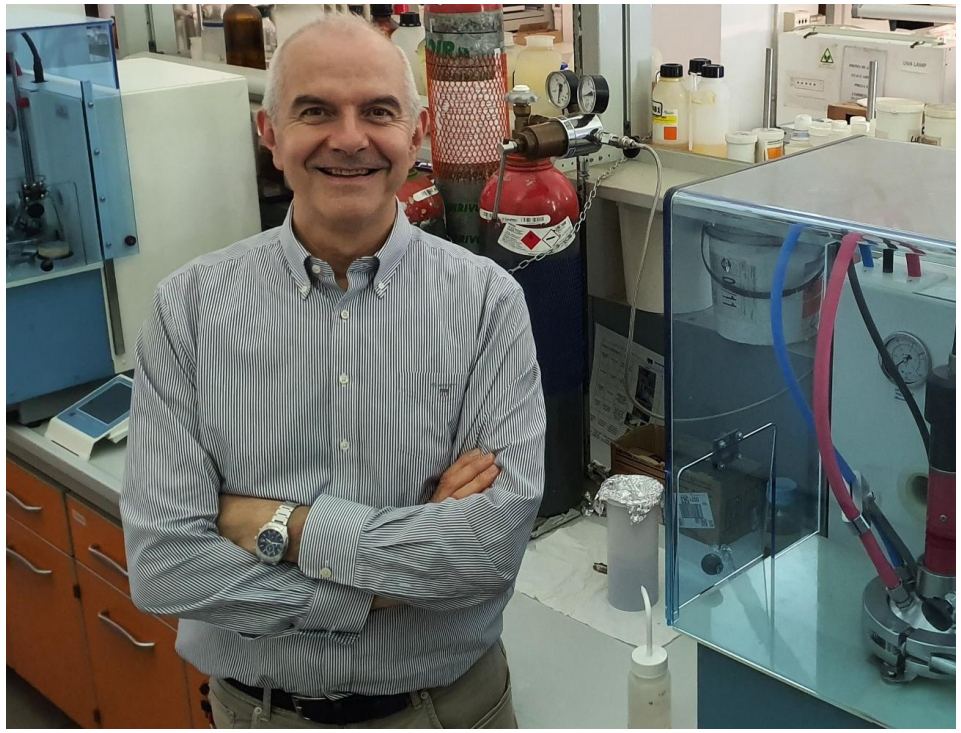

UNIVERSITÀ DI TORINO

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DIPARTIMENTO DI SCIENZA E TECNOLOGIA DEL FARMACO
UNIVERSITÀ DEGLI STUDI DI TORINO

INSTM

Università degli Studi di Torino
nis
NANOMATERIALS FOR INDUSTRY AND SUSTAINABILITY

Società Chimica Italiana
Gruppo Tematico di
Green Chemistry — Chimica Sostenibile

processes
an Open Access Journal by MDPI

PROF. DR. GIANCARLO CRAVOTTO
Editor-in-Chief of *Processes*

# The Global Energy Crisis is Reshaping the Chemical Industry: new Strategies and Technologies

June, 13th 2026


How the Energy Crisis is Reshaping the Chemical Sector


Energy Crisis Forces Chemical Plants to Scale Back Operations


Europe's Chemical Industry Cuts Output as Energy Costs Surge


Energiepreise setzen Chemieindustrie massiv unter Druck


La crise énergétique fragilise l'industrie chimique européenne

THE WALL STREET JOURNAL. WSJ

**Energy Costs Hit Chemical Makers, Triggering Global Supply Concerns**

Il Sole 24 ORE

**Crisi energetica, produzione chimica in calo in Europa**

Bloomberg

**Energy Crunch Drives Chemical Giants to Rethink Production Strategy**

Reuters

**High Gas Prices Force European Chemical Producers to Cut Capacity**

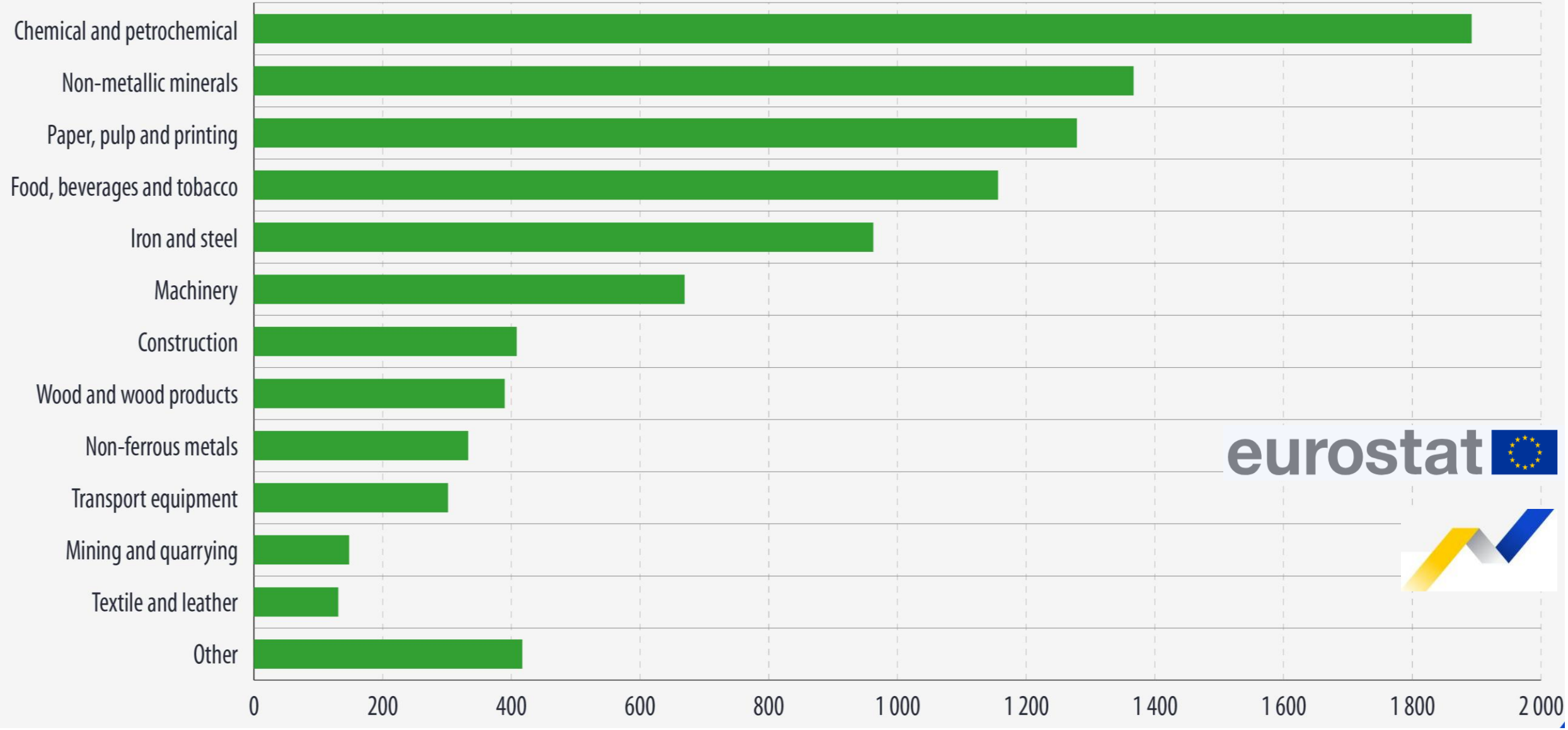
The New York Times

**Skyrocketing Energy Prices Strain Global Chemical Production**

# Total final energy consumption by industrial sector, EU, 2022

*(PJ)*

1 PJ one million billion joules ($10^{15}$) = 278 gigawatt/h




eurostat

## BULK CHEMICALS
**(petrochemicals, commodities)**

$CO_2$ **1 - 3 kg $CO_2$ per kg**

Typical energy: **10 to 40 MJ per kg**
Large scale, continuous processes, energy dominated by reaction heat, large distillation columns

## FINE CHEMICALS

$CO_2$ **5 - 20 kg $CO_2$ per kg**

Typical energy: **50 to 200 MJ per kg**
Multi step synthesis (5 to 10 steps common)
Batch processes dominate, high solvent use and recovery

## PHARMACEUTICALS (API)

$CO_2$ **10 - 100 kg $CO_2$ per kg**

Typical energy: **200 to >1000 MJ per kg**
Extremely high due to: very low yields, complex syntheses, stringent purity requirements, intensive purification (chromatography, crystallisation)

processes

Processes **2025**, *13*, 459

*Perspective*

# Reshaping Chemical Manufacturing Towards Green Process Intensification: Recent Findings and Perspectives

Giancarlo Cravotto

BASF
We create chemistry

# BASF SE, Ludwigshafen

Bloomberg

## Chemical Giant Cuts European Production as Gas Crisis Worsens

The Guardian

## BASF to cut 2,600 jobs as energy crisis puts Germany on track for recession

BASF

Europe

## The biggest corporate victim of Europe's energy crisis may be a $93 billion chemical giant whose flagship plant uses as much gas as Switzerland

**BASF Ludwigshafen** am Rhein (Germany), the largest integrated chemical complex in the world. Spanning approximately 10 square kilometers, it serves as the global headquarters and the primary production hub for **BASF SE**.


*New Agreement December 2025*

## "Shaping the Future for a Strong Site"

It runs for five years (2026–2030) and includes a commitment to invest at least **€1.5 billion annually** (target: €2 billion) in modernization and sustainable transformation


With the **RE-BORN project**, the old chemical plants have been transformed into a modern high-tech and sustainable production site

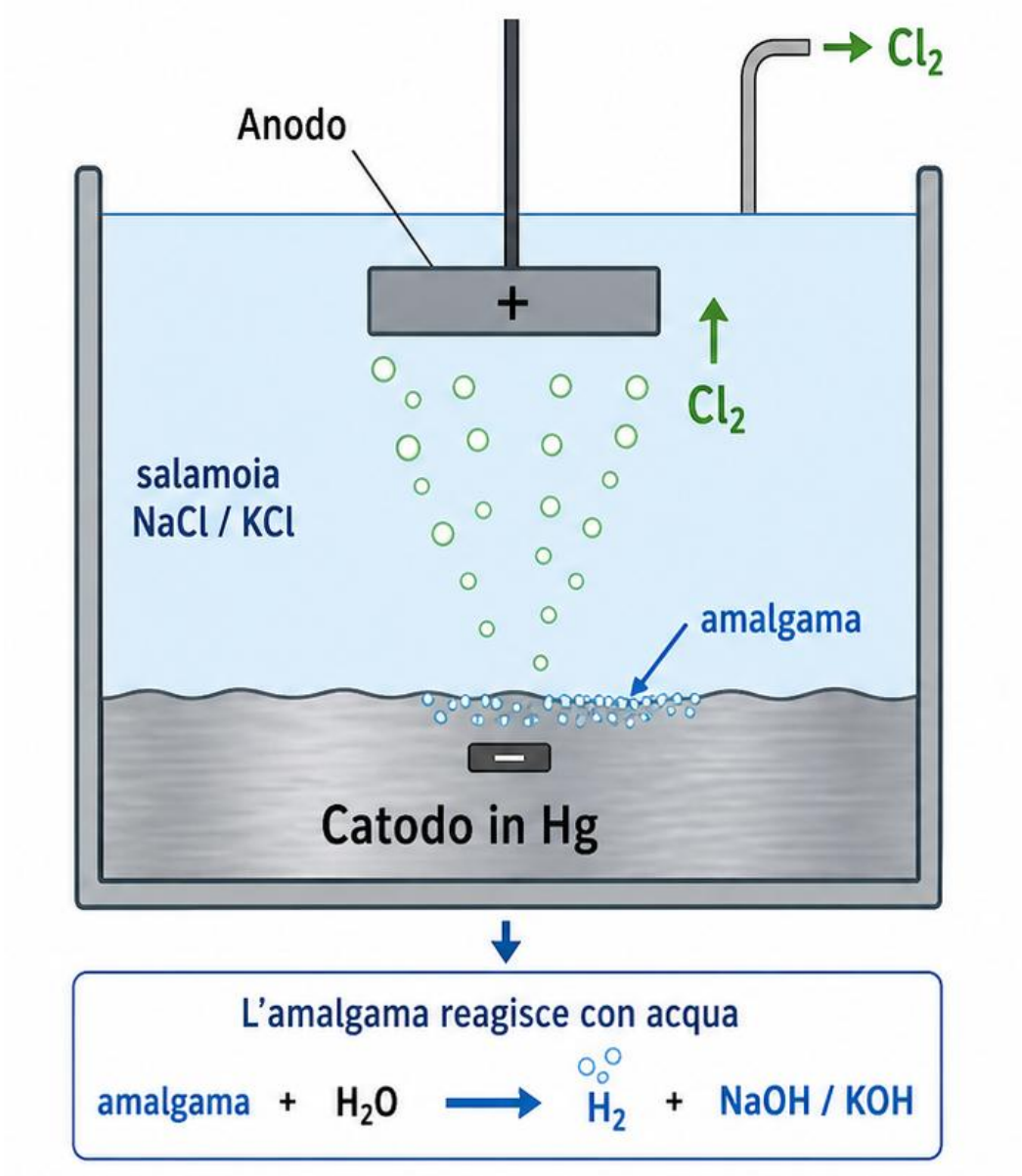
ALTAIR CHEMICAL

**RE-BORN:**

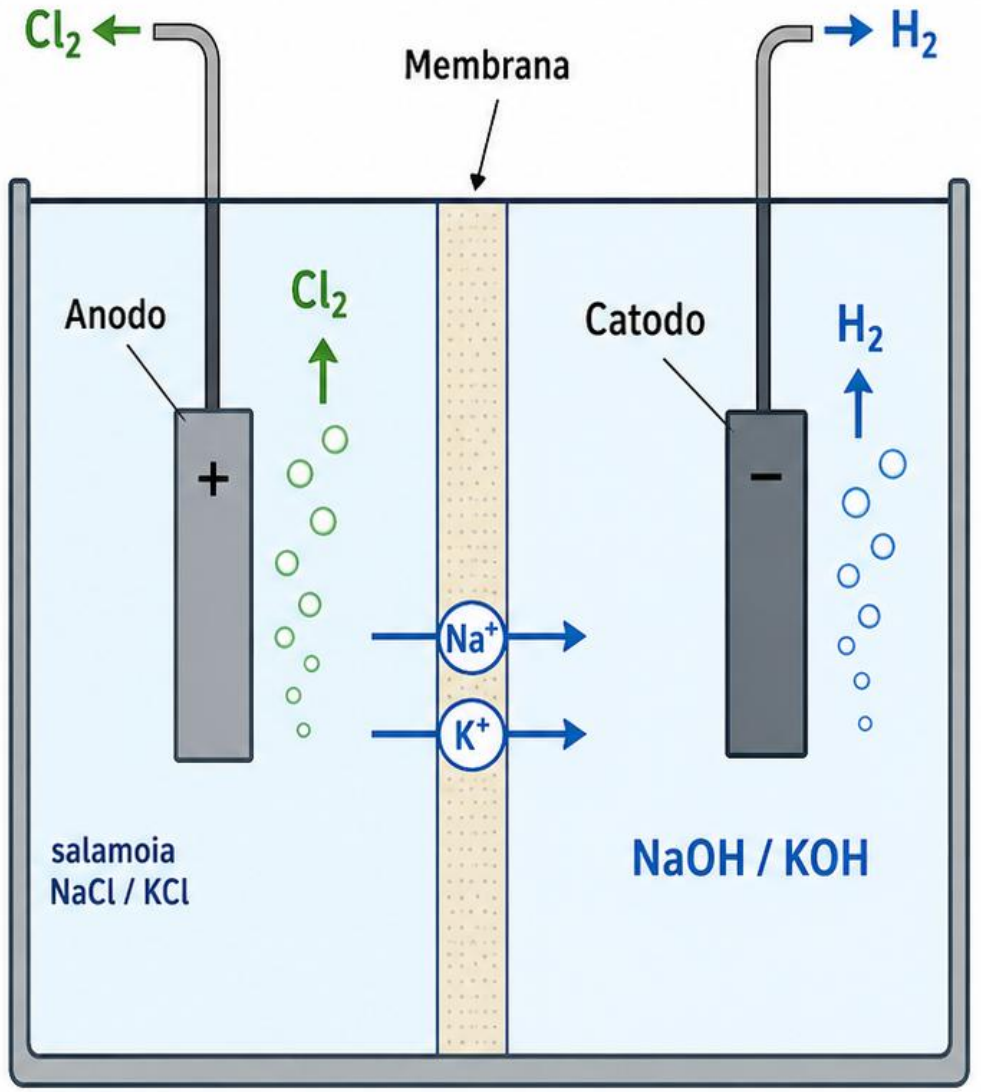
Relaunch Electrolysis-Building Optimized Rumianca New Site

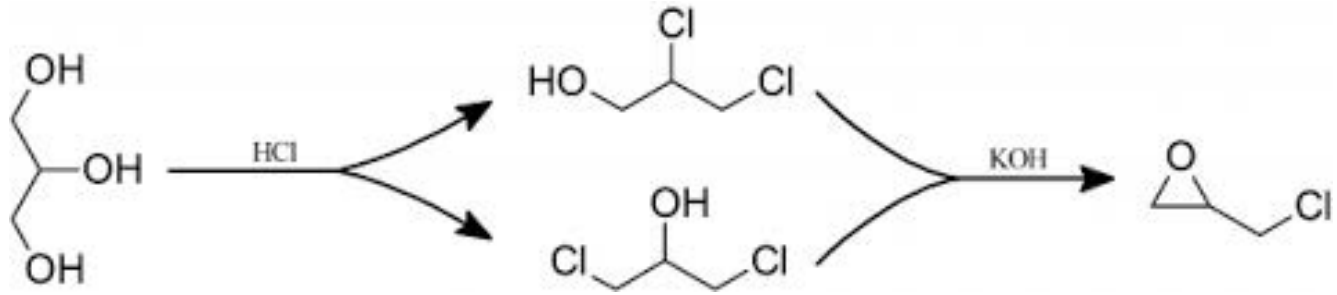
Pieve Vergonte VB

## OLD MERCURY CELLS

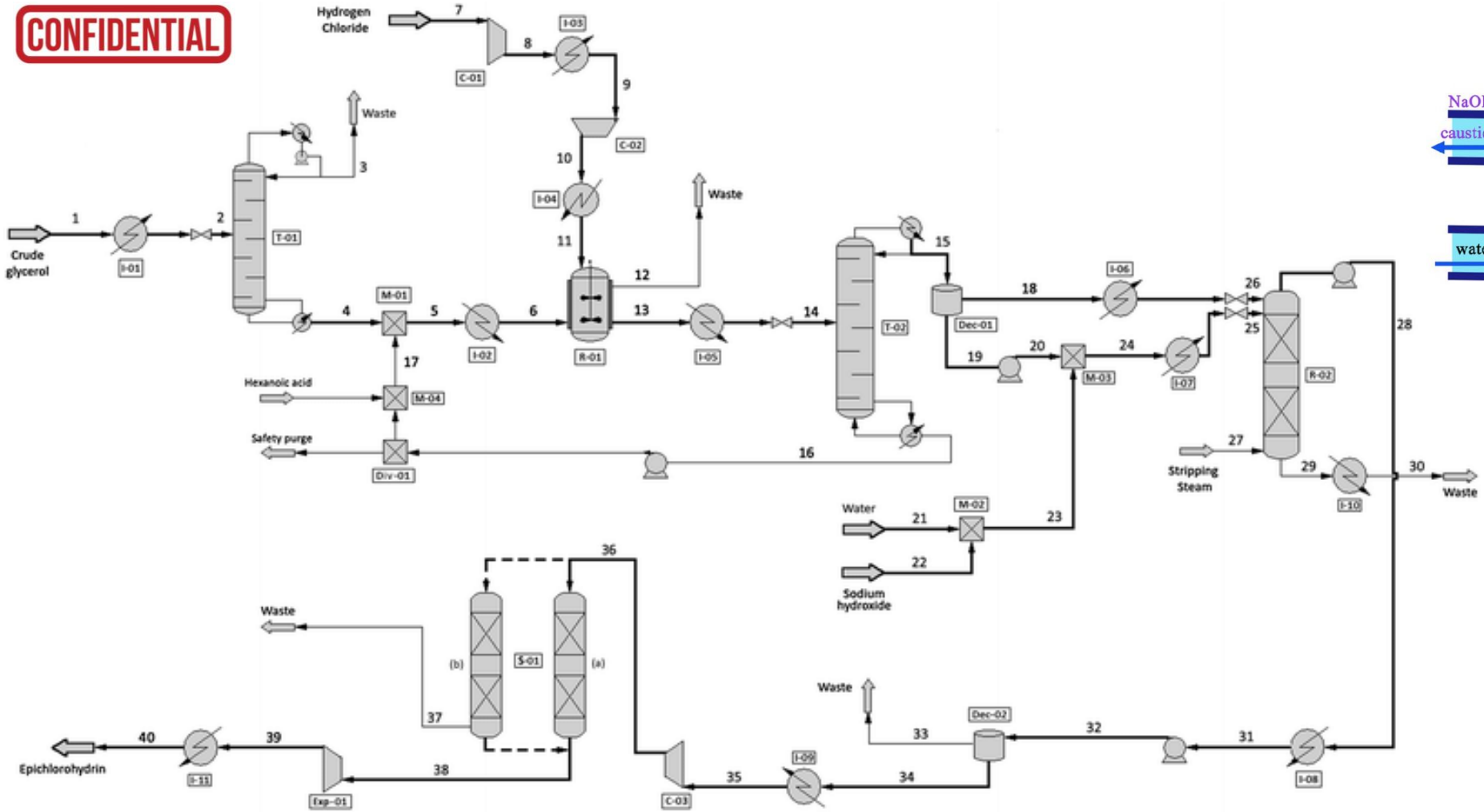


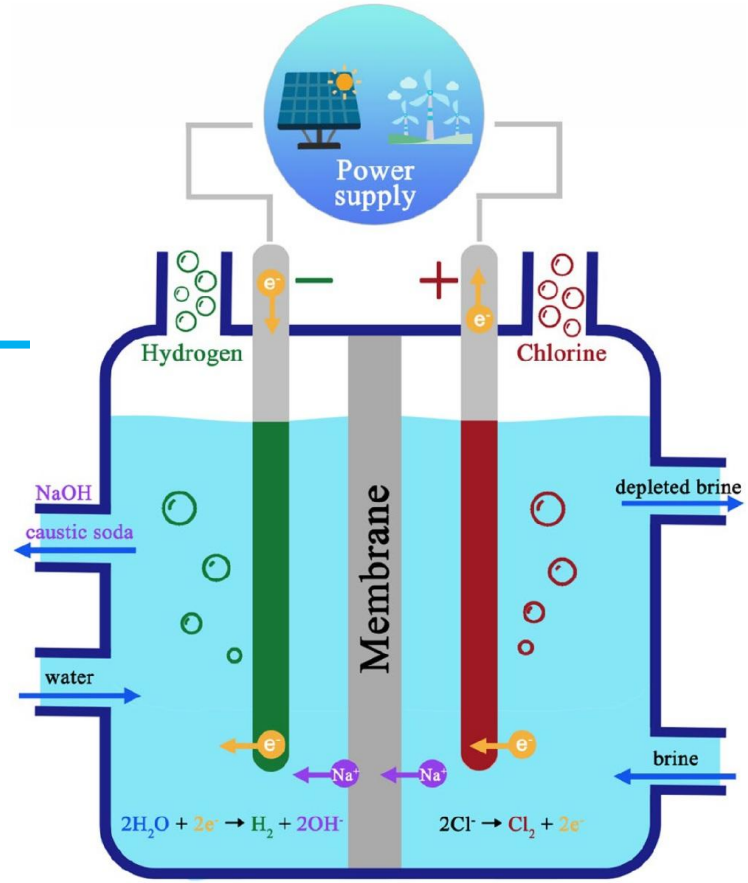

## NEW ELECTROCHEMICAL MEMBRANE CELLS






CONFIDENTIAL




ALTAIR CHEMICAL

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UNIVERSITÀ DEGLI STUDI DI TORINO

DICI
DIPARTIMENTO DI INGEGNERIA CIVILE E INDUSTRIALE


**A European Research and Technology Organisation for Chemical Systems Engineering with its headquarters in Austria**

**Scientific Advisory Board:**

Dagmar D'hooge (Ghent University), Giancarlo Cravotto (Universitá di Torino), Bettina Mihalyi-Schneider (TU Wien), Klaus Fellner (Engel Austria GmbH), Christoph Haisch (Technical University of Munich), Flavio Manenti (Politecnico di Milano), Walter Tesch (OMV Downstream GmbH), Peter Pöchlauer (Honorary Member)

## FLOW-THROUGH

MICRO- MESO- FLOW REACTORS

SONOCHEMISTRY

MICROWAVES

INDUCTION HEATING

OHMIC HEATING

## HYBRID TECHNOLOGIES

SONO-ELECTROCHEMISTRY

MECHANO-PHOTOCHEMISTRY

CAVITATION-PLASMA

SONO-EXTRUSION

## SOLVENT-FREE

BALL MILLS

EXTRUDERS

HET. SOLID CATALYSIS

## SLURRY REACTIONS

REACTIONS IN BIPHASIC MEDIA

# Non-Conventional Technologies in Chemical Laboratories

1. Microwave-Assisted Reactor

2. Ultrasonic Processor
(Sonication Reactor)

3. Continuous-Flow Microreactor

4. Photochemical LED Reactor

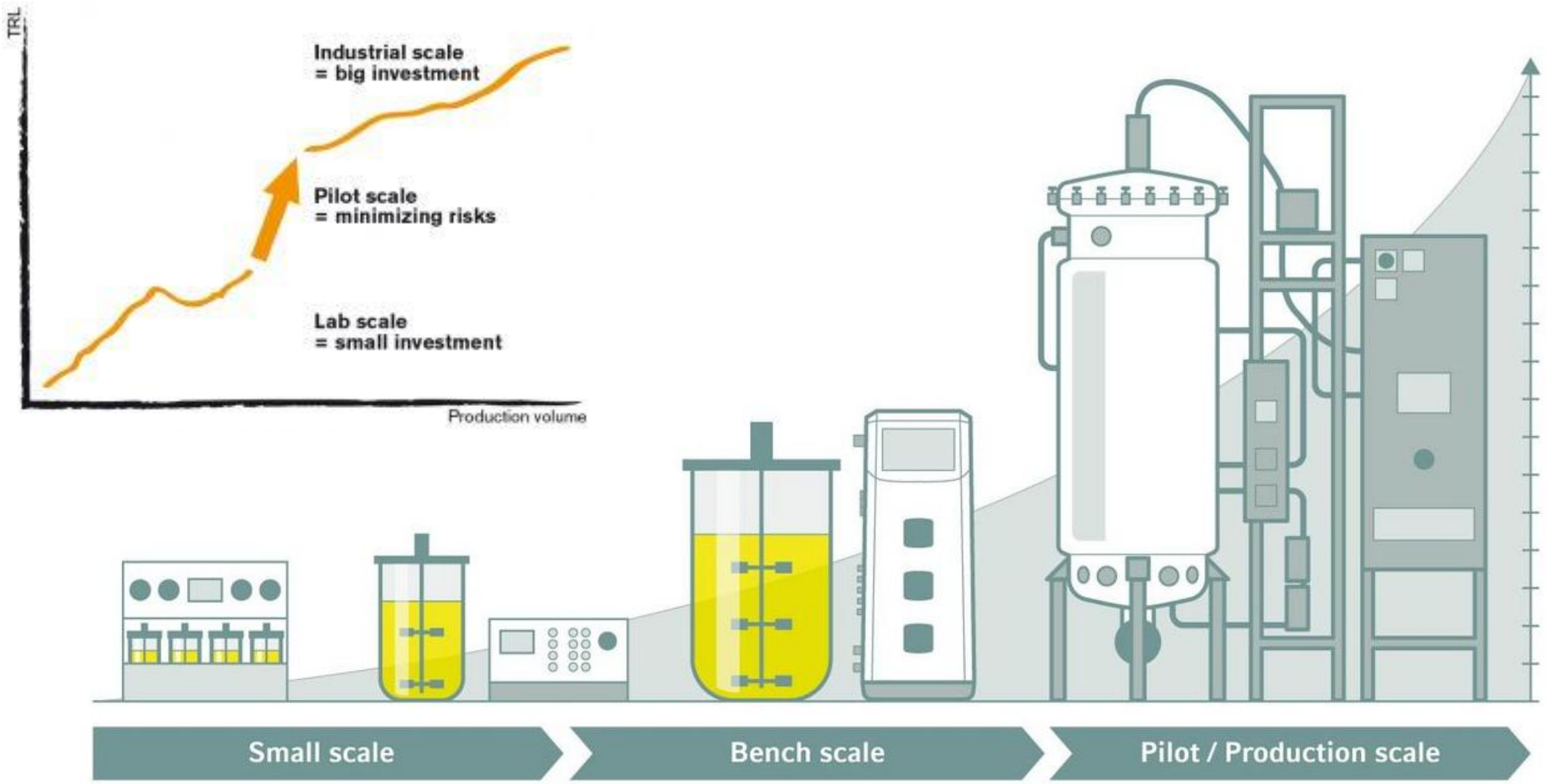
5. Plasma Reactor

6. Supercritical Fluid /
Pressurised Extraction Unit

7. Automated Robotic
Liquid-Handling System

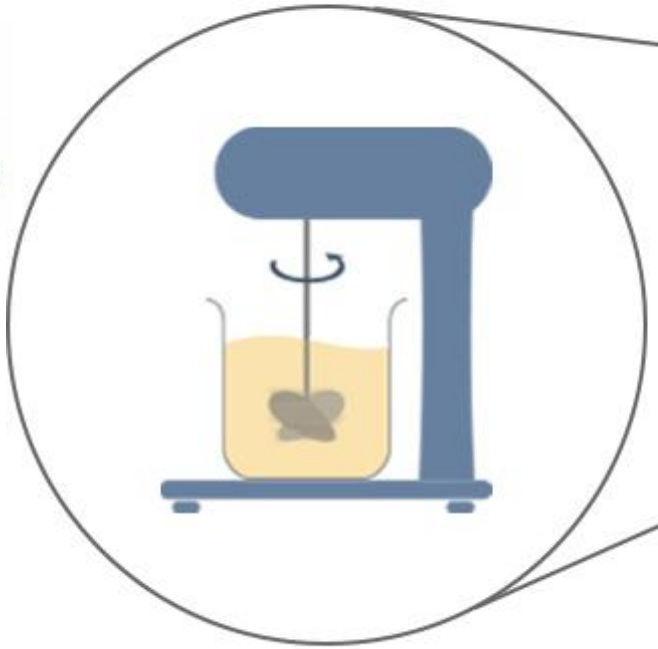
8. Green Solvent
Processing Concept

# FROM LAB TO PRODUCTION SCALE

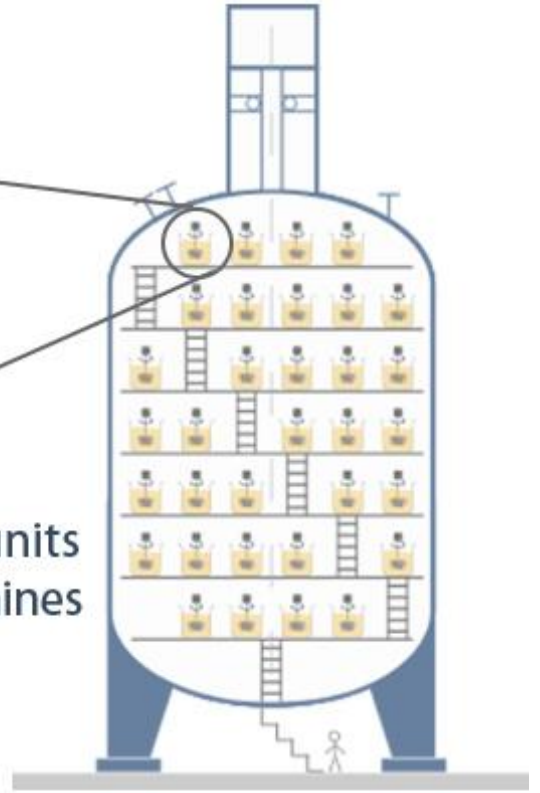


## Numbering-up

Increase capacity by multiplying identical units



Use 1,000 units
of 1 L laboratory machines



Huge paper mixing vessel
( After scaling up )

