Coordination Chemistry Reviews 566 (2026) 218229

Contents lists available at ScienceDirect

Coordination Chemistry Reviews

journal homepage: www.elsevier.com/locate/ccr

Mechanochemistry for sustainable organometallic synthesis: A review across the d-block

Daniele Zuccaccia [a,*], Leonardo Genesin [a], Talha Munir [a], Fabio Trigatti [a,b], Eleonora Aneggi [a,*]

[a] Dipartimento Di Scienze Agroalimentari, Ambientali e Animali, Sezione Di Chimica, Università Di Udine, Via Cotonificio 108, I-33100 Udine, Italy
[b] Dipartimento Di Scienze Della Vita, Università Di Trieste, Via Weiss 2, 34128 Trieste, Italy

ARTICLE INFO

Keywords:
Mechanochemistry
Transition metals
Solid-state synthesis
Coordination compounds
Green chemistry
Solvent-free synthesis

ABSTRACT

Mechanochemistry has emerged as a powerful and increasingly mature approach for the synthesis of coordination and organometallic compounds, offering access to reaction pathways and products that differ fundamentally from those observed under conventional solution-based conditions. This review provides a critical overview of recent developments in the mechanochemical synthesis of d-block coordination complexes, with emphasis on studies published over the last decade and on contemporary contributions that reflect current advances in structural control, mechanistic understanding, and sustainability assessment. Focusing on molecular, structurally characterized species rather than extended frameworks, the review surveys mechanochemical reactivity across early-, middle-, and late-transition metals, highlighting how solvent-free or minimally solvated conditions influence metal-ligand interactions, coordination geometries and product selectivity. Particular attention is devoted to comparisons between mechanochemical and solution-based approaches, addressing when the two converge, and when mechanochemistry enables qualitatively different outcomes. Beyond synthetic efficiency, mechanochemical methodologies are analyzed through the combined lens of green chemistry metrics, reaction rates, yields, product distributions and apparatus-dependent effects. By integrating recent experimental advances with critical analysis, this contribution positions mechanochemistry as a complementary and conceptually distinct field within modern coordination and organometallic chemistry, rather than as a universal replacement for solution-based synthesis.

1. Introduction

Mechanochemistry has undergone a significant conceptual evolution over the past two decades, progressing from an empirically driven, solvent-free technique to a mature synthetic strategy with profound implications for coordination and organometallic chemistry. Early systematic studies on solvent-free synthesis of metal complexes demonstrated that grinding and milling could efficiently promote coordination bond formation while avoiding bulk solvents [1]. More recently, mechanochemistry has been recognized as a general platform for sustainable synthesis and was identified by IUPAC as one of the ten chemical technologies with the potential to contribute significantly to global sustainable development [2].

Initially, mechanochemistry was embraced primarily for its alignment with green chemistry principles [3], most notably solvent minimization and reduced energy input. As emphasized in recent analyses, the absence of bulk solvent is not merely an environmental advantage, but a defining chemical parameter that reshapes the thermodynamic and kinetic landscape of reactions involving coordination bonds [4]. In this context, sustainability considerations and reactivity are intrinsically intertwined.

Coordination chemistry of the d-block underpins a wide range of applications, spanning homogeneous and heterogenous catalysis [4–11], small-molecule activation [12–17], molecular materials [18–21], luminescence [22–28], and medicinal inorganic chemistry [29–36]. Conventional syntheses of transition-metal complexes remain heavily dependent on solution-based methodologies, typically requiring large volumes of solvents, elevated temperatures, reflux conditions, inert atmospheres and multistep purification protocols. From a green chemistry perspective, such practices result in poor performance with respect to solvent consumption, energy efficiency and waste generation, as highlighted in recent life-cycle and sustainability analyses comparing mechanochemical and solvothermal processes [37].

At the same time, solvents are not chemically innocent spectators

* Corresponding authors at: Via Cotonificio 108, I-33100 Udine, Italy.
E-mail addresses: daniele.zuccaccia@uniud.it (D. Zuccaccia), eleonora.aneggi@uniud.it (E. Aneggi).

https://doi.org/10.1016/j.ccr.2026.218229
Received 20 March 2026; Accepted 15 June 2026
Available online 19 June 2026

[38]. Coordinating solvents actively influence coordination equilibria by stabilizing particular oxidation states, solvation geometries and aggregation modes. This dual role of solvents, as environmental burden and as chemical actor, has profound consequences for coordination chemistry. In systems involving N- and P-donor, and heterocyclic ligands, solution-phase products often reflect solvent-stabilized minima rather than intrinsic metal-ligand preferences, leading to solvate formation, ligand redistribution or redox processes that complicate both synthesis and interpretation [4]. Mechanochemical synthesis offers a fundamentally different reaction landscape in which bulk solvent is absent or reduced to catalytic amount. The elimination of solvent not only improves green chemistry metrics related to waste prevention and atom economy but also suppresses solvation-driven stabilization of specific coordination modes. Under mechanochemical conditions, metal-ligand interactions are governed primarily by solid-solid contact, stoichiometry, and mechanical energy input. As a result, coordination outcomes can diverge markedly from those observed in solution, in terms of molecular structure, coordination geometry, nuclearity, and polymorphism [39,40].

