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# Mechanochemistry in the undergraduate teaching laboratory

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Mechanochemistry, the facilitation of a chemical reaction through mechanical force, has seen a renaissance in recent years, largely because of its potential as an alternative sustainable synthetic route. However, while mechanochemistry supports the minimization or elimination of solvents and is a useful tool to teach green chemistry principles in an applied manner, its adoption by educators has been slow. This article provides a review of the contemporary teaching literature, highlighting its implementation in the undergraduate chemistry laboratory and its application towards integrating green chemistry principles, predominantly in organic and inorganic experiments, but also in other subdisciplines. Lastly, some perspectives are offered on the current challenges and the opportunities mechanochemistry presents for chemical education.

## Sustainability spotlight

Mechanochemistry offers the potential to minimize or eliminate solvent use for synthesis, which holds great potential as a sustainable tool. In fact, it was recognized by IUPAC as one of the “top ten technologies in chemistry” for a more sustainable future in 2019. However, its adoption in the undergraduate teaching laboratory has been slow. Our article provides a valuable resource for educators by providing a general introduction, review, and the perspectives on where and how mechanochemistry has been integrated into the teaching laboratory, aligning with SDG #4: quality education. By training chemists in these alternative synthetic tools, we also prepare the future workforce to tackle SDG #12: sustainable consumption and production relating to chemicals and waste.

## Introduction

The recent “Stockholm Declaration on Chemistry for the Future” lays out the importance of emphasizing sustainable chemistry and eliminating waste and encourages the introduction of new educational methods for sustainable chemistry.<sup>1</sup> With an ever increasing interest in green and sustainable chemistry, mechanochemistry is experiencing a renaissance, seeing adoption across all fields of chemistry, including chemical education. In fact, IUPAC recognized mechanochemistry as one of the “top ten technologies in chemistry” for a more sustainable future in 2019,<sup>2</sup> reflecting its potential as an environmentally friendly approach towards developing new processes and materials. Changes to environmental laws or policy have also helped drive the incorporation of sustainable methods into the teaching laboratory. For example, the 1976 Resource and Recovery Act (RCRA) encouraged many academic laboratories to embrace microscale chemistry.<sup>3</sup> By incorporating microscale chemistry, academic institutions reduced the amount of waste, minimized liability, saved money, and encouraged students to consider the environmental consequences of chemistry. It was a good first step toward

sustainability in the teaching laboratory and provided an opportunity to discuss green chemistry principles with students.<sup>4</sup> With the recent US Environmental Protection Agency (EPA) prohibitions and workplace protections under the Toxic Substances Control Act (TSCA) for dichloromethane in 2024,<sup>5</sup> the use of halogenated solvents is largely restricted, including in academic laboratories. This may provide a new impetus for educators to explore alternative solvents or on occasion their elimination or minimization through the use of mechanochemistry in the undergraduate laboratory.<sup>6</sup>

Mechanochemistry, using mechanical force such as impacting or shearing of reactants to complete a chemical reaction in the absence of a solvent, has been “rediscovered” as a promising sustainable synthetic tool that can minimize the use of solvents (ideally eliminating them, although reactions typically require some solvent during workup). As the use of mechanochemistry has become more mainstream, Hanusa introduced three circles arranged in a triangular fashion as a symbol to designate mechanochemical reactions,<sup>7</sup> similar to the broadly accepted symbols of thermal, microwave, and photochemical reactions. There are a number of articles available that discuss the fundamentals and intricacies of mechanochemical reactions, which are beyond the scope of the current article.<sup>8–13</sup>

At its simplest, mechanochemistry involves grinding reactants together, and the most basic approach to accomplish this is with a mortar and pestle, similar to the methods used by

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ancient alchemists dating back as early as 315 B.C.<sup>14</sup> However, the force that can be applied to the reactants by a mortar and pestle (and its inconsistency) generally limits the available chemical reactions or requires exceptionally long grinding times to achieve appreciable conversions. Fortunately, modern approaches to mechanochemical reactions typically employ commercial equipment such as the use of some type of mechanical mixer mill or planetary mill to attain greater forces with less human effort and in a shorter time, expanding the potential reactions and products that can be accessed. Commercial mills have been used industrially for years to homogenize materials, reduce particle size, and enhance extraction, including applications in the pharmaceutical industry and metallurgical field. Laboratory-scale commercial mills are available with costs in the tens of thousands range, depending on models and accessories. These tools have also been adopted in academia, finding their way into both research and teaching laboratories, where chemists continue to build a library of reactions.

Two of the most common pieces of commercial milling equipment used in academia are the mixer (also commonly referred to as “vibrational” or “shaker” mills) and planetary ball mills (Fig. 1).

In a mixer mill (MM), reactants are placed in sealable containers referred to as “jars” with added grinding balls and shaken back and forth at a constant frequency (Hz). The force originating predominately from the impact of the reactants and grinding balls facilitates the reaction, and the vessel size and number/size of balls are important variables towards moderating the energetics and kinetics of the reaction.<sup>12,16</sup> A general best practice is to use the same material for the jar and grinding balls, where stainless steel is commonly employed, although a variety of other materials are also commercially available, including tungsten carbide, zirconium oxide, PTFE, agate, and alumina. In planetary mills (PM), mechanochemical force is imparted through impact and friction generated by the centrifugal forces arising from the rotation of reaction jars

containing grinding balls at a specified rotational frequency, typically expressed in revolutions per minute (rpm).

While many mechanochemical reactions can be completed using neat (solventless) grinding, with numerous examples described herein, some chemical reactions either benefit from or require the addition of a small amount of liquid to enhance and/or control their synthesis; these are referred to as liquid-assisted grinding (LAG) reactions.<sup>17</sup> The parameter  $\eta$  is used to detail the amount of liquid used in a LAG reaction in units of  $\mu\text{L}$  of added liquid/total mass of reactants in mg. Common LAG conditions have  $\eta$  values of 0.1–0.5  $\mu\text{L mg}^{-1}$ .

An interesting parallel for the recent application of mechanochemistry and its alignment towards green and sustainable chemistry in research and teaching can be made to the embrace of microwave chemistry.<sup>18</sup> By the late 1990s and early 2000s, microwave reactors adapted to operate safely in chemistry lab became commercially available and began to be widely adopted in academia, as exemplified by the many acronyms coined during this period, including microwave-assisted organic synthesis (MAOS), microwave-enhanced chemistry (MEC), microwave organic reaction enhancement (MORE), and microwave-assisted chemistry (MAS). Similar to reducing cooking times at home, microwave reactors offer a number of advantages including quickly and efficiently heating reactions and access to higher temperatures in pressurized reactors, potentially offering increased reaction rates, yields, and reduced by-product formation.<sup>19</sup> These advantages and the alignment of microwave chemistry with green and sustainable chemistry principles have similarly led to its continued adoption by educators in the teaching laboratory.<sup>20</sup>

In the past decade or so, there has been a rapid expansion in published teaching experiments involving mechanochemistry (Fig. 2), with more educators taking the opportunity to explore this revived method each year. The following section provides a brief review of the contemporary chemistry teaching literature describing the use of mechanochemical processes with undergraduate students, mostly within organic and inorganic teaching experiments, but also with some examples more closely associated with other subdisciplines. To conclude, we provide a brief overview of the current state of affairs, as well as

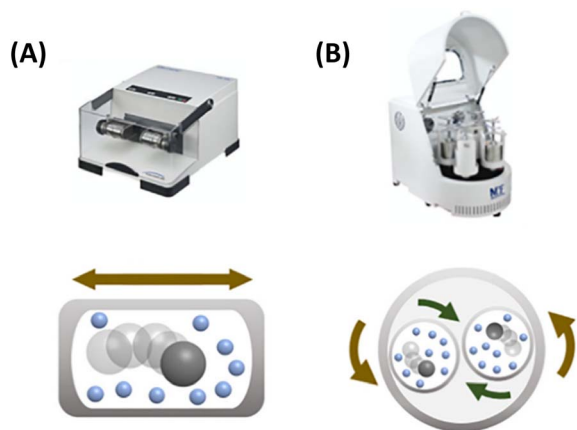


Fig. 1 Photographs of a (A) mixer mill and (B) planetary mill and diagrams of their basic modes of mechanical force generation. Adapted/reproduced from ref. 15 with permission from Elsevier, copyright 2015.