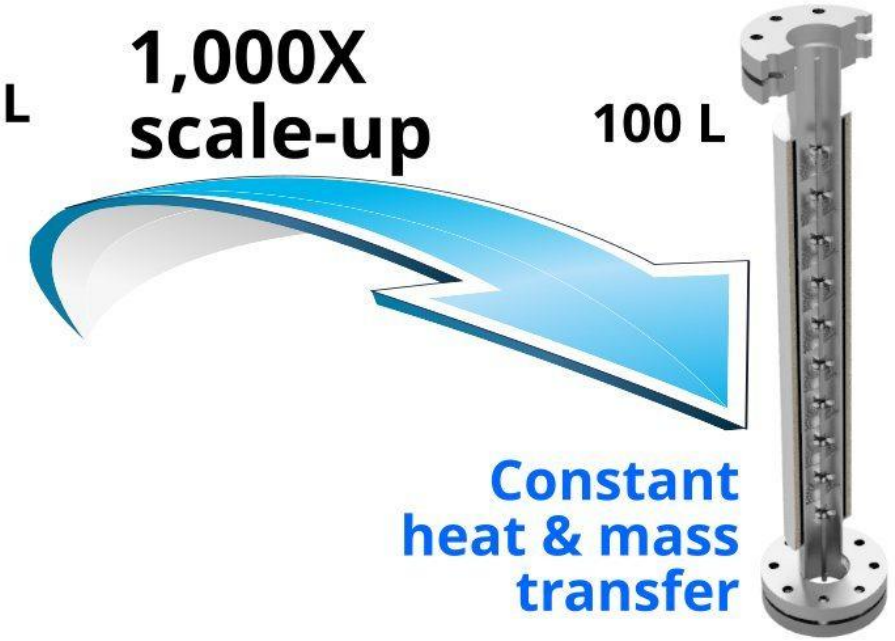
## Scaling-up

Increase capacity by enlarging one unit

0.1 L

1,000X
scale-up

100 L



Constant
heat & mass
transfer

# 1 LABORATORY SCALE

**Volume: mL to L**


**FAST SCREENING**
Rapid evaluation of formulations and reaction conditions

**TEMPERATURE CONTROL**
Precise control for reproducible results

**MIXING**
Efficient mixing at small scale

**KINETICS**
Reaction rate and kinetic studies

**SAFETY TESTING**
Hazard assessment and safe operating limits

# 2 PILOT SCALE

**Volume: 10 – 500 L**


**SCALE VALIDATION**
Verify performance when increasing scale

**HEAT TRANSFER**
Evaluate and optimize heat transfer

**MIXING BEHAVIOUR**
Assess mixing patterns and homogeneity

**RESIDENCE TIME**
Determine RTD and hold-up time

**PROCESS OPTIMISATION**
Optimize parameters for yield and efficiency

**REPRODUCIBILITY**
Ensure consistent and reliable results

# 3 INDUSTRIAL SCALE

**Volume: $m^3$ (1 – 100+ $m^3$)**

**MASS PRODUCTION**
High throughput and reliable operations

**ENERGY EFFICIENCY**
Optimize energy use and reduce operating costs

**PROCESS SAFETY**
Advanced safety systems and risk management

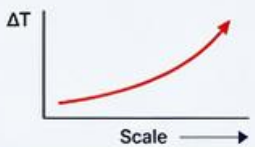
**QUALITY CONTROL**
Consistent product quality and compliance

**CONTINUOUS OR BATCH PRODUCTION**
Flexible operation based on process requirements

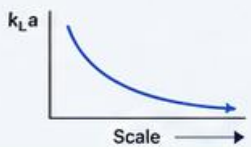
**VOLUME: $m^3$**
Large scale capacity for industrial needs

# KEY SCALE-UP CHALLENGES

**HEAT TRANSFER**
Lower surface area to volume ratio reduces heat removal efficiency



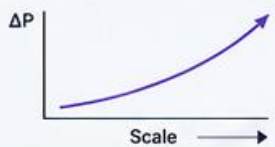

**MASS TRANSFER**
Diffusion limitations increase with scale, affecting reaction rates




**MIXING**
Mixing time increases with scale; risk of dead zones


**REACTION KINETICS**
Reaction rates may change due to temperature and concentration gradients


**PRESSURE CONTROL**
Pressure drops increase with system size and line complexity



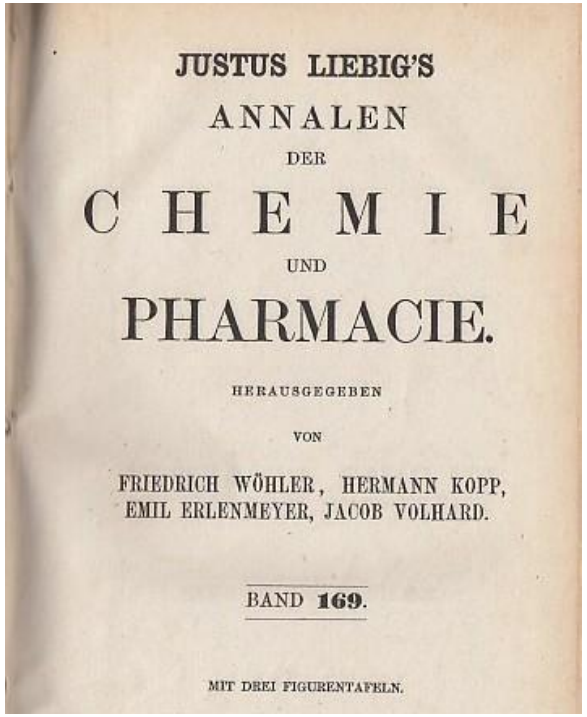

**PROCESS SAFETY**
Hazards can be amplified at larger scales—requires robust safeguards

- Increased inventory
- Runaway risk
- Relief & containment
- Emergency response

# ORGANIC SYNTHESIS IN THE ‘90s

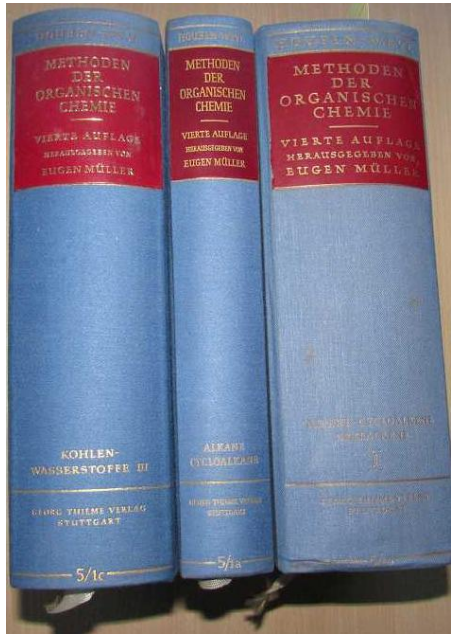
## LIEBIGS ANNALEN

**der Chemie**


JUSTUS LIEBIG'S
ANNALEN
DER
CHEMIE
UND
PHARMACIE.
HERAUSGEGEBEN
VON
FRIEDRICH WÖHLER, HERMANN KOPP,
EMIL ERLENMEYER, JACOB VOLHARD.
BAND 169.
MIT DREI FIGURENTAFELN.

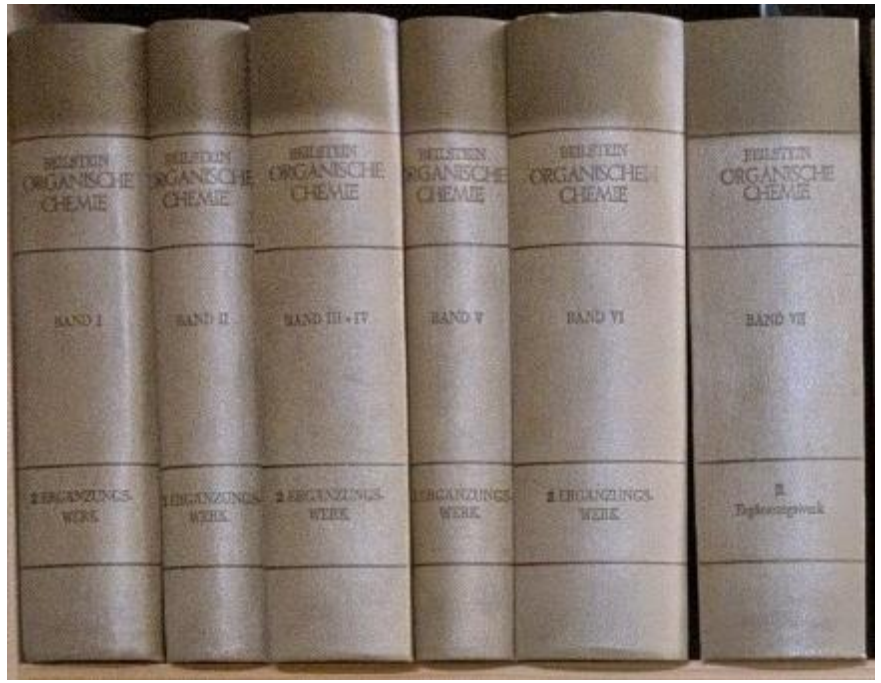
## HOUBEN-WEYL

**Methoden der Organischen Chemie**




## Der BEILSTEIN

**Handbuch der Organischen Chemie**



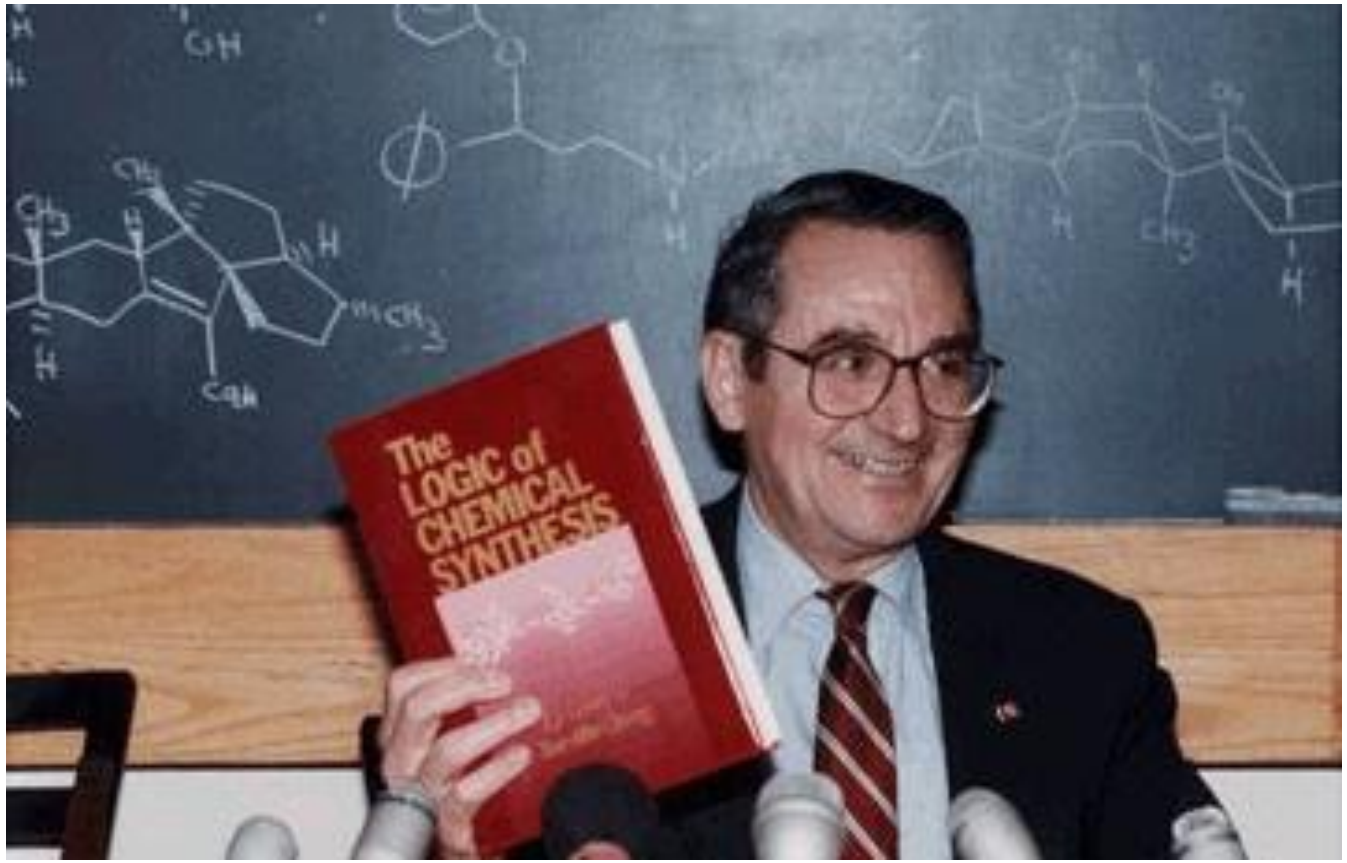
**Scientists have to follow two different research philosophies, one embodying the ideal of a deductive analysis based on known methodology and current theory, and the other…**