The green advantages of mechanochemistry extend beyond solvent elimination. Many mechanochemical transformations proceed at room temperature and pressure, often under air and within drastically reduced reaction times, resulting in lower overall energy demand compared to conventional solvothermal approaches [41]. Simplified work-up procedures, frequently limited to washing or direct isolation of solids, further reduce auxiliary materials and downstream waste, which are often dominant contributors to the environmental footprint of coordination compound synthesis [41].

Beyond its well-established role in organic synthesis [42], mechanochemistry has evolved into a broadly enabling platform across diverse areas of chemical research, including the preparation of dyes and fluorophores [43], polymer development [44], and supramolecular chemistry [45], as highlighted in recent comprehensive reviews. Nevertheless, mechanochemical coordination chemistry remains only partially consolidated, with the relevant literature distributed across accounts centered on sustainability, synthetic methodology, or specific materials classes. Broad reviews have emphasized solvent reduction and green metrics [37], while the extensive body of work on metal–organic frameworks has mainly addressed extended solids rather than discrete coordination and organometallic compounds [46]. In parallel, reviews of alternative synthetic technologies for metal complexes often treat mechanochemistry as one enabling strategy among others, rather than isolating its specific consequences for coordination reactivity, structure formation, and sustainability [47]. Thus, a unified, coordination-chemistry-centered assessment of mechanochemical approaches across the d-block is still missing.

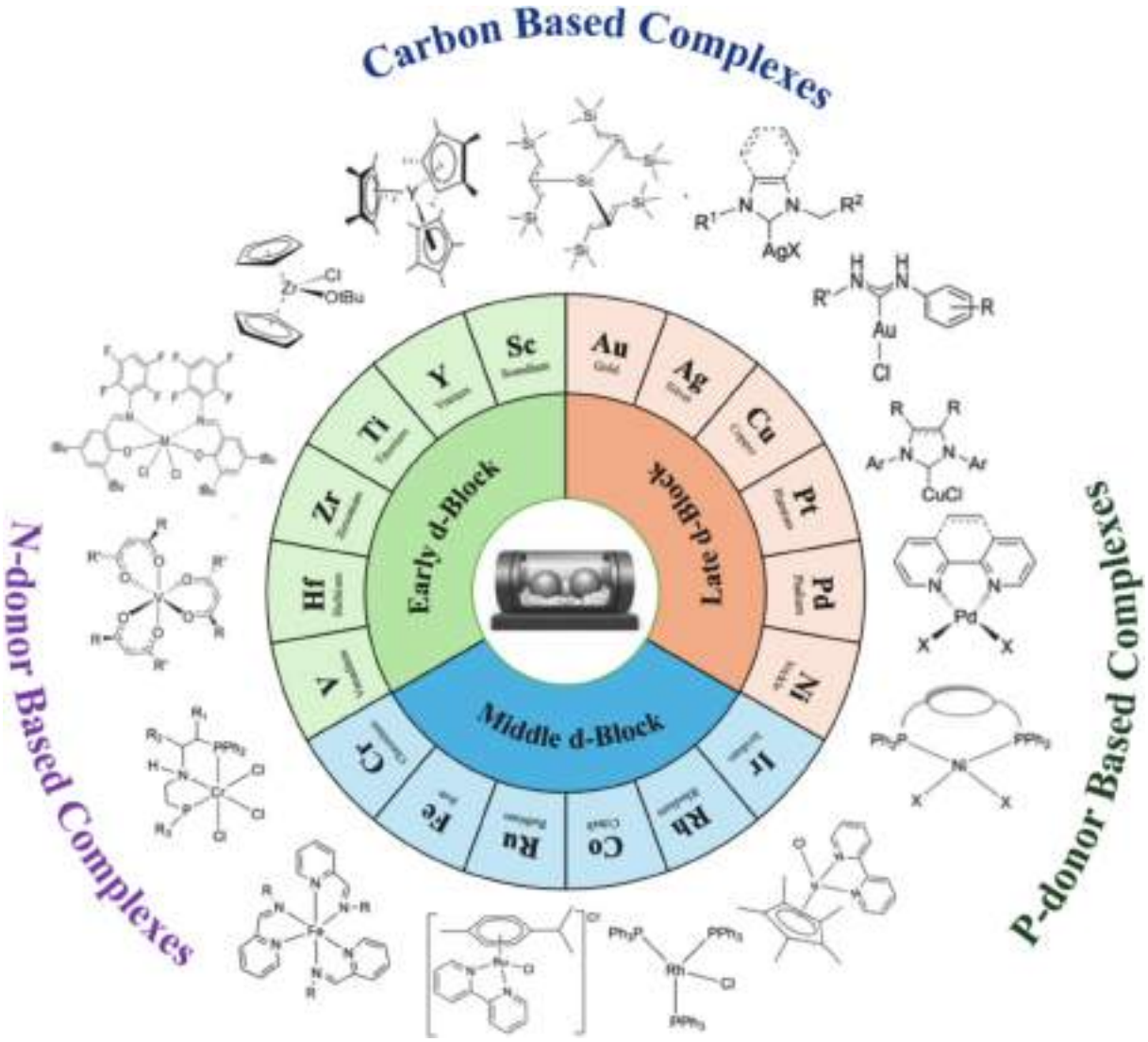


Fig. 1. Summarized details of the mechanosynthesized complexes of d-block.

