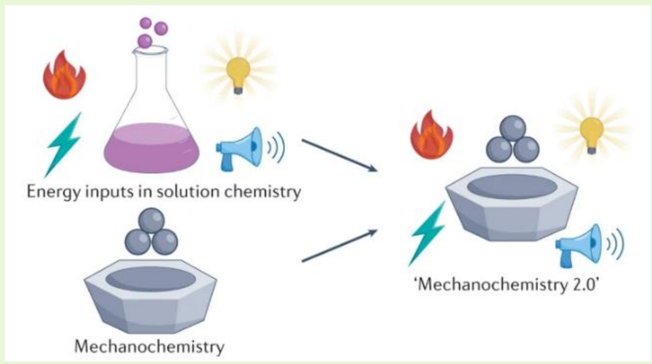
MECHANOCHEMISTRY – APPLYING THE PRINCIPLE OF GREEN CHEMISTRY TOWARD SUSTAINABILITY

Alexander Pinilla;[1] Lina López;[2] Randy Sutio[3]

[1]Pontificia Universidad Católica de Chile; [2]Universidad Nacional de Rosario; [3]Darmouth College

Definition/Description of the synthesis tool/concept

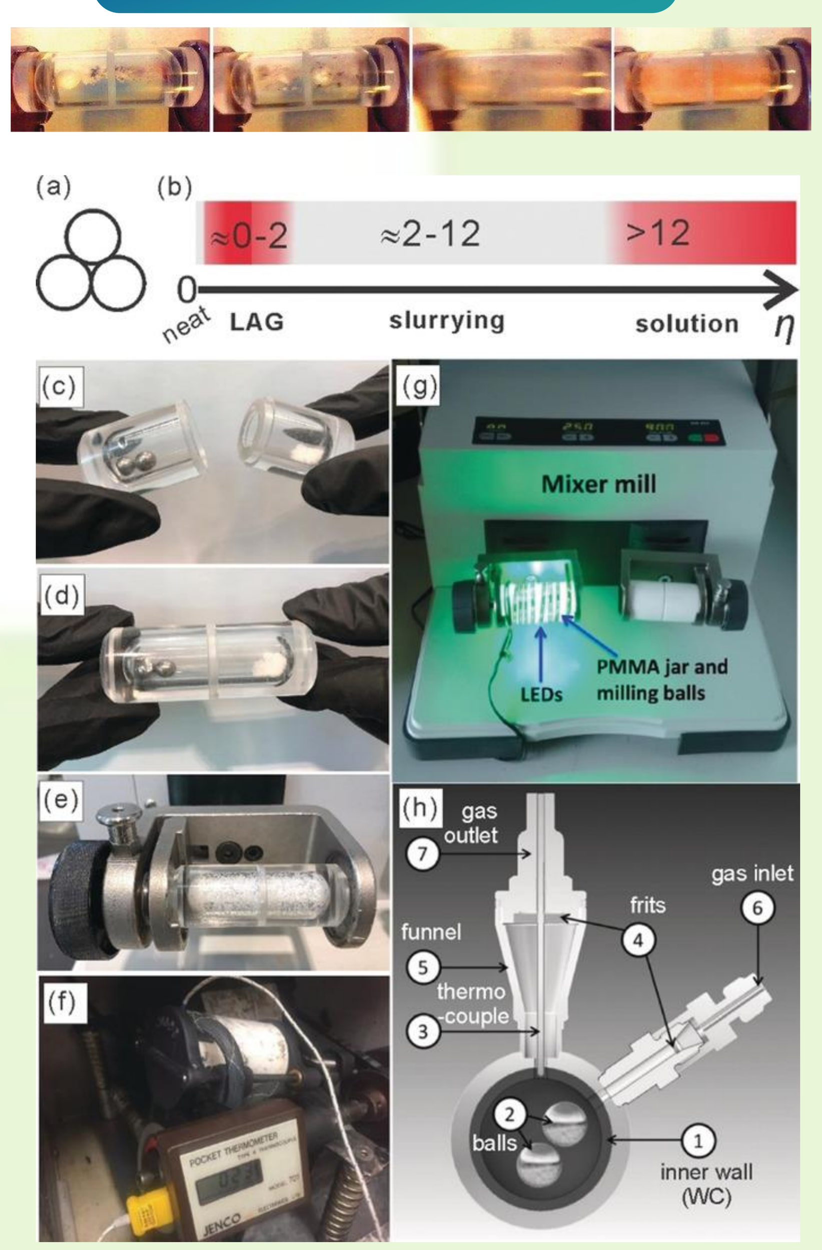
Mechanochemistry refers to a reaction that occurs by induction of mechanical energy that does not require solvent.



