



ACS Award Given for Visionary Chemistry

Collaboration Between University of Birmingham and Genentech Earned the 2024 American Chemical Society Award for Affordable Green Chemistry

P: +1 (406) 497-5333

E: info@resodynmixers.com

W: resodynmixers.com

OVERVIEW

In 2024, the American Chemical Society presented its prestigious Award for Affordable Green Chemistry to Dr. Tomislav Friščić of the U. of Birmingham, and Dr. Stefan G. Koenig and Dr. Karthik Nagapudi of Genentech, for their joint demonstration that ResonantAcoustic® Mixing (RAM) drives greener chemical synthesis across the pharmaceutical and chemical industries. [1]

Over nearly a decade of peer-reviewed research, they proved that RAM consistently

beats conventional ball milling where it matters most to industry: scalability, catalyst efficiency, product purity, and reaction control. The findings span MOF synthesis, metal-catalyzed coupling reactions, mechanoredox catalysis, direct mechanocatalysis, and pharmaceutical amination. [2][3][4][5][6]

Mechanochemistry has long been described as the future of green chemistry. This research established that RAM is the platform that makes it commercially real.



Solution

- ResonantAcoustic® Technology
- Solvent-Free, Media-Free Mechanochemical Synthesis
- Scalability from Milligrams to Multi-Gram Production
- Tunable Reaction Control



Achievement

- 2024 ACS National Award for Affordable Green Chemistry [1]
- Demonstrated Across Five Reaction Classes [2][3][4][5][6]
- 5X Reduction in Catalyst Loading vs. Ball Milling [7]
- 100-Fold Scale-Up [3]

CHALLENGES

Mechanochemistry — chemical synthesis driven by mechanical force rather than solvents or heat — has long been recognized as one of the most promising pathways to greener chemical manufacturing. But, the dominant mechanochemical technology, ball milling, carries significant limitations that have prevented it from achieving commercial scale. [1]

Milling balls introduce contamination through abrasion, a critical problem in pharmaceutical synthesis where purity standards are uncompromising. The forceful, high-speed collisions of grinding media generate heat, limiting access to thermodynamically stable polymorphs and reducing control over reaction

outcomes. Most critically, ball milling scales poorly. As loading increases in the milling vessel, the balls cannot move freely, reaction kinetics collapse, and conversion falls off rapidly. At approximately 20% filling ratio, the reaction becomes essentially unusable. [7]

Reactions that work elegantly at laboratory scale require fundamental redesign before they can be translated to commercial production. This has kept solvent-based synthesis dominant in industrial settings for decades, despite its well-documented environmental cost.

Until now, a mechanochemical platform capable of delivering clean, controllable, scalable synthesis had simply not existed.

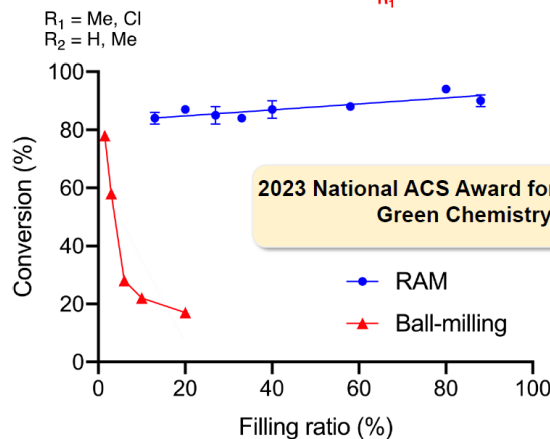
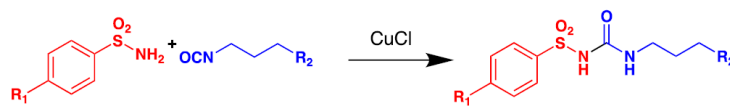
Why Conventional Mechanochemistry Hits a Wall

Ball milling conversion starts near 78% at minimal fill and collapses to approximately 17% by the time the vessel reaches 20% capacity. RAM holds steady above 84% conversion across the entire range, trending slightly upward to nearly 90% at 85% fill. The same reaction was scaled 100-fold without changing a single reaction condition. [3]

Dr. Frišćić showed the audience this comparison at Resodyn's Technical Interchange in 2023 and made his conclusion explicit:

"I'm very glad to say our team, together with Genentech, will be awarded the 2024 American Chemical Society National Award for Green Affordable Chemistry. And I blame this graph." [7]

Scaling up: 100-fold without changing reaction conditions.



Gonnet, Lennox, Do et al. *Angew. Chem. Int. Ed.* 2022, 61, e20211503.

SOLUTION

RAM, pioneered by Resodyn Acoustic Mixers, uses low-frequency, high-intensity acoustic energy to process materials in a fully sealed vessel, with the entire container oscillating uniformly to distribute energy through the full material volume simultaneously. The design requires no milling media of any kind, which means reactions stay clean, temperatures stay controlled, and performance holds as the vessel fills.

David Stirling of Genentech, speaking as a colleague of the award recipients, described what the research demonstrated:

“These three scientists have demonstrated that resonant acoustic mixing effects mild mechanochemical synthesis of diverse chemistries with drastically reduced solvent consumption. This demonstrates the potential for greener chemical synthesis as well as the power of academic-industry collaborations to advance new technologies and drive the chemical and pharmaceutical industries to more sustainable practices.”

[1]

A Research Program Built Paper by Paper

The collaboration did not arrive at this conclusion in a single experiment. It was a sustained research program that systematically expanded the scope of what RAM can do in chemistry, one reaction class at a time.