This review addresses this gap by providing a critical assessment of the recent mechanochemical synthesis of d-block coordination and organometallic compounds, focusing transition metals and on structurally characterized molecular species as indicated in Fig. 1. Extended coordination polymers and metal-organic frameworks are excluded unless directly relevant to the synthesis of coordination compounds. Emphasis is placed on complexes supported by N- and P-donor, and heterocyclic-ligands, which serve as sensitive probes for differences between solution-based and mechanochemical coordination chemistry.

In addition to its impact on coordination reactions and structural outcomes, mechanochemistry has increasingly been evaluated through the lens of green chemistry. Parameters such as solvent consumption, energy input, reaction time, auxiliary materials and work-up requirements are particularly relevant for coordination synthesis, where purification and solvent use often dominate the overall environmental footprint. However, quantitative and qualitative comparisons between mechanochemical and solution-based coordination chemistry remain highly system-dependent and are not always straightforward. For this reason, a dedicated section (Chapter 3) of this review critically examines mechanochemical coordination chemistry in comparison with conventional solution-based approaches, focusing on sustainability metrics alongside reactivity, selectivity and structural consequences.

2. Mechanochemical coordination across the d-block

2.1. Mechanochemical methodologies in coordination chemistry

Mechanochemistry has emerged as a significant tool for synthesizing organometallic complexes. It allows the overcoming of several drawbacks associated with solution methods, such as possible reactivity with the solvent, the formation of insoluble products and decomposition phenomena [2,48]. Reactions occur through the direct absorption of mechanical energy generated by movement, friction and collision of milling media together with reactants in a reactor. The official IUPAC definition of a mechanochemical reaction is “A chemical reaction that is induced by the direct absorption of mechanical energy” [49]. Energy transfer is contingent on several variables, especially in traditional methods such as manual grinding. This technique consists in the direct mixing of reagents in a mortar and mechanical energy is given by the action of a pestle [50]. The basic equipment is made in different materials and results in differences in reactivity. However, the energy dissipation is largely inconsistent, especially for time taking reactions. Hence reproducibility of such reactions is also questionable. Additionally, there are not many variables that can be altered to obtained products selectively [51]. In the contemporary era, technological advancements, exemplified by the development of planetary and shaker mills, have led to a significant enhancement in the reproducibility of experimental outcomes [52]. The classification of mills is typically divided into two primary categories. The first is the shaker mills, which are characterized by the horizontal or figure-eight movement of the reactor. The second category comprises planetary mills, which feature a rotating disk that facilitates the rotation of the reactor around its own axis [53]. The composition of reactors can vary, with reactors being constructed from diverse materials and containing an adjustable number of milling balls. Shaker-type reactors are a particular type of reactor that generate impact energy from collisions and the velocity of these reactors is expressed in Hertz (Hz) [53–55]. Conversely, planetary mills generate elevated levels of shear and stress forces resulting from the interaction between balls and reagents surrounding the walls. This phenomenon is attributed to the centrifugal force that is induced by the motion of the balls. The control parameter on this kind of apparatus is rotation speed (rpm) [53,54]. It is evident that further avenues for the mechanosynthesis of organometallic complexes exist, namely the twin-screw extrusion (TSE) and the resonant acoustic mixing (RAM) methods. The former consists of two screw elements that are closely intertwined and rotate in directions that are diametrically opposed. The continuous flow operation of the system enables superior temperature control. This technique has been utilized in the synthesis of Ni(salen) and Ni(salophen) complexes [49,52]. In contrast, the latter operates without milling media in the system, thereby reducing the risk of metallic contamination. The apparatus vibrates at a precise frequency, thereby creating acoustic waves that increase the energy of the system [49].

In the field of coordination chemistry, the efficacy of a reaction is contingent upon the surmounting of an energy barrier. It is imperative that this barrier is overcome by the total accumulated energy provided by the experimental system. This includes the kinetic energy of the balls, the material of the mills, and the time of mixing [56]. An increase in Hz or rpm generally results in a faster reaction; however, this approach could lead to a worse selectivity [49]. The frequency can also effect changes to the reaction pathway, with the potential for the formation of intermediates at lower values of Hz or rpm [57]. The time of reaction is another key parameter because it is connected to the total amount of energy and the kinetic profile of the reaction [56]. Several studies demonstrate that excessive reaction times and intensity of milling can corroborate to decomposition of the complex or the formation of side products [54,58]. The materials of jars and balls effect the energy transferred during impact and can participate in reactions by leaching materials, acting as catalysts or competing in complex formation [49,52,53]. The mass and number of the milling balls also effect the collision probability, which is critical for reaction rates, and the ball-to-powder ratio, which is related to the energy per particle. Modifying these parameters results in the emergence of divergent reaction pathways [54,57]. The stoichiometric control of organometallic reactions assumes a significant role in determining the composition of products. In fact, given that the mixture is not homogeneous, transformations are governed by particle-particle collisions with local neighbors [48,49,57]. For instance, a metathesis reaction between $K[(1,3\text{-}SiMe_3)_2C_3H_3]$ and cesium halide salts was only effective in a 3:1 ratio; in other cases, pure products could not be isolated [59]. An interesting technique for mechanochemistry is liquid-assisted grinding (LAG), where a small amount of liquid phase is inserted into the system [4,59,60]. The parameter that defines LAG conditions is denoted by η, which is defined as the ratio between the volume of liquid, in μL, and the total mass of solid reagents, in mg [4,53,54]. This approach enhances the rates and yields of reactions, whilst concomitantly increasing the crystallinity of the resultant products, by increasing molecular mobility. Furthermore, it has been shown to overcome the slow diffusion of solids [49,54,60]. Moreover, the molecules of the solvents can assume an active chemical role by coordinating metal centers and modifying the basicity or proticity of the system [4,49]. The presence of solvents exerts an effect on selectivity and polymorphism, resulting in the formation of products that are not accessible through solution chemistry. LAG reactions have the capability to proceed independently, similar as that of bulk solvent conditions, thus overcoming the limitations of solubility and solvent competition [57,60,61].

