Catalytic and Media-free Mechanosynthesis by Resonant Acoustic Mixing (RAM)

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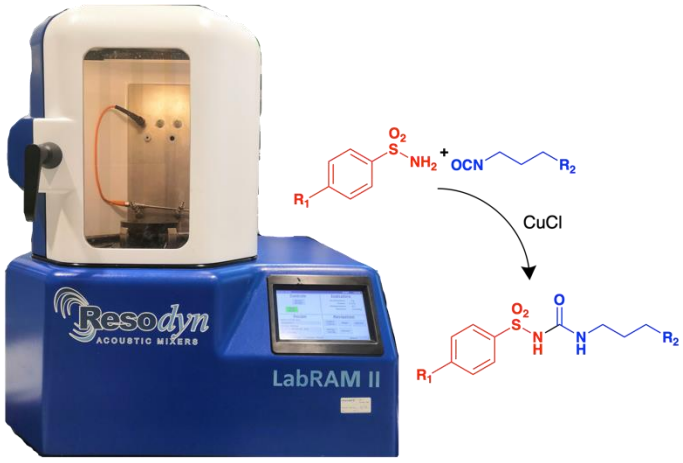
Over the past decade, organic mechanosynthesis has evolved from a laboratory curiosity into a highly developed research area.[1] Most reported cases of organic synthesis by mechanochemistry are typically based on ball milling or twin screw extrusion methodologies. While highly efficient, allowing chemical transformations in the absence of bulk solvent and even permitting access to previously not reported reactivity, such mechanochemical reactions are complicated by the need for milling media in the form of balls, pebbles, or screws.



Our team has recently reported the use of a different methodology, based on rapid acoustic-frequency mixing, for the synthesis of cocrystals, metal-organic frameworks and, in the presence of milling beads, organic molecules.[2-4] This poster will show the first use of such Resonant Acoustic Mixing (RAM) to conduct catalytic organic reactions without any milling or grinding media, including the synthesis of APIs.[5] We will present how the parameters accessible in a commercial RAM, such as time, acceleration and temperature, as well as the volume variation of liquid catalyst additives, can be used to optimize catalytic organic reactions. We highlight how the possibility to perform RAM mechanosyntheses in the absence of milling or grinding media can greatly simplify the scaling-up of mechanosynthesis.

References: [1] Friščić, T.; Mottillo, C.; Titi, H. M. *Angew. Chem. Int. Ed.* **2020**, *59*, 1018; [2] Nagapudi, K.; Umanzor, E. Y.; Masui, C. *Int. J. Pharm.* **2017**, *521*, 337; [3] Titi, H. M.; Do, J.-L.; Howarth, A. J.; Nagapudi, K.; Friščić, T. *Chem. Sci.* **2020**, *11*, 7578; [4] Fang, Y.; Salamé, N.; Woo, S.; Bohle, D. S.; Friščić, T.; Cuccia, L. A. *CrystEngComm* **2014**, *16*, 7180-7185; [5] Gonnet, L.; Lennox, C. B.; Do, J.-L.; Malvestiti, I.; Koenig, S. G.; Nagapudi, K.; Friščić, T. *Angew. Chem. Int. Ed.* **2022**, doi.org/10.1002/anie.202115030.