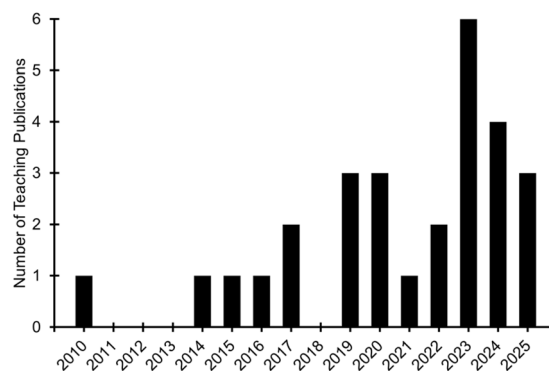


Fig. 2 Numbers of published mechanochemical teaching experiments by year from 2010–2025 discussed herein.



some of the key challenges and the opportunities that mechanochemistry offers in the undergraduate laboratory.

## Mechanochemical teaching activities

In total, 31 publications were selected for discussion from the teaching literature. These were collected using a variety of search keywords related to mechanochemistry (*e.g.* “mechanochemical”, “grinding”, “solid-state”, and “solventless”). Herein, we acknowledge that other examples utilizing mechanochemical methods within the synthetic protocols may have been missed or overlooked. Nevertheless, the examples herein should provide a reasonable survey of their incorporation into the undergraduate teaching laboratory. The teaching experiments have been organized below according to subdiscipline, primarily organic, inorganic, or other, and presented in a mostly chronological order. A summary of the main articles and their key features is provided in the SI (Table S1). The mechanochemical reactions were predominantly performed using either manual grinding (typically using a mortar and pestle) or employing commercial automated milling equipment (such as a mixer or planetary mill). As a safety note, it is important when using commercial equipment to follow both standard safety practices and the manufacturer’s specifications/protocols to ensure safe sample preparation and machine operation. Operating outside of these parameters can pose serious hazards including pressure build-up, high-temperatures, and jar failure.

The following discussion for each publication provides an overview of the teaching experiment, including the reagents and mechanochemical reaction conditions, product workup and yield, spectroscopic characterization techniques (melting point and similar methods generally not discussed), and the ways in which green chemistry principles were taught or assessed with students, when reported in each case. With respect to the latter, a common pedagogical approach adopted by several authors was the use of pre- or post-lab questions assessing students’ understanding of the green benefits of mechanochemistry, which will not be explicitly mentioned further for brevity (but are outlined in Table S1). The experiments generally fit into a single 3–4 h session and the reactions conducted at room temperature, unless otherwise stated.

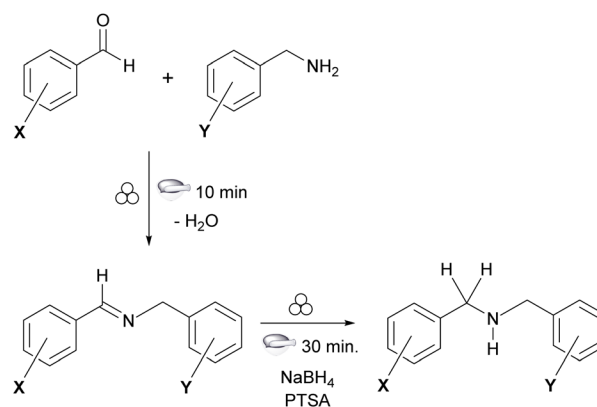
There are a number of “solvent-free” teaching experiments that employ grinding, while also using reagents that are either liquids, low-melting solids (or melted by heating), or two solids that form eutectic melts upon mixing.<sup>21–25</sup> While some of these teaching examples have not been explicitly discussed herein, it is worth noting that what is classified as a mechanochemical reaction can still be a matter of debate by even expert practitioners in the field. According to the IUPAC definition of mechanochemistry, a reaction needs to be induced by the direct absorption of mechanical energy. In any case, whether or not some of these experiments strictly fit this definition, pedagogically they are still useful in introducing the concept of mechanochemistry and making the same connections to green chemistry principles.

## Organic experiments

The organic undergraduate teaching lab was one of the earliest adopters of mechanochemistry, and thus there are numerous examples of the synthesis of organic compounds. Dicks provided a review of various solventless teaching experiments in the organic laboratory spanning 2000–2009, with several employing mechanochemical syntheses.<sup>26</sup> This section will focus on organic teaching activities published since 2010.

Following nearly a half-decade gap in the organic teaching literature, in 2015, Goldstein and Cross introduced students to a reductive amination experiment, in which a selection of liquid benzylamines and aldehydes react to form an intermediate imine *via* a dehydration reaction with grinding in an agate mortar and pestle for 15 min, followed by reduction using *p*-toluenesulfonic acid (PTSA) and sodium borohydride upon an additional 30 min of grinding (Scheme 1).<sup>23</sup> The authors noted that both the benzylamine and aldehyde needed to be liquids for a successful and clean reaction, raising the question of whether the condensation reaction is necessarily facilitated in a true mechanochemical manner, as discussed previously. Following ethyl acetate extraction (57–85% yield), the hydrochloride salts could also be formed and recrystallized from ethanol (8–32% yield), with the products characterized by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy.

In 2016, Margetić and Štrukil published a book chapter highlighting promising reactions from the primary literature that could be used to introduce mechanochemistry into the undergraduate curriculum.<sup>27</sup> They proposed a selection of mechanochemical syntheses of different organic compounds, including carbon–carbon coupling, C–H functionalization, carbon–nitrogen coupling, metal–ligand complexation, and cycloaddition reactions. In 2020, Colacino and Porcheddu published another book chapter offering additional mechanochemical reactions that were deemed appropriate for the organic undergraduate teaching laboratory, including both metal-catalyzed and metal-free reactions.<sup>28</sup> In both chapters, the reactions were selected from the primary literature using several



Scheme 1 Reductive amination reaction by manual grinding (X = H, 3-Cl, 4-OCH<sub>3</sub>, and 4-CH<sub>3</sub> and Y = H and 4-CH<sub>3</sub>). Adapted/reproduced from ref. 23 with permission from the American Chemical Society, copyright 2015.

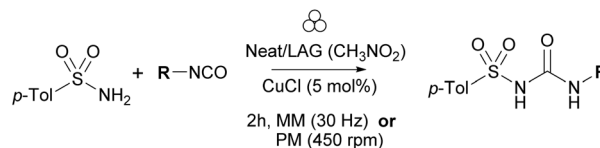


important criteria for teaching experiments (*e.g.* cost, commercial availability, time, yield, and workup), and automated ball-milling techniques were implemented. However, it is unclear whether these experiments have been directly implemented with students.

In 2018 in Brazil, Cunha and colleagues developed a mechanochemical chlorination of acetanilide using the less hazardous reagent trichloroisocyanuric acid (TCCA) to afford 4-chloroacetanilide (Scheme 2).<sup>29</sup> While the synthesis could be accomplished by hand grinding in a mortar and pestle, they reported a very long 1 h synthesis performed by students working in pairs and alternating every ~10 min, with relatively low yields (36–40%). Alternatively, they provided one of the earliest examples using a commercial planetary ball mill (PM) in the teaching laboratory, which resulted in a higher yield (52% in 1.5 h at 500 rpm) and, presumably, less fatigue in students' wrists. It is important to note that agate-lined reaction vessels and balls were recommended as TCCA may corrode stainless steel. Workup after milling included extractions with ethyl acetate and product recrystallization from water/ethanol before characterization by IR. Cunha *et al.* incorporated green chemistry principles into the activity by having students calculate E-factor metrics and by comparing the results with those from an alternative synthetic route employing sulfuric acid as the solvent.

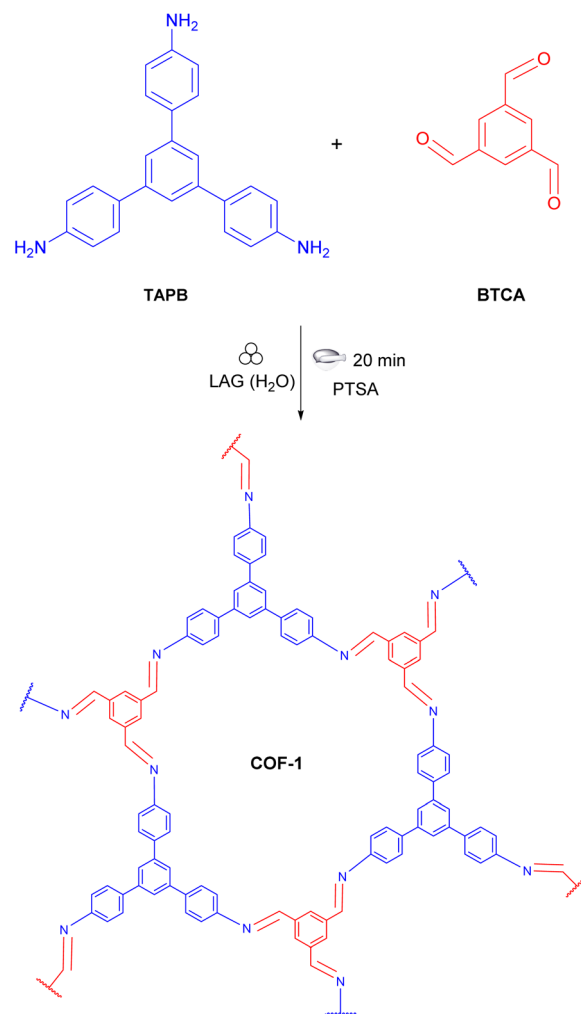
In 2019, Colacino *et al.* reported an experiment exploring the mechanochemical synthesis of a small library of sulfonylureas, including the pharmaceutical ingredient tolbutamide, through the catalytic coupling (*via* CuCl) of *p*-toluenesulfonamide with four different isocyanates. They used either neat or liquid-assisted grinding (LAG) with a small amount of nitromethane as the liquid to accelerate the reaction (Scheme 3).<sup>30</sup> The synthesis was performed in either a mixer mill (at 30 Hz) or a planetary ball mill (at 450 rpm) for 2 h. Workup included EDTA-based complexation directly in the reaction jar, followed by vacuum filtration and washing with water to fully remove the catalyst, resulting in 65–98% yield of the sulfonylureas, which were characterized by <sup>1</sup>H and <sup>13</sup>C NMR. A unique facet of this activity is the ability to highlight how the two different mechanochemical-reaction conditions enable the formation of two different polymorphs of tolbutamide.