Mechanochemical synthesis may sometimes require solvents for workup and purification steps. However, even in such cases, the volume of solvent required is significantly lower compared to conventional solution-based chemistry, which typically involves extensive workup procedures and large amounts of solvent during synthesis. Similarly, under LAG conditions, the amount of solvent used is comparatively very low, and in many cases, the residual solvent can be easily removed without additional workup. Furthermore, in one-pot reactions, the absence of intermediate purification steps drastically reduces the overall solvent consumption [62–64].

In the context of organometallic systems, it is imperative to consider the molar equivalents of solvent per metal center. Minor LAG volumes can attain coordinative saturation, a state that may facilitate reactions without the need for external thermal activation [4]. However, it should be noted that this method is not without its drawbacks, as it can give rise to the formation of undesirable solvate products, the decomposition of reactive species, issues pertaining to selectivity, and a concomitant

increase in empirical complexity [4,49,54,60]. In d-block organometallic mechanochemistry, additives have the capacity to participate in the reaction beyond the limits of simple physical assistance. These compounds function as bases, catalysts, stabilizers, or selectivity-directing agents, thereby modulating metal-ligand binding environments and directing phase selectivity [49,54]. In the context of chemical reactions, inorganic salts function as essential catalysts, particularly in the context of metalation reactions. By removing protons, these salts facilitate the formation of covalent bonds between metal and nitrogen or metal and carbon atoms [65]. Inorganic salts are often employed as promoters or structural templates, capitalizing on the thermodynamic stability of byproducts to influence the shift in reaction equilibria [4,66]. Non-ionic solids, such as silica or alumina, function as solid solvents and are employed to regulate the physical state of the reaction mixture. It has been demonstrated that the process of agglomeration of reagents can be controlled; however, it should be noted that excessive amounts can result in a decrease in yields. Furthermore, these additives have the capacity to influence stereo and regio selectivity [54].

Mechanochemistry alters the coordination sphere of complexes through the exclusion of coordinating solvents. This fact enables access to compounds that are not possible in solution chemistry: base free or unsolved complexes, which often exhibit enhanced reactivity. Moreover, in some cases some uncommon geometries are possible; the mechanochemical activated state may differ from the thermal one. Also, the hapticity modes differ from solution chemistry, without solvent ligands can have higher η [4,53,59].

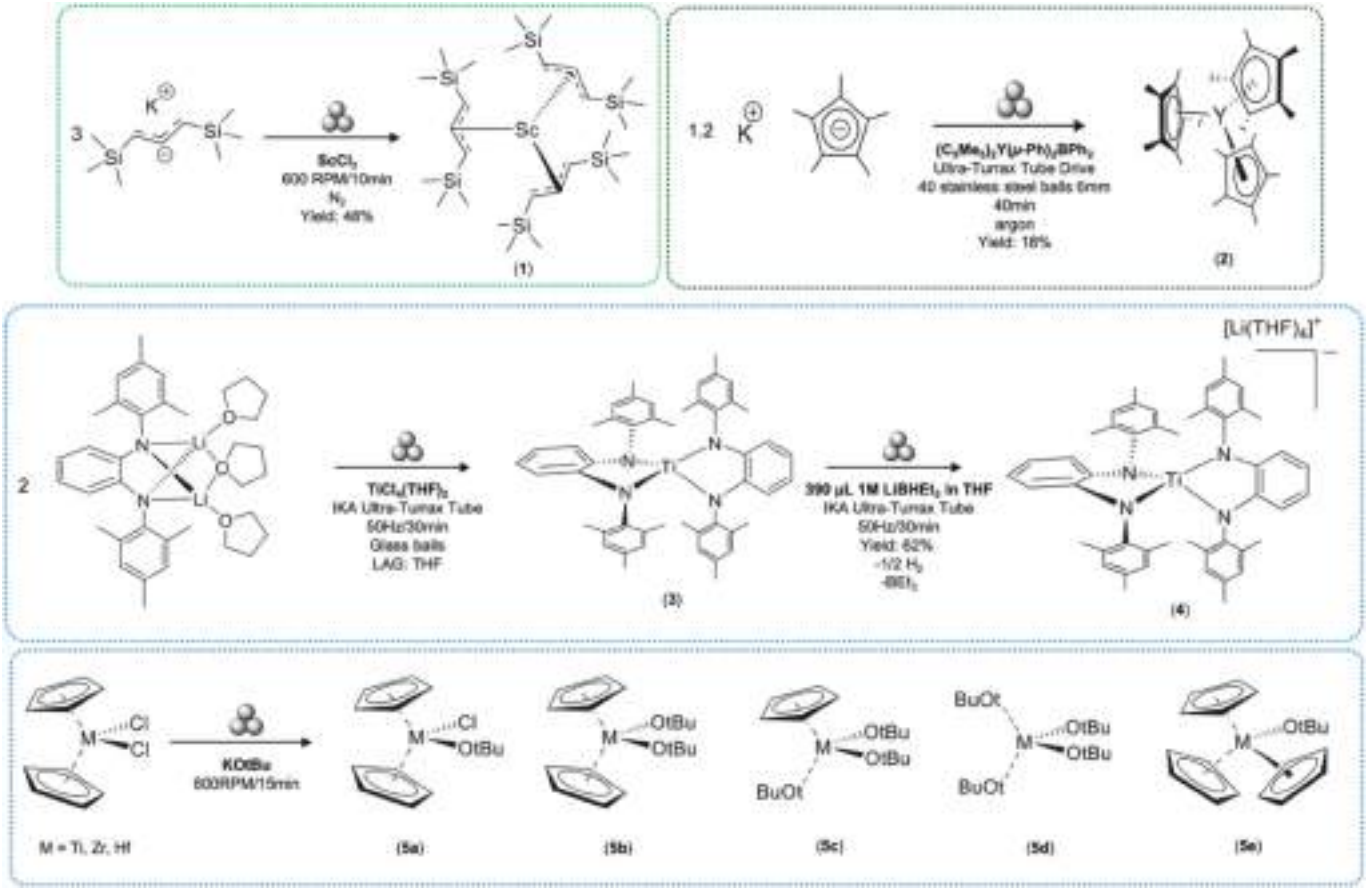
The coordination in mechanochemistry can be achieved in a one-pot protocol, thus overcoming the limitations imposed by solubility. Substitution of ligand, trans-metalation and redox reaction occur with different energy barriers when compared to solution synthesis. Reactions involving complexes have been shown to be faster and less energy-consuming, thereby avoiding the risk of ligand and metal deactivation [54,59,60].