**emphasizing innovation and even speculation**

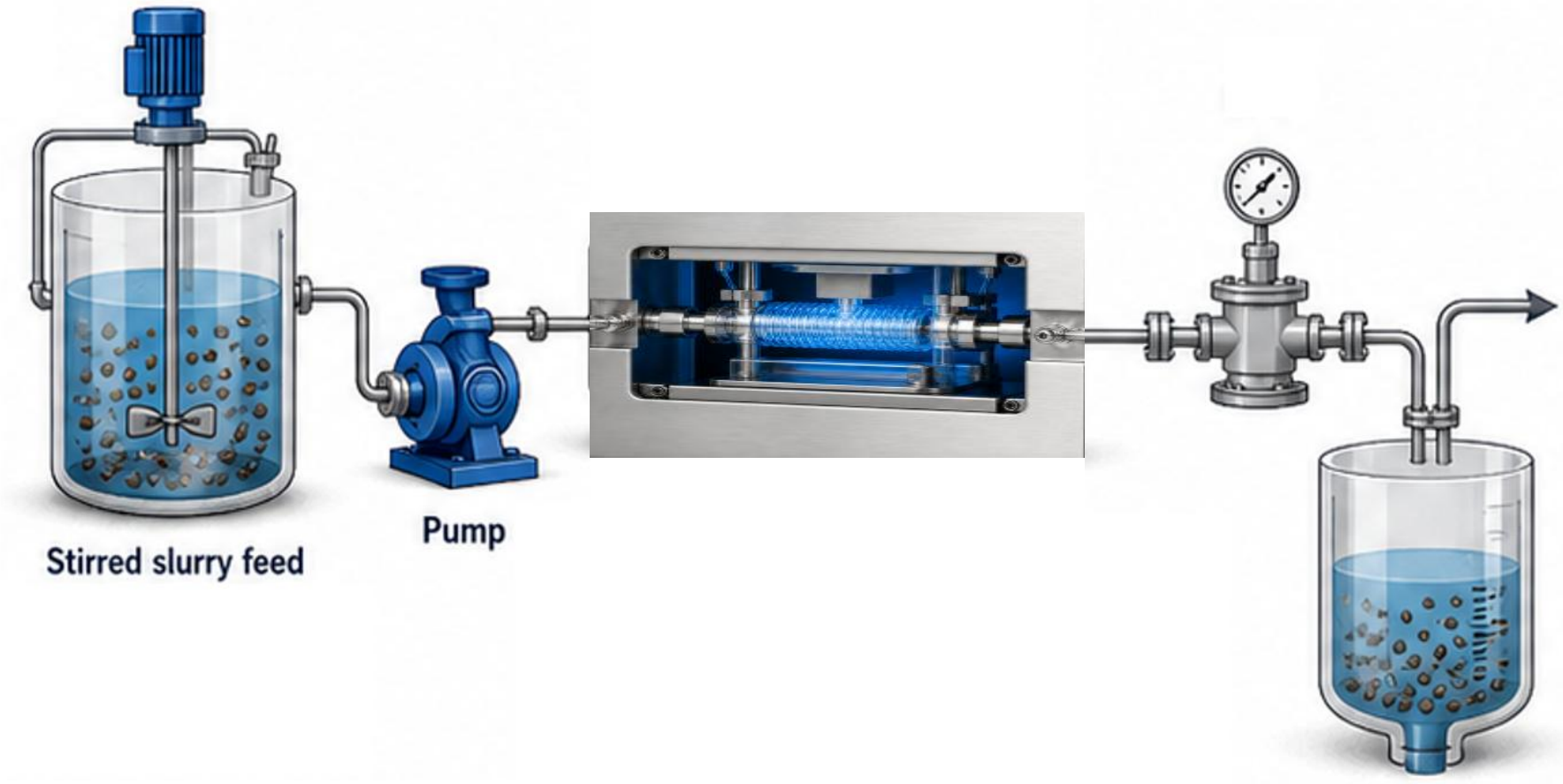
## Elias James Corey

**1990**

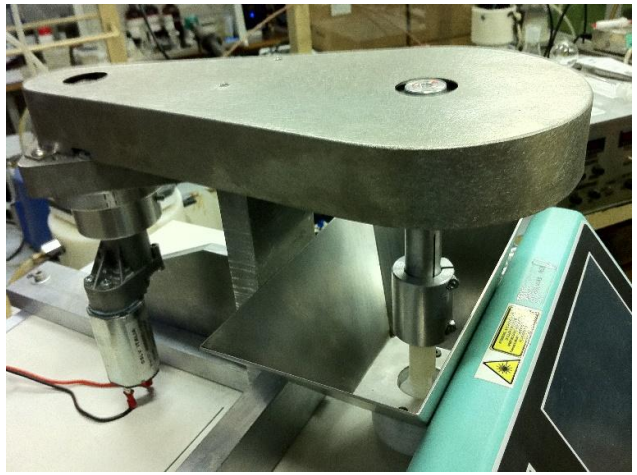

Nobel Laureate

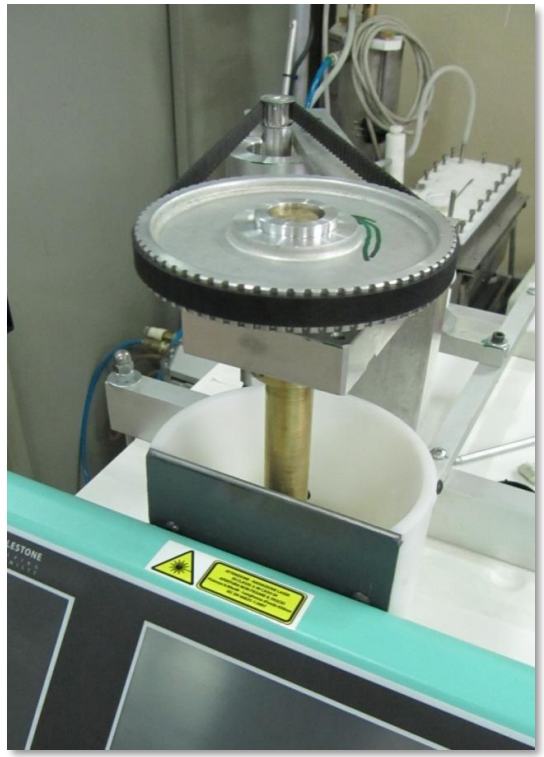


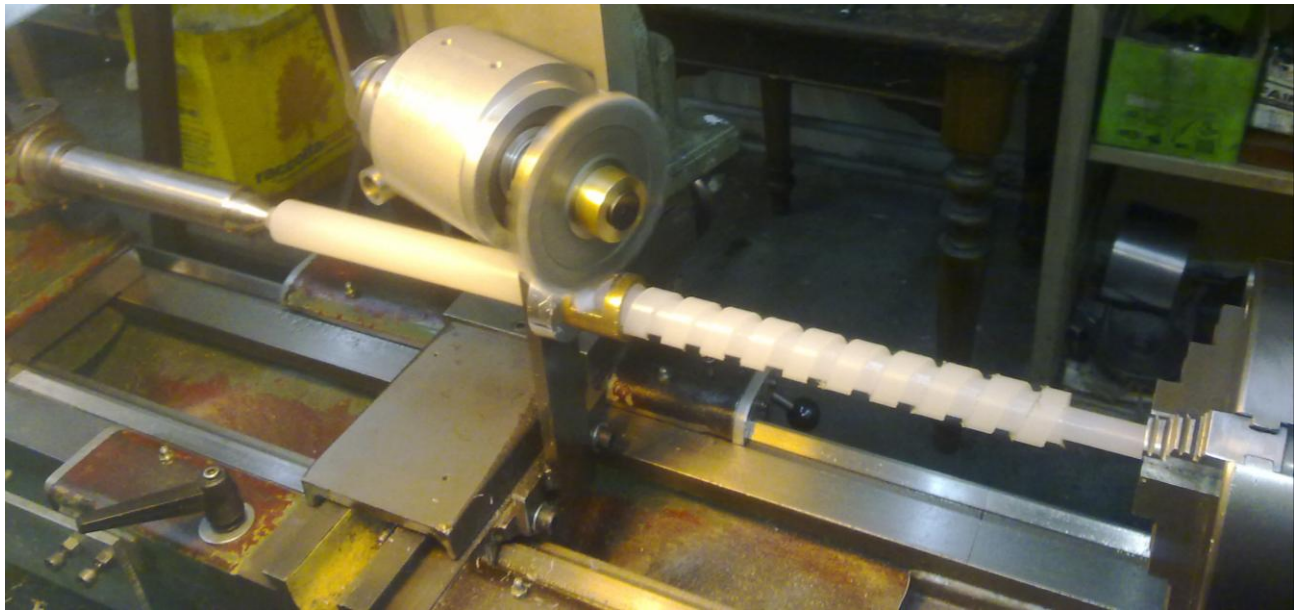
# SLURRY OR SOLVENT-FREE REACTIONS UNDER FLOW-MICROWAVES

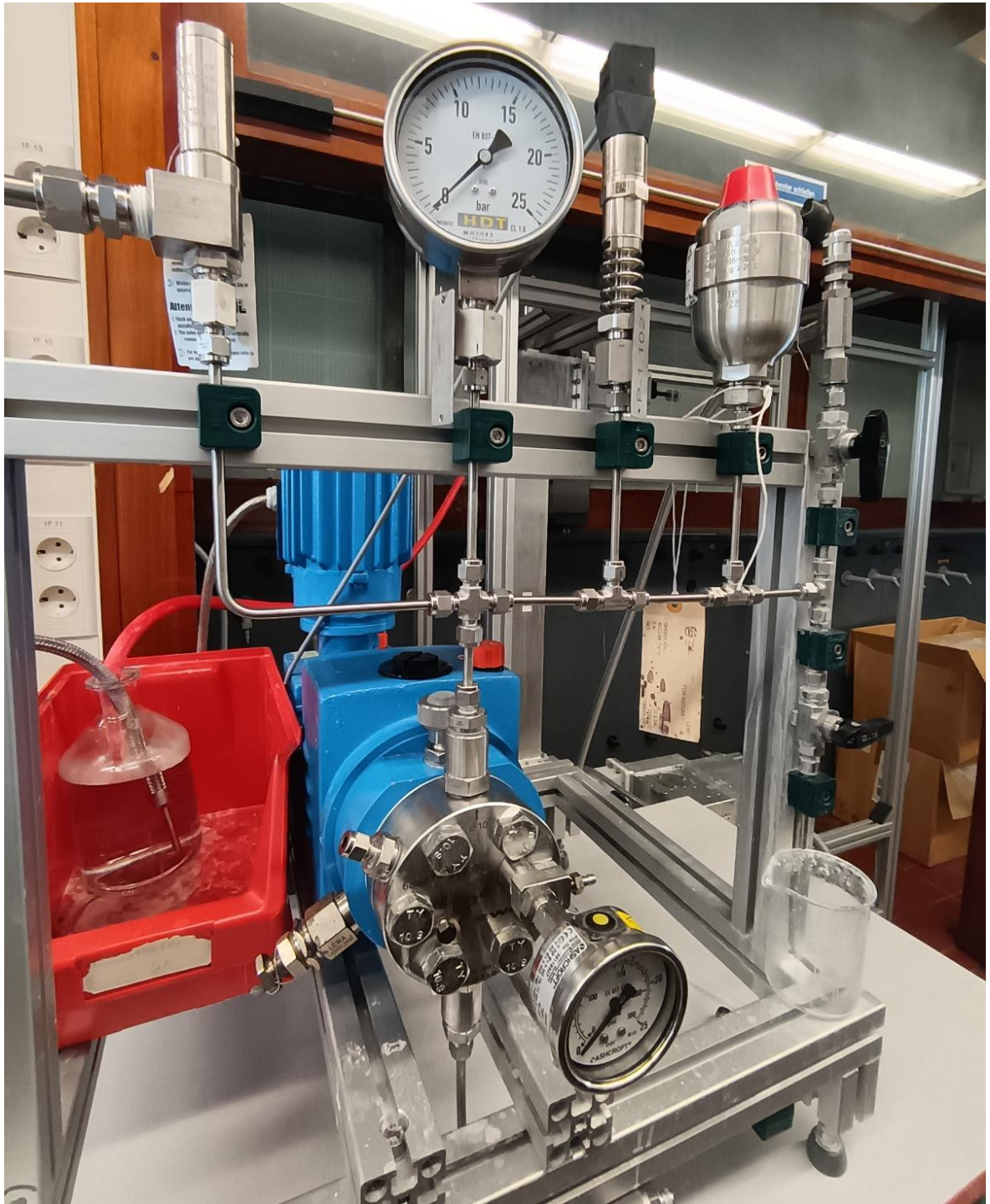


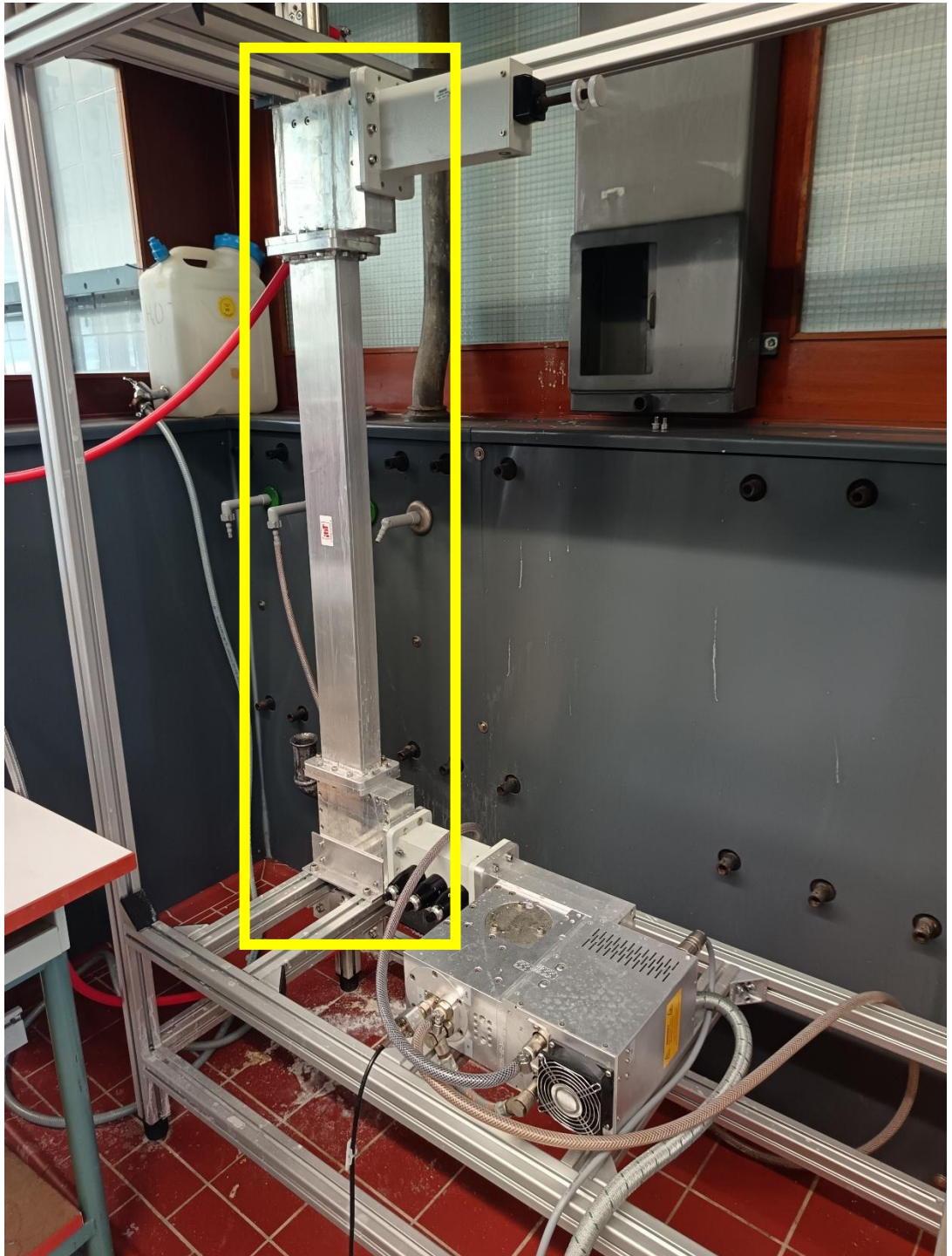
# SLURRY REACTIONS IN MW






10
15
5
20
8
25
bar
HDT



# MW-ASSISTED SLURRY REACTIONS

Labotron 6000, 2450 MHz 6 kW,

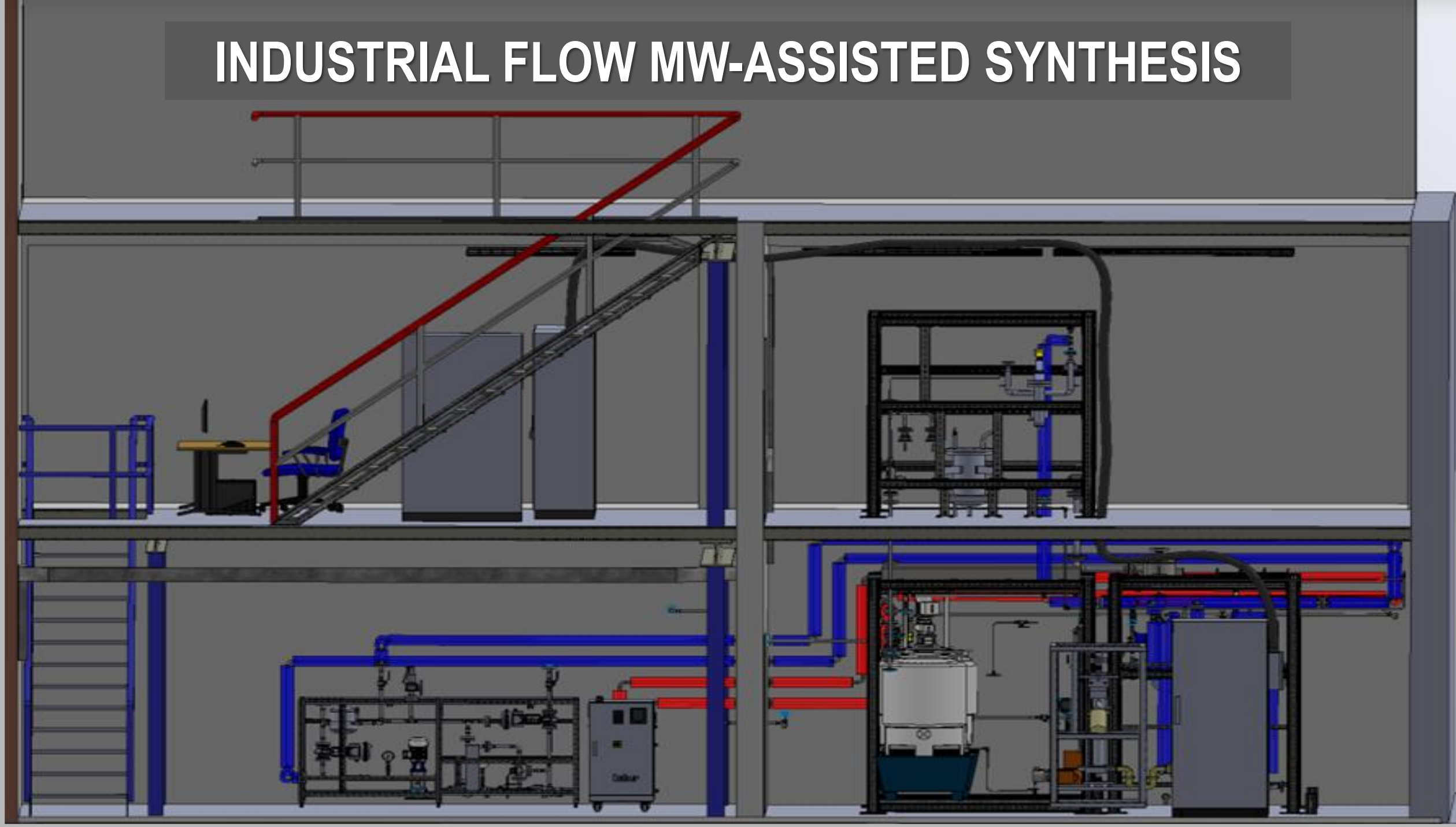

## µWave Flow Reactors

**1.2 – 20 kW - 2450 MHz**

## Pilot MW reactor

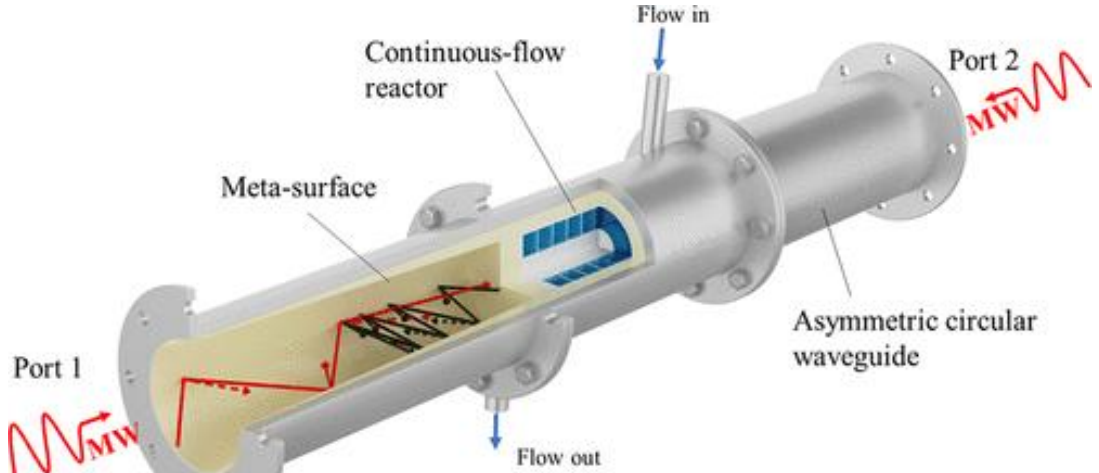
**up to 250bar/350°C**

# INDUSTRIAL FLOW MW-ASSISTED SYNTHESIS




R-6100


B-2.210
H-2.207
H-2.208
F-2.211
H-2.213
P-2.200




**Reflected energy is cut off to achieve efficient microwave heating.**


Kühlwasser Vorlauf
Schrauben anziehen HOT
Hohlleiter
Mittelteil

# INDUSTRIAL FLOW MW-ASSISTED SYNTHESIS


**Energy Efficiency = kilojoule/mole**

Europäisches Patentamt
European Patent Office
Office européen des brevets

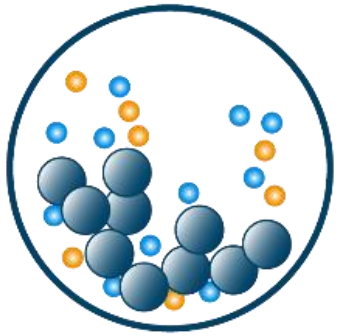
(11) **EP 3 860 966 B1**

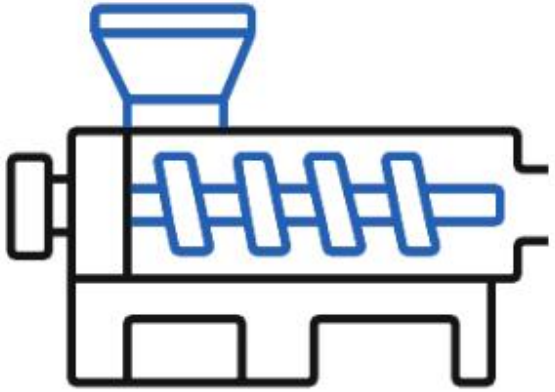
**EUROPEAN PATENT SPECIFICATION**

**SQUALENE OF HIGH QUALITY PRODUCED BY MICROWAVE ASSISTED PROCESS**

DURCH MIKROWELLENUNTERSTÜTZTES VERFAHREN HERGESTELLTES QUALITATIV HOCHWERTIGES SQUALEN

# MECHANOCHEMISTRY: BALL MILLS & REACTIVE EXTRUDERS

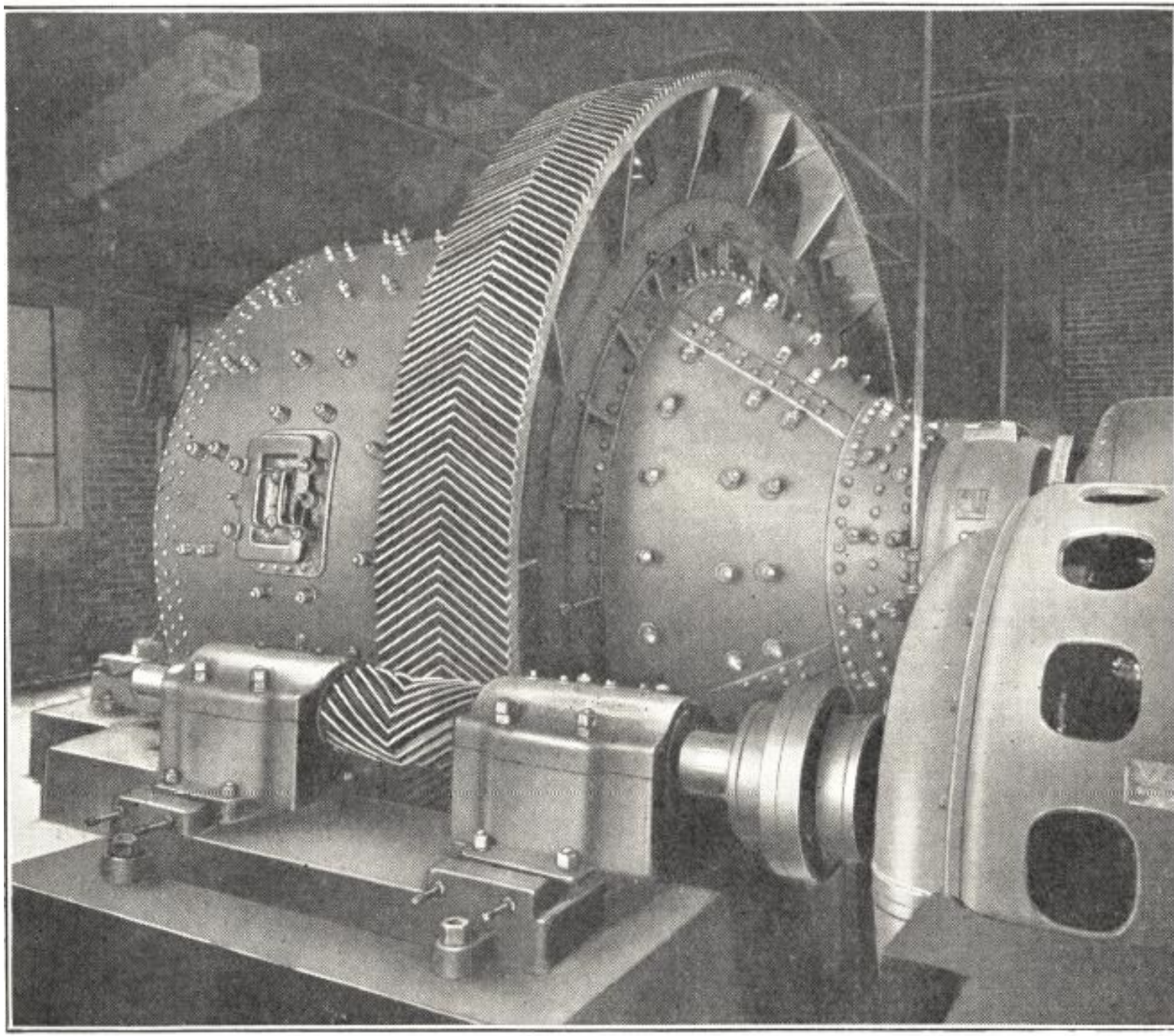




## *Mühlenbetriebe*

# BASF GmbH (Germany)

In the 19th century, BASF (Germany), used giant mills to grind materials into synthetic organic dyes. Factory workers would load a ball mill's large cylindrical drum with starting material and metal balls. The balls would grind the materials as the drum spun. One of the dyes made in these mills was **Heliogen blue, an intense sapphire dye made by crumbling copper chloride and phthalonitrile**.



DOUBLE HELICAL DRIVE FOR BALL MILL.

Cite this: *Chem. Sci.*, 2012, **3**, 295

www.rsc.org/chemicalscience

PERSPECTIVE

Chemical Science

# Harnessing mechanochemical effects with ultrasound-induced reactions

nature chemistry

*Nature Chem.* **2012**, *4*, 77-78

MECHANOCHEMISTRY

# Measuring the force of sound

Chem Soc Rev

*Chem. Soc. Rev.*, 2013, **42**, 7521 RSC Publishing

TUTORIAL REVIEW

# On the mechanochemical activation by ultrasound


# PLANETARY BALL MILL

ChemComm
Chemical Communications
www.rsc.org/chemcomm

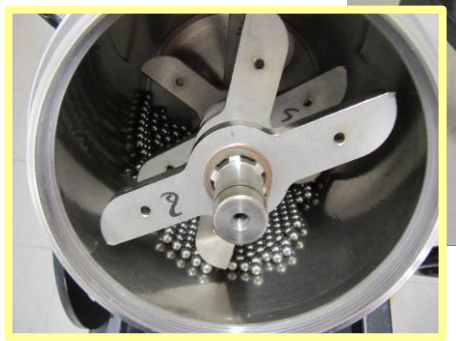
# High throughput mechanochemistry: application to parallel synthesis of benzoxazines

*Chem. Commun.*, **2018**, *54*, 551-554

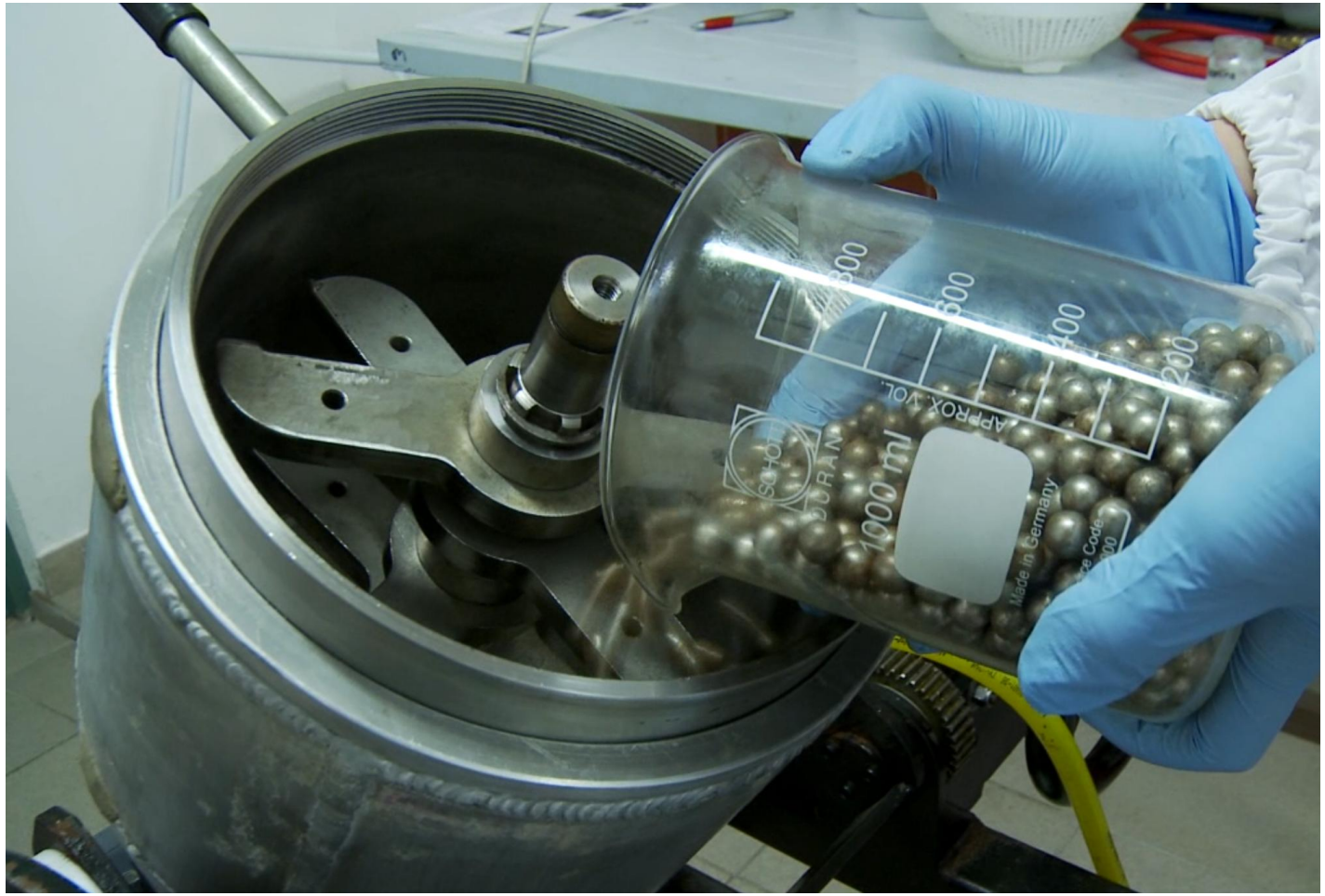
c&en
CHEMICAL & ENGINEERING NEWS

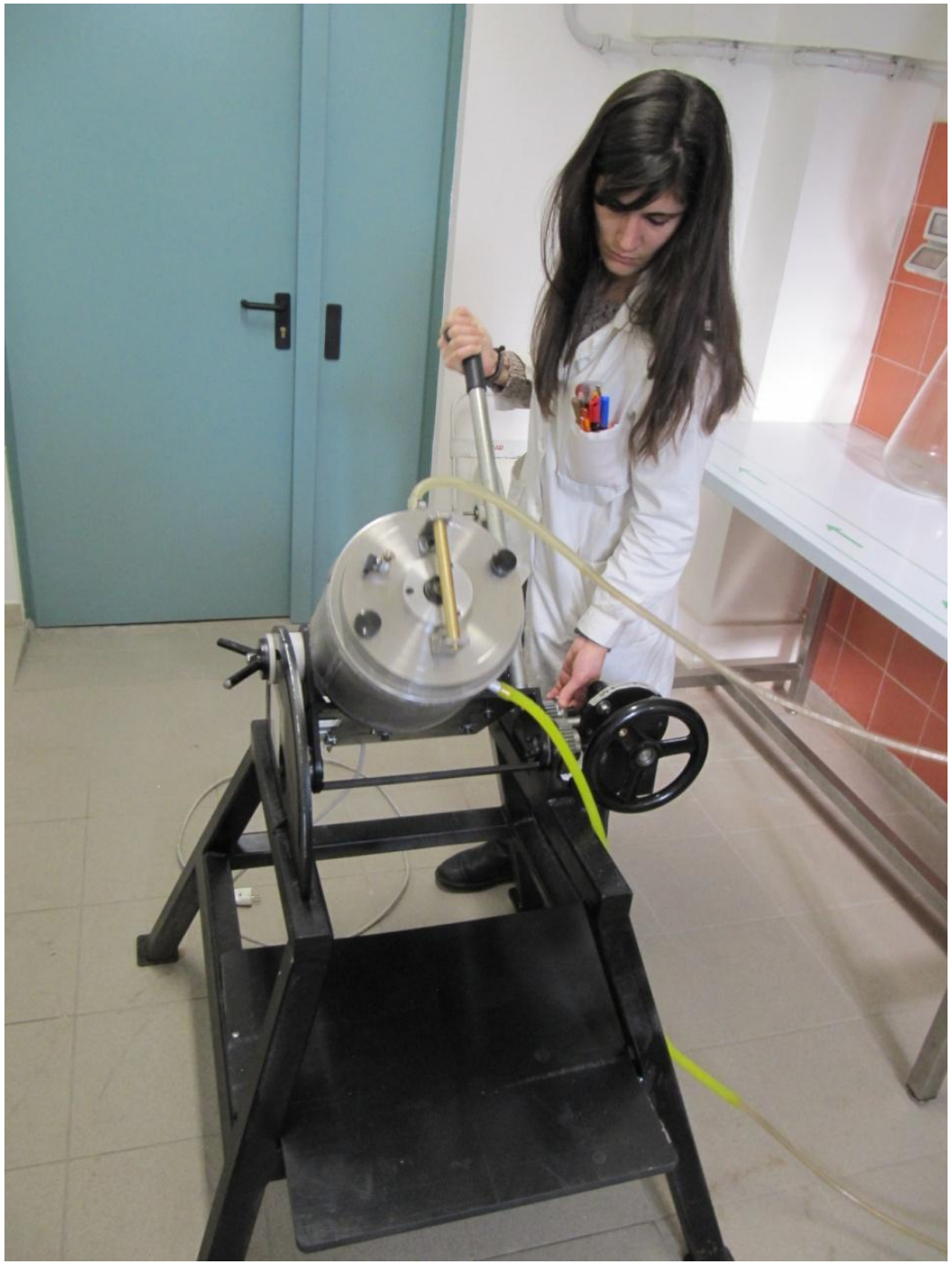
# Mechanochemists want to shake up industrial chemistry


# SLURRY OR SOLVENT-FREE SYNTHESIS IN BALL MILLS




# SLURRY OR SOLVENT-FREE SYNTHESIS IN BALL MILLS



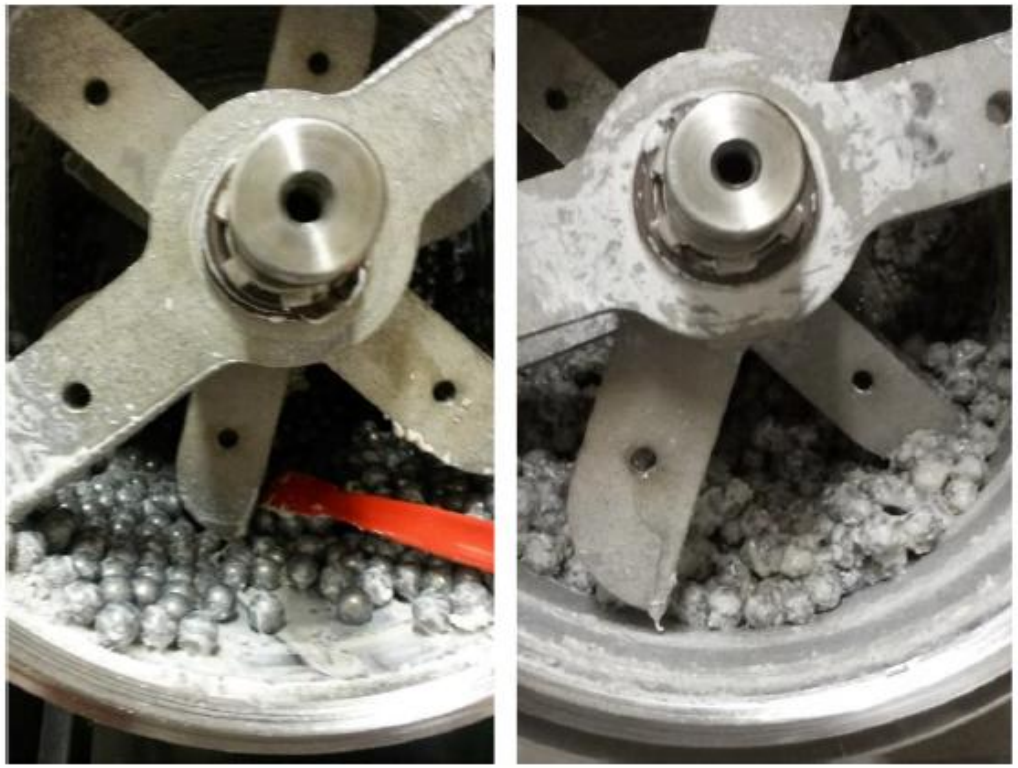
ACS Sustainable Chemistry & Engineering

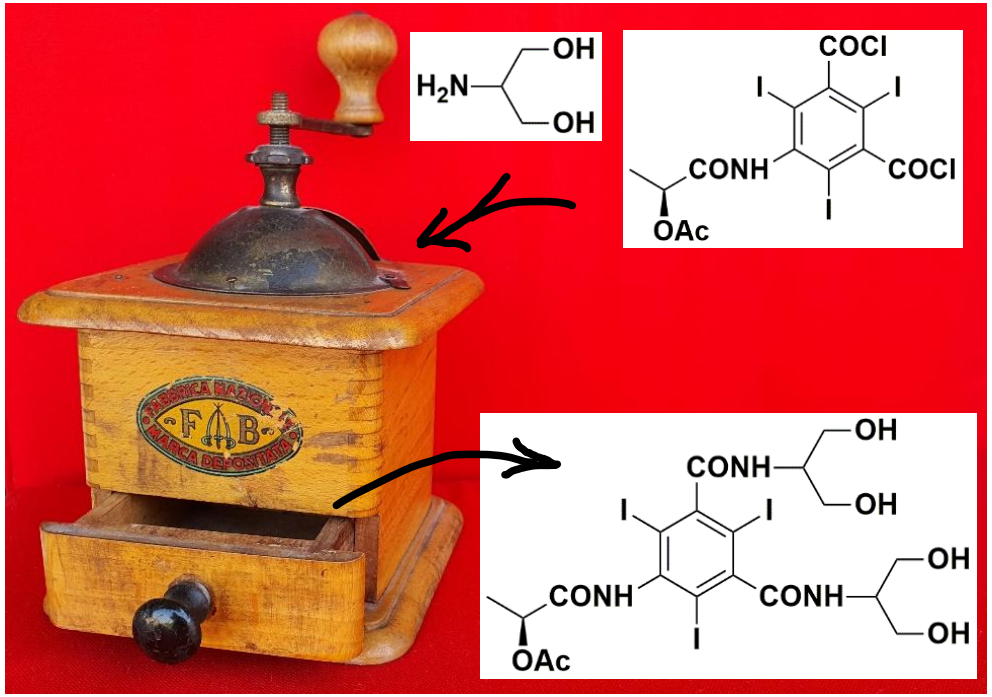
ACS Sustainable Chem. Eng. 2020, 8, 12825−12830

pubs.acs.org/journal/ascecg


# Mechanochemistry Applied to the Synthesis of X-ray Contrast Agent

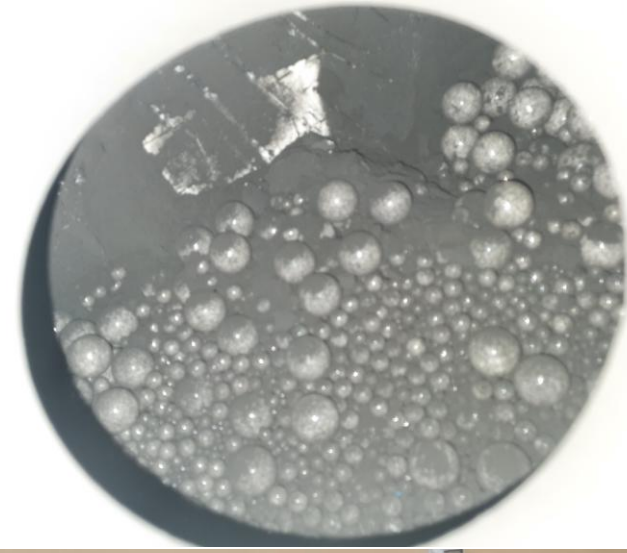
ISOVUE®
(iopamidol injection)





# SEMI-INDUSTRIAL MECHANOCHEMICAL SYNTHESIS


Frequency Controller
Changsha Tianchuang Powder Technology Co., Ltd.



