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Review Paper

Mechanochemistry: A green chemistry for green technology

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Abstract

Mechanochemistry involves the physicochemical transformation of materials or substances induced by external mechanical energy or forces. In recent years, the application of mechanochemistry as a green synthetic method for the preparation or production of new functional materials has gained significant interest by many researchers. This paper reviewed the relationship between mechanochemistry and the principles of green chemistry, mechanochemistry as green technology, mechanochemical reactions, peculiarities of mechanochemical processes, applications, and the challenges of mechanochemistry. However, based on the review, with improved or advanced technologies, it is strongly believed that mechanochemistry is probably going to be one of the most efficient way to improve greenness in chemical industries and beyond.

Keywords: Mechanochemistry, green chemistry, green technology, mechanochemical reaction, applications.

Introduction

An ideal chemical reaction should be simple, safe, effective, economical and free or have less hazardous byproducts among others[1,2]. However, the concept of green chemistry was introduced to achieve these attributes[3]. Thus, Green chemistry can be described as a branch of chemistry that deals with synthesis or manufacturing of chemical products and processes that are sustainable, simple, safe, effective, economical and reduce the use or generation of hazardous substances[4]. Furthermore, green chemistry is a multidisciplinary field, which is applicable to all branches of chemistry (physical, organic, inorganic, nanochemistry, mechanochemistry, pharmaceutical etc), chemical industry and materials sciences.

However, the concept of mechanochemistry which is the main subject matter can be described as the aspect of chemistry in which chemical reaction involving two or more substances are induced by external mechanical energy or forces at room temperatures[5]. Thus, in the laboratory, most mechanochemical reactions involving solid reactants are carried out by a simple manual grinding using a mortar with a pestle. However, various types of ball mills, or alternatively single- or twin-screw extruder which have advantages such as control of the reaction conditions and obtaining reproducible results over the use of pestle and mortar are also used[6,7].

Moreover, in recent years, the application of mechanochemistry as green synthetic method for the preparation or production of new functional materials has gained significant interest by many researchers[7-9]. This method depends on the physical and chemical transformations of the materials through induced mechanical forces by grinding and milling[8]. In addition, scientific studies revealed that due to the application of mechanical forces, the efficient energy dispersion and mass transportation has led to the unnecessary used of solvents and gave way for greener and more direct chemical syntheses than the normal solvent-synthetic reactions[9,10].

Furthermore, the applications of mechanochemistry as green approach to various fields of sciences including pharmaceuticals, fertilizers, catalysis, nanotechnology, ceramics, waste management, metallurgy etc have been reported[11-13].

In pharmaceuticals for instance, a large amount of energy is consumed during the synthesis of active pharmaceutical ingredients (API) due to many stages involve which are associated with the use of large volume of solvents[14]. The waste products of the reactions enter the soil through wastewater or a sludge thereby contaminating the environment. However, the large use of solvents, which is one of the major key players in the pharmaceutical industry during the synthesis, is of great concern as it affects the production cost and the environment[9]. Interestingly, these challenges have been addressed to some extent bymechanochemistry[15].

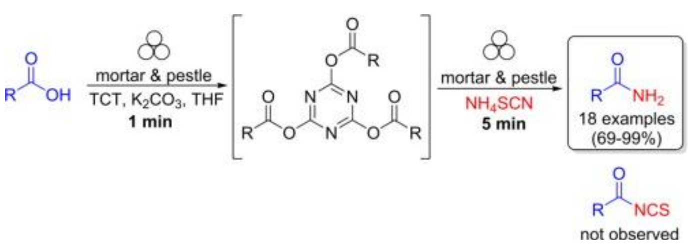
Therefore, this paper reviewed the concept of mechanochemistry in relation to green chemistry for green technology.

Mechanochemical Reactions

According to literature, mechanochemical reactions are not restricted to any state of matter (solid, liquid or gas)[16,17]. However, a large number of mechanochemical reactions have been demonstrated and published globally. For instance, the preparation of Hg from cinnabar (HgS) in the presence of vinegar carried out using pestle and mortar all made up of a Cu which was dated around 315 B.C. was among the several early discovered inorganic mechanochemical reactions carried out in mortar and pestle[18]. Furthermore, mechanochemical reactions involving organic, inorganic substances, ceremics, nanparticles among others have been reviewed[19]. These include syntheses of polymers, acylation of various oganic compounds, complex ceramic oxide, nanocrystals, of sulfides, hydrides, nitrides, simple oxides, and selenides, and their phase transformations and materials for hydrogen production and storage. The facile mechanochemical syntheses of coordination complexes of transition metals with organic ligands which led to mononuclear complexes and coordination clusters, cages, and other one-, two-, and three-dimensional architectures have been achieved[19]. Scheme-1a & b illustrate examples of inorganic and organic mechanochemical reactions involving reduction of ferricyanide to ferrocyanide and synthesis of primary amide from carboxylic acid, 2,4,6-trichloro-1,3,5-triazine (TCT) and ammonium thiocyanide (NH_4SCN) respectively.