In comparison with solution chemistry, mechanochemical synthesis is distinguished by its divergent structural control, stoichiometry and capacity to isolate species that are not obtained in the presence of a solvent [4,48]. However, mechanochemistry is more sensitive to equipment specifications. Indeed, the total energy for the reaction can change easily and result in different products [2,49,56].

Products and intermediates of mechanochemical reactions are characterized principally *via* Raman and PXRD. Both the techniques work *in situ* and *ex situ* mode allowing different applications depending on the system. PXRD *in situ* usually requires a synchrotron source for the X-Ray [67]. Although it is quite difficult to analyze and forecast what is actually happening in the jar, these *in situ* characterization techniques can help get mechanistic understandings of solid-state reactions in the mill. Several research groups have tried to carry out these *in situ* monitoring of such reactions, mainly due to modified systems [55,57,68–70]. More comprehensive and details characterizations can be performed using well-established analytical techniques such as NMR, IR, and UV spectroscopy.

2.2. Metals of groups 3, 4 and 5

Mechanochemical approaches to early d-block organometallic complexes remain comparatively less developed than those for middle- and late-transition metals, largely due to the high oxophilicity and air sensitivity of many early-metal precursors. However, extant studies demonstrate that mechanical activation can provide access to highly reactive species under solvent-free conditions, often revealing selectivity patterns that are distinct from those observed in solution. Rightmire et al. synthesized a tris(allyl) complex of scandium (**1**) through two



Scheme 1. Summary of Sc(III), Y(III), Ti(III/IV), Zr(IV) and Hf(IV) complexes prepared by mechanochemical synthesis.

different mechanochemical approaches. In the initial synthesis, $ScCl_3$ was milled in a dispersing tube with stainless-steel balls with an excess of the ligand's potassium salt. In the second protocol (Scheme 1), the reaction of the same reagents took place in a planetary ball mill. In both cases, the use of a nitrogen atmosphere was necessary to obtain the desired product [71].

Tris(pentamethylcyclopentadienyl) complexes (**2**) were obtained by Woen and colleagues by milling inside an argon-filled glovebox. The specific procedure involved the use of the following reagents: $[(C_5Me_5)_2Y(\mu\text{-}Ph)_2BPh_2]$ with a small excess of KC_5Me_5 (Scheme 1). The reaction was conducted within an Ultra-Turrax Tube Drive and the crystals were collected after a liquid extraction process [72]. With yttrium, a borohydride complex was also synthesized through mechanochemistry. Huot and coworkers subjected YCl_3 to a two-hour milling process at a rate of 200 rpm using a planetary mill, employing a jar as the milling vessel. Another method reported in the article required the milling of YH_3 under B_2H_6 atmosphere. The second technique demonstrated to have the advantage of not producing a solid by-product that needs to be removed [73].

Titanium(III) with N-donor ligands complex can be obtained through a one pot two step protocol (Scheme 1) [74]. In the initial step, a mixture of $[Li_2(^{Mes}PDA)(THF)_3]$ and $[TiCl_4(THF)_2]$ is milled under LAG conditions to form $Ti(^{Mes}PDA)_2$ (^{Mes}PDA = *N*,*N*′-bis(2,4,6-trimethylphenyl)-*o*-phenylenediamide) (**3**) quantitatively. The second step in the process is the reduction of Ti(IV) to Ti(III) with a solution of $LiBHEt_3$ in THF to achieve $[Li(THF)_4][Ti(^{Mes}PDA)_2]$(**4**).