No conventional laboratory stirrer or stirrer is required.

This technique uses an automated ball mill and the reaction occurs in a flask containing the grinding medium. The ball mill allows a solvent-free reaction.

General Overview of Mechanochemistry

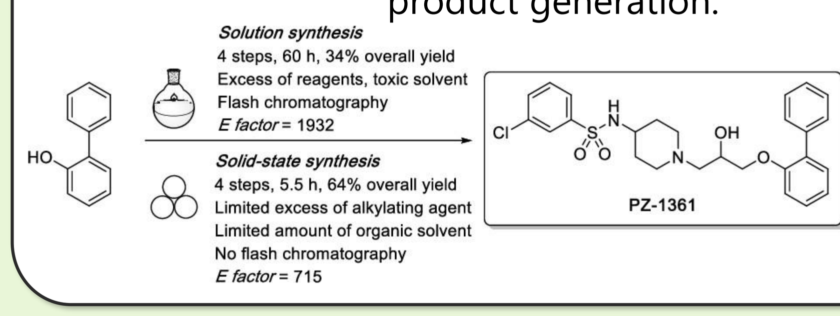


The use of ball mills grants control over the exact milling time and allows minutes control over the energy input throughout the milling process.

¿Why does the tool relate to Green and Sustainable Chemistry?

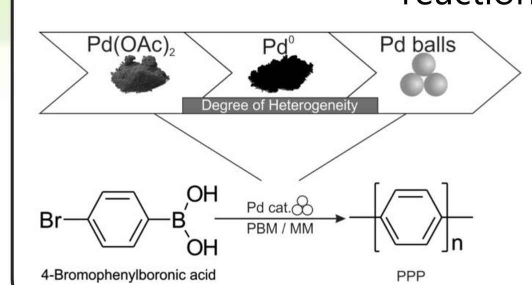
Waste Prevention

Synthesis of potent 5-HT_7 receptor antagonist (antidepressant) **PZ-1361** highlight the benefit of ball-milling technique in reducing reaction time, limiting the usage of solvent and by-product generation.



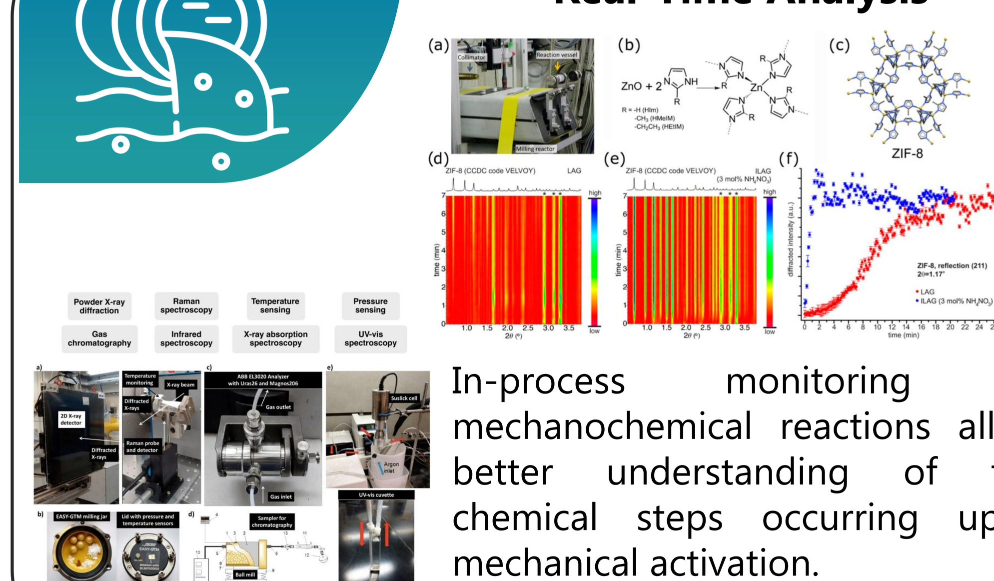
Catalysis

Ball milling technique is envisioned to allow direct catalyst recovery while minimizing contamination from the reaction mixture.