$$Fe(CN)^{-3}_{6} + Br^{-}Fe(CN)^{-4}_{6} \longrightarrow + \frac{1}{2} Br_2 \text{ (ball mill)}$$

Scheme-1a: Reduction of ferricyanide to ferrocyanide[19].



Scheme-1b: Synthesis of primary amide from carboxylic acid, TCT and NH_4SCN[20].

Peculiarities of Mechanochemical Reactions

Studies revealed that there are significant number of chemical reactions that take place via mechanochemical reactions but very difficult to occur or do not occur at all in solutions[21-23]. This was attributed to their unique reaction mechanisms. Oh *et al.*[24] observed that in the synthesis of functionalized fullerenes, mechanochemical nucleophilic behavior of CN^- differed from its behavior in solutions which led to the formation a new compound, C_{120} with 18% yield. Additionally, a novel C−N coupling of arylsulfonamides and carbodiimides, which failed or gave poor conversions in solutions was made possible via mechanochemical reaction which occurs readily by liquid assisted grinding solvent (LAG)[11].

Rightmire *et al.*[25] reported the mechanochemical synthesis of a tris(allyl)aluminum complex based on the sterically hindered bis(trimethylsilyl)allyl ligand. On contrary, solvent based synthesis of such complexes immediately dissociated upon dissolution. Another possible and unique molecule synthesized via mechanochemical process was adamantoid P_4N_6-phosphazane substituted by tert-butyl groups. However, according to literature, different substituted adamantoid phosphazanes were synthesized via solvent based synthesis but this product remains very rare and was cited as an example of a sterically inaccessible target molecule. Other peculiar products not obtainable from solvent based syntheses but possible with mechanochemical reaction include cyclooctatetraene derivatives synthesized from ethyl propiolate (an alkyne) using a Nickel vial and Nickel pellets as catalysts and different large Iptycenes synthesized using double Diels Alder cycloadditions have been reported in the literature[26-28].

Moreover, Rak *et al.*[29], studied the mechanosynthesis´ of ultra-small monodisperse amine-stabilized gold nanoparticles with controllable size. In the study, it was observed that milling with capping agents permits the solvent-free synthesis of monodisperse gold nanoparticles with sizes between 1 and 2 nm, while the solvent syntheses are normally conducted at high dilution in order to maintain control over aggregation and size of the particles.

Stoichiometry of Mechanochemical Reactions

Jean-Louis Do and Tomislav Frisčič[21], reported that one of the excellent qualities of mechanochemical reactions is the control over the quantitative evaluation of the reaction. Thus, mechanochemical reactions allow the targeted and precise synthesis of stoichiometrically different reactants' including organic, inorganic, organometallic reactants, ceramics and nanoparticles by simply monitoring the reaction mixture composition[30-32]. Investigations confirmed that the control the over the stoichiometry of the reaction is remarkably superior to that of conventional solvent based synthesis, where control of product selectivity is difficult and requires a large amount of reactants[33].

Furthermore, the control over the stoichiometric of mechanochemical syntheses or reactions have been observed and reported in the literature. For example, Pavlović *et al.*[68] carried out mechanochemical synthesis of stoichiometric $MgFe_2O_4$ spinel by milling of a mixture of three different sources of magnesium (MgO, $MgCO_3$, and $Mg(OH)_2$) separately withα-Fe_2O_3 powders in a planetary ball mill. The study yields a précised and quantity of $MgFe_2O_4$ spirites. In addition, milling of aromatic diamines with one or two equivalents of an aryl isothiocyanate gave cleanly and selectively mono- or bis (thioureas), while milling of mesitylene with different amounts of Oxone and a sodium halide led to its selective mono-, di-, or trihalogenation[34,35].