(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 June 2018 (14.06.2018)

WIPO | PCT

(10) International Publication Number
WO 2018/104228 A1

BRACCO

## MECHANOCHEMICAL SYNTHESIS OF RADIOGRAPHIC AGENTS INTERMEDIATES

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
01 April 2021 (01.04.2021)

WIPO | PCT

(10) International Publication Number
WO 2021/058591 A1

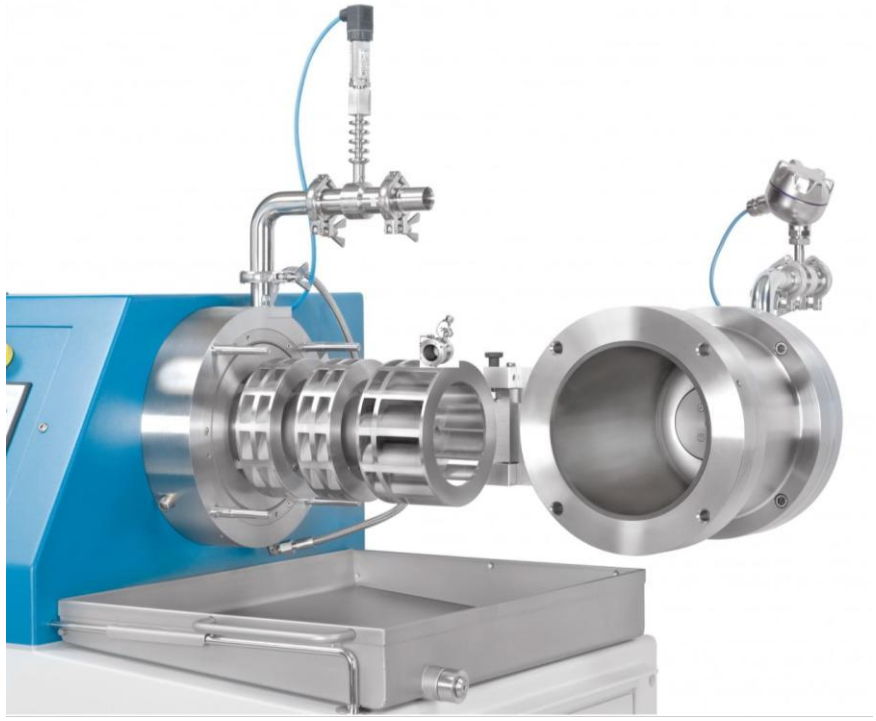
**(54) Title:** METHOD FOR THE PRODUCTION OF METAL OXIDE PIGMENT COMPOSITE OF CONTROLLED AGGLOMERATING PROPERTIES AND RESPECTIVE PRODUCT