Solvent-free environment ball-milling allow Suzuki polymeration to take place utilizing Pd black catalyst instead of Pd^{II} ligand while avoiding the needs of expensive ligand.

Real-Time Analysis



In-process monitoring of mechanochemical reactions allow better understanding of the chemical steps occurring upon mechanical activation.

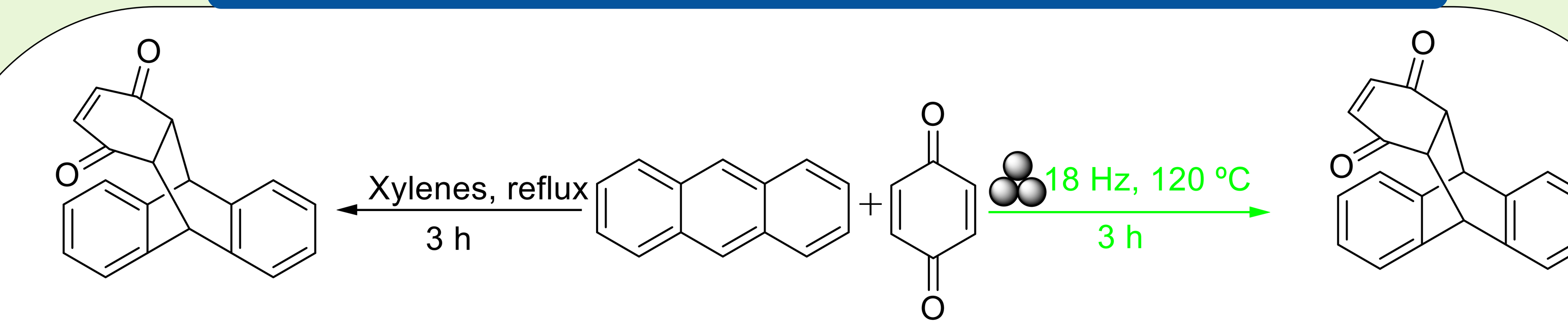
Advantage

- Room temperature or slightly elevated
- One pot synthesis (time efficiency)
- Solvent-free or minimum amount of solvent
- Waste minimization
- Conventional catalyst can be replaced by metallic surfaces
- Access to molecules whose isolation has so far been impossible