Titanium(IV) tert-butoxy halides, $[Cp_xTiX_y(OtBu)_{4-(x+y)}]$ ($0 < x, y < 3$) (**5a-e**) complexes have been studied by Boyde et al. The milling of $[Cp_2TiCl_2]$ with different equivalents of KOtBu was conducted in a planetary mill, in a jar equipped with a safety clamp to ensure air-sensitive grinding conditions. The formation of four different species was observed when a ratio of 2:1 ligand to metal center was established. The species were identified as $[Cp_xTiCl_y(OtBu)_{4-(x+y)}]$ (**5b-e**) and the authors reported that modifying the molar ratio of reagents resulted in a more selective reaction [75]. The same authors investigated this aspect in subsequent paper of 2018, where they studied the reaction of two distinct Ti(IV) precursors with various alkoxides and Cp donors [64]. In the initial case, they utilized $[Cp_2TiCl_2]$ with different alkoxides, yielding a pure product $[Cp_2TiCl(OtBu)]$ exclusively for the equimolar reaction with KOtBu. The group obtained superior results by employing a combination of $TiBr_4$, LiCp and LiOtBu milled in varying proportions. Subsequent to the reactions, the compounds $[Cp_2TiBr(OtBu)]$, $[CpTiBr_2(OtBu)]$ and $[CpTiBr(OtBu)_2]$ could be collected.

In the article by Boyde and colleagues, Zr(IV) and Hf(IV) complexes were also obtained (Scheme 1) using the same procedure previously reported. The aforementioned metals exhibited a more selective synthesis. Indeed, the reaction of $[Cp_2ZrCl_2]$ with two equivalents of KOtBu resulted in the formation of solely $[Cp_2ZrCl(OtBu)]$ and $[Cp_2Zr(OtBu)_2]$ (**5a, 5b**). It was demonstrated that increasing the amount of alkoxide resulted in the formation of only the second product. In the presence of an equimolar ratio of Hf(IV) or more than 3 equiv. of alkoxide, the mechanochemical reaction results in the selective formation of $[Cp_2HfCl(OtBu)]$(**5a**) or $[Cp_2Hf(OtBu)_2]$(**5b**), respectively. In the instance of two equiv. of KOtBu, a mixture of two products was formed $[Cp_2HfCl(OtBu)]$ and $[Cp_2Hf(OtBu)_2]$, as demonstrated in Table 1. The discrepancy in outcomes observed in the Ti(IV) case can be attributed to the enhanced binding affinity exhibited by the Cp ligand, which is known to form more robust bonds with heavier metal centers [75].

Table 1
Mechanochemical synthesis of $[Cp_xMCl_yO_{4-(x+y)}]$ of Ti, Zr and Hf and table of composition of the products.

M	equiv. KOtBu	$[Cp_2MCl(OtBu)]$	$[Cp_2M(OtBu)_2]$	$[CpM(OtBu)_2]$	$[M(OtBu)_4]$	$[Cp_3M(OtBu)]$
Ti	2.0	–	32%	47%	18%	3%
Ti	3.4	–	–	88%	12%	–
Zr	2.0	81%	19%	–	–	–
Zr	3.4	–	100%	–	–	–
Hf	1.0	100%	–	–	–	–
Hf	2.0	56%	41%	–	–	–
Hf	3.4	–	100%	–	–	–

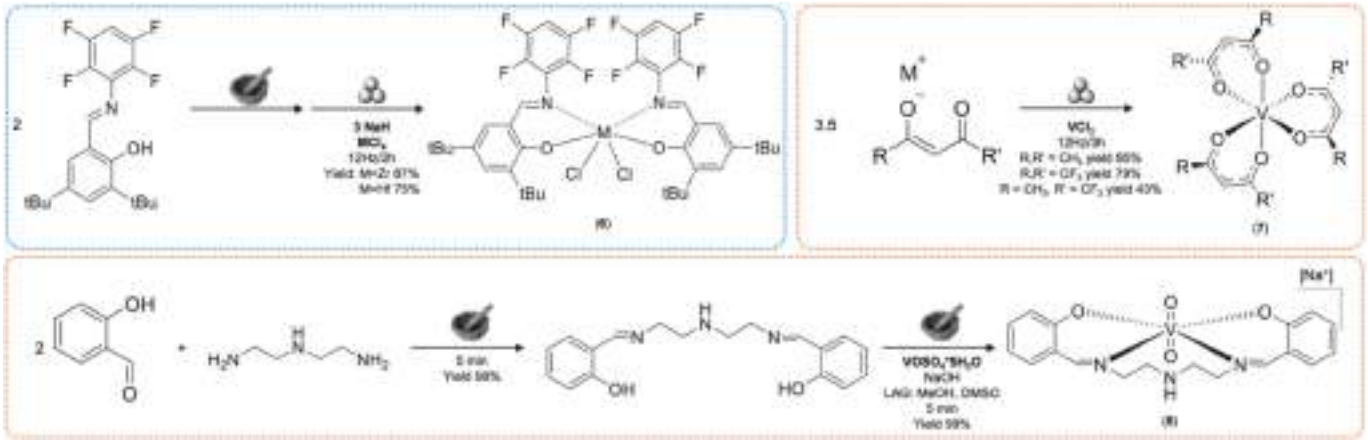
A protocol has been developed for the synthesis of phenoxyimine complexes of Zr(IV) and Hf(IV) (**6**) (Scheme 2), starting from MCl_4 with the ligand LH (LH = N-(3,5-Di-tert-butyl-salicylidene)-2,3,5,6-tetrafluoroaniline). The reaction necessitated a series of additional steps. Initially, a mixture of MCl_4, LH and NaH was triturated in an agate mortar. Thereafter, the mixture was transferred into a reactor of an eccentric vibromill and milled. Subsequent to milling, the mixture was subjected to heating *in vacuo*, after which the products were isolated by means of liquid extraction. In this reaction, the presence of sodium hydride (NaH) is necessary for the formation of the ligand anion. The authors reported that further studies are required to elucidate the reasons why the reaction between an equimolar ratio of ligand and metal center gives more pure complex (**6**) [76]. In the existing literature, other organometallic complexes of zirconium that have been documented include $Zr(BH_4)_4$, as reported by Gennari et al. [64] The reaction between $ZrCl_4$ and a substantial excess of $LiBH_4$ or $NaBH_4$ was conducted in a planetary ball mill within an argon atmosphere. The product is collected by sublimation. The authors reported that the yield of the reaction is affected by a variety of parameters. The optimal molar ratio of reagents is different when $NaBH_4$ is used as opposed to $LiBH_4$, with the latter being more reactive. It is imperative to regulate the temperature to avert the decomposition of the ligand into B_2H_6 and H_2. Consequently, a 10 min interval of rest is imperative after every 15 min of milling [77].