# TRANSLATING MILLS TO EXTRUDERS AND FLOW MILLS

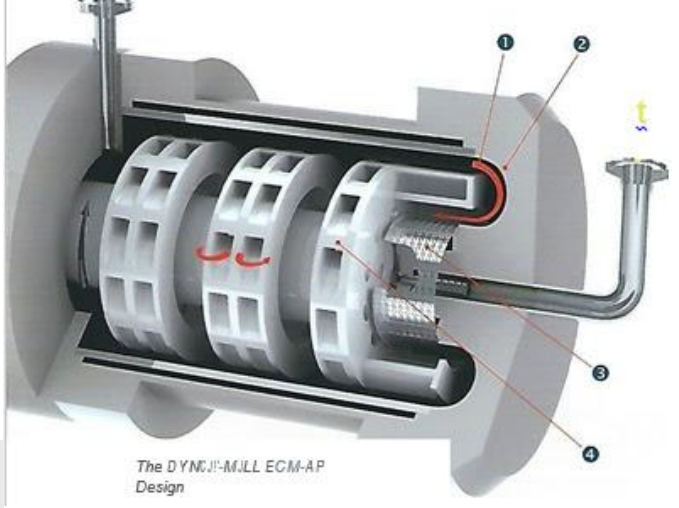


***from Batch to Continuous flow***

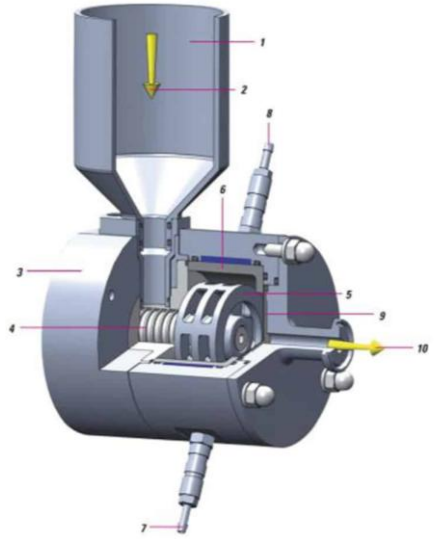
# DYNO®-MILL MULTI LAB

WAB


The DYNO®-MILL ECM-AP Design

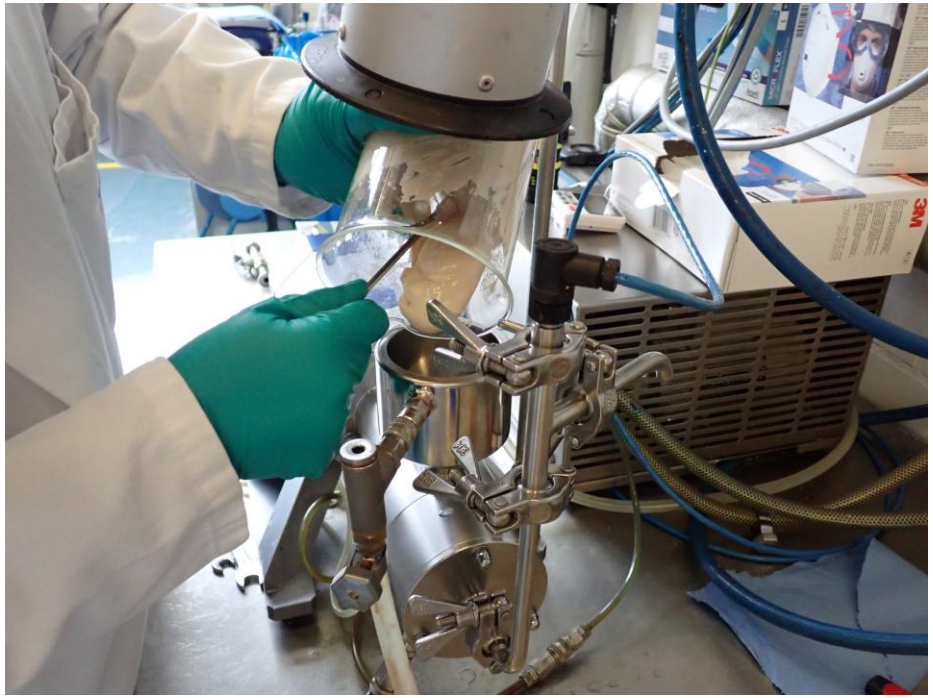


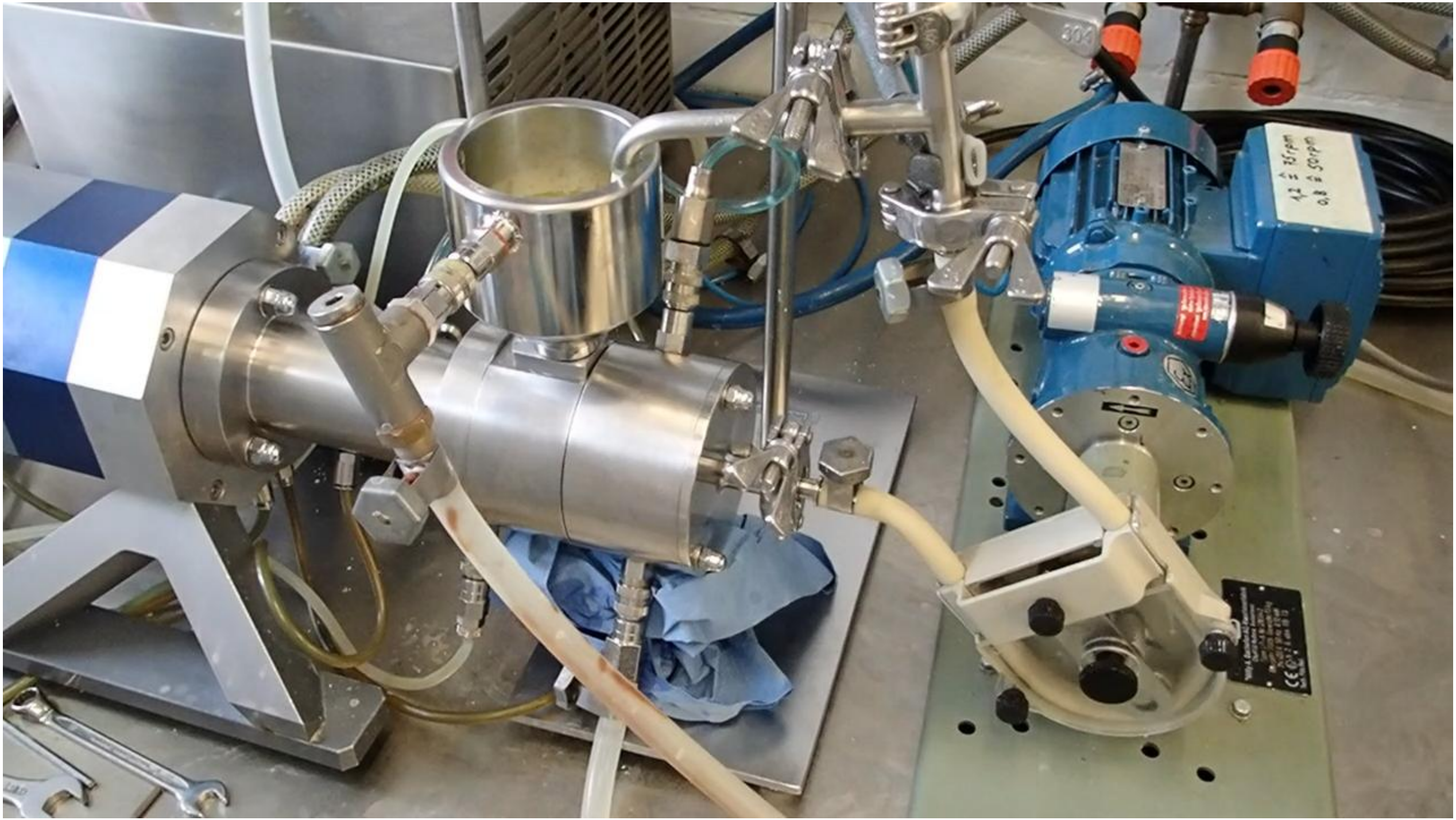

ChemSusChem

Research Article
doi.org/10.1002/cssc.202301921

## Sustainable Beckmann Rearrangement using Bead-Milling Technology: The Route to Paracetamol

# SLURRY OR SOLVENT-FREE SYNTHESIS IN ROTATING MILLS



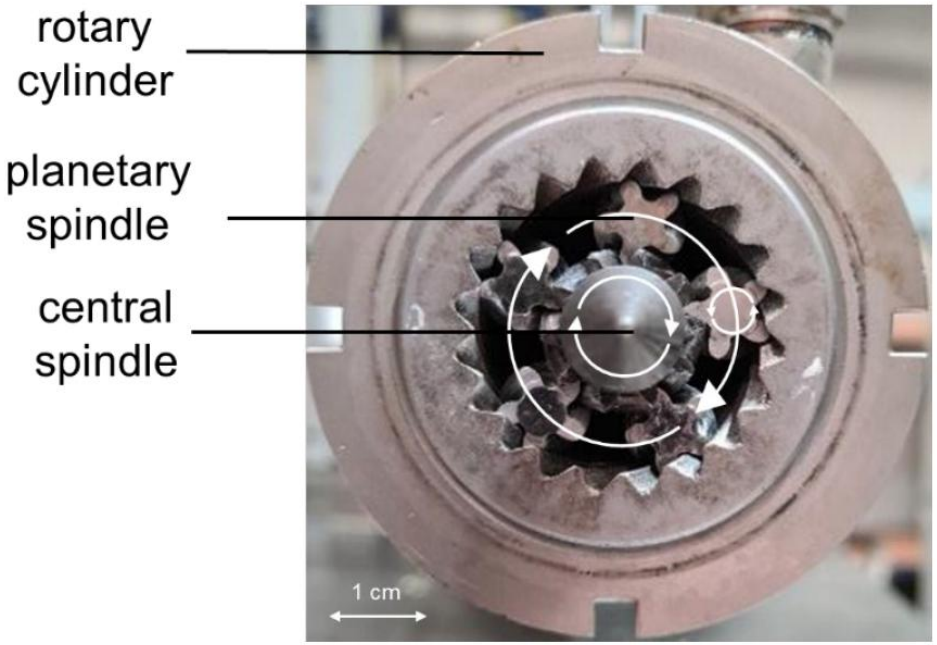
# FROM GRAMS TO TONS

## G SCALE

## KG SCALE

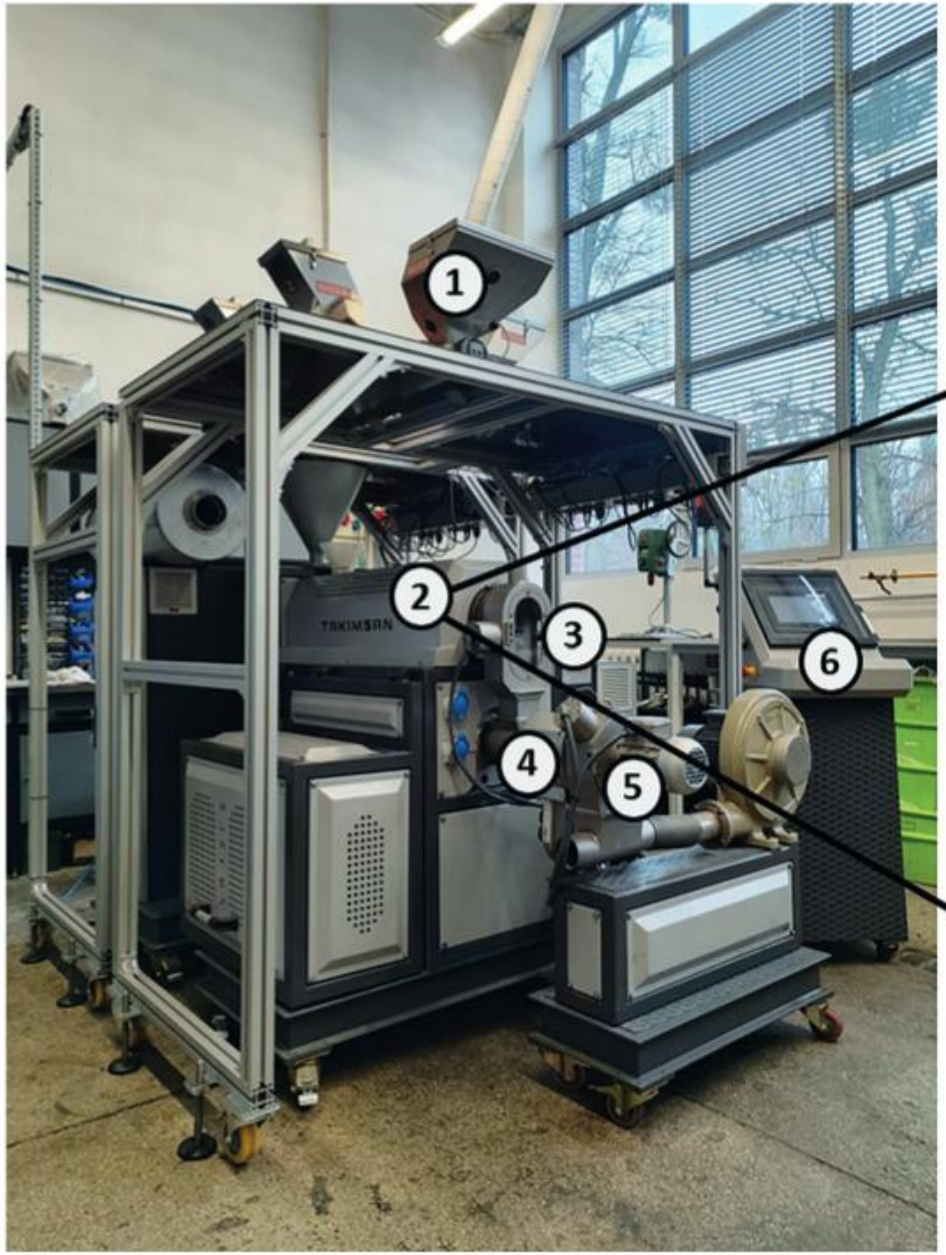

## T/ MT SCALE

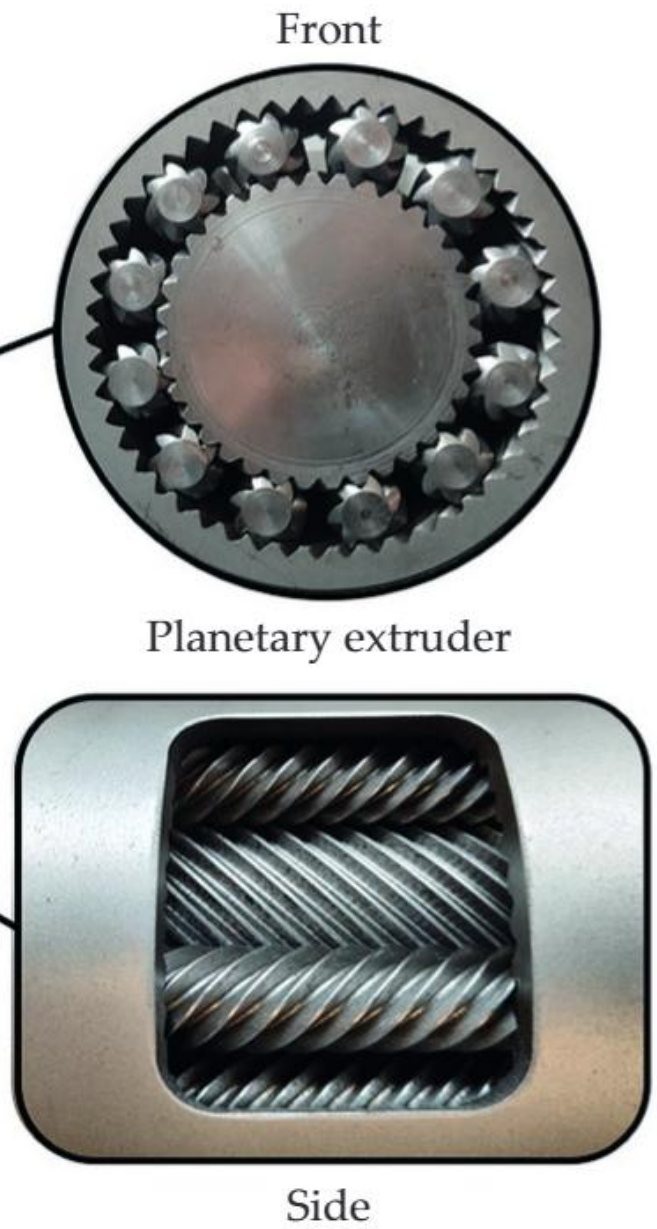
# PLANETARY ROLLER EXTRUDER




ENTEX

# PLANETARY EXTRUDER




1- gravimetric feeders' system

2 - planetary extruder

3 - vacuum-degassing chamber

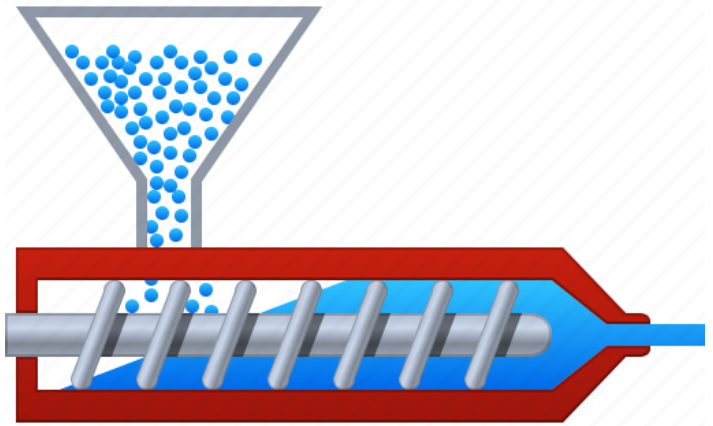
4- single-screw extruder

5 - granulation system

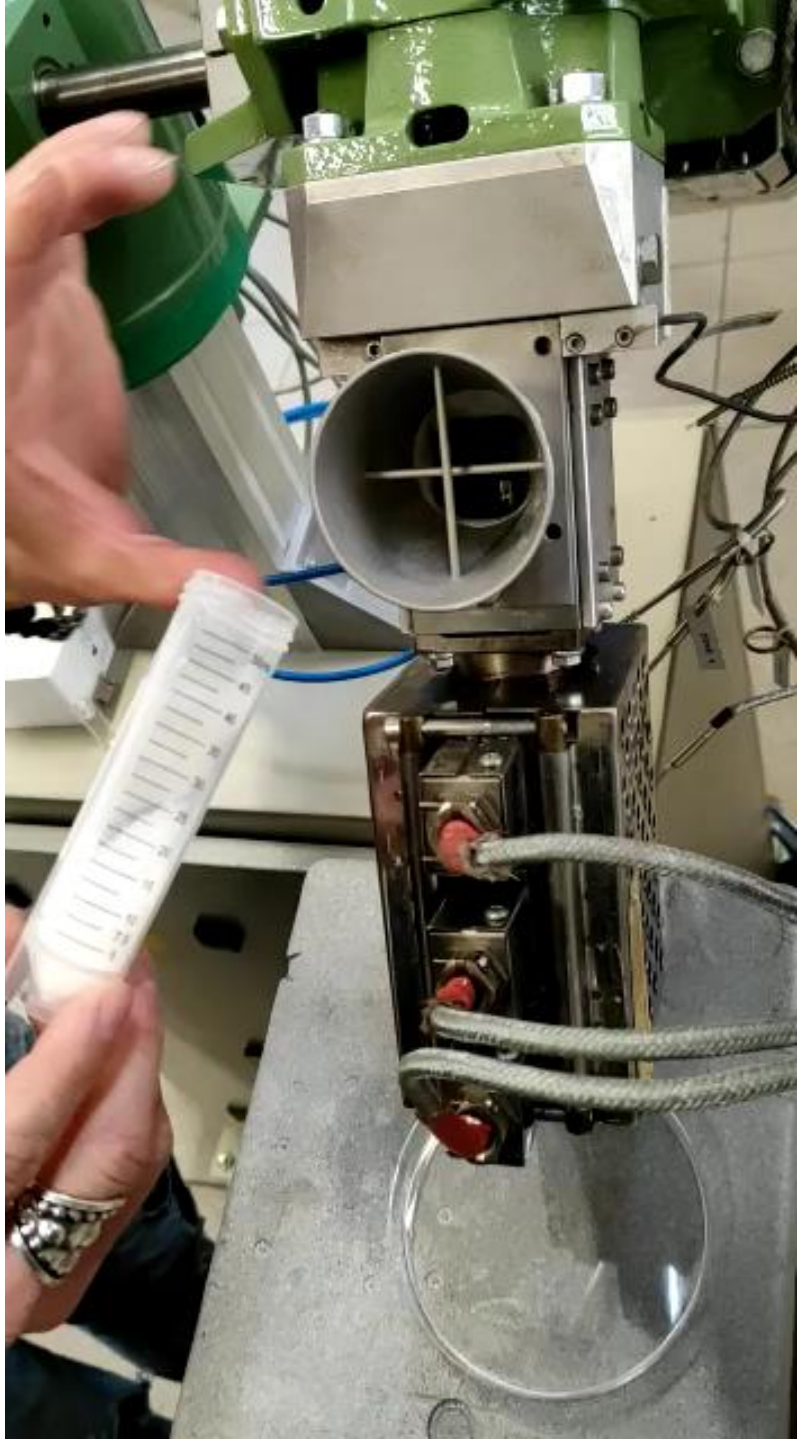
6 - control panel

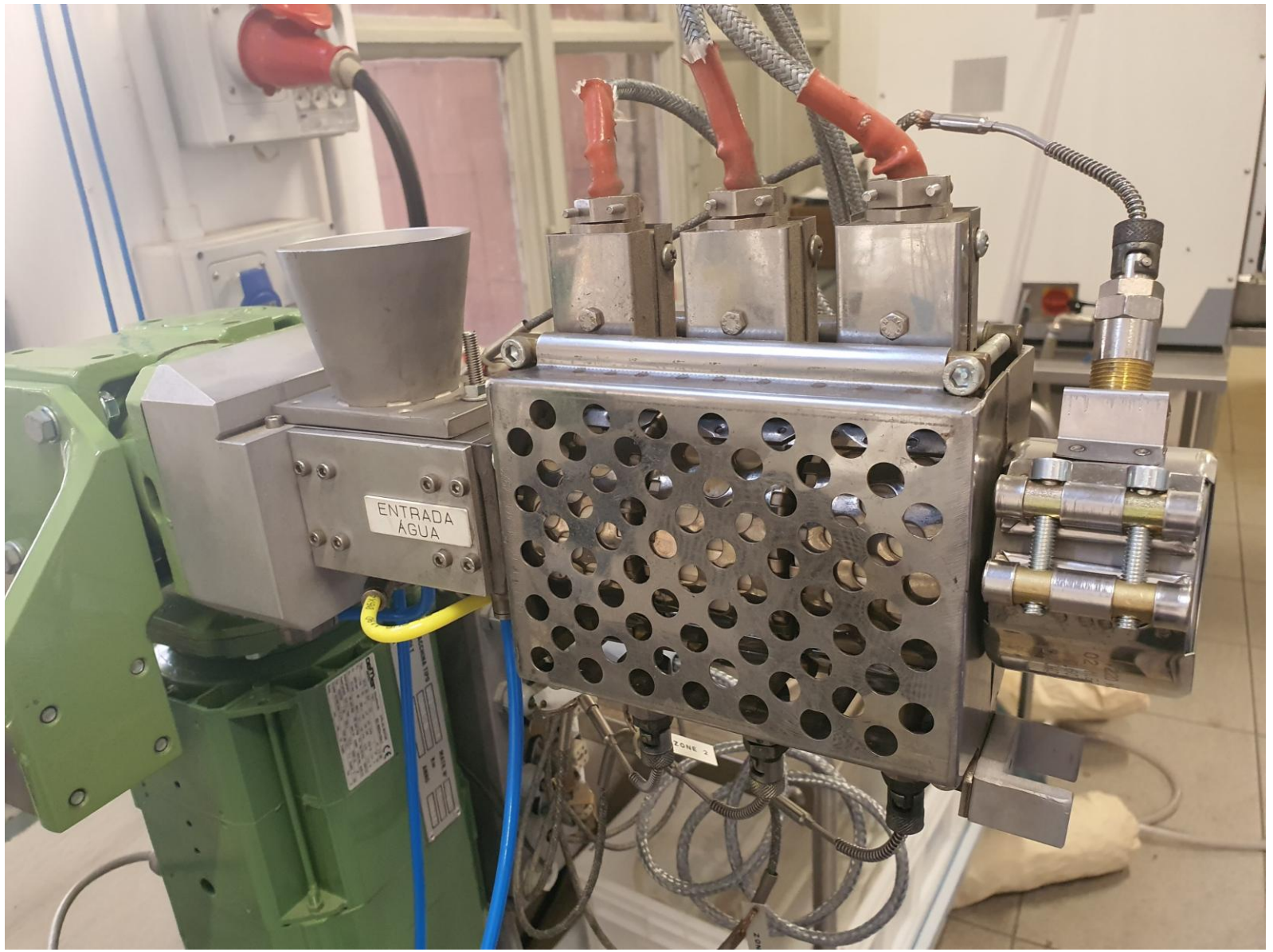
technovel

# CHALLENGES IN REACTIVE EXTRUSION



# SINGLE-SCREW EXTRUDER





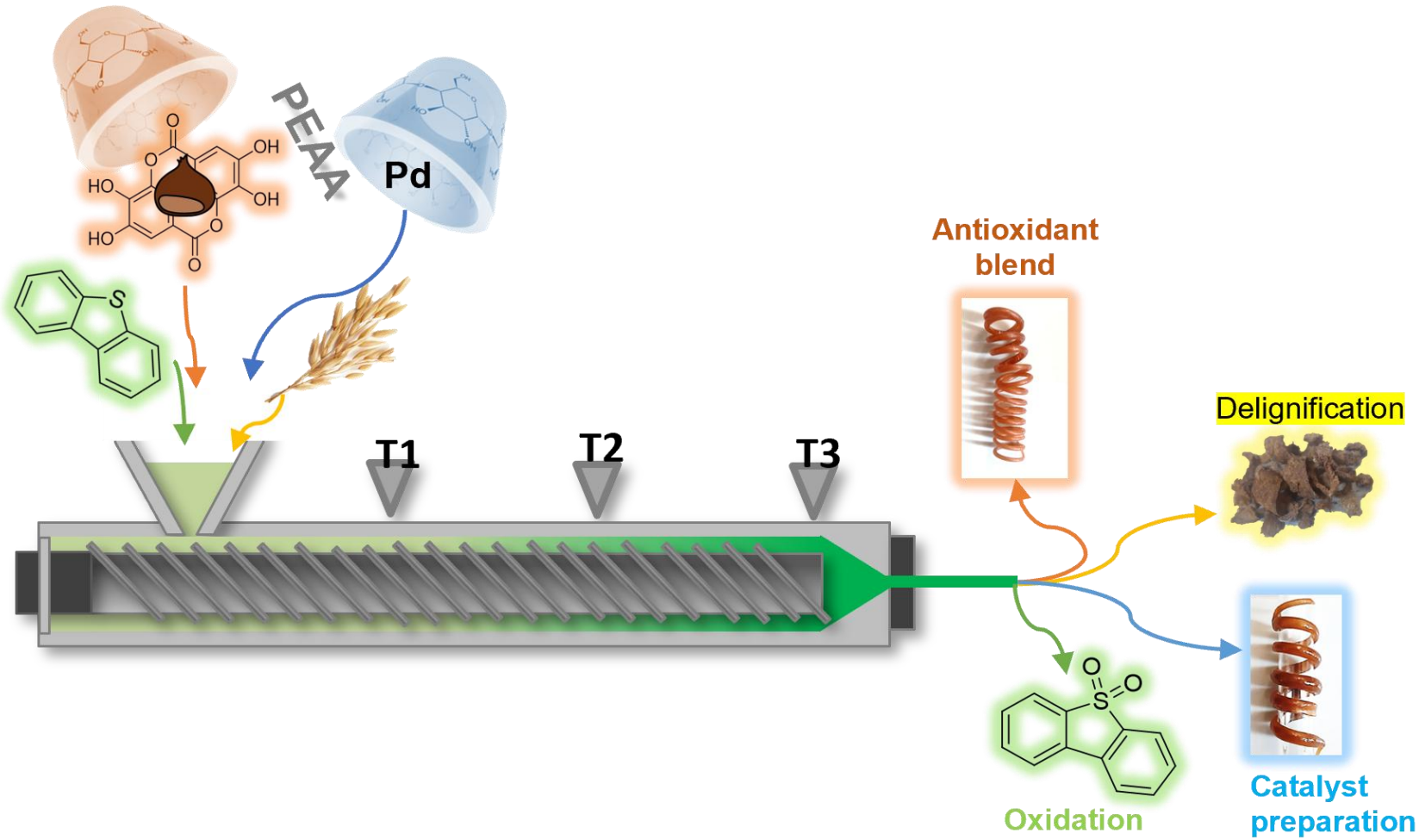
molecules

MDPI

*Molecules* **2022**, 27, 449

*Article*

# Mechanochemical Applications of Reactive Extrusion from Organic Synthesis to Catalytic and Active Materials

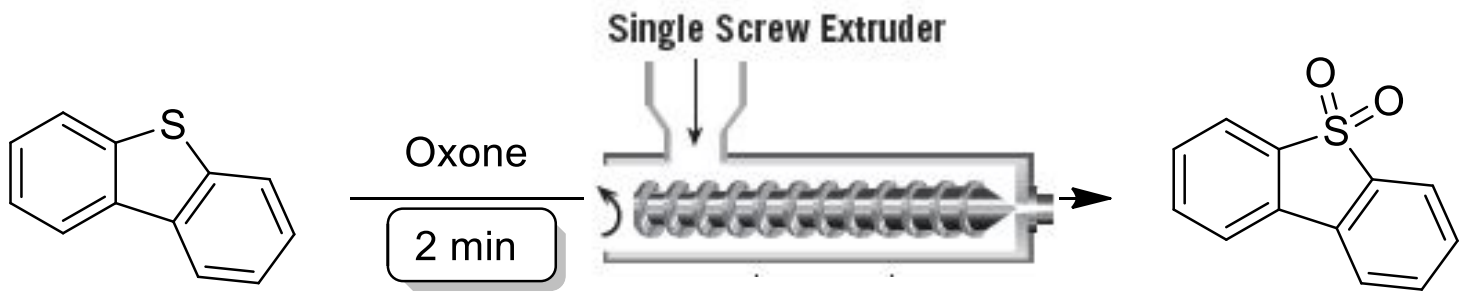


# OXIDATION OF DIBENZOTHIOPHENE

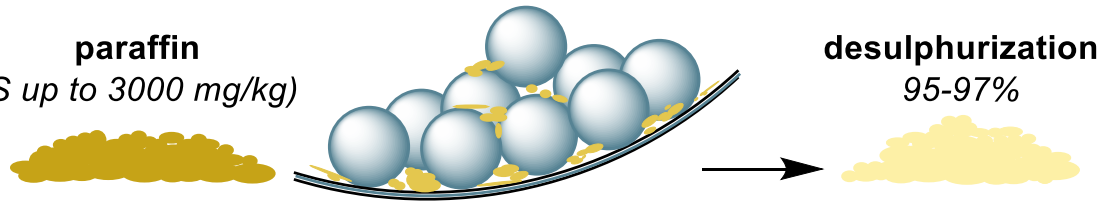
***Cravotto et al 2012***


**5** **6** (99%)

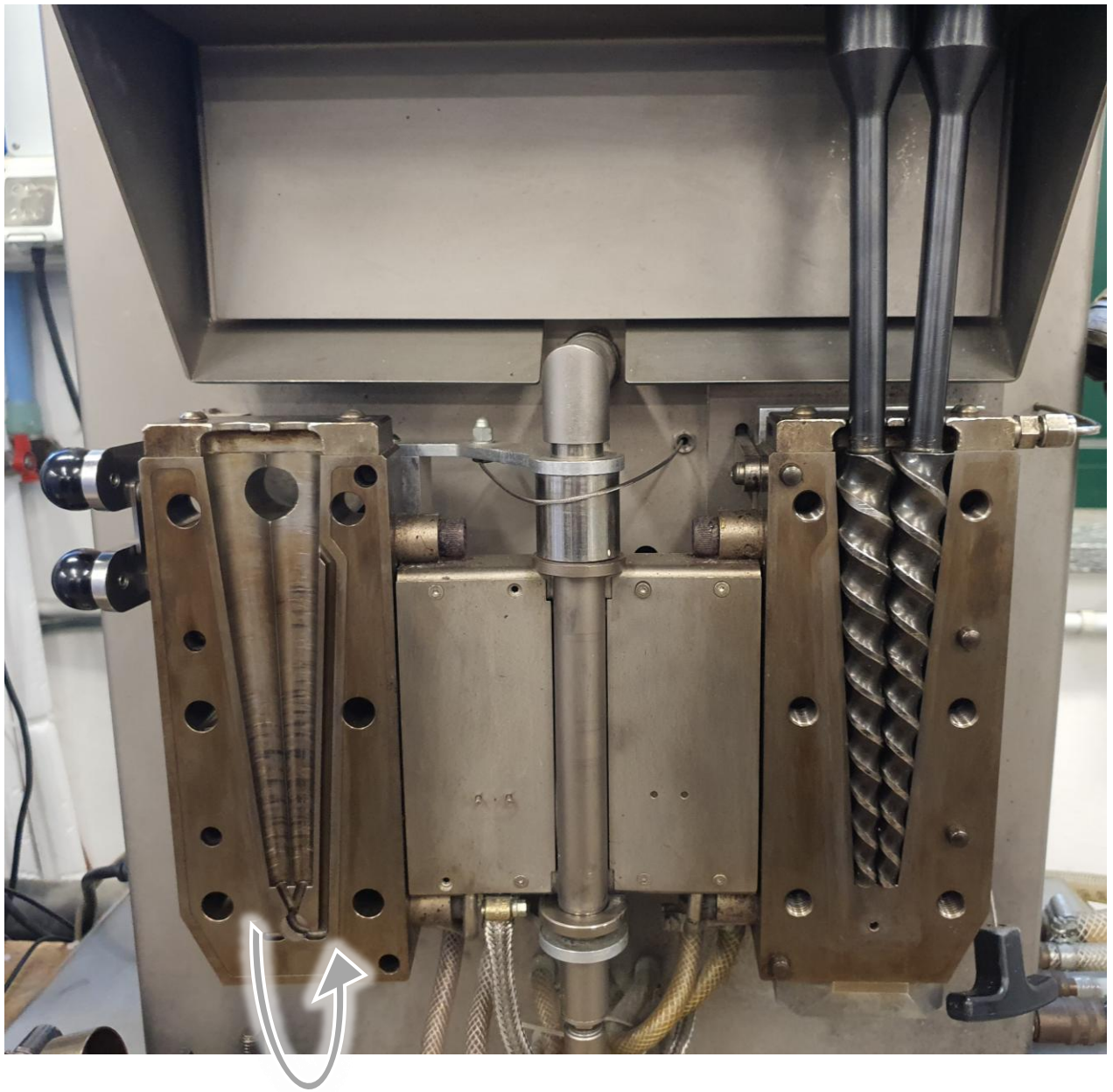
***This work***




**5** **6** (98%)




# TWIN-SCREW EXTRUDER WITH RICYCLE

RSC Mechanochemistry

ROYAL SOCIETY OF CHEMISTRY

REVIEW

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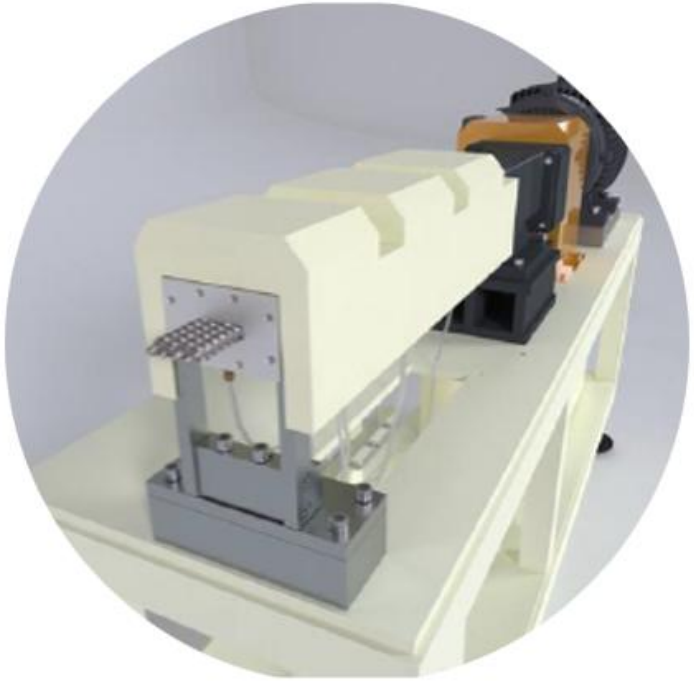
View Journal | View Issue

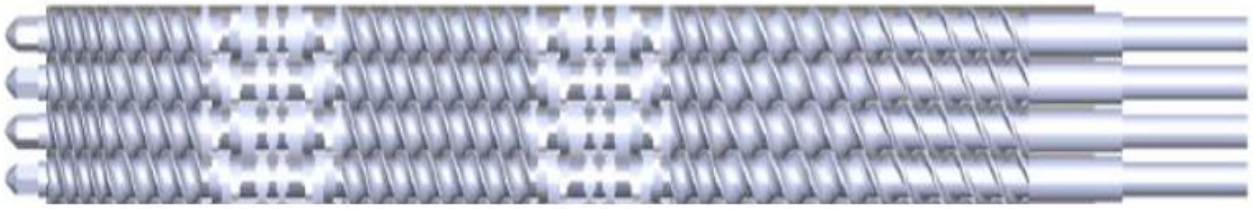


Cite this: *RSC Mechanochem.*, 2026, 3, 144

# Flow-through mechanochemical synthesis by reactive extrusion

Paolo Freisa, [a] Luciano Lattuada, [b] Alessandro Barge [a] and Giancarlo Cravotto *[a]





# MULTI EXTRUDER UNIT

**EXTRUDER 3 - Double screw**

**EXTRUDER 1**

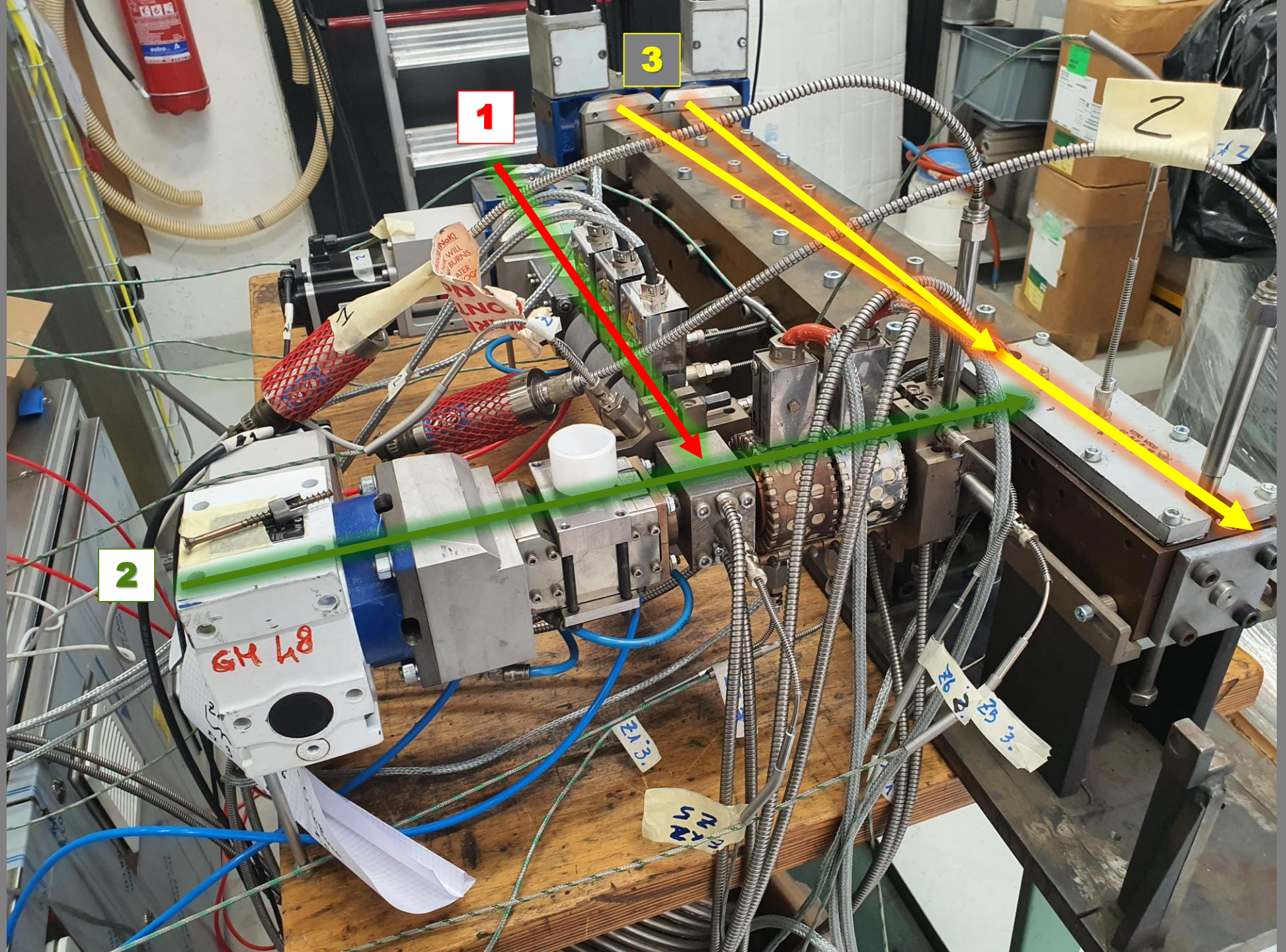
**EXTRUDER 2**



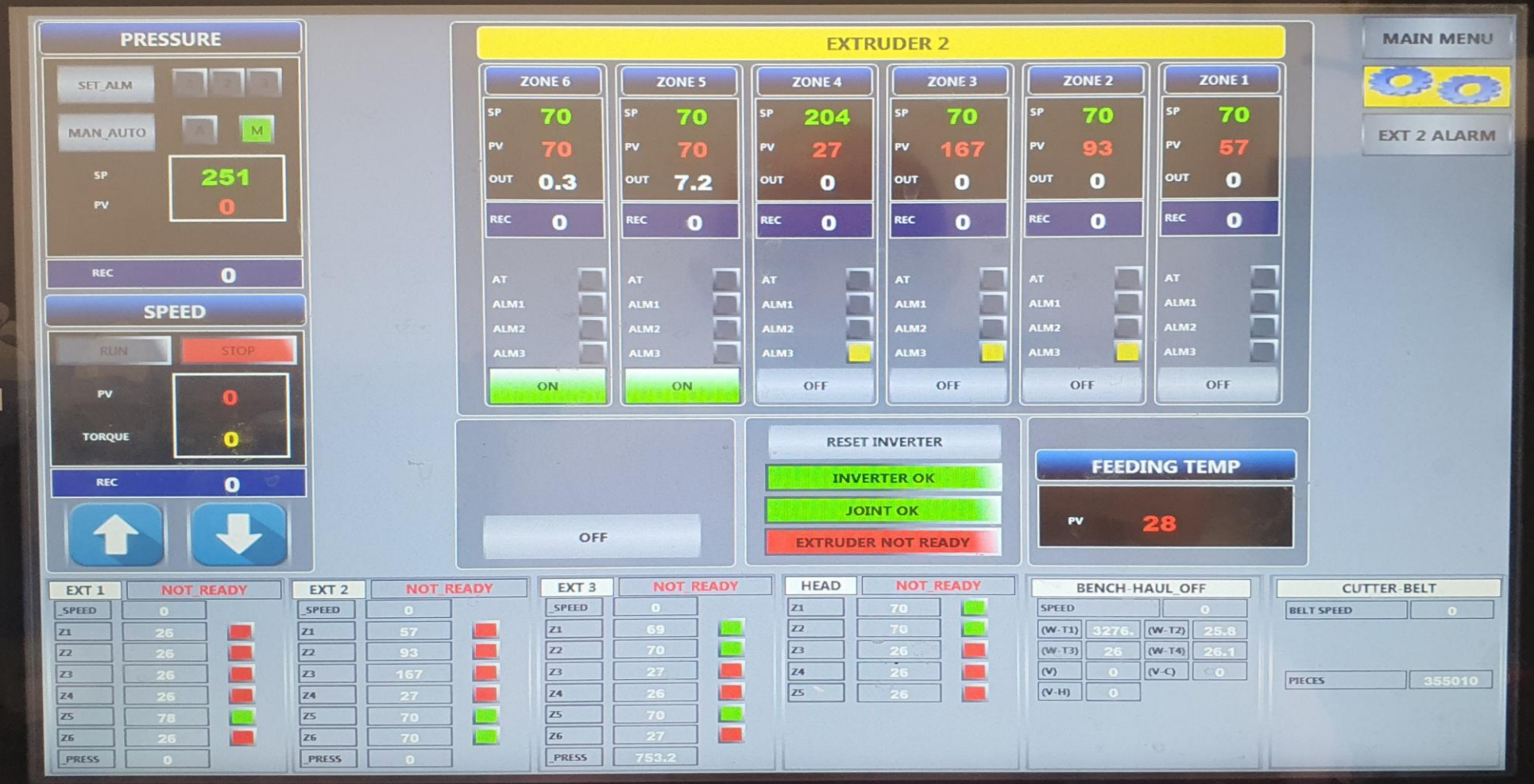

**BETTER MIXING & RESIDENCE TIME**

CONFIDENTIAL

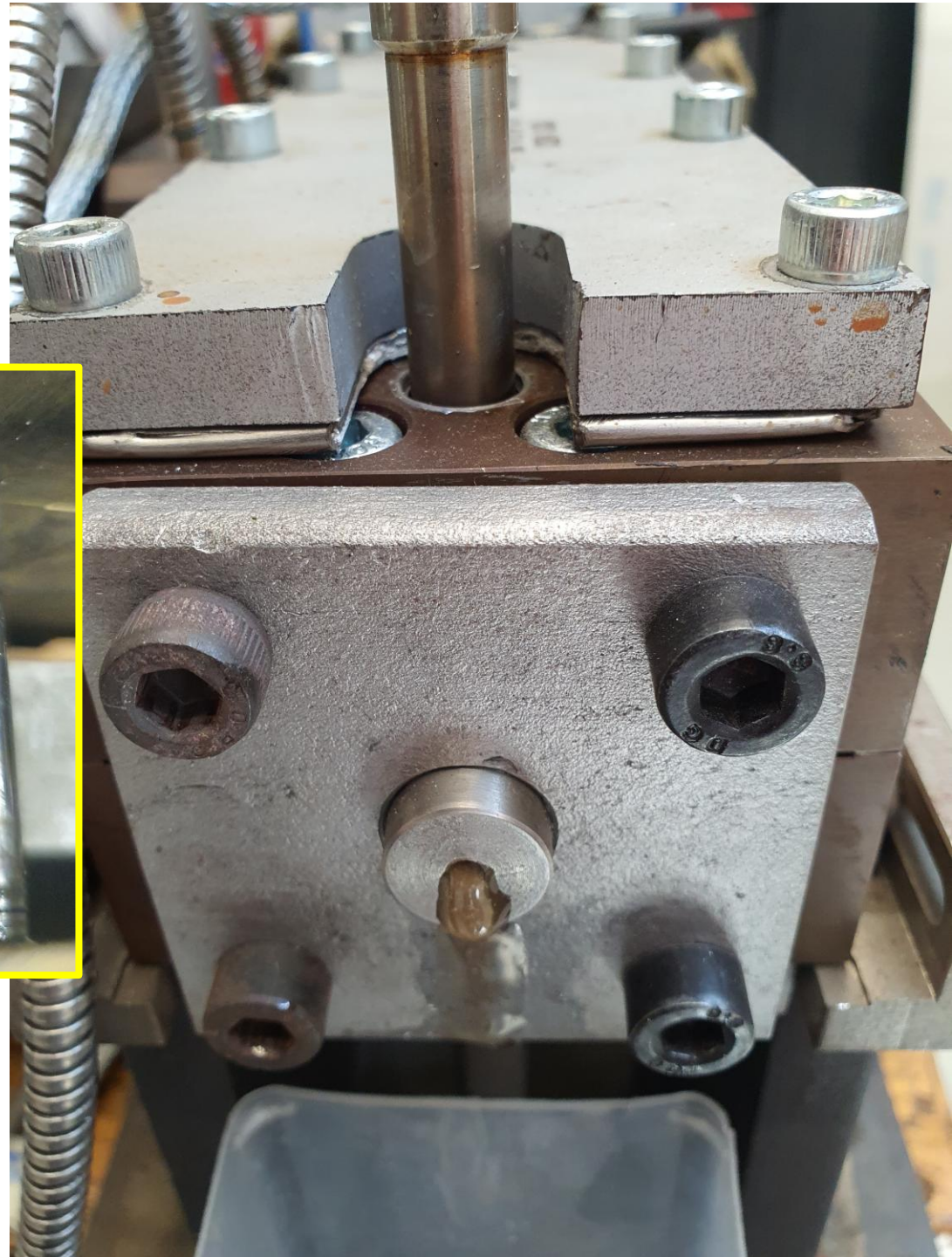
# MULTI EXTRUDER UNIT



# PARAMETERS REGULATION AND MONITORING



# SPECIAL TWIN-SCREW EXTRUDER



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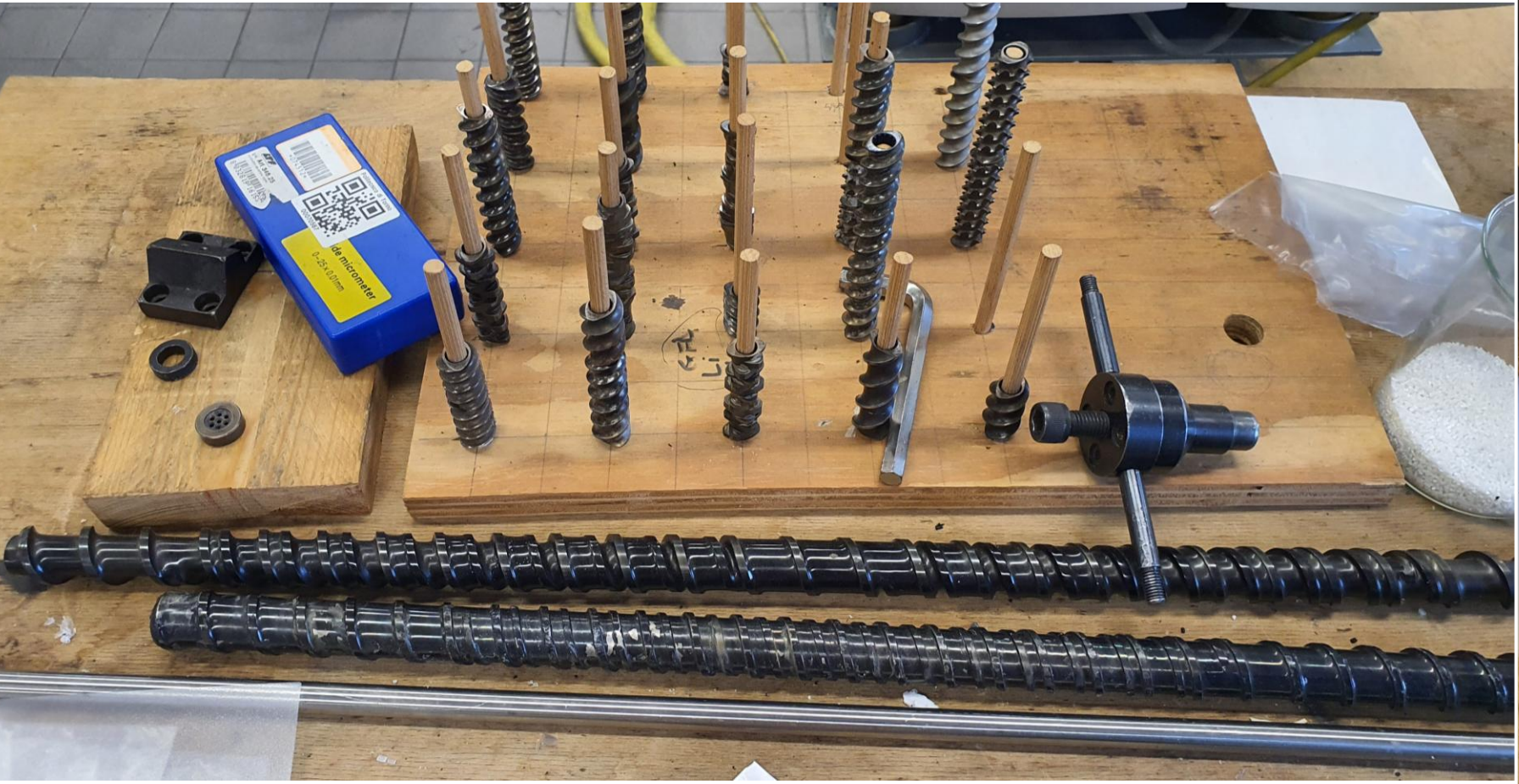