Mechanochemical Instruments/Equipments

Different equipment/instruments have been used for mechanochemical syntheses. The simplest and common equipment used in the laboratory is mortar and pestle[36]. Others used asides a simple mortar and pestle for manual grinding, include vibratory or mixer, ball mills of the planetary and attrition types[37]. Moreover, Schmidt *et al.*[38] reported that when higher amount of energy and milling time are required for the reaction, ball mills are normally used. Furthermore, it was observed that for small samples, laboratory vibrators of the Wiggle-Bug type are also very efficient while for prolonged high energy milling as in mechanical alloying or amorphization of hard crystalline solids, very high energy vibrators such as high speed attritors or stainless steel ball mills of high impact (Spex type) are used. Ultrasonic can also be used for mechanochemical reactions[38]. Figure-1 shows examples of some equipment used for mechano-chemical syntheses[19].

Silvina[19] described the working principles of the instruments with the exception of mortar and pestle as follows; firstly, the reactants are introduced into the ball mill through the feed port to the barrel where the reaction occurs, on completion of the reaction, the products are obtained through the exit port. Figure-1(d) illustrates the operation mode of the planetary ball mill where the reactors or reaction vessels and discs are rotated or oscillated within their own axes at certain angular frequencies but in opposite directions (horizontallyω_d and verticallyω_r), this is done in order to acquire and maintain kinetic energy of the milling media during a preset milling time. However, these rotations generate forces known as centrifugal forces which result to a net force that undergoes periodic changes during the mill working cycle. This force is acquired by the balls which make them collide continuously among themselves and with the reactor walls thereby trapping the reactants in inelastic collisions and transferring part of the energy to them through continue impacts. Furthermore, twin-screw extruders are also used to carry out mechanochemical reactions though they are less common but their implementation is gradually gaining interest. The equipment consists of intermeshing and interlocking screws within the barrel as shown in Figure-1(e) which forces the reactants to undergo mechanochemical transformation[15]. One of major advantages of this equipment is its remarkable mixing capability which makes its product exceptional from mechanochemical equipments[69].

Mechanochemisry as Green Technology

According to Ying *et al.*[39], green chemistry or technology, is the major reason and inspiration behind the reemergence of mechanochemistry, specifically apply to pharmaceutical and chemical industries for cleaner, safer, and more efficient physicochemical transformations. Studies revealed that out of the many reasons behind promoting the study of mechanochemistry, is its sustainability and versatility[40]. Furthermore, mechanochemistry accommodates different chemical processes that do not require the use of reaction solvents which by implications, reduces waste generation and pollution while significantly reduces production costs[41]. Additionally, literature that revealed larger yields are often obtained by mechanochemical processes than the conventional solvent based reactions. Other remarkable advantages of mechanochemical processes over the normal solvent processes include good stoichiometry control, enhanced product selectivity and reduced reaction times[42,43].

Moreover, Silvina[19] reported the twelve principles of green chemistry in relation to mechanochemistry. Table-1 described these principles and their relationship with mechanochemistry.

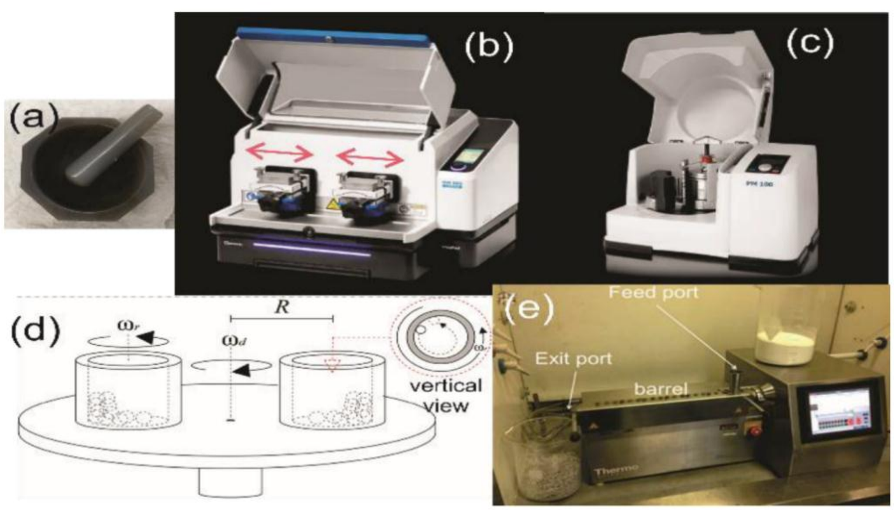


Figure-1: (**a**) An agate mortar and pestle for manual grinding (b) Mixer-type ball mill with optional control of temperature. (**c**) A Retsch GmbH (Haan, Germany) planetary ball mill model PM 100 (d) Illustration of the mode of operation of a planetary ball mill (**e**) A twin-screw extruder[19].

