

Resonant Acoustic Mixing (RAM): Fast, impact-less metal-catalysed mechanosynthesis

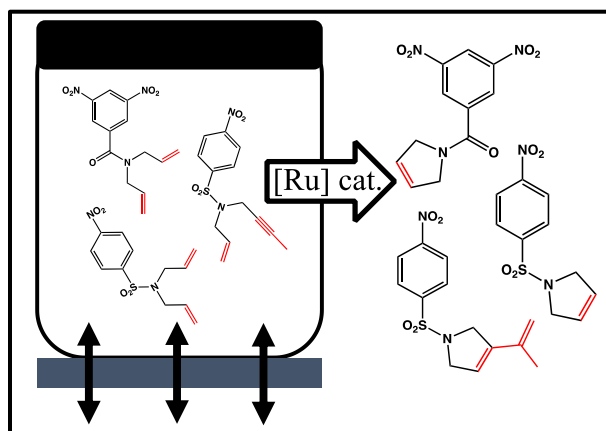
Cameron B. Lennox^a, Lori Gonnet^a, Jean-Louis Do^a, Stefan G. Koenig^b, Karthik Nagapudi^b, Tomislav Friščić^a

a) Department of Chemistry, McGill University, Montreal, Canada

b) Small Molecule Pharmaceutical Sciences, Genentech, Inc. South San Francisco, USA

Mechanochemistry is an attractive and valuable methodology for synthetic and materials discovery, while being positioned to be the cornerstone of alternative, sustainable synthesis.^[1,2] Current milling and extrusion systems rely on milling, grinding or crushing media to impart mixing and chemical reactivity, often resulting in material contamination through wear and tear.^[3]

We herein report methodologies that promotes catalytic organic mechanosynthesis by Resonant Acoustic Mixing (RAM) – an emerging mechanochemical technology that does not require bulk solvent or milling media. Using as the model reactions ruthenium-catalyzed ring-closing metathesis, RAM mechanosynthesis is now shown to be faster, operationally simpler than conventional ball-milling, while also providing the first example of a mechanochemical strategy for ene-yne metathesis.^[4]



[1] James *et al.* *Chem. Soc. Rev.* **2012**, *41*, 413; [2] Do, Friščić *ACS Cent. Sci.* **2017**, *3*, 13; [3] Friščić, Mottillo, Titi *Angew. Chem. Int. Ed.* **2020**, *59*, 1018; [4] Gonnet, L.; Lennox, C. B.; Do, J.-L.; Malvestiti, I.; Koenig, S. G.; Nagapudi, K.; Friščić, T. *Angew. Chem. Int. Ed.* **2022**, doi: 10.1002/anie.202115030.