Vanadium β-diketonates (**7**) were first synthesized in 2017 (Scheme 2). VCl_3 was subjected to a reaction with an excess of different β-diketonate salts in a mill under inert atmosphere. The reaction time is typically three hours, with the exception of Vanadium(III) tetramethylheptanedionate and Bis(tetramethylheptanedionato)oxovanadium (IV) reactions, which needed one hour. The authors of the study experimented with a variety of acetonate salts as reagents, including acetylacetonate, hexafluoroacetylacetonate, trifluoroacetylacetonate, and tetramethyleptandionate. Bis(tetramethylheptanedionato)oxovanadium(IV) was obtained in analogous conditions to those employed for the synthesis of other complexes; however, the purification process was conducted under air instead of an inert atmosphere. The authors of the study reported the results of the elemental analysis, which suggests that the chemical formula for the substance is $[C_{22}H_{38}O_5V]$ [78]. The vanadium(V) Schiff base complex (**8**) was obtained by Boruah et al. through a two-step process (Scheme 2). The initial step of the process involved the grinding of two equiv. of salicylaldehyde in a mortar, in the presence of diethylenetriamine. The second step entailed the grinding of the ligand in LAG condition with $VOSO_4{\cdot}5H_2O$ and an excess of NaOH. The solvent employed in this study was a solution of methanol and DMSO. The mixture was subjected to a trituration process for a duration of 30 min, after which it was allowed to rest for a further 15 min, with intermittent grinding. Following a thorough cleansing and vacuum drying process, the complex **8** was obtained in quantitative amounts [79]. It is evident that early-transition-metal systems manifest numerous characteristics that are intrinsic to mechanochemical coordination chemistry. These include a marked sensitivity to stoichiometry and energy input, a pronounced dependence on inert handling for highly oxophilic centers, and, in certain instances, an enhanced selectivity relative to solution routes. Collectively, these studies indicate that, although the experimental conditions are demanding, early d-block mechanochemistry offers access to reactive and compositionally tunable complexes under conditions that minimize solvent interference.

