MOF Synthesis Scales 1,000X with RAM

How Liquid-Assisted ResonantAcoustic® Mixing Unlocked a Scalable, Media-Free Route to Metal-Organic Framework Synthesis

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OVERVIEW

Metal-organic frameworks are among the most commercially promising materials. Their extraordinary surface areas, tunable pore structures, and chemical versatility have driven applications across gas storage, drug delivery, catalysis, and more. The global MOF market is projected to reach USD 1.7 billion by 2030. [3] However, manufacturing is a major hurdle. Specifically, it is the inability to scale MOF synthesis without contamination, loss of yield, or fundamental redesign of reaction conditions.

Researchers at McGill University and Genentech demonstrated that ResonantAcoustic® Mixing (RAM) resolves that barrier. Published in Chemical Science in 2020 and recognized as a HOT Article by the Royal Society of Chemistry, the work introduced liquid-assisted RAM (LA-RAM) as a rapid, media-free route to diverse MOF synthesis. Scale-up from hundres of milligrams to 350 grams has been demonstrated without changing reaction conditions. [1][4]

Solution

- ResonantAcoustic® Technology
- Liquid-Assisted RAM (LA-RAM) Methodology
- Media-Free MOF Synthesis at Room Temperature
- Linear Scale-Up Without Reoptimization

Achievement

- 1,000X Scale-Up w/o Changing Reaction Conditions [1][4]
- First-Ever Mechanochemical Synthesis of ZIF-L [1]
- High MOF Purity [1][2]
- Commercially Relevant ZIF-8 and HKUST-1 Produced [1]

CHALLENGES

Conventional MOF synthesis relies on solvothermal methods, dissolving metal salts and organic linkers in large volumes of solvent, then applying heat over hours or days to drive crystallization. The process is energy-intensive, generates significant solvent waste, and produces inconsistent results when scaled. For commercially important MOFs like ZIF-8 and HKUST-1, those inconsistencies directly affect purity, porosity, and performance in downstream applications. [3]

Mechanochemical synthesis, using mechanical force rather than bulk solvent, emerged as a greener alternative. Ball milling can produce MOFs without solvents, but introduces its own problems. Ceramic and metal grinding media wear down during milling and contaminate the product. This is a serious limitation for pharmaceutical-grade materials and high-purity applications. Ball milling also generates heat through friction, which can damage sensitive frameworks or push reactions toward unwanted phases. As vessel loading increases, the grinding media cannot move freely, mixing efficiency collapses, and product quality falls. [1][2]