de micrometer


DEMAG
MARIS

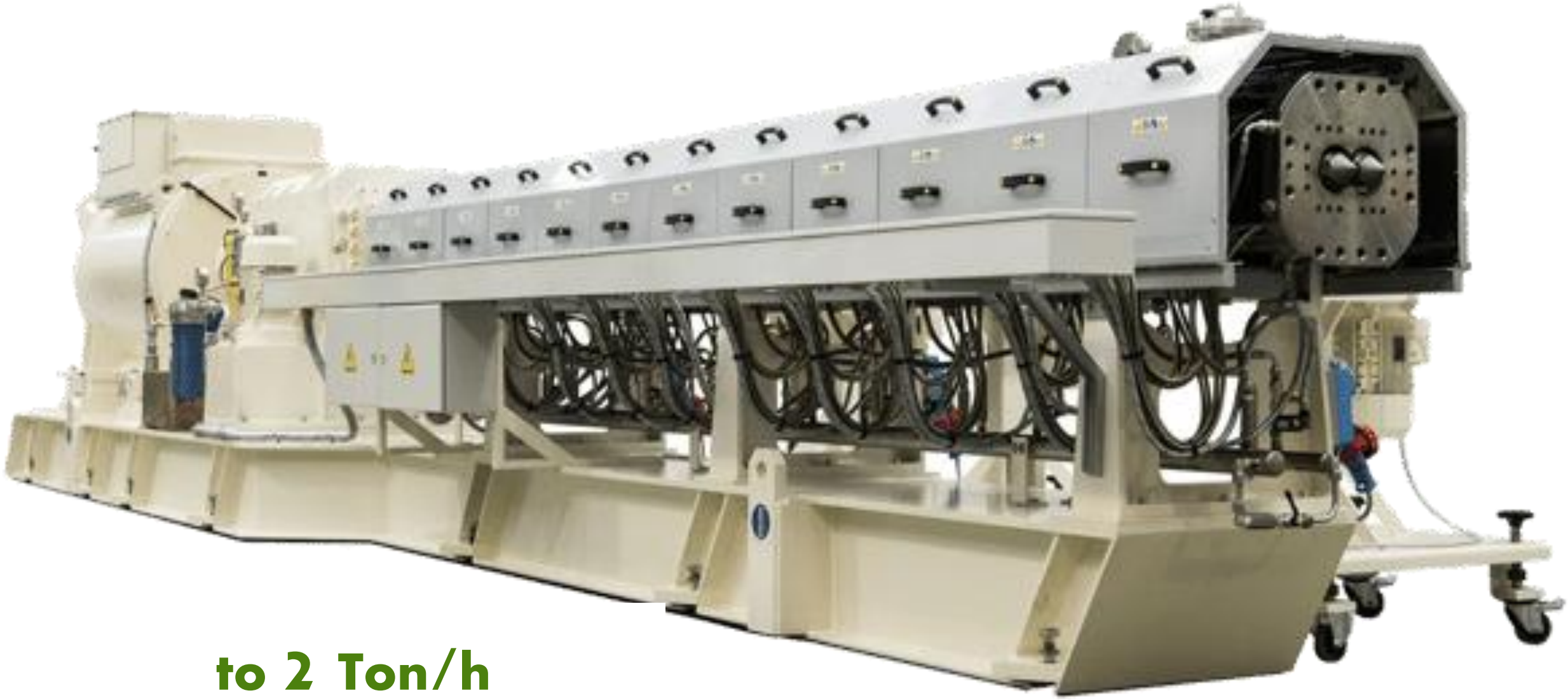
# PILOT TWIN EXTRUDER

**from 10-100 kg/h**



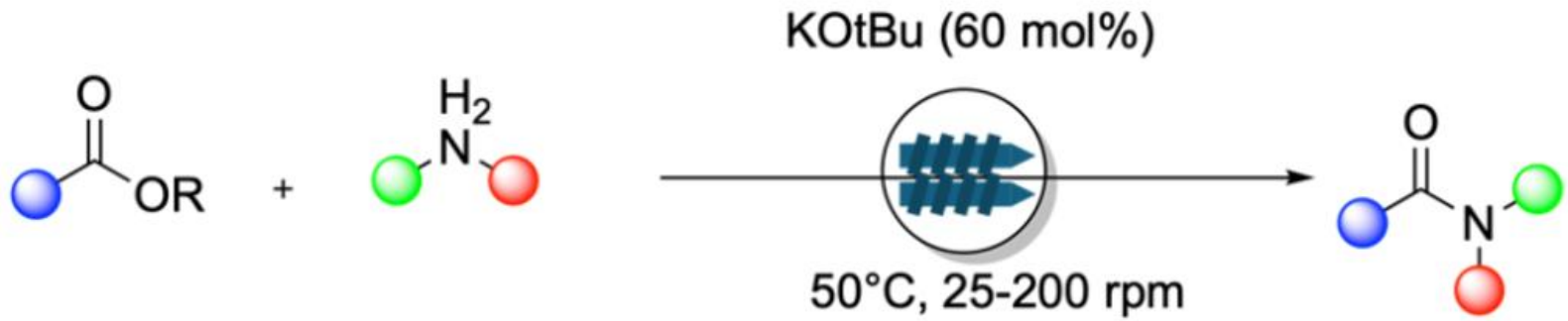

64

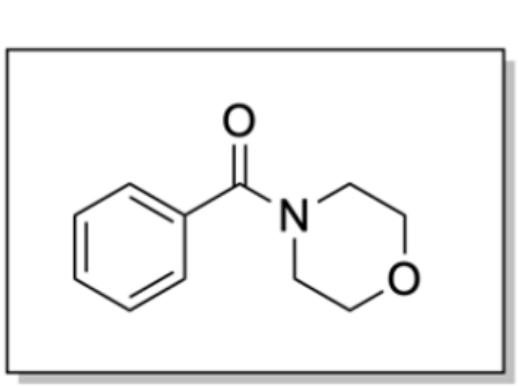
# INDUSTRIAL REACTIVE EXTRUSION



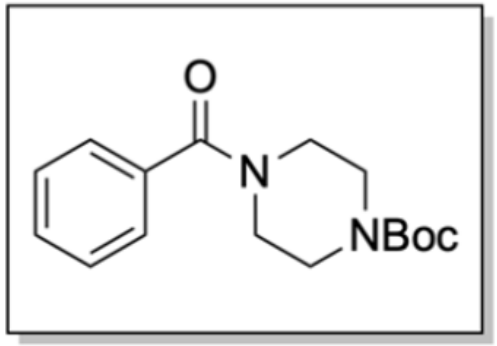
**to 2 Ton/h**

# AMIDATION REACTION FROM ESTERS (COUPLING-AGENT FREE)

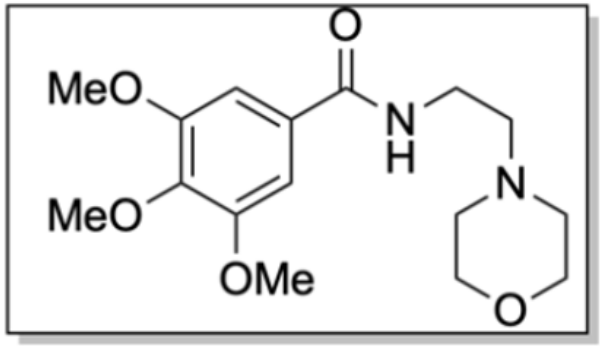


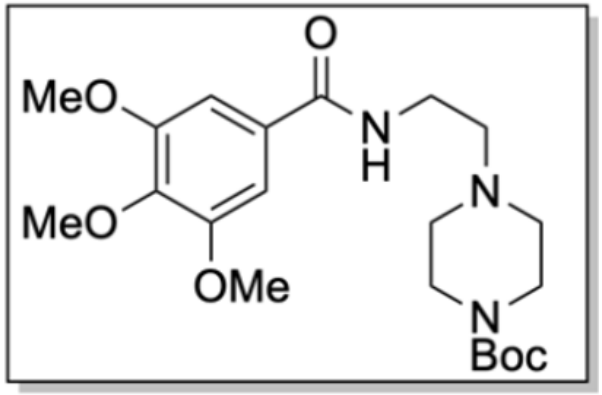

50 rpm, 96% yield




100 rpm, 93% yield




25 rpm, 78% yield



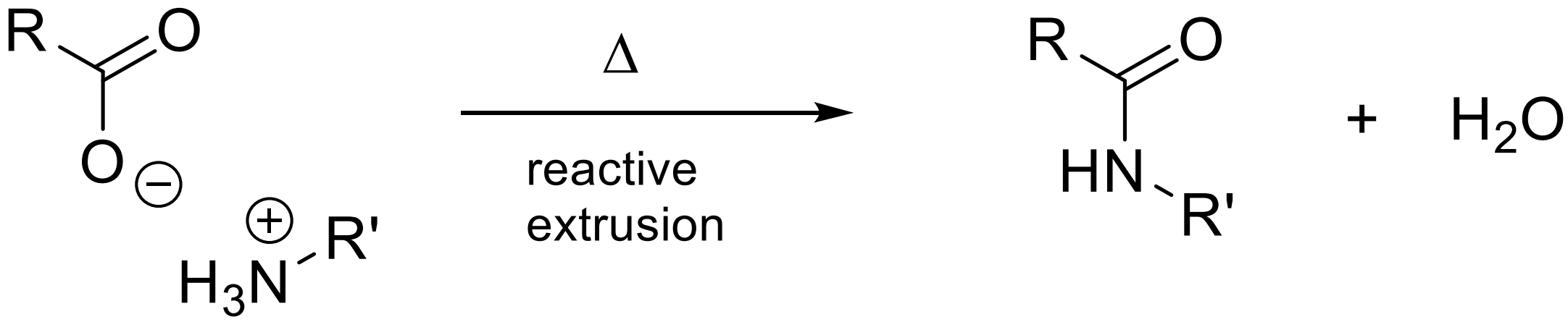

200 rpm, 81% yield

= Conveying

= 30° forward kneading zone

= 90° alternating kneading zone

# DIRECT AMIDATION BY REACTIVE EXTRUSION

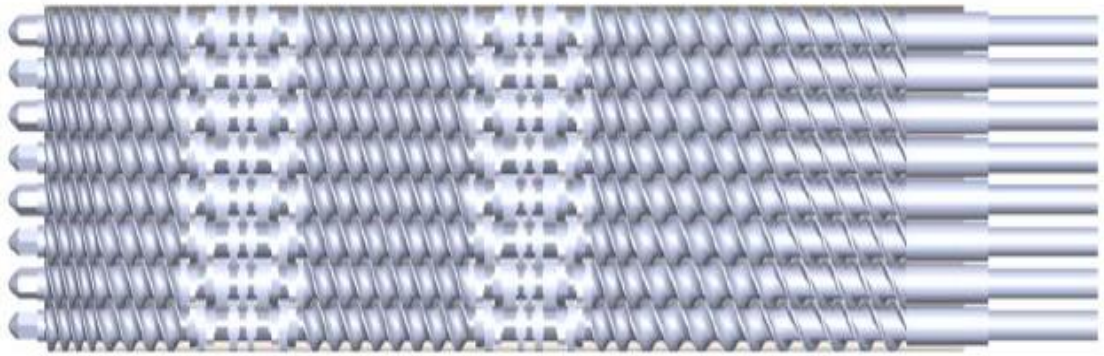



- Solvent-free reaction
- NO acyl chlorides
- NO activators
- Effective control of reaction (residence) times and temperature
- Efficient heat transfer
- Effective elimination of water produced

# HOW TO EXTEND THE RESIDENCE TIME?

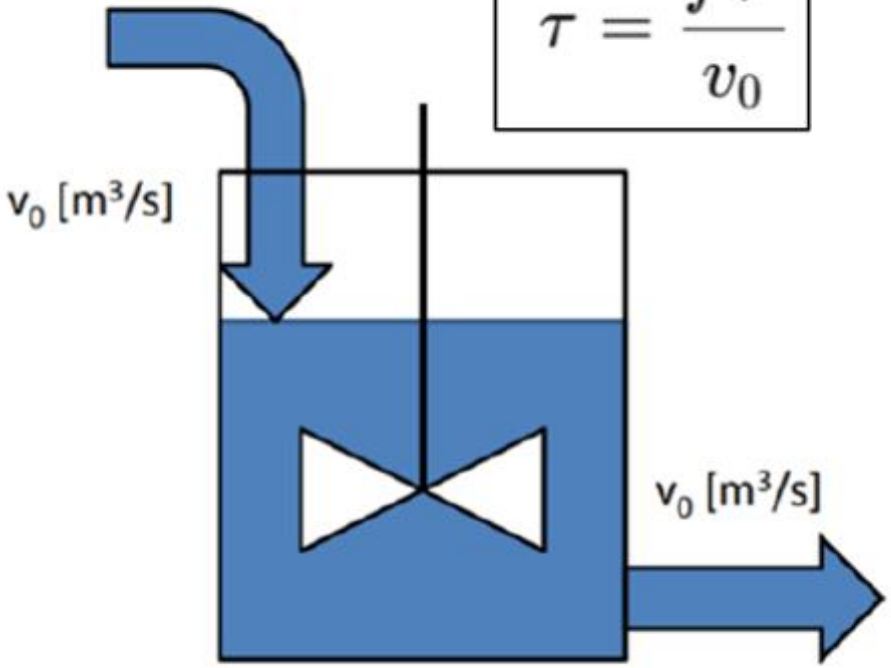
**LONGER SCREW LENGTH**

**INCREASE SCREW NUMBER**



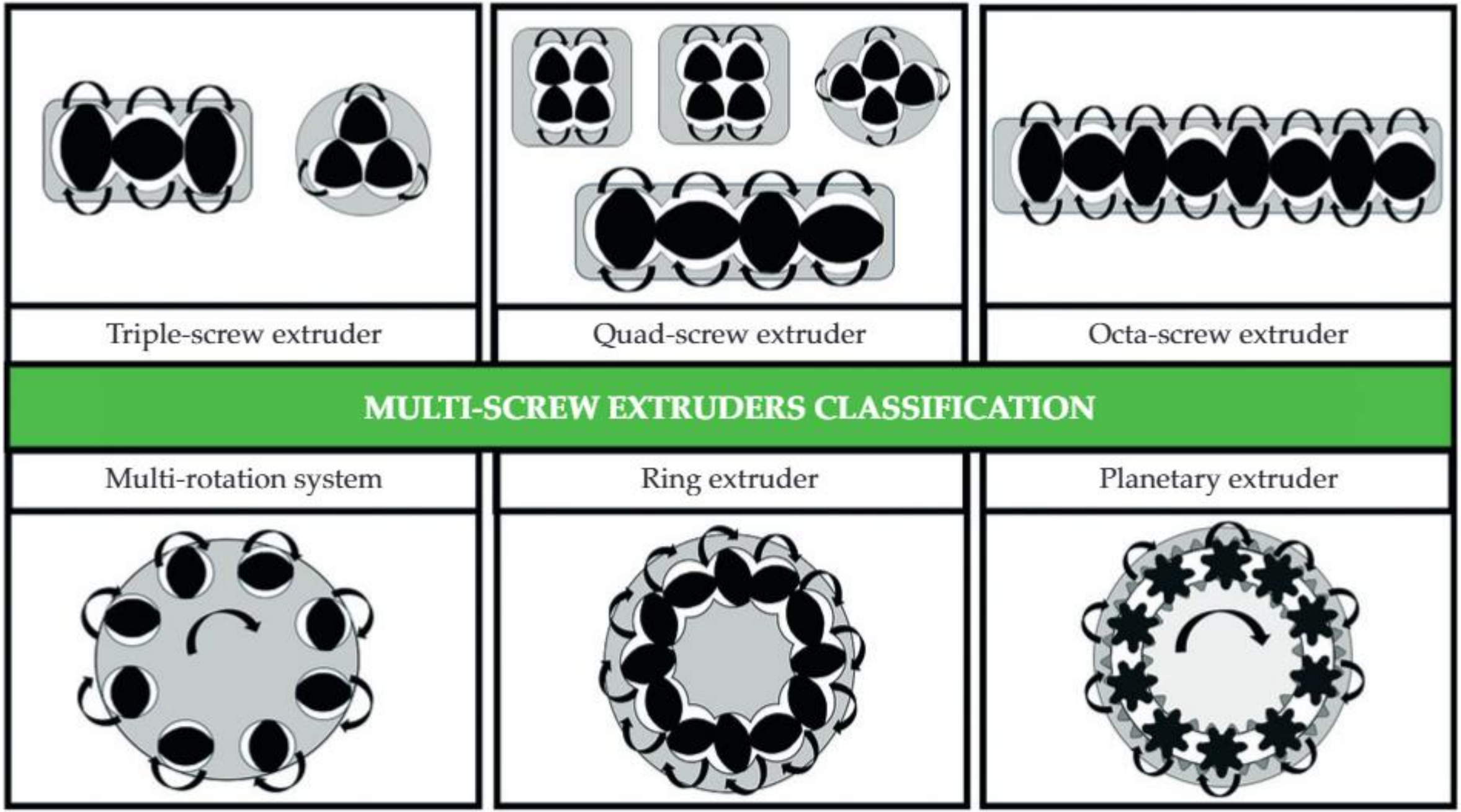
# HOW TO EXTEND THE RESIDENCE TIME?

$$\tau = \frac{fV}{v_0}$$




- $v_0$ [m³/s]: Feed rate
- $v_0$ [m³/s]: Discharge rate
- $V$ [m³]: Volume between the barrel and the screw
- $f$ [-]: Filling factor

**↑V ↑f = ↑Residence Time**




General classification of multi-screw extruders

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

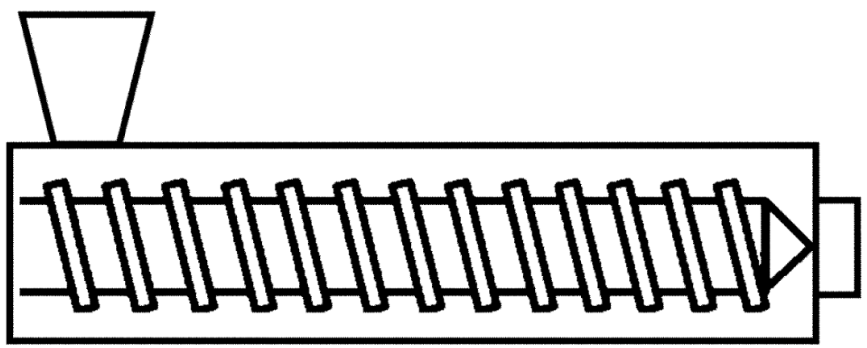
(19) World Intellectual Property Organization
International Bureau

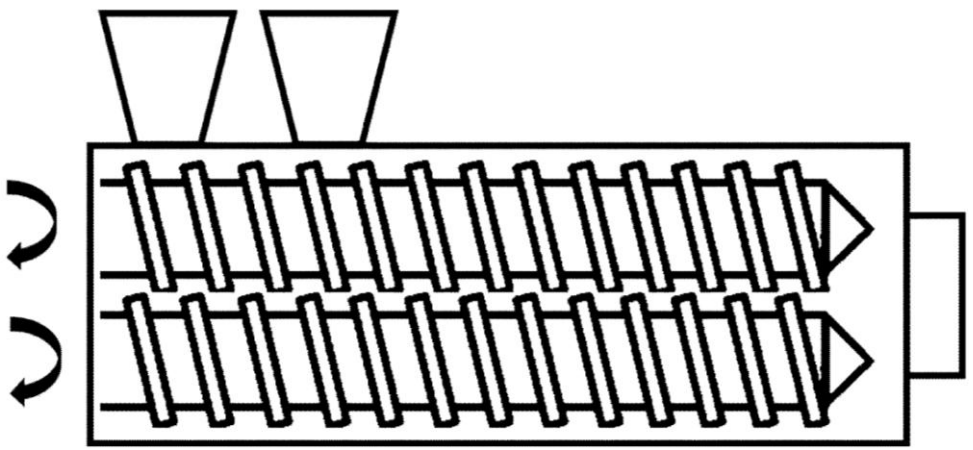
(43) International Publication Date
19 December 2024 (19.12.2024)

WIPO | PCT

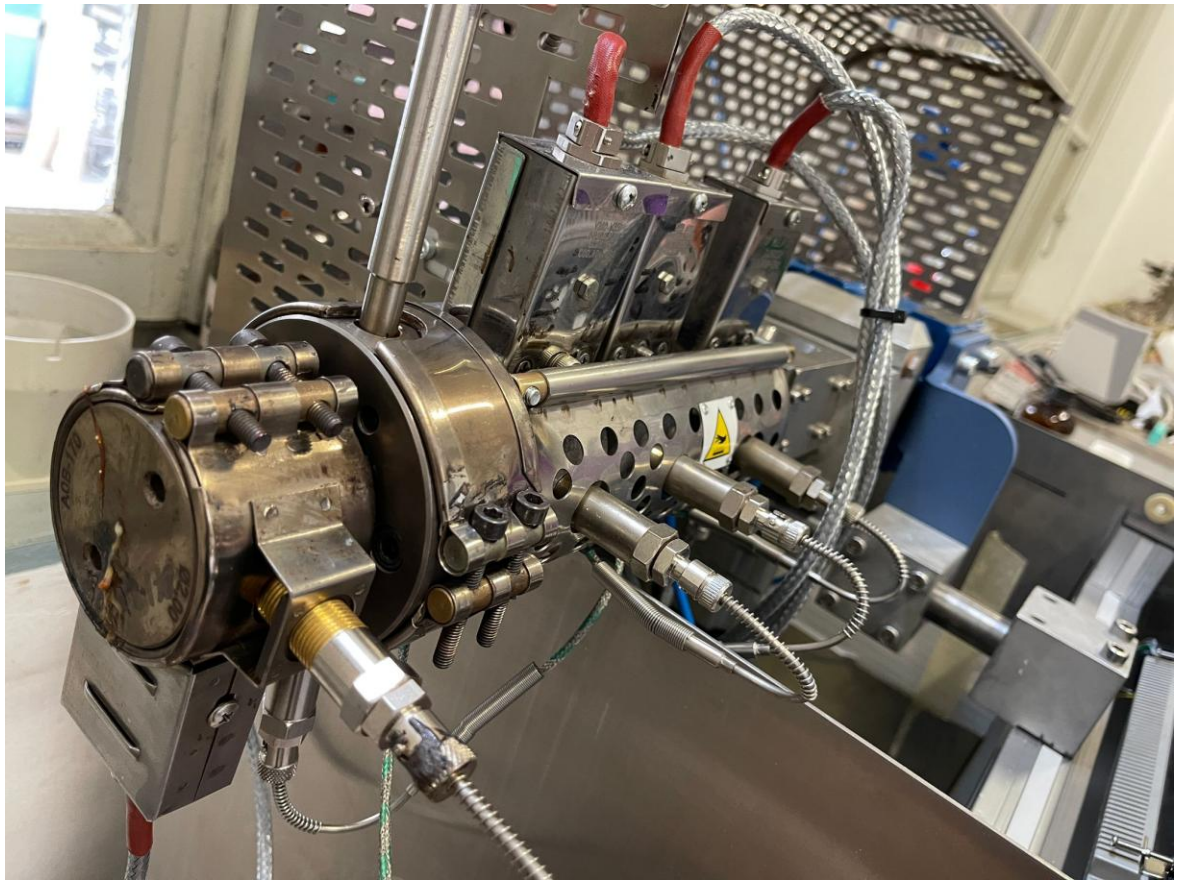
(10) International Publication Number
WO 2024/256322 A1

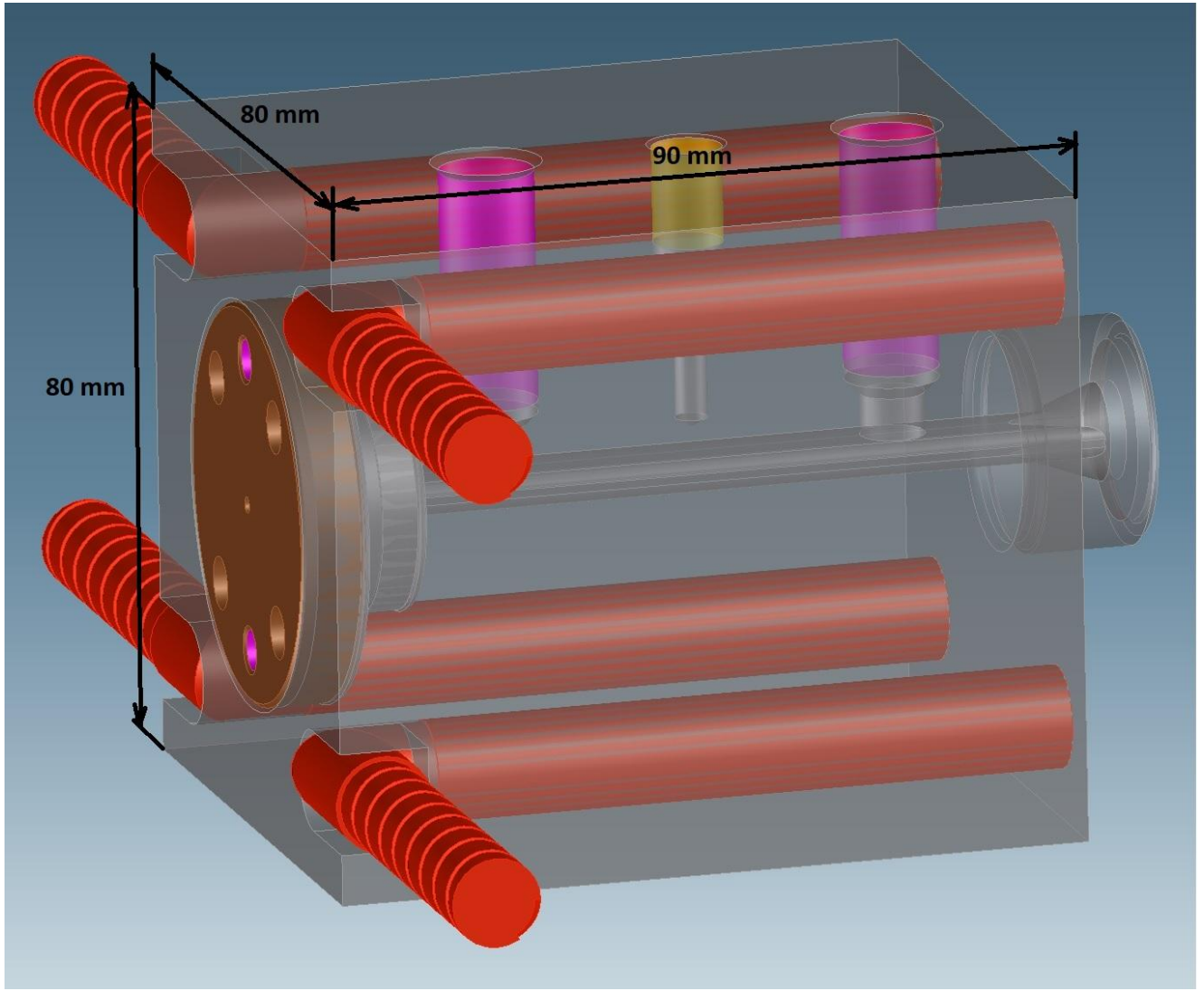
# Title: SYNTHESIS OF NON-IONIC RADIOGRAPHIC CONTRAST AGENTS BY MEANS OF REACTIVE EXTRUSION