In the same year, Mancheno *et al.* introduced students to the only example of a mechanochemical synthesis of a covalent organic framework (COF-1) (Scheme 4). The solids 1,3,5-tris(*p*-aminophenyl)benzene (TAPB) and 1,3,5-

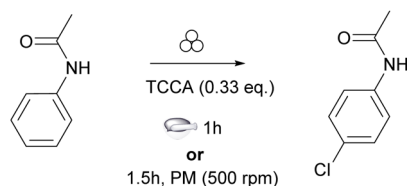


**Scheme 3** Mechanochemical synthesis of sulfonylureas *via* CuCl-catalyzed coupling of *p*-toluenesulfonamide with isocyanates (R = CH<sub>3</sub>CH<sub>2</sub>–, CH(CH<sub>3</sub>)<sub>2</sub>–, PhCH<sub>2</sub>–, and CH<sub>3</sub>(CH<sub>2</sub>)<sub>3</sub>–; *p*-Tol = 4-methylphenyl). Adapted/reproduced from ref. 30 with permission from the American Chemical Society, copyright 2019.

benzenetricarbaldehyde (BTCA) were first ground together in a 1 : 1 molar ratio, together with *p*-toluenesulfonic acid (PTSA) using an agate mortar and pestle for 5 minutes.<sup>31</sup> Next, a small amount (20 μL) of water was added and an additional 15 minutes of LAG grinding was performed. The product workup involved quick oven drying, followed by washing with water, filtration, and additional washing with methanol and THF



**Scheme 4** LAG synthesis of a covalent organic framework (COF-1) from 1,3,5-tris(*p*-aminophenyl)benzene (TAPB) and 1,3,5-benzenetricarbaldehyde (BTCA). Adapted/reproduced from ref. 31 with permission from the American Chemical Society, copyright 2019.

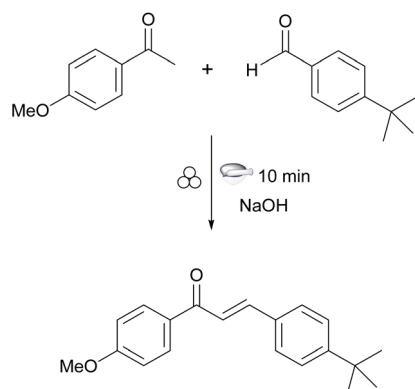


**Scheme 2** Mechanochemical chlorination of acetanilide using trichloroisocyanuric acid (TCCA) by manual grinding or using a planetary mill (PM). Adapted/reproduced from ref. 29 by the Brazilian Chemical Society under Creative Commons CC-BY-4.0, copyright 2018.



(60%–80% yield). The teaching activity was run over five different 3.5 h sessions and involved students also carrying out a solvent-assisted synthesis and characterization of the COFs using several solid-state methodologies including IR,  $^{13}\text{C}$  CP-MAS NMR, powder X-ray diffraction (PXRD) and thermogravimetric analysis (TGA). While green chemistry principles did not appear to be the focus of the activity, performing the solvent-assisted synthesis provides a potential opportunity for instructors to introduce comparisons, either qualitative or with metrics, which could enhance students' learning of sustainability.

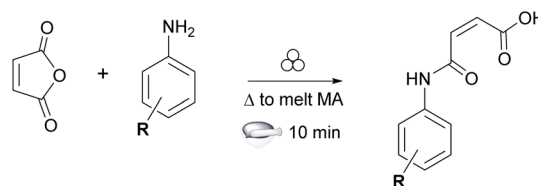
In 2019, Bastin and co-authors published a teaching activity in for a two-step synthesis of substituted *N*-phenylmaleimides and their subsequent use in a Diels–Alder reaction.<sup>24</sup> The first step involved a solventless amine acylation reaction between maleic anhydride and a substituted aniline. This was achieved by melting the former reactant in a small porcelain mortar on a hotplate before removing the reaction from heat and adding the aniline, followed by manual grinding with a pestle for 10 min (Scheme 5). The product was extracted and washed with ethyl acetate, giving average student yields of 66%. As noted before, Bastin *et al.* did not explicitly identify this reaction as mechanochemical, as it may not necessarily be induced by the mechanical force of grinding, but instead facilitated by solventless mechanical mixing.<sup>32</sup> This illustrates some of the nuance of what may or may not be considered mechanochemistry. Alternative solution-based syntheses for this reaction were also provided using ethyl acetate. The experiment is amenable to spectroscopic characterization by IR or  $^1\text{H}$  NMR spectroscopy, and the entire experiment could be completed in two or three 3 h sessions. This solvent-free reaction exhibits high atom economy, which was assessed by students, and they also performed a green chemistry assessment through the analysis of reagent hazards and metrics including effective mass yield (EMY) and E-factor. The alternative solvent-based routes also provide the potential for student comparisons between these approaches.



**Scheme 5** Solvent-free amine acylation reaction between maleic anhydride and a substituted aniline ( $\text{R} = 4\text{-Cl}$ ,  $4\text{-OCH}_3$ ,  $4\text{-CH}_3$ , and  $3\text{-NO}_2$ ) by heating and manual grinding. Adapted/reproduced from ref. 24 by the Taylor & Francis Group under Creative Commons CC-BY-4.0, copyright 2019.

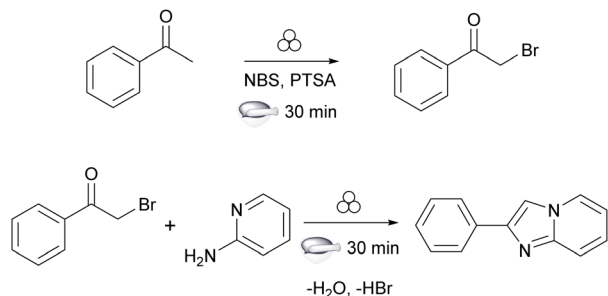
In 2022, Jordan and co-workers developed an experiment involving the four-step synthesis of avobenzone, which is an active component in sunscreens, that can be completed in two 4 h sessions.<sup>25</sup> In the first session and step in the sequential synthesis, a chalcone was made using an approach adapted from Palleros,<sup>33</sup> where a solvent-free aldol condensation between 4-methoxyacetophenone and 4-*tert*-butylbenzaldehyde with NaOH was performed in a mortar and pestle (Scheme 6). Once a sticky white paste was formed ( $\sim 10$  min of manual grinding), the product was worked up using hot water and recrystallized from hot ethanol before spectroscopic characterization by  $^1\text{H}$  NMR. Similar to the previous example, it could be argued whether this formally fits the definition of mechanochemistry. As stated by Palleros in their work, at least one liquid reactant (in this example, the benzaldehyde) or the formation of eutectics is required, which produces liquid phases with a high reactant concentration environment that may be responsible for the observed acceleration of reaction rates. In the subsequent lab session, three different synthetic reactions transform the chalcone into avobenzone, two of which also employ microwave heating.