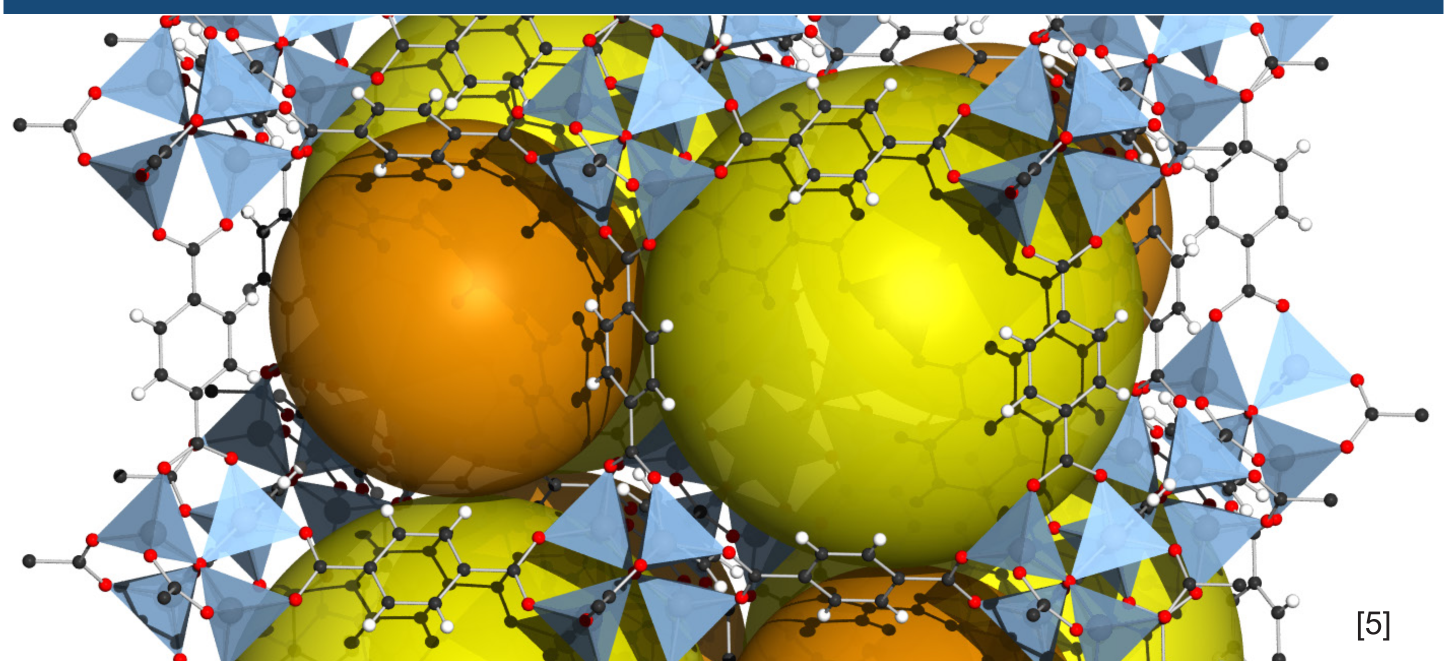
Producing MOFs cleanly, accessing sensitive frameworks, and scaling to commercial quantities had not been achieved by a single technology. That gap is what RAM closes.

What Are MOFs — and Why Does Scale-Up Matter?

Metal-organic frameworks are porous crystalline materials built from metal ions connected by organic ligands. Some frameworks exceed 7,000 m^2 of surface area per gram, combined with precisely tunable pore sizes that can selectively adsorb, store, or filter specific molecules. [3]

These properties have attracted intense industrial interest across energy storage, carbon capture, drug delivery, and chemical separations. Over 13,000 MOF-related patents have been filed to date, and several frameworks including ZIF-8 and HKUST-1 are already commercialized. The persistent challenge is that synthesis routes optimized at research scale typically require significant redesign before they can run at production volumes, adding cost and development time that slow commercial adoption. [3]

RAM offers a scalable, greener alternative to traditional methods.



[5]

SOLUTION

Liquid-assisted ResonantAcoustic® Mixing uses low-frequency, high-intensity acoustic energy to process solid and liquid reagents in a fully sealed vessel, with no grinding media of any kind. A small amount of liquid additive, far less than in traditional solution synthesis, is added to the reaction mixture. The acoustic energy field distributes that liquid uniformly throughout the vessel, promoting intimate contact between reagents and driving crystallization without the mechanical wear, heat generation, or contamination associated with ball milling.

Dr. Friščić described the significance of the approach in Chemistry World:

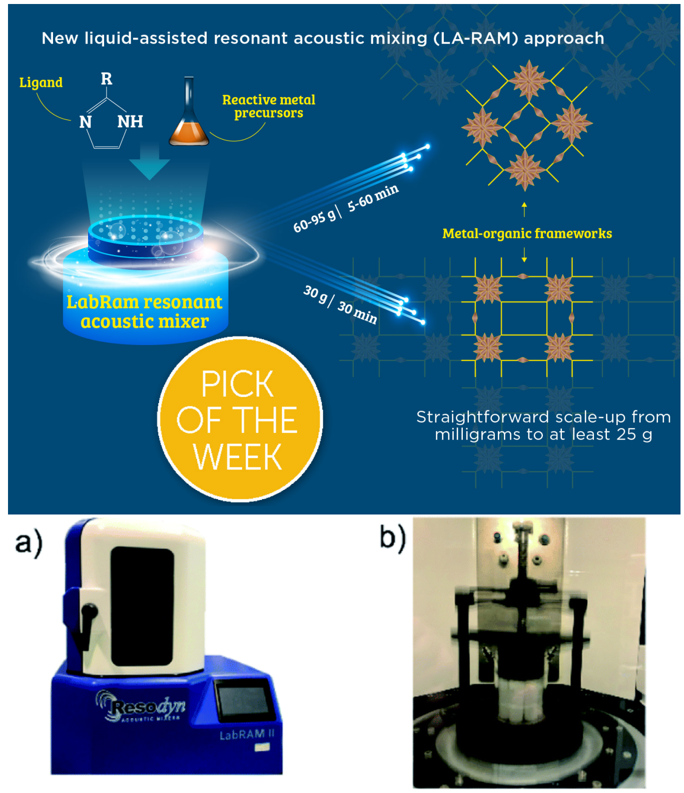
> *"There is a big problem in how chemistry makes things. We want to find ways of doing chemistry without creating toxic solvent waste."* [2]

LA-RAM addresses that problem at the source. By using only a minimal liquid additive rather than bulk solvent, it dramatically reduces waste compared to solvothermal synthesis. By eliminating grinding media entirely, it removes the contamination risk that has limited mechanochemistry's utility for high-purity applications.

A New Framework — and a New Standard for MOF Synthesis

The 2020 Chemical Science paper demonstrated LA-RAM synthesis across a range of MOF systems: commercially relevant ZIF-8 and HKUST-1 based on Zn(II) and Cu(II) respectively, a mixed-ligand Co(II) system, and the 2D layered framework ZIF-L. [1]

The ZIF-L result was particularly significant. Ball milling had never produced ZIF-L. LA-RAM, operating without grinding-based particle damage, accessed the framework for the first



Liquid-assisted RAM featured "Pick of the Week" by RSC for MOF synthesis. [1][6]

time in any mechanochemical environment. Ball milling also provided poorer control of product composition in the mixed-ligand system, while LA-RAM produced materials with no discernible difference from those made by traditional synthetic methods. [1][2]

Dr. Friščić noted what this opens up for future materials work:

> *"I'm really excited about how we could potentially use this acoustic mixing to make very sensitive MOFs, with very high porosity and extremely low density frameworks, which are difficult to make chemically."* [2]

The Scale-Up That Changes the Commercial Equation

The published paper demonstrated straightforward scale-up from milligrams to at least 25 grams using ZIF-L as the model system, with the same reaction conditions applied at both ends of the range. [1] Subsequent work extended that further. Dr. Friščić described the progression at Resodyn's Technical Interchange in 2023:

> *"What we could do is go step by step and scale this up to something like 200 grams. I heard from the person who did the work, they actually went to 350 grams at some point recently without any optimization. So you define reaction conditions at 200 milligrams and you linearly scale them up. I'm blown away by that. That's over a thousand times scale-up."* [4]

A chemist can develop a reaction at research scale and transfer it directly to production with the same conditions and the same outcomes. That is the commercial unlock that MOF manufacturing has been waiting for.

CONCLUSION

The LA-RAM MOF synthesis work published in Chemical Science by Titi, Do, Howarth, Nagapudi, and Friščić documented a mechanochemical synthesis methodology that is cleaner than ball milling, capable of producing frameworks that ball milling cannot access, and linearly scalable to production quantities without reoptimization. [1]

For a market growing at 22.1% annually toward a projected USD 1.70 billion by 2030, manufacturing capability is a meaningful commercial constraint. [3] LA-RAM addresses it directly. From the first synthesis of ZIF-L by any mechanochemical route to a 1,000X scale-up verified without changing reaction conditions, the results document a platform ready to take MOF chemistry from the research bench to the production floor. [1][4]

Contact Resodyn Acoustic Mixers, Inc. to discuss how ResonantAcoustic® Mixing can transform your advanced materials synthesis process.

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CITATIONS

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