It began with materials synthesis. In 2020, the team published the first demonstration of metal-organic framework synthesis using liquid-assisted RAM, producing commercially significant frameworks including ZIF-8 and HKUST-1, as well as ZIF-L — a framework that had never previously been obtained by any mechanochemical method. Scale-up



LabRAM II in use by the Friščić Group at the University of Birmingham.

from hundreds of milligrams to 25 grams was demonstrated with the same reaction conditions applied at both ends of the range. [2]

From materials the program moved to catalytic organic synthesis. In 2022, the team demonstrated ruthenium-catalyzed and copper-catalyzed reactions by RAM without bulk solvents, and in a media-free environment, producing results faster and with greater operational simplicity than ball milling. The antidiabetic drug Tolbutamide was synthesized at scale from hundreds of milligrams to at least 30 grams with no changes to reaction conditions. [3]

In 2023 the program extended into mechanoredox catalysis, using a piezoelectric material to drive electron-transfer reactions under RAM conditions, scalable to gram scale and faster than the analogous ball milling approach. [4] That same year, direct mechanocatalysis was demonstrated using a simple copper coil for click-coupling reactions, showing that catalysis can proceed in a purely impact-free acoustic environment with surface-based kinetics. [5] By late 2024 the program had moved into Buchwald-Hartwig amination — one of the most industrially important reaction classes in pharmaceutical synthesis

— establishing systematic design parameters for scalable RAM reactions. [6]

Each paper broadened what RAM chemistry could accomplish. Taken together, they make the case that RAM is a platform, not a specialized tool for any single application.

What RAM Enables Beyond Ball Milling

The research documented two additional advantages that go beyond scalability.

The first is catalyst efficiency. Dr. Friščić documented that RAM can reduce catalyst loading by five to ten times compared to ball milling for the same reactions. For pharmaceutical synthesis, where precious metal catalysts represent a significant portion of manufacturing cost, that reduction has direct commercial value. [7]

The second is polymorph access. RAM operates at controlled, low temperatures, which means it can reach thermodynamically stable polymorphs that ball milling has historically missed. In one documented case, the RAM process produced the room-temperature stable structure of a target material — a result that was inaccessible under ball milling because the heat generated during milling pushed the system past the relevant transition temperature. In pharmaceutical development, polymorph control is both a regulatory requirement and a commercial imperative. [7]

The breadth of the research program reflects the spectrum of RAM's applicability. From materials science to catalytic synthesis to pharmaceutical amination, the same platform delivered consistent advantages across fundamentally different chemistry. That consistency is what the ACS recognized.



OmniRAM installed for scale up testing and industry collaboration at the Birmingham Centre for Mechanochemistry and Mechanical Processing.

CONCLUSION

The 2024 ACS Award for Affordable Green Chemistry is a powerful recognition of good science. It is also the chemistry community's formal endorsement of ResonantAcoustic® Mixing as a platform technology for the next generation of green chemical synthesis.

Across MOF synthesis, metal-catalyzed reactions, mechanoredox catalysis, direct mechanocatalysis, and pharmaceutical coupling,

RAM delivered consistently superior results on scalability, catalyst efficiency, product purity, and reaction control. [2][3][4][5][6] The research of Friščić, Koenig, and Nagapudi built that case systematically, with the rigor and breadth that earned such a high recognition from the American Chemical Society.

Mechanochemistry has a scalability solution. It is acoustic mixing.



Contact Resodyn Acoustic Mixers, Inc. to discuss how ResonantAcoustic® Mixing can transform your chemical synthesis and manufacturing process.

P: +1 (406) 497-5333

E: info@resodyn.com

W: www.resodynmixers.com

CITATIONS

1. "2024 ACS National Award Winners." Chemical & Engineering News, American Chemical Society. January 2024. <https://cen.acs.org/people/awards/2024-ACS-National-Award-winners-Part-I/102/i1>
2. Titi, H.M., Do, J.-L., Howarth, A.J., Nagapudi, K., and Friščić, T. "Simple, scalable mechanosynthesis of metal–organic frameworks using liquid-assisted resonant acoustic mixing (LA-RAM)." Chemical Science 11: 7578–7584. 2020. <https://pmc.ncbi.nlm.nih.gov/articles/PMC8159441/>
3. Gonnet, L., Lennox, C.B., Do, J.-L., Malvestiti, I., Koenig, S.G., Nagapudi, K., and Friščić, T. "Metal-Catalyzed Organic Reactions by Resonant Acoustic Mixing." Angewandte Chemie International Edition 61(13): e202115030. 2022. <https://onlinelibrary.wiley.com/doi/abs/10.1002/anie.202115030>
4. Effaty, F., Gonnet, L., Koenig, S.G., Nagapudi, K., Ottenwaelder, X., and Friščić, T. "Resonant acoustic mixing (RAM) for efficient mechanoredox catalysis without grinding or impact media." Chemical Communications 59: 1010–1013. 2023. <https://pubs.rsc.org/en/content/articlehtml/2023/cc/d2cc06013b>
5. Lennox, C.B., Borchers, T.H., Gonnet, L., Barrett, C.J., Koenig, S.G., Nagapudi, K., and Friščić, T. "Direct mechanocatalysis by resonant acoustic mixing (RAM)." Chemical Science 14: 7475–7481. 2023. <https://pmc.ncbi.nlm.nih.gov/articles/PMC10337763/>
6. Gonnet, L., Lennox, C.B., Borchers, T.H., Askari, M., Wahrhaftig-Lewis, A., Koenig, S.G., Nagapudi, K., and Friščić, T. "Rapid, Scalable Buchwald-Hartwig Amination by Resonant Acoustic Mixing (RAM): Establishing Parameters for RAM Reaction Design." ChemRxiv preprint. December 2024. <https://chemrxiv.org/doi/full/10.26434/chemrxiv-2024-qb5wr>
7. Friščić, T. Keynote presentation, Resodyn Acoustic Mixers Technical Interchange 2023. Transcript on file.