In 2024, Neto *et al.* developed a teaching lab for the sequential mechanochemical preparation of 2-phenylimidazo [1,2- $\alpha$ ]pyridine (Scheme 7).<sup>34</sup> In the first step, 2-bromoacetophenone was synthesized on the gram scale by students from acetophenone using manual grinding in the presence of *N*-bromosuccinimide (NBS) and *p*-toluenesulfonic acid (PTSA), either in a mortar and pestle or in a thick-walled (4 mm) test tube using a glass rod. After 30 minutes of grinding (with alternating students), the product was extracted with ethyl acetate and washed with aqueous sodium thiosulfate and aqueous sodium bicarbonate to remove the remaining NBS and acid catalyst, respectively, giving an average isolated product yield of 96%. The second step involved the reaction of 2-bromoacetophenone with 2-aminopyridine, again with 30 minutes of manual grinding, followed by workup with hot acetone and cold hexane for precipitation of 2-phenylimidazo [1,2- $\alpha$ ]pyridine with an average yield of 77%. The authors also noted that this procedure could be performed using a homemade ball-mill apparatus consisting of a plastic Falcon tube filled with several small steel balls and agitated using a vortex mixer. Replacing the total of 1 h manual grinding with 10 min using this apparatus resulted in comparable yields. The product was spectroscopically characterized by  $^1\text{H}$  and  $^{13}\text{C}$  NMR and IR spectroscopy. If desired, students could compare the



**Scheme 6** Solvent-free aldol condensation between 4-methoxyacetophenone and 4-*tert*-butylbenzaldehyde by mortar and pestle grinding. Adapted/reproduced from ref. 25 with permission from the American Chemical Society, copyright 2022.



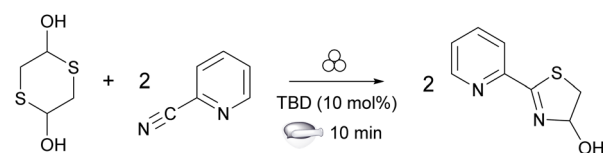


**Scheme 7** Sequential mechanochemical preparation of 2-phenylimidazo[1,2-*a*]pyridine from 2-bromoacetophenone. Adapted/reproduced from ref. 34 by the Brazilian Chemical Society under Creative Commons CC-BY-4.0, copyright 2024.

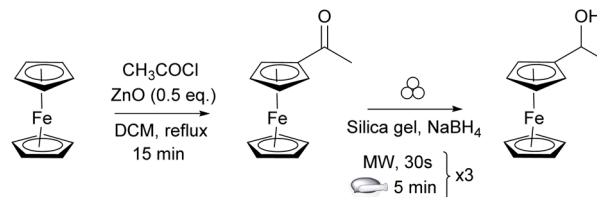
mechanochemical route for the  $\alpha$ -bromination of acetophenone, which was reported here for the first time, to a more traditional solution-based protocol that requires 12 h of reflux.

In 2025, Ma and colleagues published an optimized route for the synthesis of a thiazoline heterocycle from 1,4-dithiane-2,5-diol and two equivalents of 2-cyanopyridine, catalyzed by triazabicyclodecene (TBD) base, *via* mechanochemical grinding with a mortar and pestle for 10 minutes (Scheme 8).<sup>35</sup> Simple recrystallization from hot ethanol resulted in 65–78% isolated yields for students, followed by characterization using TLC, GC-MS, and  $^1\text{H}$  NMR spectroscopy. The authors also screened several conditions, including different bases and solution-based syntheses with different solvents, and had students explore different grinding protocols and mortar-and-pestle materials, all of which have the potential to be adapted by instructors to embed student inquiry or comparison activities with a green chemistry lens, if desired.

Another example was provided by Pokharel *et al.* in 2025 with a two-session (3 h each) experiment involving the synthesis of acetylferrocene, followed by its mechanochemical/microwave reduction to ( $\pm$ )-1-ferrocenylethanol (Scheme 9).<sup>36</sup> The latter reduction of ketone to alcohol is facilitated by  $\text{NaBH}_4$  and silica gel, where 30 seconds of heating in a household microwave (MW) oven was followed by 5 minutes of grinding in a mortar and pestle, which was repeated three times. It is worth noting here that the function of grinding appears to predominately be facilitating the formation of the silica-supported sodium borohydride reducing agent.<sup>37</sup> The authors noted that heat could be avoided, but this required a longer grinding time (20 min). Solvent workup with ethyl acetate and water for the



**Scheme 8** Synthesis of a thiazoline heterocycle from 2-cyanopyridine and a half-equivalent of 1,4-dithiane-2,5-diol *via* mechanochemical grinding. Adapted/reproduced from ref. 35 with permission from the American Chemical Society, copyright 2025.



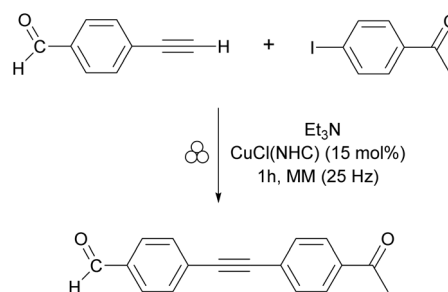
**Scheme 9** Acetylation of ferrocene and the subsequent reduction to ( $\pm$ )-1-ferrocenylethanol using a microwave (MW) oven and grinding. Adapted/reproduced from ref. 36 with permission from the American Chemical Society, copyright 2025.

mechanochemical reduction resulted in reported student yields as high as 87%, with the product being characterized by IR,  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectroscopy.

The last example of an organic mechanochemical experiment to be discussed herein was provided by Shunnar and colleagues in 2025.<sup>38</sup> Over three 2–2.5 h sessions, students first synthesized a copper *N*-heterocyclic carbene (NHC) complex, which can be transmetalated to a gold complex; both reactions are performed *via* mixer milling (see Inorganic experiments section). The  $\text{CuCl}(\text{NHC})$  complex (NHC=*N,N'*-bis(2,6-diisopropylphenyl)imidazole-2-ylidene or “IPr”) was then used as a catalyst (15 mol%) for the mechanochemical Sonogashira cross-coupling of 4-ethynylbenzaldehyde and 4-iodoacetophenone using triethylamine as the base in a mixer mill for 1 h (25 Hz) (Scheme 10). The reaction was quenched with water and the product was extracted with dichloromethane (DCM), resulting in average student yields of 78%, followed by spectroscopic characterization by  $^1\text{H}$  NMR and GC-MS. Students also explored the same cross-coupling reaction with  $\text{Pd}(\text{PPh}_3)_4$  as a co-catalyst, which improves the conversion to 88% under analogous milling conditions. In this activity, students learned about green chemistry principles through several pre-laboratory activities and calculating various metrics (AE, RME, OE, MI, and E-factor).

### Inorganic experiments

Several inorganic teaching experiments have also been published employing mechanochemical syntheses, although it is worth noting that the majority have emerged within the past five



**Scheme 10** NHC-catalyzed mechanochemical Sonogashira cross-coupling of 4-ethynyl benzaldehyde and 4-iodoacetophenone. Adapted/reproduced from ref. 38 by the American Chemical Society under Creative Commons CC-BY-4.0, copyright 2025.



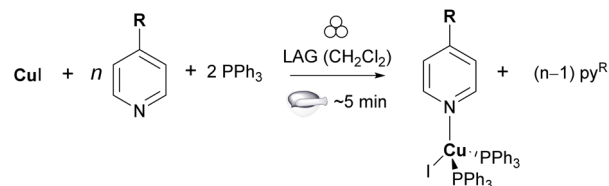
## Tutorial Review

years. Margetić and Štrukil's chapter in the 2016 Mechanochemical Organic Synthesis book also proposes two promising teaching reactions involving the mechanochemical syntheses of an organometallic Ru complex and Zn-salen complexes;<sup>27</sup> however, as stated for the organic reactions, it is unclear if and how these may have been implemented with students in the teaching laboratory.

An early inorganic example of mechanochemistry from the contemporary teaching literature was reported by De Vos and Verdonk in 1985,<sup>39</sup> where they discussed a demonstration involving grinding lead nitrate and potassium iodide using a mortar and pestle to form lead(II) iodide *via* salt metathesis, producing a colour change from white reagents to yellow product as a visual indication of reaction progress. Interestingly they noted that even simple shaking of the reagents in a closed test tube was sufficient for the reaction to proceed. This reaction is a solid-state version of the popular solution-state demonstration commonly referred to as the “golden rain” experiment.