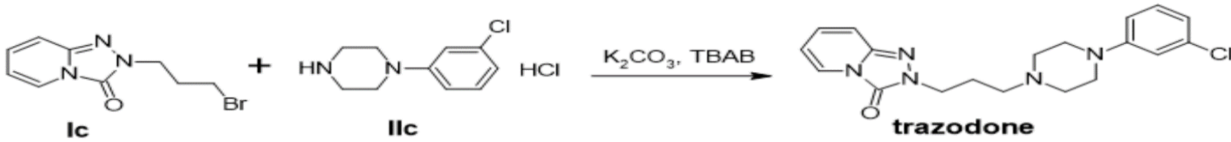
Applications of Mechanochemistry

Applications of mechanochemistry as green technology in selected areas including pharmaceuticals, fertilizers, catalysis, waste management, metallurgy are discussed below.

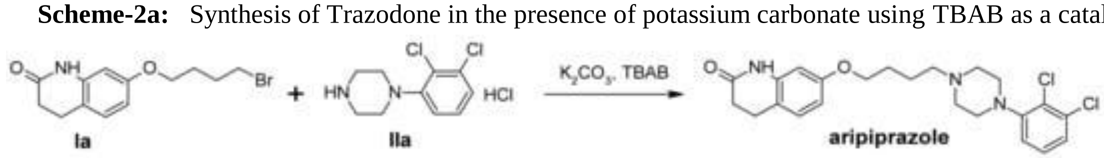
Pharmaceutical: In this century, where sustainability is of great concern, mechanochemistry shines as a green and sustainable approach to drug synthesis[40]. Thus, by eliminating the need for large volumes of solvents and minimizing waste production, mechanochemistry significantly reduces the environmental impact associated with drug manufacturing[44,45]. This technique promotes the principles of green chemistry by minimizing the use of hazardous chemicals and maximizing atom economy. Furthermore, these economical and environmental friendly aspects of mechanochemistry align with the growing demand for sustainable practices in pharmaceutical industries[9]. However, a lot of drugs have been synthesized using this technique. For examples, mechanochemical synthesis of Isoniazid and Pyrazinamide co-crystals with glutaric acid using solid state grinding and liquid assisted grinding by Ngilirabanga *et al*.[9], synthesis of Trazodone in a mortar and Aripiprazole in ball mill, mechanochemical synthesis of Flucytosine and acetylsalicylic acid in a ball mill have been achieved respectively[46,47]. Scheme-2a and b illustrate the chemical equations for the mechanochemical syntheses of Trazodone and Aripiprazole drugs respectively.

Table-1: Twelve principles of green chemistry and their relationship with mechanochemistry.

Principles of Green Chemistry	Mechanochemistry
Prevention of waste	Due to limited or no use of solvents to carry out mechanochemical reactions or syntheses, waste is prevented or minimized at of the reaction.
Atom economy	Because mechanochemical method minimizes the incorporation of more substances aside the main reactants, high product yield is obtained. Example: Mechanochemical syntheses of MOFs directly from metal oxides instead of metal salts.
Syntheses of less toxic chemicals	This method helps in synthesizing less toxic chemicals by avoiding the use solvents that are highly toxic and uses highly reactive substances that not require the use of solvents. E.g, mechanochemical activation of CaC_2 using safer oxidants such as oxoneand avoiding the use of gaseous acetylene.
Design of safer chemicals	Application of mechanochemical method for the synthesis of active pharmaceutical ingredient (API) is achieved and considered better alternative in terms of safety. Example; mechanochemical syntheses of new metalloid drugs with reduced toxicity
Safer solvents and auxiliaries	Solubility of a reactant is not unnecessary. Also, solvents that less are toxic, cheaper and safe are used as liquid assisted grinding (LAG) where necessary.
Design for energy efficiency	Less energy is required and the process occurs mostly at ambient temperature and pressure whenever possible. Therefore, consumes less fossil fuel
Renewable feedstock use	Extraction of oil from biomass (renewable feedstock) used for biofuel production is also achieved via Mechanical method of extraction.
Reduced derivatives	Generation of unnecessary derivatives such as the use of protecting groups or intermediates is minimized or avoided. Such steps which may require some to proceed are also avoided.
Catalysis	Milling media/vessels can be used as catalysts. Many enzymes remain active in ball milling and reactive extrusion.
Design for Reactors degradation	Efficient degradation of waste including metal and polymer waste such as metal oxide and polyethylene terephthalate respectively is achieved through mechanochemical processes.
Real-time analysis	In situ monitoring of product formation is achieved using Raman spectroscopy.
Safer chemistry for accident prevention	Accident is prevented or minimized because mechanochemical method reduces exposure of humans and the environment to hazardous chemicals especially toxic solvents which some of them are even highly inflammable.