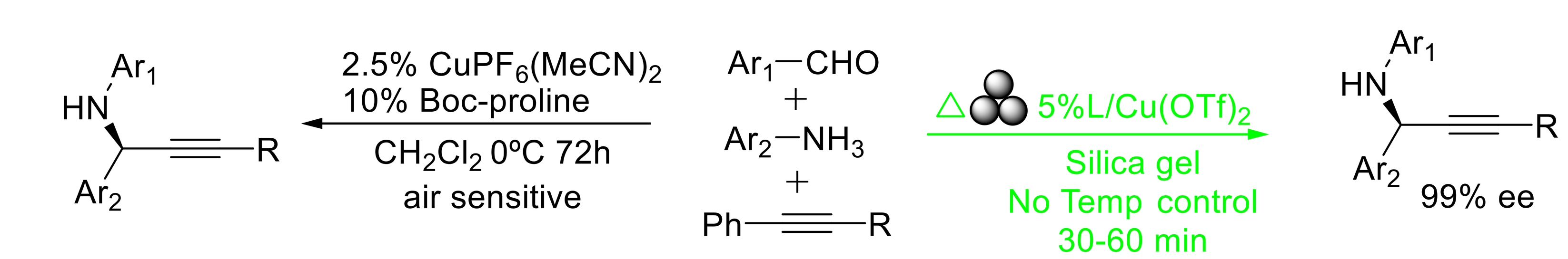
Disadvantage

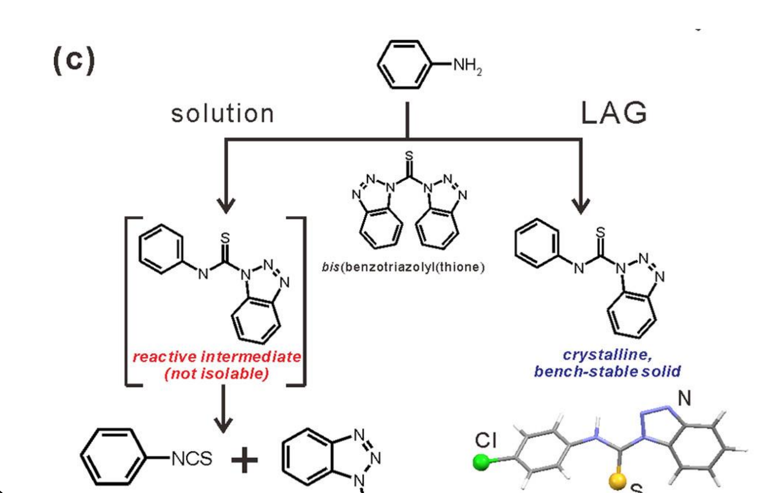
- Amorphization may occur during neat grinding
- Contamination from milling reactors
- Necessitate specialized equipments
- Arduous control for precise synthesis
- Separation and recycling of homogeneous catalyst is difficult

APPLICATIONS IN CHEMICAL SYNTHESIS



Condensation products ← Solvent required — knoevenagel condensation, imine formation, aldol reaction — continuous kg-h^{-1} scale, pure product fed directly into receiving vessel → Condensation products

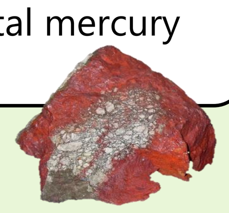


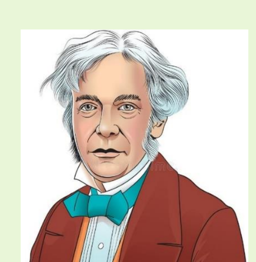


Aryl N-thiocarbamoyltriazoles which is proposed as the intermediates during the synthesis of thioureas were never isolated. This stems from its rapid dissociation in solution; this issue was solved by the usage of liquid -assisted grinding to allow the isolation of the elusive intermediate.

A brief history

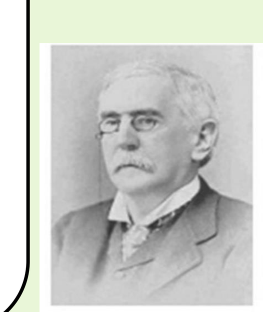
IV b.C. (Theophrastus)
Grinding cinnabar with acetic acid in a copper vessel to give elemental mercury





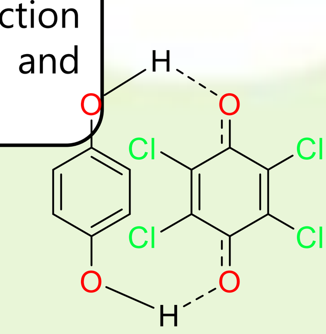
XIX (1820)
Michael Faraday reducing AgCl to Ag with Zn, Cu and pestle and mortar

XIX (1890)
Carey Lea showed that mechanochemistry could give different products to thermal ones favouring decomposition of mercury and silver halides

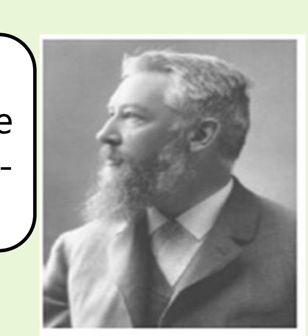


Matthew Carey Lea
(1823 – 1897)

XIX (1893)
First mechanochemical reaction (cocrystallization) by Ling and Baker



XX (1932)
Wilhelm Ostwald classify the mechanochemistry as one of four sub-disciplines of chemistry



Wilhelm Ostwald
(1853 – 1932)

1980-1990
Particularly cocrystallization,developed significantly.

1997-2018
- **IUPAC:** Defintion of Mechanochemistry
- **J. Marck group:** First Sonogashira reaction with Cu equipment
- **J. Marck group** CuAAC reaction
- **Y. Sayama group:** Hydrogenation reaction

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