In 2010, Berry *et al.* published an experiment for the mechanochemical synthesis of a dimeric  $[\text{PdCl}_2\{\text{Ph}_2\text{P}(\text{CH}_2)_5\text{PPh}_2\}]_2$  complex *via* the reaction of  $\text{PdCl}_2$  with the bidentate phosphine 1,5-bis(diphenylphosphino)pentane.<sup>40</sup> For the milling procedure, a home-made apparatus was constructed from a well-secured overhead stirrer (fabricated using an old-style food mixer) used to spin a four-winged propeller that mixed 3/16 inch steel ball bearings inside a 50 mL round-bottomed flask. While the authors reported no structural failures caused by the steel balls breaking the glass, caution should be exercised when using homemade apparatus such as this due to potential safety risks in the teaching laboratory. After overnight milling and workup using DCM to extract the product, isolated yields of 20–45% were obtained by students, and characterization by  $^1\text{H}$ ,  $^{13}\text{C}$ , and  $^{31}\text{P}$  NMR spectroscopy showed a mixture of *trans* and *cis* isomers. A subsequent step involved students deprotonating the dimeric product *via* overnight reflux in DMF, and recrystallization from DCM afforded the pincer complex  $\text{PdCl}\{\text{CH}[(\text{CH}_2)_2\text{PPh}_2]_2\}$ , a known catalyst for Suzuki–Miyaura coupling. The latter could provide a possible extension for instructors to apply the green chemistry principle of catalysis within this activity. The entire experiment and characterization were completed in two 3 h lab sessions.

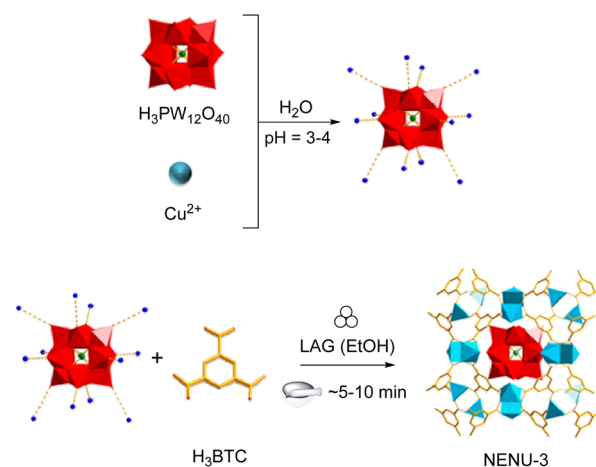
After a decade interlude, Förster and Heinze reported an inorganic teaching experiment in 2020 for the LAG mechanochemical syntheses of  $\text{CuI}(\text{PPh}_3)_2\text{L}$  ( $\text{L} = \text{py}$  or  $\text{py}^{\text{CN}}$ ) complexes, which exhibit luminescence thermochromism.<sup>41</sup> Using a mortar and pestle,  $\text{CuI}$  was combined with either pyridine ( $\text{py}$ ) or 4-cyanopyridine ( $\text{py}^{\text{CN}}$ ) and a few drops of dichloromethane and ground for 1 min. This was followed by the addition of  $\text{PPh}_3$  and further grinding for a few minutes (Scheme 11). *Tert*-butyl methyl ether was then used to collect and wash the products by filtration, and after drying, the solid product was characterized by attenuated total reflectance (ATR) IR spectroscopy, along with qualitative observations under UV light. The authors noted that other substituted pyridines and nitrogen heterocycles have been successfully used for analogous Cu complexes but suggested avoiding some due to their toxicity and cost.



Scheme 11 LAG mechanochemical synthesis of  $\text{CuI}(\text{PPh}_3)_2\text{L}$  ( $\text{L} = \text{py}$  or  $\text{py}^{\text{CN}}$ ;  $\text{R} = \text{H}$  and  $\text{CN}$ ) complexes. Adapted/reproduced from ref. 41 with permission from the American Chemical Society, copyright 2020.

The same year, Yuan *et al.* developed and implemented the only example in the undergraduate laboratory of the mechanochemical preparation of a metal–organic framework (MOF), specifically an encapsulated polyoxometalate (POM) guest (POM@MOF).<sup>42</sup> The POM@MOF, NENU-3, with the composition of  $[\text{Cu}_2(\text{BTC})_{4/3}(\text{H}_2\text{O})_{2/6}[\text{HPW}_{12}\text{O}_{40}] \cdot (\text{C}_4\text{H}_{12}\text{N})_2 \cdot 25\text{H}_2\text{O}$ , was formed by first dissolving equimolar  $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$  and  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  (HPW) in water adjusted to acidic pH, followed by evaporation to yield a light green powder. The product powder was combined with 1,3,5-benzenetricarboxylic acid ( $\text{H}_3\text{BTC}$ ) and a small amount of ethanol for LAG and ground for 5–10 minutes in a mortar and pestle until the blue NENU-3 product was obtained (Scheme 12). The product was collected by centrifugation and washed with water and ethanol to remove unreacted precursors before characterization by PXRD, IR and UV-vis spectroscopy,  $\text{N}_2$  adsorption, and TGA during additional sessions. The authors also detailed traditional synthetic protocols involving hydro(solvo)thermal or solution-based methods, which, when combined with characterization, would require three typical lab sessions in total; however, this provides an opportunity for potential green chemistry comparisons and discussions by students.

In 2023, Kraft reported a mechanochemical teaching experiment involving three synthetic routes to form the inorganic



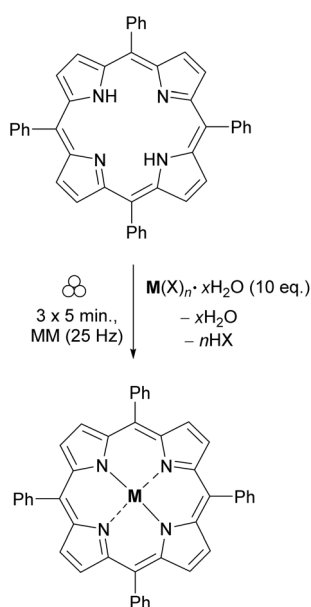
Scheme 12 Preparation of POM@MOF  $[\text{Cu}_2(\text{BTC})_{4/3}(\text{H}_2\text{O})_{2/6}[\text{HPW}_{12}\text{O}_{40}] \cdot (\text{C}_4\text{H}_{12}\text{N})_2 \cdot 25\text{H}_2\text{O}$  (NENU-3) from  $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ ,  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  (HPW), and 1,3,5-benzenetricarboxylic acid ( $\text{H}_3\text{BTC}$ ) using LAG. Adapted/reproduced from ref. 42 with permission from the American Chemical Society, copyright 2020.



pigment “Prussian blue”,<sup>43</sup> a.k.a. iron(III) hexacyanoferrate(II) or  $K_3Fe^{III}[Fe^{II}(CN)_6]$ , by simple mortar and pestle grinding. The routes involved manual grinding for up to 5 minutes the hydrated salts of either  $Fe^{III}Cl_3$  with  $K_4[Fe^{II}(CN)_6]$ ,  $Fe^{II}SO_4$  with  $K_3[Fe^{III}(CN)_6]$ , or both as iron(II) salts of  $Fe^{II}SO_4$  with  $K_4[Fe^{II}(CN)_6]$ , where “Prussian white” or “Everitt’s salt” is first formed, but is readily oxidized to Prussian blue by oxygen in the air after being left on the bench for a few hours.

The same year, Nitka *et al.* published an experiment for the greener synthesis of tetraphenylporphyrin ( $H_2TPP$ ) and subsequent metalation, where a microwave-synthesized porphyrin ligand could be metallated *via* either solution-based reflux or mechanochemically using a mixer mill (Scheme 13).<sup>44</sup> In the latter, a ten-fold excess of metal(II) acetate hydrate salt ( $M = Zn, Cu, Ni, Co, Ag$  as  $AgNO_3$ ) relative to  $H_2TPP$  was used and three 5 minutes milling intervals at 25 Hz were shown to lead to its complete incorporation according to UV-vis after extraction with ethyl acetate. Green chemistry principles related to mechanochemistry were highlighted in the student manual introduction and in a student pre-lab question. The alternative solution-based metalation route by reflux, as well as an additional microwave-based route mentioned by the authors,<sup>45</sup> also provide the potential opportunity for instructors to include deeper discussions and comparisons between these synthetic approaches using green chemistry principles.

Jenkins *et al.* also provided a simple experiment in 2023 where mortar and pestle grinding for a few minutes facilitated the conversion of  $CuCl_2$  to  $CuO$  using two equivalents of  $NaOH$ .<sup>46</sup> Washing with water removed the  $NaCl$  byproduct before drying (52.2% yield) and the product was characterized by IR as both a solid and in solution, as well as by PXRD. The

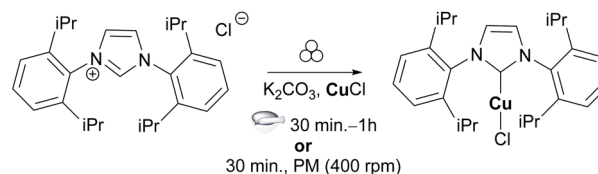


**Scheme 13** Mechanochemical metalation of tetraphenylporphyrin ( $H_2TPP$ ) with  $MX_2 =$  metal(II) acetate hydrate salts ( $M = Zn, Cu, Ni,$  and  $Co$ ;  $x = 1-4$ ) or  $AgNO_3$ .  $Ph = -C_6H_5$ . Adapted/reproduced from ref. 44 by the Taylor & Francis Group under Creative Commons CC-BY-4.0, copyright 2023.

conversion was compared to solution-state syntheses using three different solvents (water, isopropanol, and acetone; yields 86.4–90.1%), which extends the experiment over two 3 h sessions. This allowed for comparisons in the context of green chemistry principles, with the notable advantage that the solventless mechanochemical route reached completion within a few minutes compared to the hours required for the solution-based methods, albeit with significantly lower yields.