Scheme-2a: Synthesis of Trazodone in the presence of potassium carbonate using TBAB as a catalyst.



Scheme-2b: Synthesis of Aripiprazole in the presence of potassium carbonate using PTC as a catalyst.

Fertilizer: Several studies have been reported on the application of mechanochemistry in the synthesis of fertilizers as green alternative to conventional methods. Recently, Ehab *et al.*[48] carried out a study on mechanochemical preparation of a novel slow-release fertilizer based on K_2SO_4-kaolinite. Chen *et al.*[13] reported the *m*echano chemical transformation of apatite to phosphoric slow-release fertilizer and soluble phosphate. Mohammad *et al*.[49] reported their study on mechanochemical preparation, properties and kinetic study of kaolin–N, P fertilizers for agricultural applications. Scheme-3 shows the equation for the reaction. Bhardwaj *et al*.[50] also discussed the fine milling in applied mechanochemistry and its application in agriculture for the production fertilizers. Tongamp *et al*.[51] have reported the incorporation of the nitrate ion into the Mg –Al–NO_3 type layered double hydroxide structure using mechanochemical process. Their findings revealed that, the mechanochemical process allows the intercalation of target materials in which the crystal structure of kaolin and the layered double hydroxide are maintained. Solihin[52] also reported the mechanochemical route for synthesizing $KMgPO_4$ and NH_4MgPO_4 for application as slow-release fertilizers.

$$2Ca_5(PO)_3OH+3(NH_4)_2SO_4+7H_2SO_4 \rightarrow 6NH_4\ H_2PO_4+10CaSO_4 +2H_2O$$

Scheme-3: Mechanochemical synthesis of kaolin–N, P fertilizers for agricultural application.

Catalysis: According to Amrute *et al*.[53] mechanochemistry enables the synthesis of various forms of catalytic substances in a more sustainable and convenient way than the conventional methods. However, the case of nanostructure systems for instance, mechanochemical synthesis of catalysts is concerned with the synthesis of materials with desired properties such asmorphology, porosity, crystallization degree, component distribution, dispersion and phase composition[54]. Moreover, mechanochemical synthesis of different metal nanoparticles used as catalysts including iron, copper, nickel, silver, gold, and palladium has been reported[55]. Mechanochemistry is also a versatile platform for the synthesis of organocatalytic and metal-catalyzed transformations, such as the Suzuki− Miyaura coupling as illustrated in Figure-2, Huisgen cycloaddition and olefin metathesis[56-58].

Waste Management: Mechanochemistry is also applied in solid waste management. In recent years, it has been demonstrated that mechanochemistry has many advantages over other conventional chemical methods in solid waste disposal, such as metal and metal oxide wastes, fly ash modification, rubber and plastic recycling[59]. However, a significant number of researches on the application of mechanochemical processes in solid waste management has been published. Thus, in China, Zhang *et al.*[60] studied the devulcanisation of natural rubber vulcanizate with self-designed mechanochemical reactor of pan mill type. The study revealed that solid state mechanochemical milling primarily resulted in the devulcanisation through the scission of cross-linking bond rather than the natural rubber main chain. Jana and Das[61] applied the mechanochemical devulcanization process to treat the waste generated from scrap tyres. Furthermore, Bilgili *et al.*[62] reported that a mechanochemical technique based on stress induced chemical reactions and structure changes of materials has shown a potential application in devulcanisation of cross-linked rubber. Zhang *et al.*[64] and Wang *et al.*[63] developed a novel metal recycling process using two kinds of waste containing nonferrous metals (in oxide or metal) and iron/aluminium metals and ground them with sulphur sample to mechanically induce solid-state reaction to form nonferrous metal sulfides and iron/aluminium oxides, which allows the use of the current mineral processing technologies to recover metals from various kinds of wastes. Scheme-4 illustrates the chemical equation for the mechanically induced solid-state reaction of zinc oxide, iron and sulphur as an example of metal recycling process.