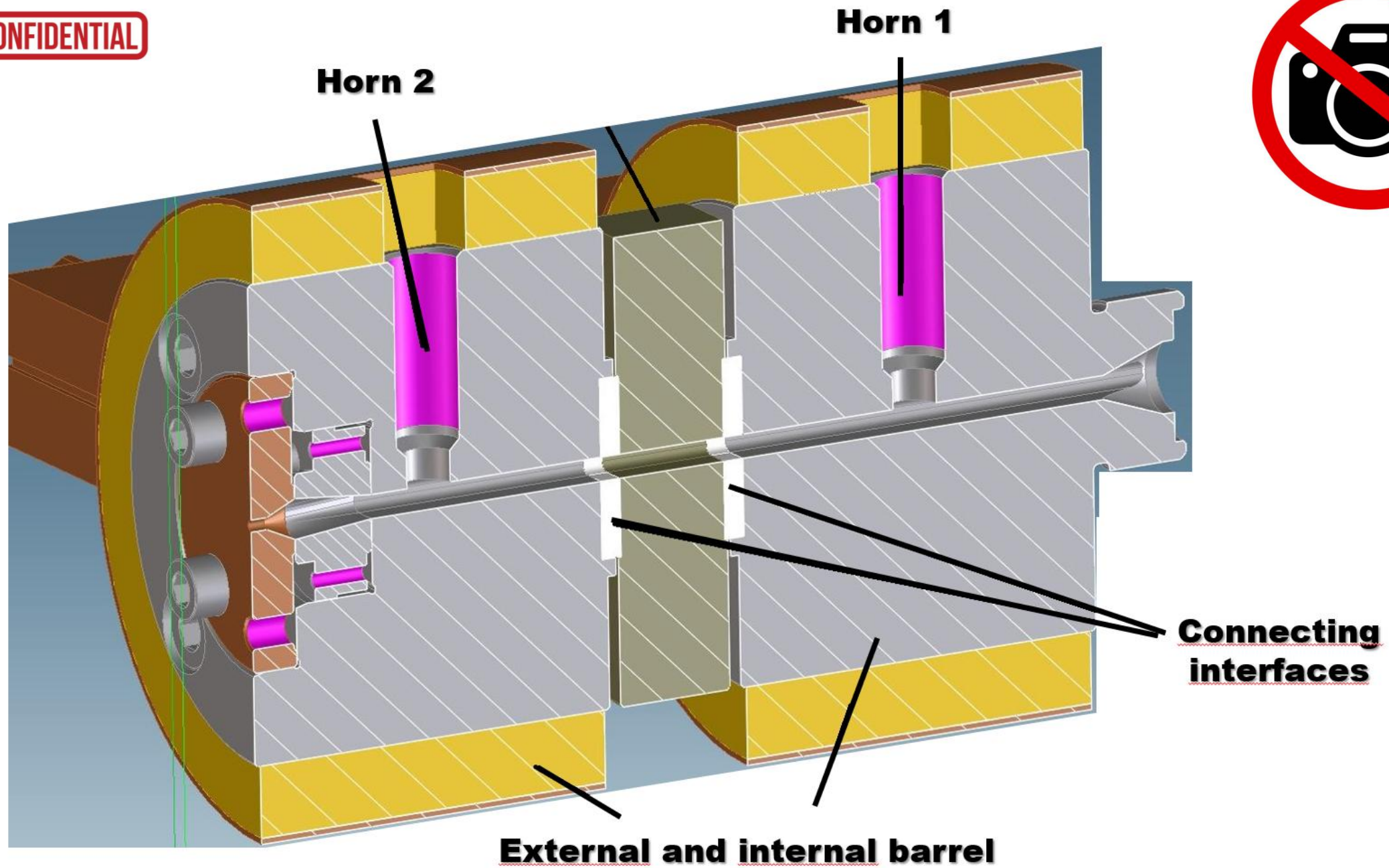


# ULTRASOUND-ASSISTED EXTRUSION

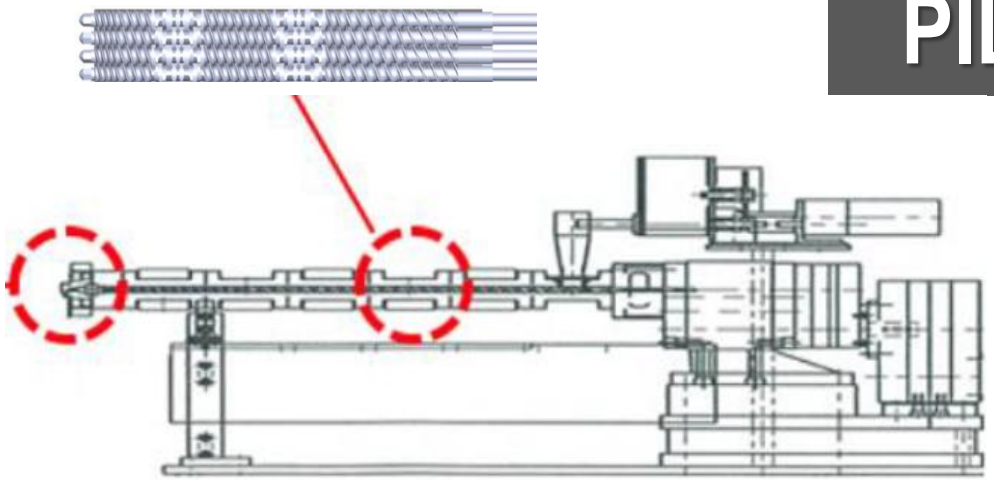


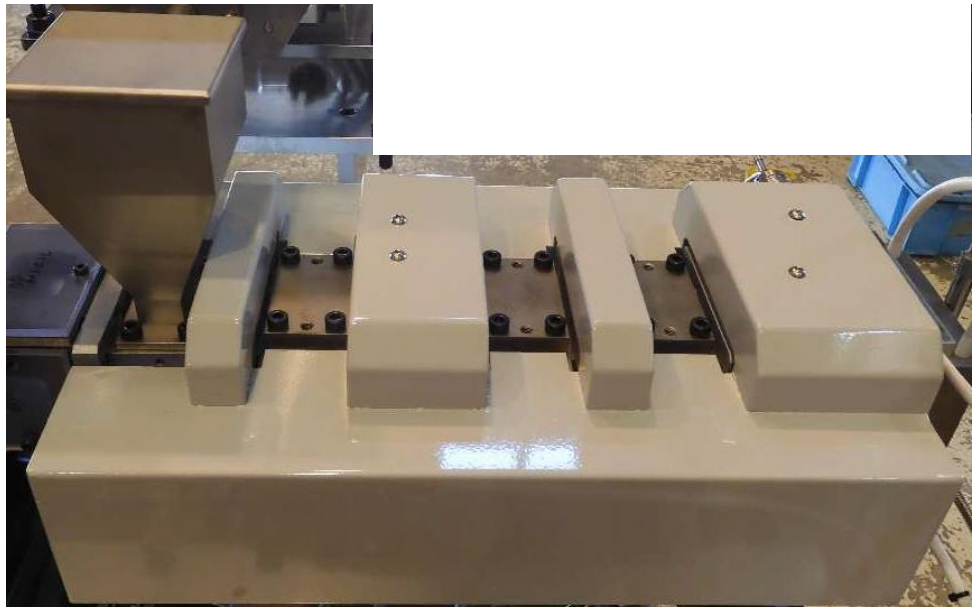


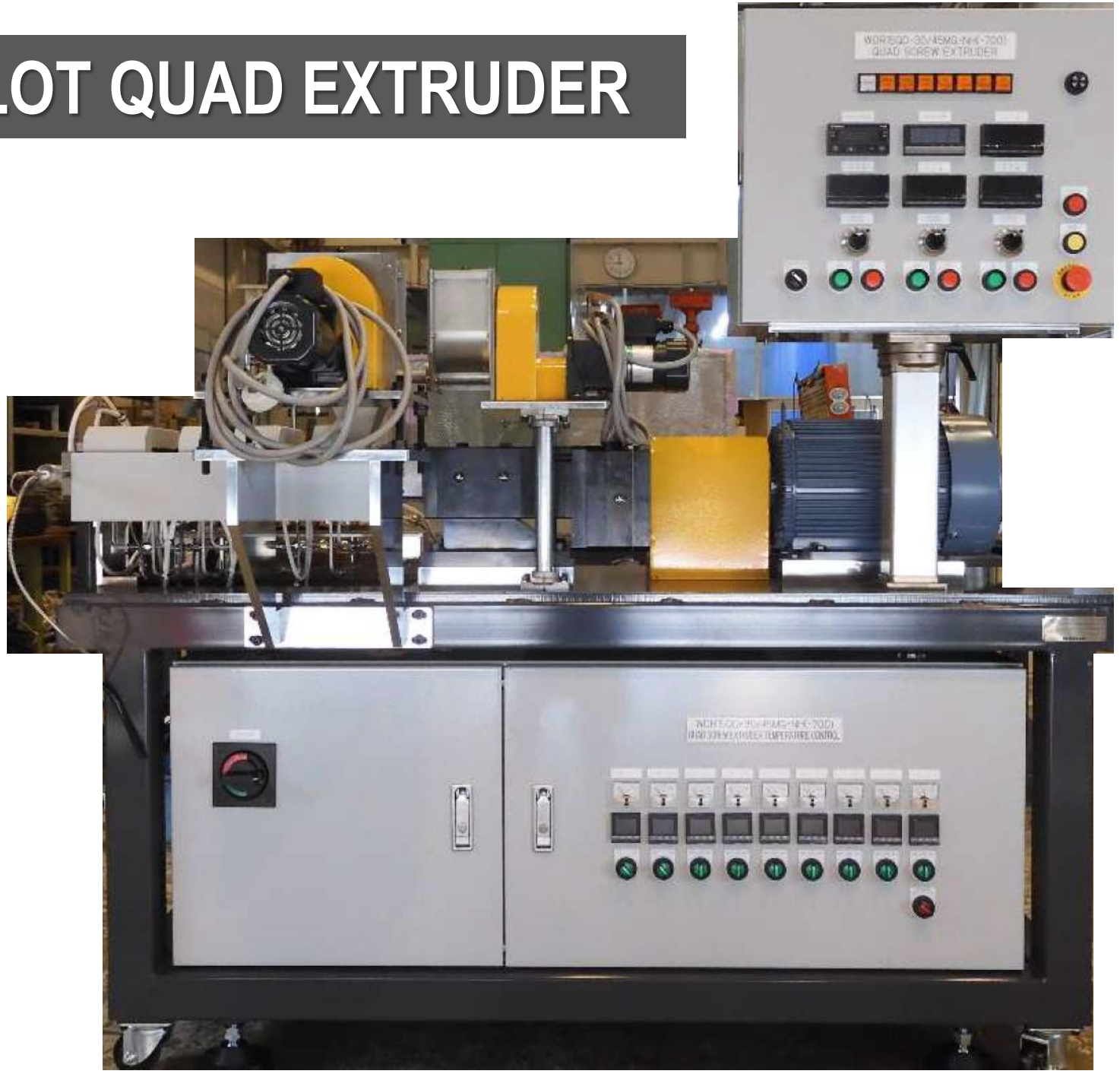
CONFIDENTIAL



# PILOT QUAD EXTRUDER







**Paolo Freisa**
PhD student

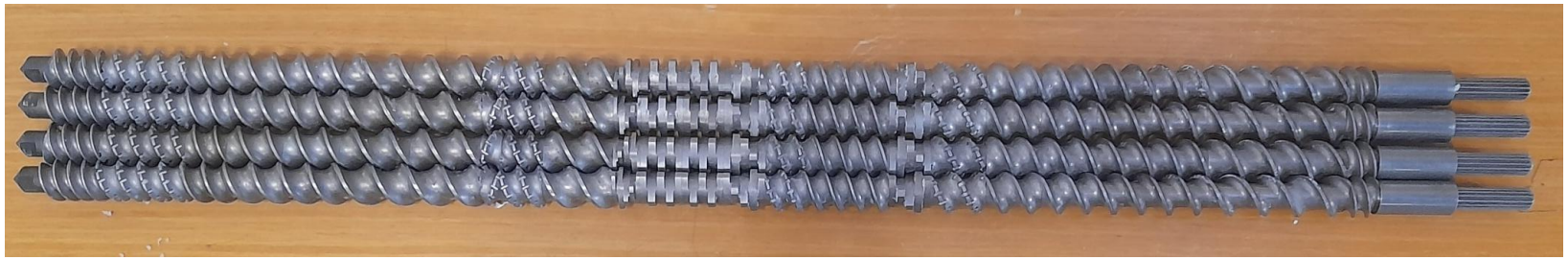
**Alessandro Barge**
Associate Professor

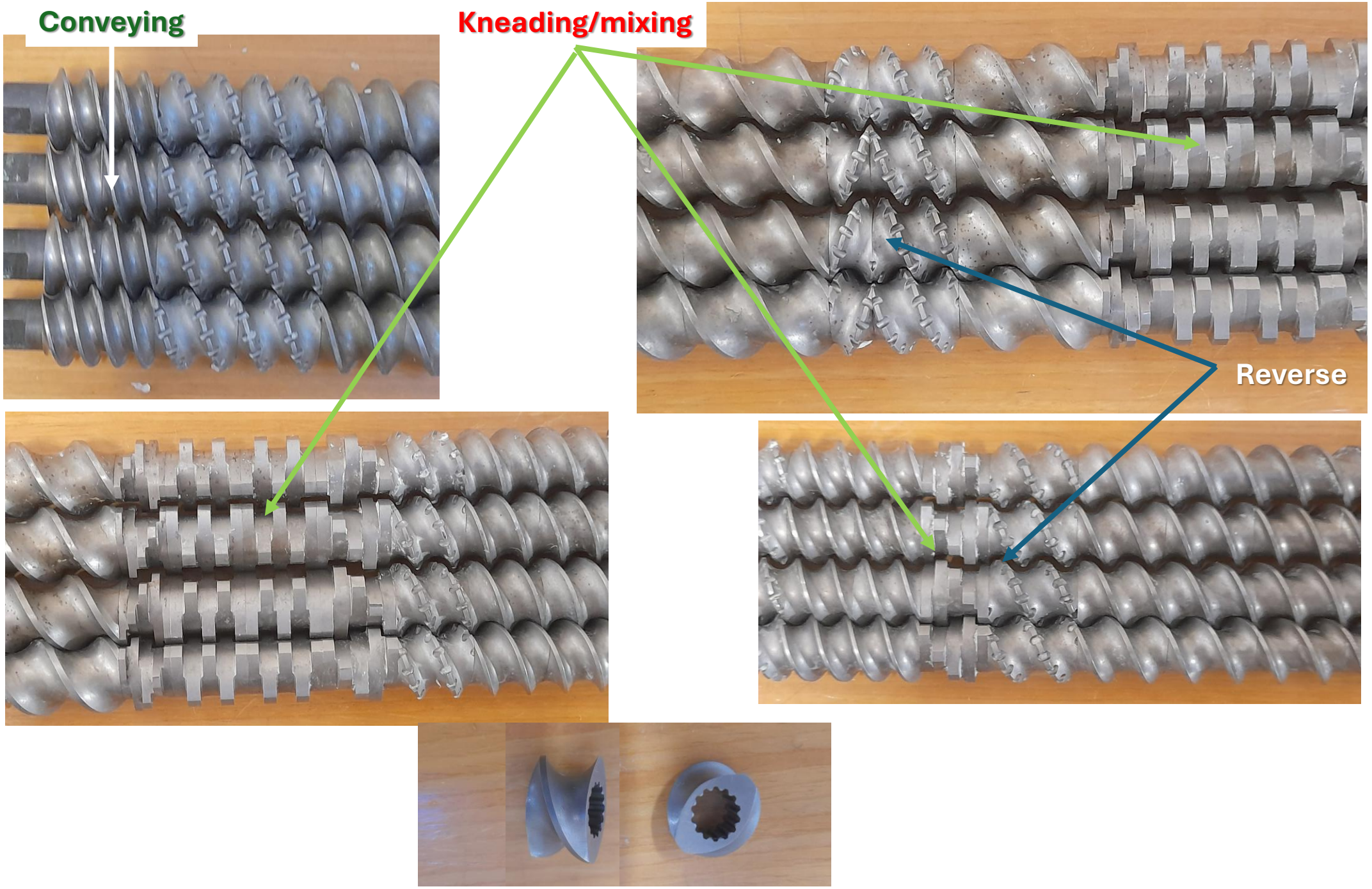
**Chiara Scarpa**
PhD candidate

# PILOT QUAD EXTRUDER

The **residence time** in the extruder, as well as the **mechanical effects** exerted, depends on three factors: the **speed at which the extruder screws rotate**, **the quantity of product fed in**, and the **geometry of the screws**.

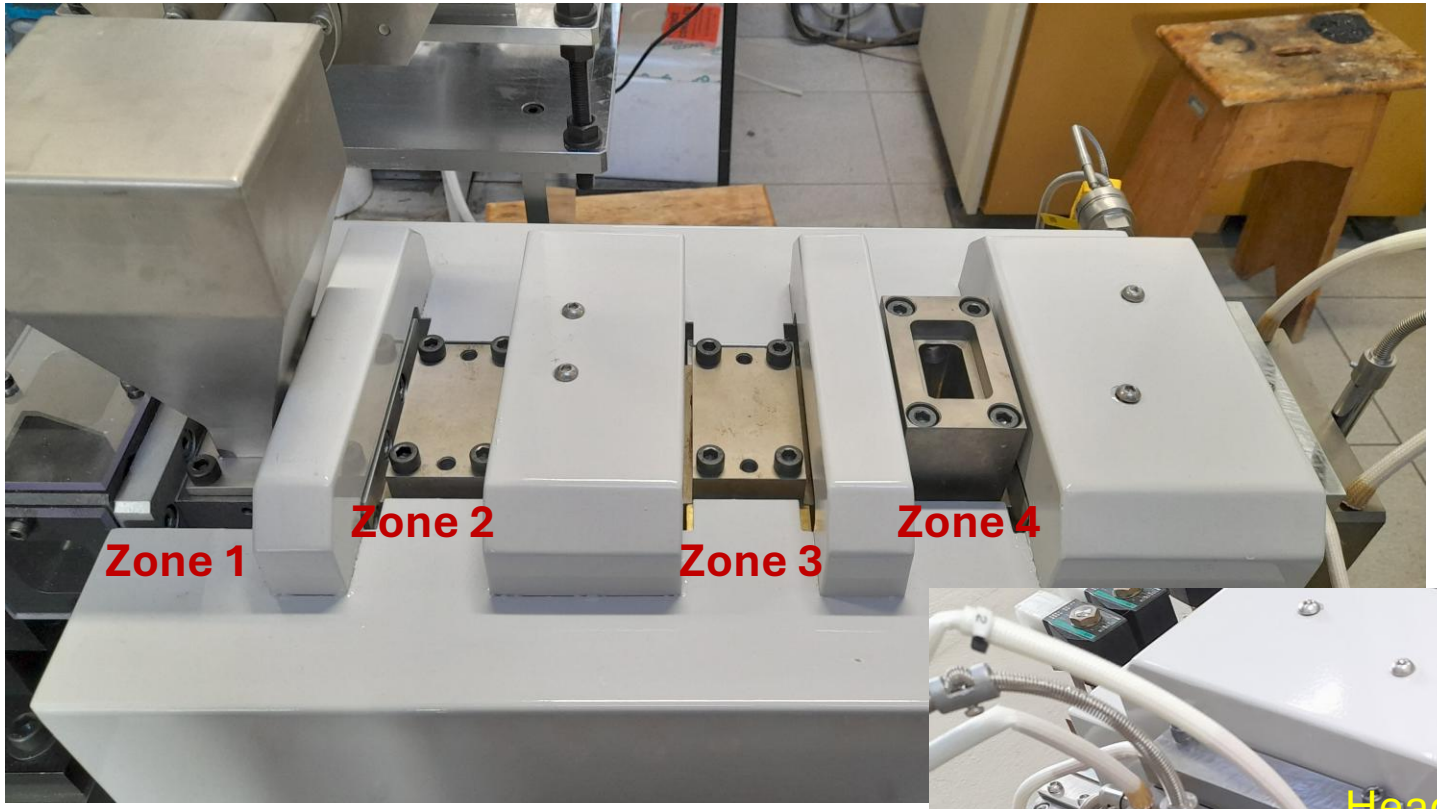
- **The geometry of the screws remains unchanged.**
- **The speed of the extruder screw has been changed**
- **The amount of mixture fed in has been changed**

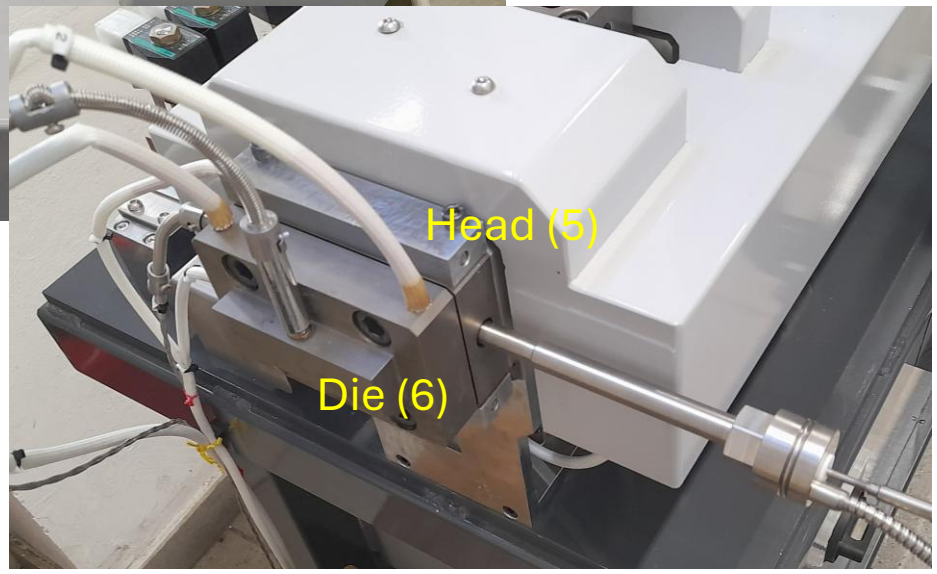



Conveying
Kneading/mixing
Reverse

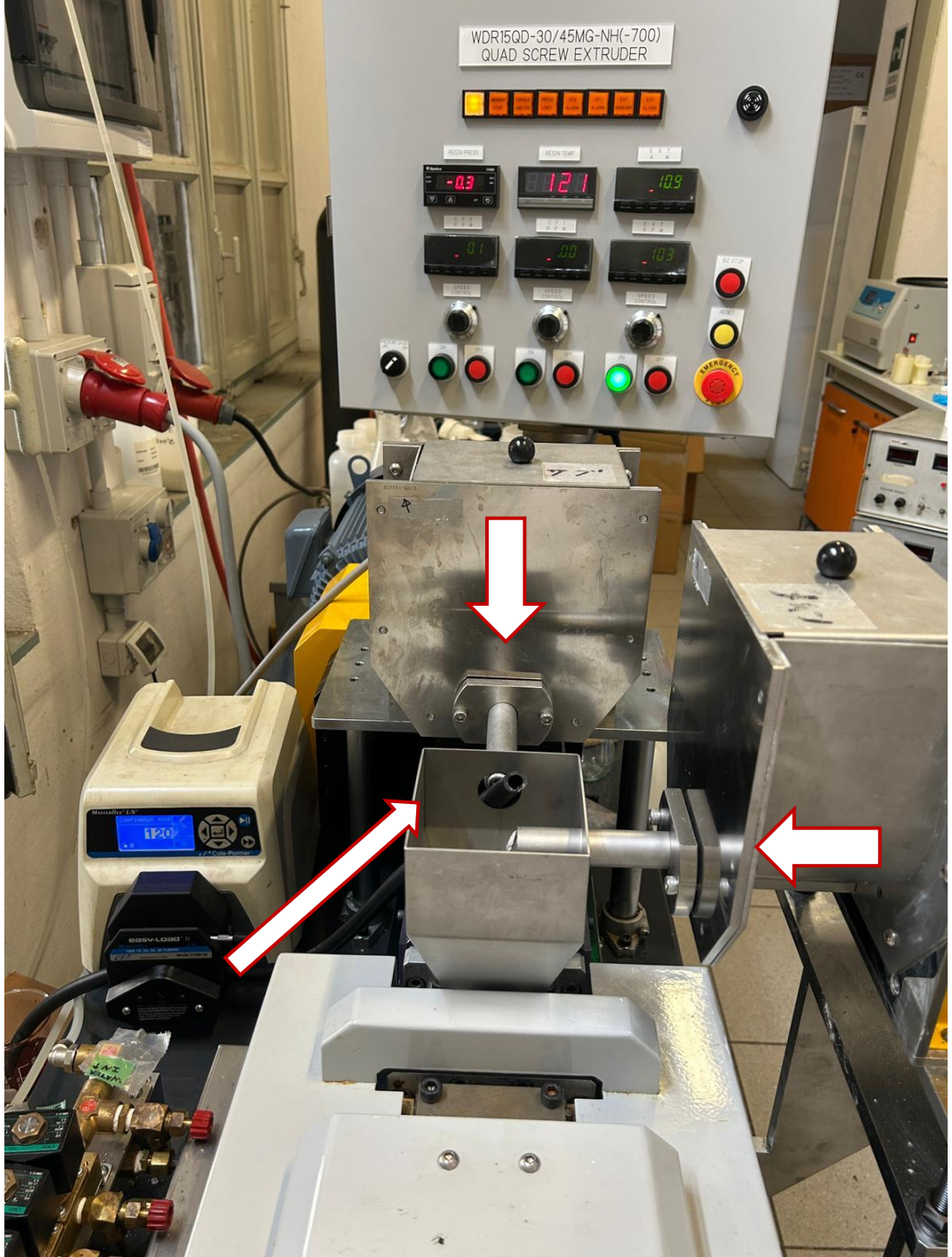
**Two independent feeders allow the mixture components to be introduced in accordance with predefined stoichiometric ratios.**