The final inorganic example from 2023 by Bru and colleagues provided mechanochemical routes for the synthesis of the N-heterocyclic carbene (NHC) complex  $[Cu(Cl)(IPr)]$  ( $IPr = N,N'$ -bis(2,6-diisopropylphenyl)imidazole-2-ylidene) (Scheme 14).<sup>47</sup> Equimolar amounts of  $CuCl$  and the imidazolium salt  $IPr \cdot HCl$  were reacted in the presence of  $K_2CO_3$  base using either (1) automated planetary ball milling for 30 min at 400 rpm or (2) manual mortar and pestle grinding for 30 min to 1 h (with isolated yields of ~64% after half an hour). Both routes required work-up by dissolving the product in DCM and then precipitation with pentane before filtration and drying *in vacuo*. The authors provided an alternative “greener” work-up to avoid DCM by substituting with acetone, followed by Celite filtration and then precipitation with heptane or cyclohexane, resulting in comparable yields. In this activity, students also applied six green chemistry metrics (AE, E-factor, MI, RME, OE, and Green Star) to compare the mechanochemical synthesis to other solution-based routes that were also performed over the two 3 h sessions, and all products were characterized by  $^1H$  NMR. Students unanimously agreed that the mechanochemical route was the greener synthetic method. Interestingly, the publication by Bru *et al.* was the only one discussed herein that explored the experience and views of students on green and sustainable chemistry following the activity; amongst several insights gained, one important outcome was that students developed a new perspective on mechanochemistry as a powerful tool with the potential to avoid/diminish solvent use.

As first discussed in the Organic experiments section, in 2025, Shunnar and colleagues introduced an experiment in which students also synthesized  $[Cu(Cl)(IPr)]$  *via* a similar synthetic route as Bru *et al.*,<sup>47</sup> and then used the complex as a catalyst for a mechanochemical Sonogashira cross-coupling.<sup>38</sup> In their synthesis, the  $Cu$  complex was prepared using a mixer mill with two cycles of 30 minutes each at 25 Hz. Extraction with acetone and filtration through Celite, followed by precipitation with pentane resulted in a 66% average student yield. Shunnar *et al.* also prepared an  $Au(Cl)(IPr)$  complex through the transmetalation of  $Cu$ -NHC with  $AuCl$  using analogous ball milling



**Scheme 14** Mechanochemical synthesis of  $[Cu(Cl)(IPr)]$ . Adapted/reproduced from ref. 47 with permission from the American Chemical Society, copyright 2023.



## Tutorial Review

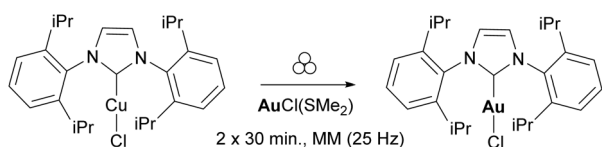
conditions and similar workup, giving an average student yield of 70% (Scheme 15), followed by spectroscopic characterization by  $^1\text{H}$  NMR. As discussed previously, their activity introduced students to green chemistry principles through several qualitative pre-laboratory questions and quantitative metrics calculations.

In 2024, Domínguez-Martín *et al.* developed an experiment for their inorganic medicinal chemistry course involving the mechanochemical synthesis of an antibiotic coordination framework (ACF),<sup>48</sup> specifically a coordination complex conjugated with a pharmacologically active molecule based on the known antibiotic nalidixic acid and zinc as the metal center. The Zn-ACF was formed by manual grinding in a mortar and pestle of a mixture of nalidixic acid and zinc nitrate with a small amount of aqueous ammonia solution for 5 minutes of LAG (Scheme 16), followed by washing with ethanol to remove the ammonium nitrate byproduct and drying in a desiccator. Typical student yields ranged from 10.8–92.4%, and the product was spectroscopically characterized by IR and PXRD. The synthesis and characterization were divided into two 2 h sessions, with the antimicrobial activity tested during a third session.

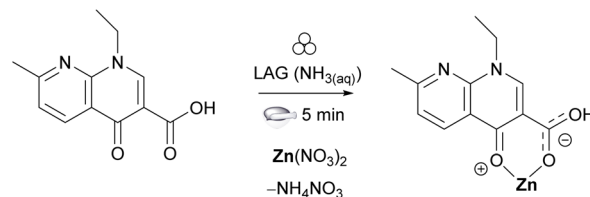
The last example from 2024 in the inorganic teaching literature is by Dong *et al.* with the mechanochemical synthesis of  $[\text{Ni}(\text{Me}_3\text{en})(\text{acac})][\text{BPh}_4]$ .<sup>49</sup> In a mortar, equimolar amounts of  $\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ , acetylacetonone (Hacac),  $\text{NaBPh}_4$ , aqueous  $N,N,N'$ -trimethylethylenediamine ( $\text{Me}_3\text{en}$ ) solution, and a half-equivalent of  $\text{Na}_2\text{CO}_3$  were ground with a pestle for 10 min. The use of liquid reagents and aqueous solution suggests this would likely be classified as LAG if induced mechanochemically. The product was then extracted and washed with water before being dried in an oven at 90 °C for 30 min. Students explored the solvatochromic and thermochromic properties of the products using UV-vis spectroscopy, and both single-crystal and powder XRD data were obtained for the product(s), which could be used for analyses if desired by the instructor. An aqueous synthesis of this product was also described, which provides instructors an opportunity to incorporate student comparisons if desired.

## Other subdiscipline experiments

A few other mechanochemical teaching experiments have been published that are aligned more closely to other sub- or inter-disciplines of chemistry beyond that traditionally considered organic or inorganic chemistry (*e.g.* polymer/materials, pharmaceutical, and computational), which are discussed below.



Scheme 15 Mechanochemical synthesis of  $[\text{Au}(\text{Cl})(\text{IPr})]$  by transmetalation with  $[\text{Cu}(\text{Cl})(\text{IPr})]$ . Adapted/reproduced from ref. 38 by the American Chemical Society under Creative Commons CC-BY-4.0, copyright 2025.

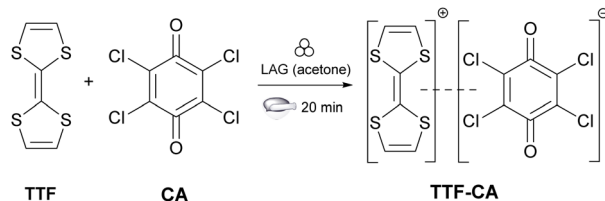


Scheme 16 Mechanochemical synthesis of a zinc-antibiotic coordination framework (Zn-ACF) using nalidixic acid. Adapted/reproduced from ref. 48 by the American Chemical Society under Creative Commons CC-BY-4.0, copyright 2024.

Wixtrom *et al.* provided an example of LAG in 2014 for the synthesis of two polymorphs of the charge transfer salt tetrathiafulvalene-chloranil (TTF-CA) (Scheme 17).<sup>50</sup> After 20 minutes of manual grinding in a mortar and pestle, the green polymorph could be obtained using a small amount of acetone, whereas using a small amount of water during grinding afforded the black polymorph. The two products were characterized by infrared spectroscopy (IR), and the authors incorporated green chemistry metrics including atom economy and E-factor analyses for students.

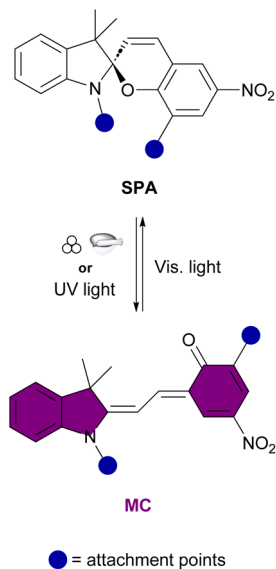
In 2017, Brown and colleagues published an outreach demonstration involving a mechanochromic poly(dimethylsiloxane) (PDMS) elastomer covalently cross-linked by spiroopyran (SP).<sup>51</sup> The SP molecule functions as both a photochemical and mechanochemical switch, where mechanical stimuli (*e.g.* pulling the polymer, hitting with a hammer, or dragging a blunt object across the surface) results in a reversible change from colourless to bright purple. The underlying chemistry involves the mechanochemical ring-opening of spiroopyran (SP) to give the highly coloured merocyanine (MC), as shown in Scheme 18. The elastomer slowly relaxes back to the colourless state under ambient conditions, or this can be expedited upon exposure to visible light. The authors noted a commercially available material with SP physically dispersed in PDMS (not covalently cross-linked) is also available but required special safety precautions and the colour change is much less intense.