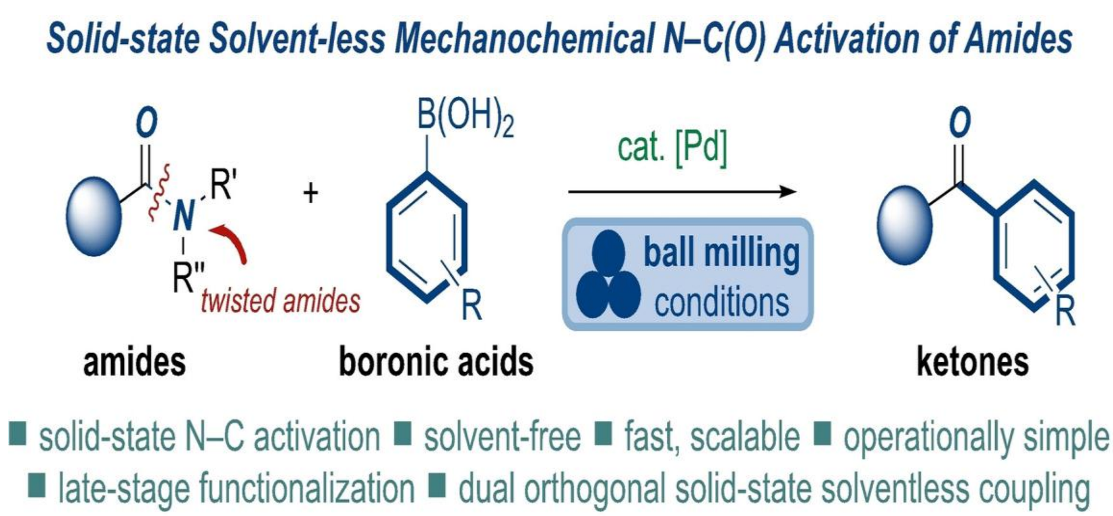


Figure-2: Suzuki− Miyaura coupling of N-C(O) in presence Polladium Catalyst.

$4ZnO + 4S + 3Fe$ ¼ $\rightarrow$ $4ZnS + Fe_3O_4$

Scheme-4: Mechanically induced solid-state reaction using zinc oxide, iron and sulphur.

Metallurgy: The extraction of metals from various ores or minerals such as magnetite, haematite, limonite, tungsten concentrate, molybdenite, monazite, rutile etc or recovery of Metal from second-hand resources via mechanochemical technique has been demonstrated over the years[65]. McDonald, R.G. & Muir[66] reported that one of the techniques used to obtain fast kinetic recovery of copper from Chalcopyrite has been ultrafine grinding (mechanical activation) with particle sizes (d80) down to 5-15µm. A study conducted by Kano *et al*.[65] revealed that indium oxide could be reduced to metal in a non-thermal process utilizing mechanochemistry. In the study, which was carried out in a planetary ball mill, lithium nitride was used as reductant and nitrogen gas was used to have a shielding atmosphere. The proposed mechanism for the reaction is illustrated in Scheme-5. Saito and co-workers developed a novel process where LIBs electrodes and PVC were milled in a planetary ball mill[67]. It was observed that the recovery of Li and Co was dependent on grinding time and recoveries of Li and Co reached 100% and 90% respectively after 30 h of grinding. Scheme-6 also shows the chemical equation for the reaction.

$2O_3 + Li_3N + NH_3 \rightarrow 2In + 3LiOH + N_2$ (a)
$In_2O_3 + 2Li_2N + N_2 \rightarrow 2In + 3Li_2O + 2N_2$ (b)

Scheme-5: The proposed mechanism for the reduction of indium oxide to indium metal.

$LiCoO_2 + 3[–CH_2–CHCl–]n \rightarrow CoCl_{2\,+}$ LiCl + CxHyOz.

Scheme-6: Milling of Lithium batteries with PVC.

Challenges of Mechanochemistry

Currently, the study of mechanochemistry is still at infancy especially on commercial scale. However, details on the empirical analyses of the fundamental physicochemical parameters of mechanochemical processes in relation to thermodynamics, reaction kinetics and mechanism is scarcely available in the literature. Additionally, isolation, purification and recovery of mechanochemical products still remain a change[19]. Furthermore, it is obvious that, mechanochemistry could not make all of chemical synthesis 100% solvent-free. Therefore, the use of solvent no matter how little it's remains a challenge.

Conclusion

The study of mechanochemistry can be described as inherently interdisciplinary involving multiple scientific disciplines. However, from the review, mechanochemistry is found to be sustainable, feasible, economical and technologically green with vast potential applications in chemical industries and other science related disciplines, but it also has some challenges that need further researches to be addressed.

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