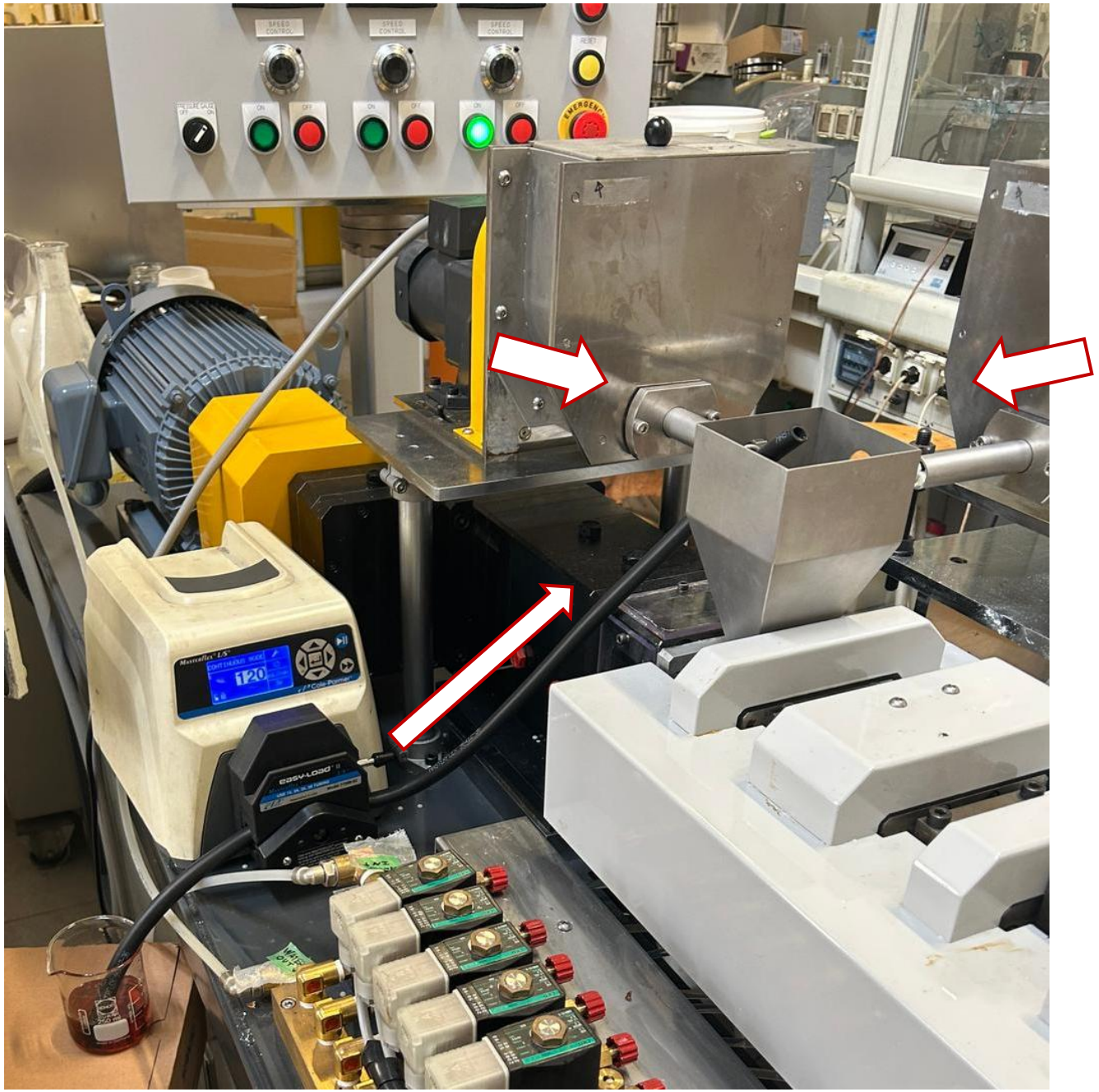
**The feed rate affects the mechanical forces and residence time in the extruder.**



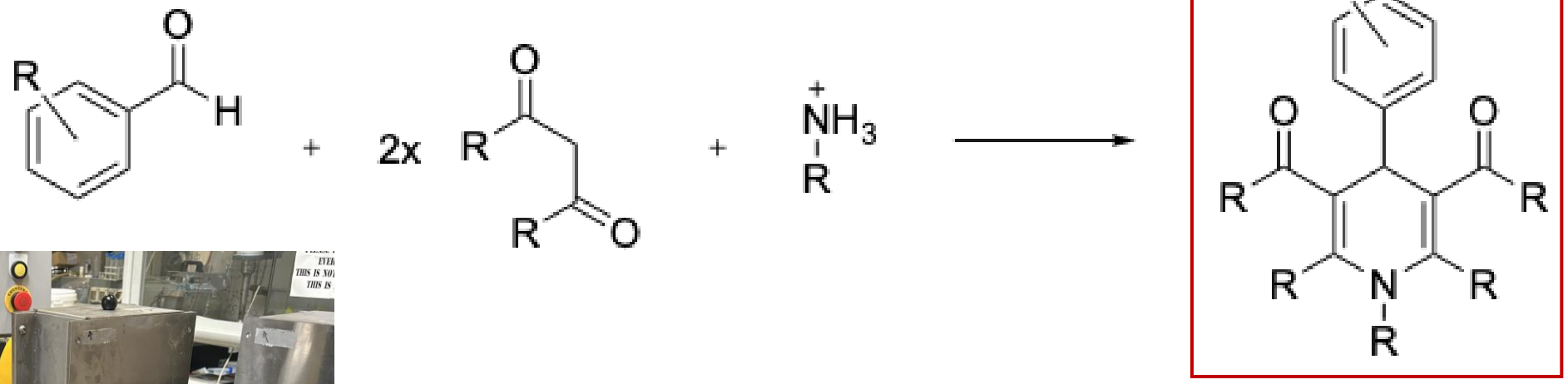

**The temperature can be controlled across six independent zones. Four of these zones cover the entire length of the screws, while the remaining two are dedicated to the head and die at the end of the tool.**


WDR15QD-30/45MG-NH(-700)
QUAD SCREW EXTRUDER



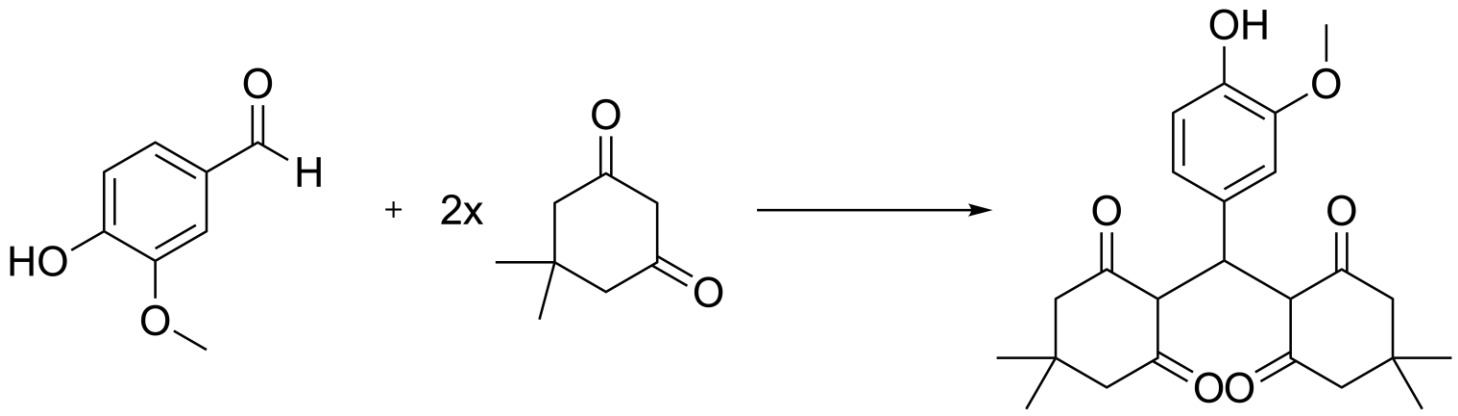
# MULTICOMPONENT REACTION

## Quad extruder



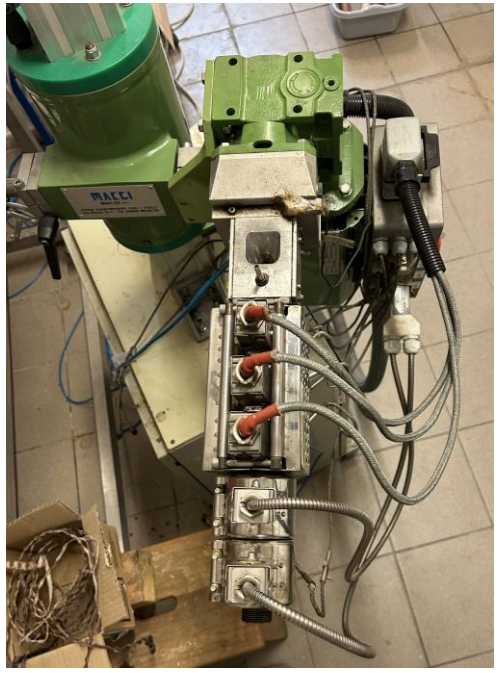

- Temperatures of the 6 zones: **100, 140, 140, 140, 140, 140 °C**
- Screw speed: 200 rpm (Time of residence: < 5 min)
- **Solvent or liquid-assisted grinding not required**
- **Solid reagents introduced by independent feeders and the liquid with a peristaltic pump**

# Knoevenagel condensation and Michael addition of vanillin with dimedone

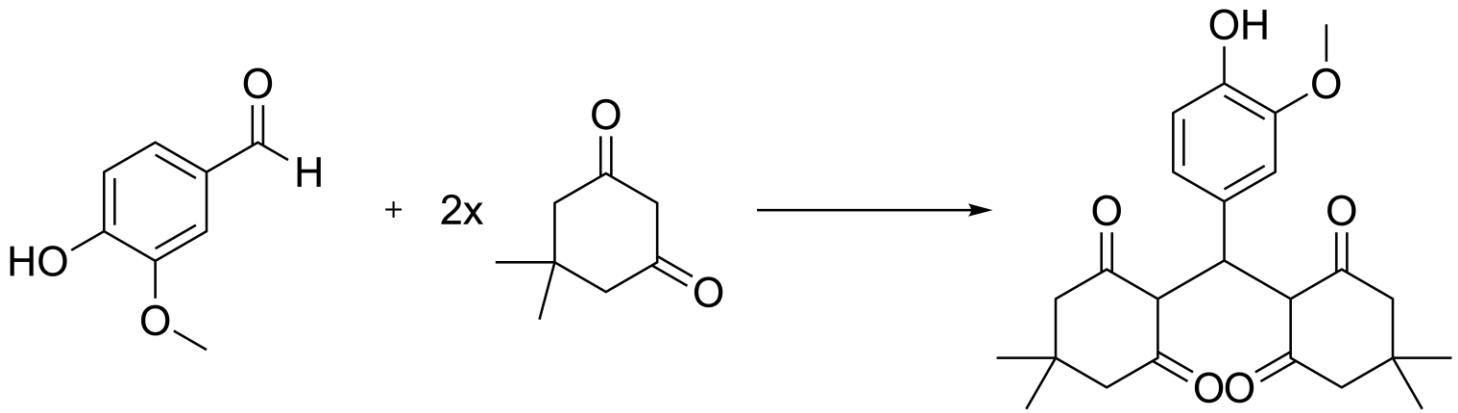



**Single-screw extruder**

- Temperatures of the 4 zones: **100, 140, 140, 140 °C**
- Screw speed: 11.1 rpm (residence time: 7-10 mins)
- The product was isolated through successive precipitation steps, achieving **over 95% purity** (confirmed by HPLC-MS and NMR).
- **Solvent or liquid-assisted grinding not required**



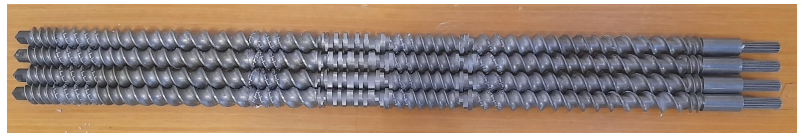
# Knoevenagel condensation and Michael addition of vanillin with dimedone

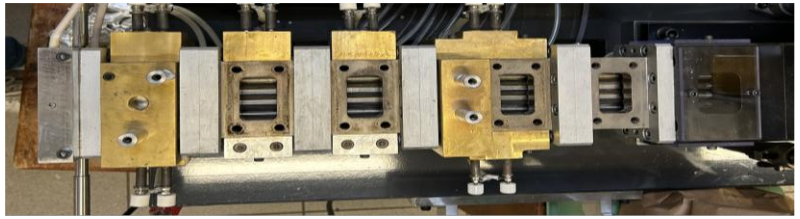



- Temperatures of the 6 zones: **100, 140, 140, 140, 140, 120 °C**
- Screw speed: 100 rpm (Time of residence: < 5 min)
- The product was isolated through successive precipitation steps, achieving **over 95% purity** (confirmed by HPLC-MS and NMR).
- **Solvent or liquid-assisted grinding not required**

technovel

## Quad-screw extruder





# EXTRUDERS COMPARISON

## Single-screw extruder

- Screw geometry: conveying
- RPM: 11.1
- 1 screw

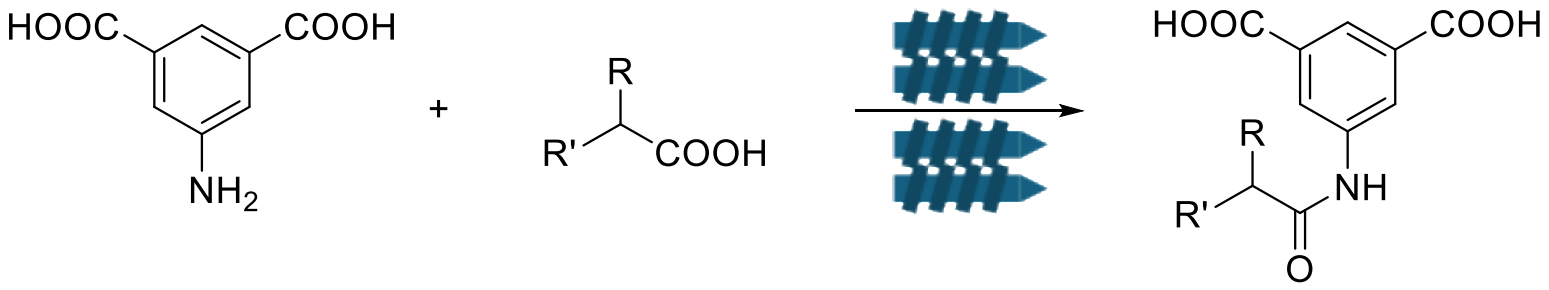
## Quad-screw extruder

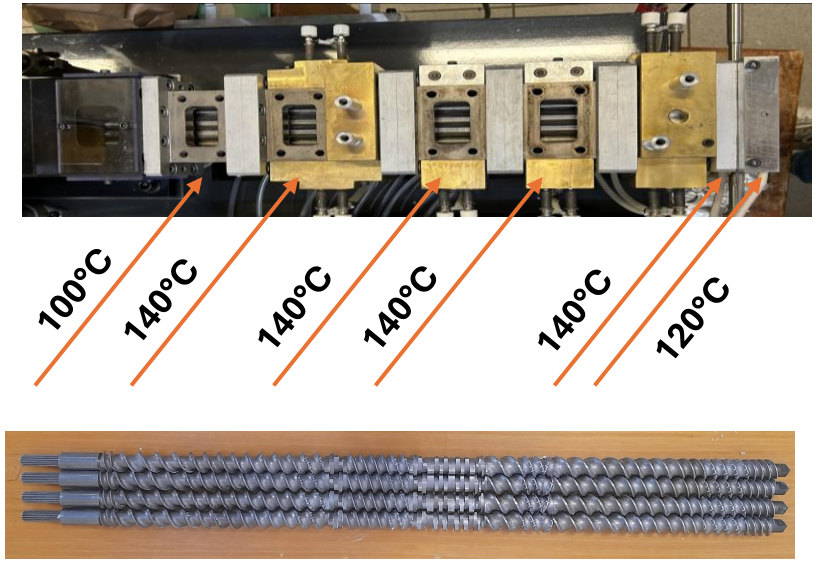
- Screw geometry: different elements (conveying, reverse, kneading)
- RPM: 100
- 4 screws

**The quad-screw extruder gave better conversion**

Hoever with appropriate optimization of the screw geometry and reaction conditions, the single-screw extruder would also guarantee the **same result**.

# DIRECT AMIDE FORMATION (quad-screw extruder)

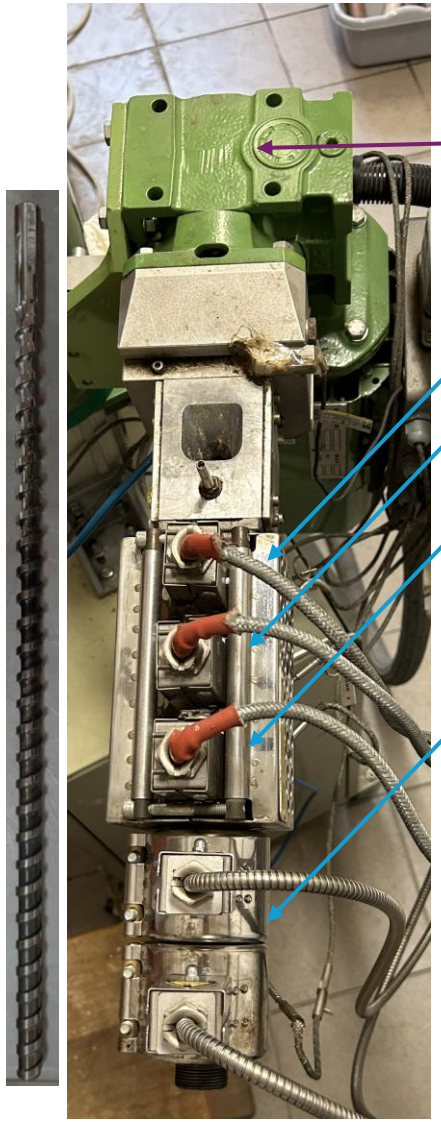


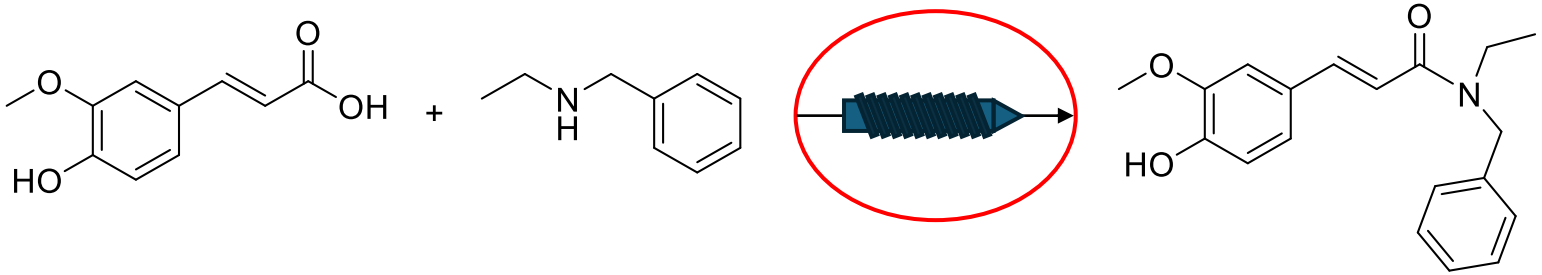




| Screw speed (rpm) | Conversion (%) |
|---|---|
| 100 | 91 |
| 300 | 96 |

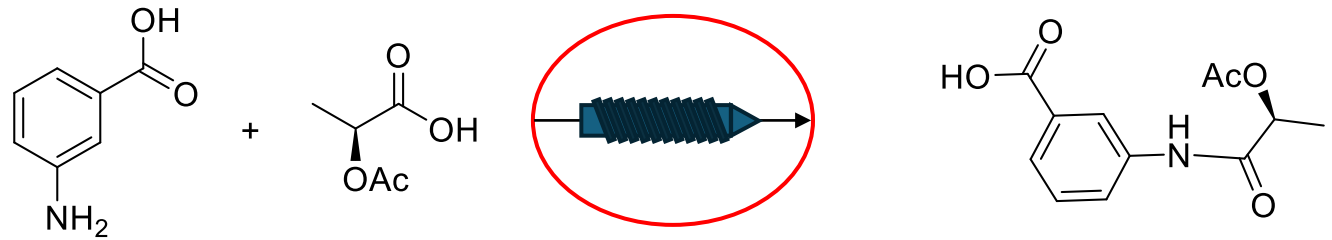
Greater mechanical effect, better conversion

# DIRECT AMIDE FORMATION (single-screw extruder)




53%

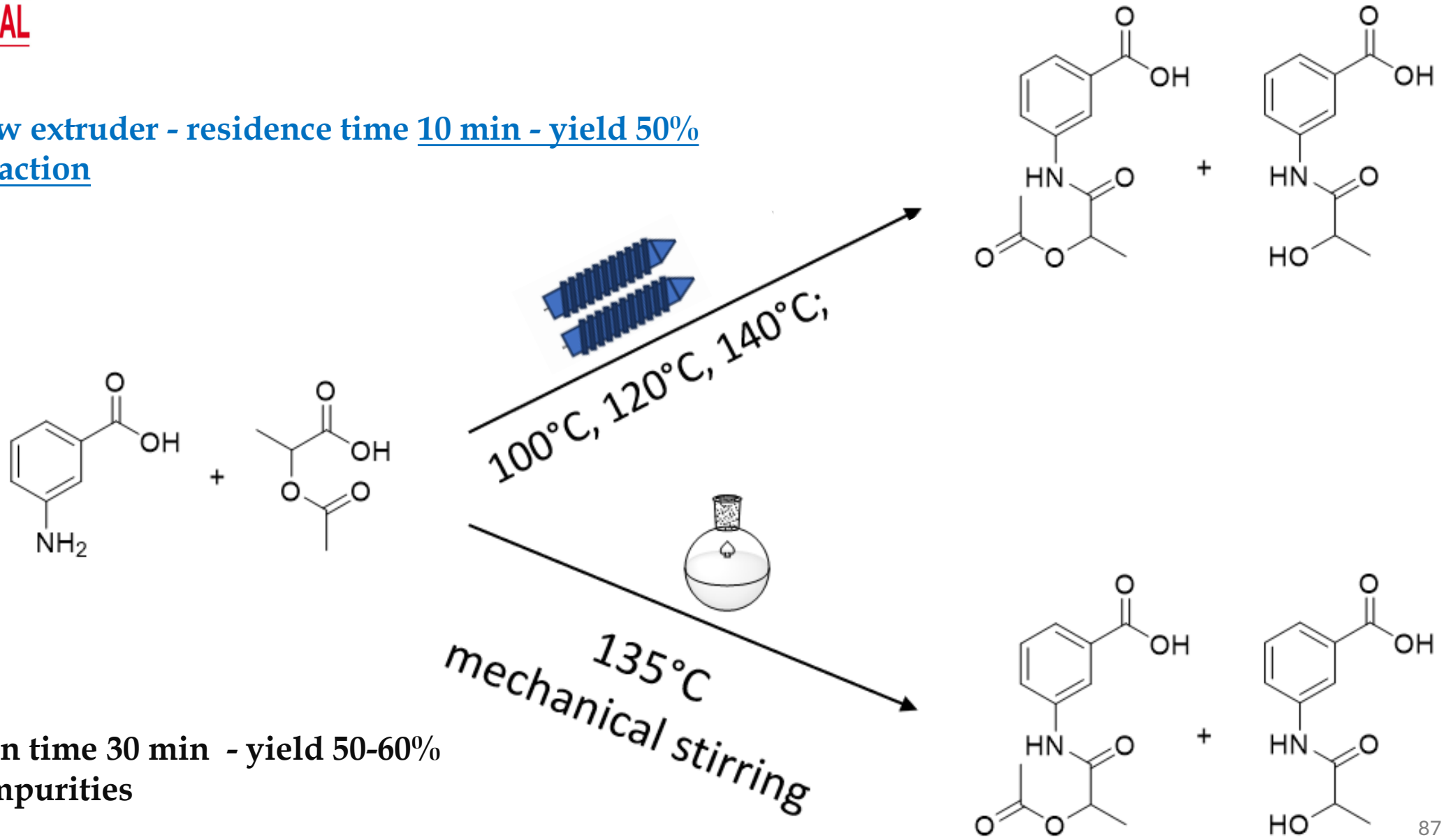



45%

# REACTIVE EXTRUSION *vs* CONVENTIONAL

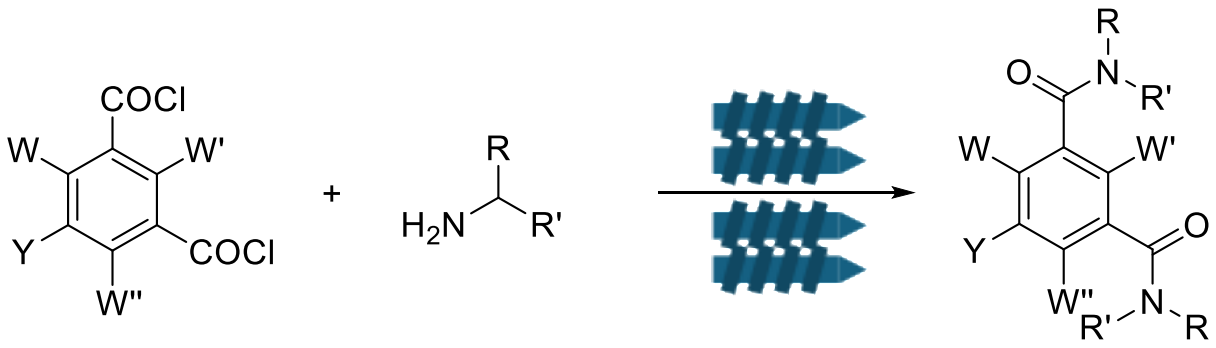
CONFIDENTIAL

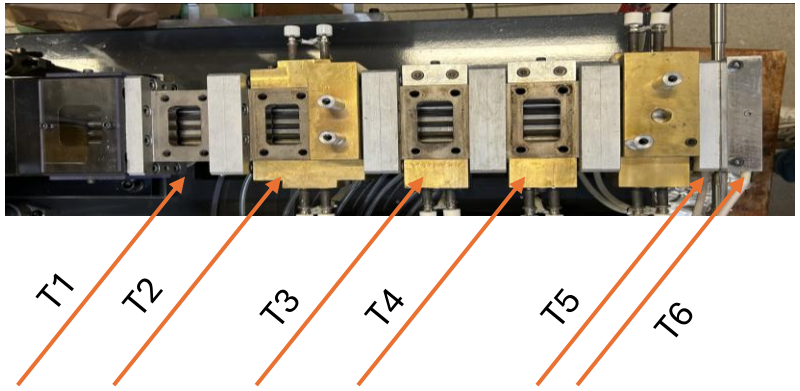
**Twin-screw extruder - residence time 10 min - yield 50%**
**cleaner reaction**




**Reaction time 30 min - yield 50-60%**
**more impurities**

# DIFFICULT AMIDE FORMATION (quad-screw extruder)



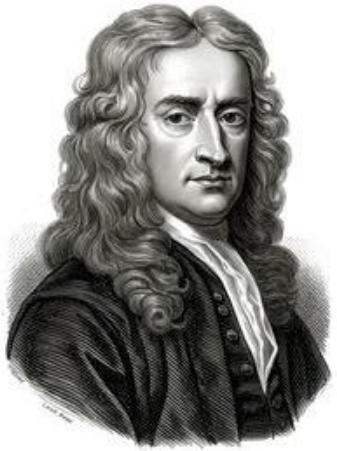




Phthaloyl chloride is substituted with electron-withdrawing and/or steric groups. Under standard conditions, the reaction that forms the amide does not proceed efficiently.

| T1 (°C) | T2 (°C) | T3 (°C) | T4 (°C) | T5 (°C) | T6 (°C) | rpm | Yield (%) |
|---|---|---|---|---|---|---|---|
| 70 | 70 | 70 | 70 | 70 | 70 | **100** | **61** |
| 80 | 85 | 80 | 70 | 70 | 65 | **100** | **60** |
| 85 | 85 | 85 | 85 | 85 | 85 | **70** | **70** |
| **25** | **25** | **25** | **25** | **25** | **25** | **500** | **88** |
| **15** | **15** | **15** | **15** | **15** | **15** | **500** | **90** |

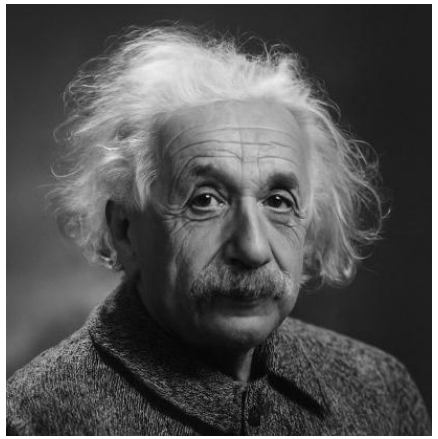
temperatures above the melting point

**temperatures below the melting point**



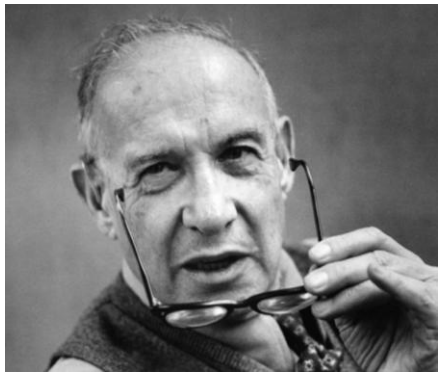
**ISAAC NEWTON**

“If I have seen further, it is by standing on the shoulders of giants”



**ALBERT EINSTEIN**

“Many times a day I realise how much my own work depends on the labours of others”



**PETER DRUCKER**

“Knowledge has to be improved, challenged, and increased constantly, or it vanishes”


Napoli, 7-8 Maggio 2026