In 2021, Winum *et al.* reported another unique experiment involving tribochromism, where mechanical grinding results in a colour change.<sup>52</sup> In their experiment, students first synthesized Maya blue pigments from their indigo derivatives *via* microwave-assisted reactions with clay. Drying of the solid products results in a thermochromic colour change generally to



Scheme 17 LAG synthesis of the charge-transfer salt tetrathiafulvalene-chloranil (TTF-CA) by manual grinding.<sup>50</sup>





**Scheme 18** Mechanically responsive poly(dimethylsiloxane) (PDMS) elastomer network covalently functionalized with spiroropyran (SP) cross-linkers. Adapted/reproduced from ref. 51 with permission from the American Chemical Society, copyright 2017.

a greyish/greenish colour. Upon crushing in a mortar, the material reverts to its initial blue colour due to strain-induced disruption of the solid-state structure, which increases surface contact with air and facilitates reabsorption of water onto the Mg sites in the sepiolite mineral. The products were characterized using UV-vis reflectance spectroscopy, and TGA was used to assess the water loss from the solid structures.

In 2022, Bychkov and Matveeva published a biopolymer experiment exploring the mechanochemical degradation of  $\alpha$ -cellulose over the course of five 4 h sessions.<sup>53</sup> Using a planetary ball mill, senior undergraduate students investigated different process conditions (0 to 960 s of milling). Students then investigated the properties of the treated samples using granulometric measurements of average particle size, viscometric determination of degree of polymerization, and degree of crystallinity by XRD. A unique aspect of this experiment was the use of a wattmeter to measure the energy consumption of the planetary mill for the cellulose destruction process, which could be used to introduce connections to green chemistry principle #6: design for energy efficiency.

In 2023, Silva and colleagues provided an advanced pharmaceutical experiment involving the mechanochemical synthesis of a dual-drug naproxen-cimetidine co-amorphous system (NPX-CIM) through neat co-milling of a 1 : 1 ratio of each component combined in a mixer mill for 60 min at 30 Hz.<sup>54</sup> The product required no solvent workup and was characterized by differential scanning calorimetry (DSC), PXRD and ATR-IR spectroscopy. It is worth noting that they implemented it with their first-year graduate students in a 5 h session, but it may also be amenable to adaptation for advanced undergraduate courses. This topic offers a unique application of mechanochemistry and is of interest for active pharmaceutical ingredients, as amorphous solids lack long-range order and intermolecular

interactions. As a result, they can exhibit higher solubilities relative to the crystalline phases of poorly water-soluble drugs, thereby enhancing drug bioavailability.

In 2023, Hu *et al.* provided a more specialized, multisession materials chemistry teaching activity based on their group research, which utilized a mechanochemical method to produce ultrathin two-dimensional MoS<sub>2</sub> nanosheets that could be applied as catalysts.<sup>55</sup> The MoS<sub>2</sub> nanosheets were prepared from a 1 : 6 molar ratio of MoO<sub>3</sub> to sulphur powder with 24 h milling in a planetary ball mill (580 rpm), followed by annealing under N<sub>2</sub> at 600 °C for 2 h. To fabricate S defect-rich MoS<sub>2</sub> nanosheets (which improve the catalytic efficiency), a “swift ball milling method” was used, where the later product was milled under a reducing atmosphere for an additional hour before being washed with DI water and then subjected to ultrasonication for 1 h, followed by several additional DI water washings, centrifugation, and freeze-drying protocols. The products were characterized using XRD, transmission electron microscopy (TEM), and X-ray photoemission spectroscopy (XPS). The two ultrathin 2D MoS<sub>2</sub> were also applied by students as catalysts for the oxidation of 3,3',5,5'-tetramethylbenzidine (TMB) and for the detection of ascorbic acid, quantified by UV-vis spectroscopy.

The only example exploring mechanochemical concepts using computational tools was published by Wang and Wang in 2024.<sup>56</sup> Using quantum chemistry calculations, this study provided students with insights into the underlying mechanisms and intricacies of mechanochemistry by computationally exploring several parameters for an ethanol model molecule including system energy, bond lengths, bond orders, and spin density. Within the study, students used the COGEF (constrained geometries simulate external force) method, which is a widely used computational approach in mechanochemistry to simulate the effects of external mechanical forces on molecules to predict chemical reactivity.<sup>57</sup>

## Perspectives, challenges, and opportunities

Mechanochemistry provides an interesting opportunity for educators to adapt a growing synthetic technique for use in the teaching laboratory. It provides a platform for thinking differently about how chemical reactions proceed, for integrating green chemistry principles, and applying tools that support more sustainable chemistry. As with any “new” method, educators must also overcome some challenges and barriers towards its integration, as trade-offs and practical considerations are inevitable in the teaching space. This section provides some perspectives and discussion reflecting on how mechanochemistry has been implemented in chemical education to date, the opportunities it may hold for undergraduate students, and some of the current challenges associated with its broader adoption by educators.

Most universities are looking for routes to increase their sustainability practices, and within the undergraduate chemistry curricula, green chemistry principles are also becoming



widely adopted.<sup>58</sup> The importance and impetus towards including green chemistry in the undergraduate curricula is evidenced by its requirement in many chemistry program accreditations, for example the American Chemical Society (ACS) just recently updated its guidelines for Bachelor's degree programs to require a working knowledge of the Twelve Principles of Green Chemistry since 2023.<sup>59</sup> Mechanochemistry offers a clear opportunity to simultaneously introduce and evaluate green chemistry principles. As a solvent-free or minimized synthetic method, a clear and commonly discussed aspect focuses on green chemistry principles #1 and #5, the prevention of waste and use of safer solvents, respectively. As mentioned in the introduction, with the prohibition of the widely used halogenated solvent dichloromethane, mechanochemistry also offers a sustainable opportunity for educators to break away from traditional solution-based approaches. However, it is worth highlighting that nearly every teaching example discussed herein generally required some solvent use during the workup of the mechanochemical reactions. While a large majority used "preferred" solvents according to green principles (such as water, ethyl acetate, and ethanol), their use may still provide an opportunity for instructors to introduce solvent-selection guides to students. While no examples of this were reported herein, the potential for students to use solvent-selection guides in workup decisions offers opportunities to explore higher-level learning and/or inquiry-based activities. Catalysis, green chemistry principle #9, is another area that mechanochemistry can introduce in the undergraduate laboratory, as shown by several examples above.<sup>30,35,38</sup> In fact, connections to all twelve green chemistry principles have been made for examples of mechanochemistry,<sup>60</sup> which may offer new opportunities for educators to integrate these principles into their undergraduate curriculum. Unfortunately, many of the teaching experiments discussed herein solely apply mechanochemistry in a "show and tell" fashion, leaving potential opportunities for active student learning and the application of green chemistry principles in practice behind "on the lab bench". A common pedagogical approach employed in many of the mechanochemical teaching experiments was limited to the use of generalized pre- or post-lab questions, such as "What is green chemistry? Which principles of green chemistry do mechanochemical syntheses align with?" (see Table S1). This is a missed opportunity to fully capitalize on the learning potential mechanochemistry has to offer. However, there are some good higher-order learning examples that describe having students explicitly evaluate green metrics and/or making comparisons with traditional synthetic approaches.<sup>29,35,44,47,50</sup> These offer a valuable instructional framework for educators looking to adopt mechanochemical experiments. It is also worth restating that only Bru *et al.* assessed and surveyed their students' experience and views around green and sustainable chemistry after completing their mechanochemical teaching activity.<sup>47</sup> This may be an area that warrants further investigation for mechanochemistry-focused teaching experiments to assess the pedagogical approaches and their impact on student knowledge of green and sustainable chemistry.

Manual grinding by mortar and pestle is an accessible, easily scalable and reasonably low-cost route towards integrating mechanochemistry into the undergraduate curriculum, with several teaching experiments discussed herein applying this approach. However, the more limited and inconsistent mechanical force generated through this method can result in long grinding times, introducing a practical challenge with respect to instructional timeframes and student enjoyment/fatigue caused by long grinding (in our experience, grinding for more than ~5 minutes becomes rather tedious for students). Instructors have been creative in finding affordable solutions to manual grinding, for example Neto *et al.* applied a home-made ball mill-type apparatus made using plastic Falcon tubes and small steel balls with a vortex mixer,<sup>34</sup> which reduced an hour of manual grinding down to 10 minutes. The authors herein have also heard anecdotal reports of educators adapting equipment such as the Wig-L-Bug® Mixer for mechanochemical reactions. When using equipment outside of their designed function, instructors should be mindful of the potential hazards and ensure that proper safety measures are in place to avoid accidents, especially when undergraduate students are involved in their operation.

As mentioned earlier, commercial equipment such as mixers and planetary mills offer advantages in terms of automating the mechanical process and greatly reducing the required milling time for most reactions. However, the associated costs may be a barrier towards gaining access to these tools in the undergraduate facility. In our experience, in addition to the mixer costing in the potentially tens of thousands of dollars, the reaction jars can also be expensive, often costing a few thousand dollars each (depending on their specifications). Another important practical consideration for using this type of equipment is potential capacity limits regarding the number of samples that can be run simultaneously, which is particularly important for larger class sizes and reactions requiring longer milling times. Typical commercial instruments only have a few "sample stations" that can operate at one time, and with even reasonably short reaction times, this can introduce practical bottlenecks within a teaching session lasting only a few hours. A hypothetical example to illustrate this point is a lab session with a group of 20 students working in pairs, where ten individual reactions are required, and if the mill instrument is limited to two simultaneous reactions, then five separate runs are required. If the reaction requires 30 min of milling, even beginning immediately at onset of the session would result in a best-case scenario where the final set of reactions only start milling 2.5 h into the session. Other teaching examples reported herein reported much longer milling times, such as 2 h,<sup>30</sup> or even 24 h.<sup>55</sup> While there are possible workarounds by integrating other activities and/or staggering what students are performing either within or between lab sessions, the timing when using commercial equipment can be a complicating factor for some potential experiments that should be taken into consideration. An exciting opportunity to potentially address some of these complications may be offered by new adaptors and reaction vessels available for specialized applications, which could be explored in the undergraduate laboratory to



increase throughput or enable longer batch grinding times. For example, the commercial brand Retsch® offers smaller jars that are stackable in its planetary mills (e.g. up to eight 12 mL samples simultaneously on their PM400 instrument, two in each of the four grinding stations) or adapters for their mixer mill that can simultaneously run four 5 mL or ten 2 mL stainless-steel grinding jars per station (with MM400, possessing two sample stations, enabling eight or twenty samples simultaneously). Other specialized attachments designed for other applications may also offer opportunities for instructors to adapt them for teaching purposes. For example, Retsch® offers an adaptor marketed for co-crystal screening on its planetary mills, which can each hold up to twenty-four 1.5 mL glass vials (which can be loaded with a few 3 mm or 4 mm steel balls), enabling up to 64 samples to be processed simultaneously. For comparison, De Vos and Verdonk noted that their simple teaching demonstration of lead(II) iodide formation from lead nitrate and potassium iodide could be facilitated by just shaking the reactants together in a glass tube.<sup>39</sup> For their mixer mills, adaptors for “single-use” plastic vials intended for homogenizing biological samples also allow for up to ten small vial (0.2–5 mL) or four 50 mL Falcon tubes to run simultaneously per grinding station, albeit at a lower milling frequency. This is similar to the Falcon tube and vortex mixer approach implemented in the teaching lab by Neto *et al.*<sup>34</sup> and described elsewhere,<sup>61</sup> which are accessible at considerably lower costs. Beyond those commercially available, custom adapter fabrication or 3D printing may also offer new opportunities for instructors to innovate and adapt milling equipment to fit the needs of the undergraduate teaching laboratory, although once again the authors emphasize that appropriate safety considerations and precautions must be assessed for these items, particularly in contexts involving students. Although no examples were reported in the current teaching literature, other commercial devices could also be explored in the undergraduate laboratory, such as twin-screw extruders and resonant acoustic mixers. These instruments may already be available at some institutions for instructors to explore and may also be suitable for larger-scale reactions. For example, the authors envision that these could be applied by instructors for the batch preparation of a reagent used by students in the entire class, with student observing the reaction as a means of exposure to mechanochemistry and an opportunity to introduce metrics and other teaching moments.

In the book chapters by Margetić and Štrukil's in 2016,<sup>27</sup> and by Colacino and Porcheddu in 2020,<sup>28</sup> several potential organic and inorganic experiments to introduce mechanochemical synthesis into the undergraduate curriculum were proposed, with the authors applying several thoughtful considerations when selecting experiments for the teaching space. These include (i) affordable and commercially available reagents, (ii) reasonable reaction times to fit experiments within typical practical sessions, (iii) high yields and reaction selectivity, (iv) relatively simple workups, (v) flexibility on grinding materials and mechanochemical equipment, and (vi) where feasible, environmentally conscious or renewable reagents. While it is unclear if the proposed experiments had been tested or

implemented with undergraduate students, these thoughtful guidelines are a useful guide in selecting relevant syntheses from a growing body of mechanochemical reactions emerging from the primary literature to be adapted or developed into the undergraduate teaching laboratory.

Mechanochemical approaches also offer some unique advantages that could be harnessed to access new and previously inaccessible chemistries within the teaching space. There are a growing number of examples in the research literature where unique material systems and reaction pathways are possible, which are difficult or impossible to access through conventional solution or thermal-based methods.<sup>62–65</sup> There are also examples in the literature where mechanochemistry offers new, safer alternative synthetic routes. For example, in 2023, Patel *et al.* demonstrated a mechanochemical process for generating fluorochemicals from fluorspar, which bypasses the highly toxic and hazardous HF.<sup>66</sup> Other unique examples include mechanochemical syntheses that circumvent traditional requirements of inert atmospheres and dry solvents. For example, in 2025, Kondo and colleagues reported the direct generation of organolithium reagents in air from organic halides and lithium metal under bulk-solvent-free conditions without any special precautions.<sup>67</sup> The authors noted that this approach enabled reactions with poorly soluble aryl halides as well as direct C–F bond lithiation that are usually inefficient under conventional solution-based conditions. Similarly, mechanochemistry has been applied for the synthesis of sensitive organometallic reactions in air that otherwise would require a glove box or Schlenk line.<sup>68</sup> While these selected examples may or may not necessarily be well suited for the teaching lab, they illustrate that mechanochemistry can offer unique advantages and opportunities, which to the best of our knowledge, have generally not yet been capitalized on within the teaching laboratory to date.

Beyond its green and sustainable chemistry benefits such as solvent reduction/elimination, mechanochemistry also provides a unique “teachable moment” for students to consider the role solvents play and offers a renewed perspective towards how chemical reactions proceed. In our experience, many undergraduates assume that the presence of a solvent is always necessary. Indeed, some reactions greatly benefit from the presence of a solvent, and of course traditional reflux and other fundamental techniques are essential technical foundations that every chemist should learn. By no means should all solution-based undergraduate experiments be replaced with mechanochemical methods; however, advanced students will have already gained a great deal of experience with traditional syntheses, and introducing new and modernized approaches can be an effective way to enhance their skills. Colacino and Porcheddu insightfully wrote:<sup>28</sup>

“Is solvent-based chemistry a religion? No, but the current mindset of chemists and chemical educators needs to change to encompass alternatives to solution-based reactions. In this context, mechanochemistry offers new perspectives for sustainable thinking and conception of a chemical reaction...”

Educators must decide in a meaningful way when, where, and how to add mechanochemistry to their curriculum,



ensuring that it aligns with their teaching goals, and not just include it solely for the sake of doing so. As shown in several of the examples discussed herein, having students run a parallel synthesis using a traditional method (e.g. reflux) next to the mechanochemical approach holds pedagogical value by allowing comparisons of the synthetic and green chemistry metrics. Similarly, for some educators, having students evaluate solvent substitutions for a solution-based synthesis is an important learning opportunity, although, as highlighted in the teaching examples discussed, solvents are almost always required for workup in mechanochemical approaches, which still provides a similar opportunity for instructors to integrate the idea of solvent substitutions if desired.

The revival of mechanochemistry as a synthetic tool poses some challenges but offers substantial opportunities for educators and students, particularly as a straightforward means of engaging with green chemistry principles. As the research and teaching literature on mechanochemistry continues to grow, and as equipment is further developed or adapted to meet the needs of synthetic chemists and educators, fertile ground is emerging for its continued expansion into undergraduate teaching laboratories.

## Author contributions

All authors contributed equally.

## Conflicts of interest

There are no conflicts to declare.

## Data availability

Supplementary information: a summary of the key features from the articles reviewed (Table S1). See DOI: <https://doi.org/10.1039/d5su00971e>.

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