2.3. Metals of groups 6, 7, 8 and 9

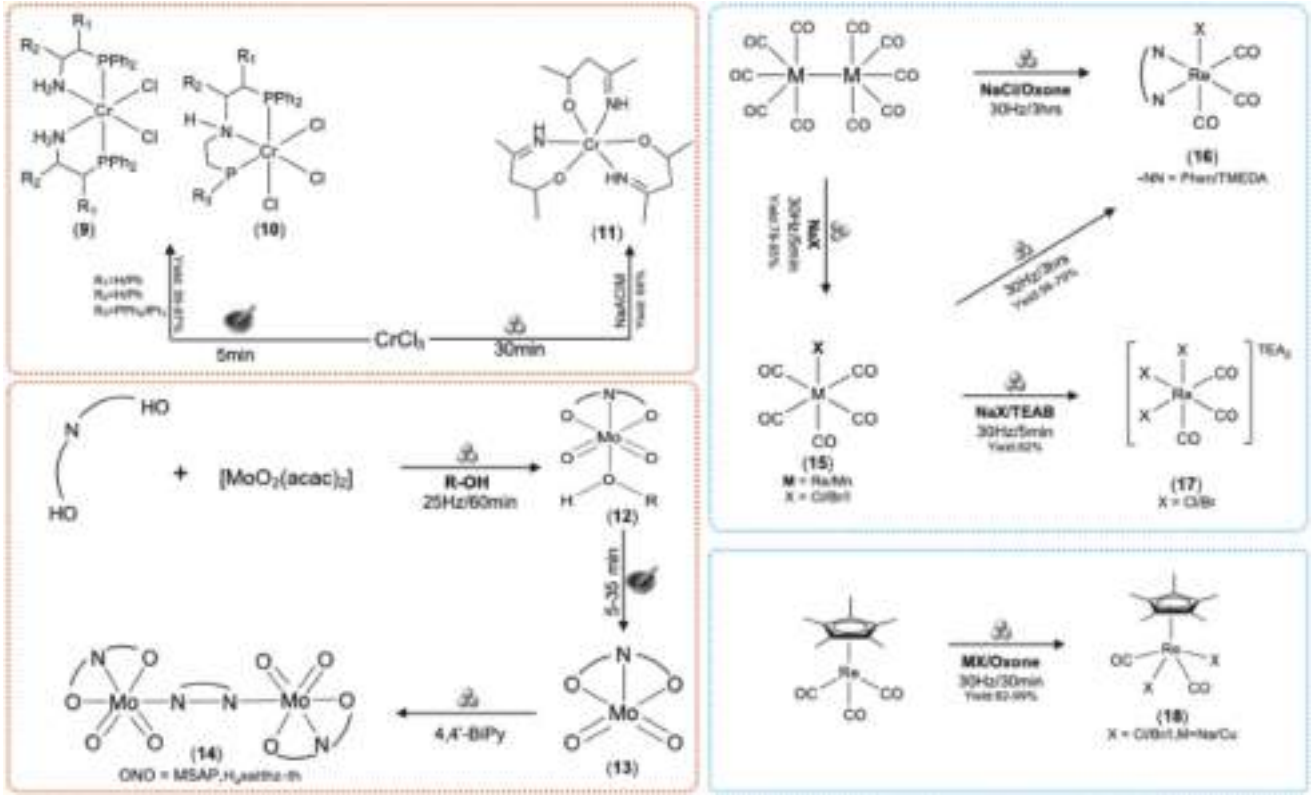
2.3.1. Mechanochemical synthesis of Cr(III) and Mo(IV) complexes

Chromium complexes offer persistent challenges in terms of



Scheme 2. Summary of V(III/V), Zr(IV), Hf(IV) complexes prepared prepared by mechanochemical synthesis.

solubility mismatch between ligands and metal precursor. Especially in the case of chromium-imine complexes, these opposing trends of solubility create phase effects (as chromium salts are soluble in aqueous media and ligands readily hydrolyze in the same) [47]. To address these issues, Makhaev and coworkers reported one of the earliest examples of solid-state chromium complex synthesis, reacting $CrCl_3$ with sodium 4-imino-2-pentanonate (NaACIM) in a simple vibratory ball mill to afford chromium ketoiminate derivatives (**11**) (Scheme 3) [80]. This solvent-free strategy effectively bypassed solubility constraints and prevented imine hydrolysis. Despite these early contributions, mechanochemical synthesis of chromium complexes has remained largely unexplored until the recent work of Morris et al. in 2024 [81]. They reported Cr(III) complexes (**9, 10**) bearing bidentate P,N- (such as $(NH_2(CH_2)_2PPh_2)$, (*S*,*S*)-$(NH_2(CHPh)_2PPh_2)$) and tridentate P,N,P ligands (such as (*S*,*S*)-$(NH_2(CHPh)_2PPh_2)$, $((NH_2(CH_2)_2PPh_2)$, $(Ph_2P(CH_2)_2N(H)(CH_2)_2PPh_2)$ and (*S*,*S*)-$(iPr)_2PCH_2CH_2N(H)CH(Ph)CH(Ph)PPh_2)$), obtained rapidly under milling conditions without the elaborated procedures typical of classical solution approaches. The authors observed metal-ligand interactions analogous to those reported in solution [82], thereby raising important questions regarding the actual mechanistic role of solvents in conventional chromium coordination chemistry. Beyond these examples, solid-state routes to chromium complexes remain scarce, highlighting a significant opportunity for further development. Mechanochemical strategies have also been extended to Mo(IV) chemistry, particularly for the synthesis of dioxomolybdenum complexes with hydrazone ligands [83]. In contrast to solution chemistry, where competitive solvation and solubility effects strongly influence coordination, mechanochemical approaches enable the direct assembly of O,N, O-type ligands with molybdenum precursors under solvent-minimized conditions. Recent studies describe the synthesis of MoO_2(VI)



Scheme 3. Summary of Cr(III), Mo(IV) and Mn(I/II), Re(I/III) complexes prepared by mechanochemical synthesis.

complexes ([MoO_2(L)(MeOH)] and [MoO_2(L)]$_n$) derived from thiophene-2-carboxylic acid hydrazone ligands (O,N,O-ligand) [84]. A related system was analyzed by Friščić and coworkers who mechanochemically activated [MoO_2(MSAP)(ROH)] (where H_2MSAP = N-3-methoxysalicylidene-2-amino-3-hydroxypyridine) first removing volatile components (**12,13**) by grinding, followed by coordination of neutral N-donor ligands to yield complexes such as [(MoO_2(MSAP)$_2$)(4,4′-bipyridine)](**14**) in quantitative yields [85]. Collectively, these chromium and molybdenum examples illustrate how mechanochemistry can overcome solubility-driven limitations while often reproducing, under solvent-free conditions, coordination motifs known from solution chemistry.

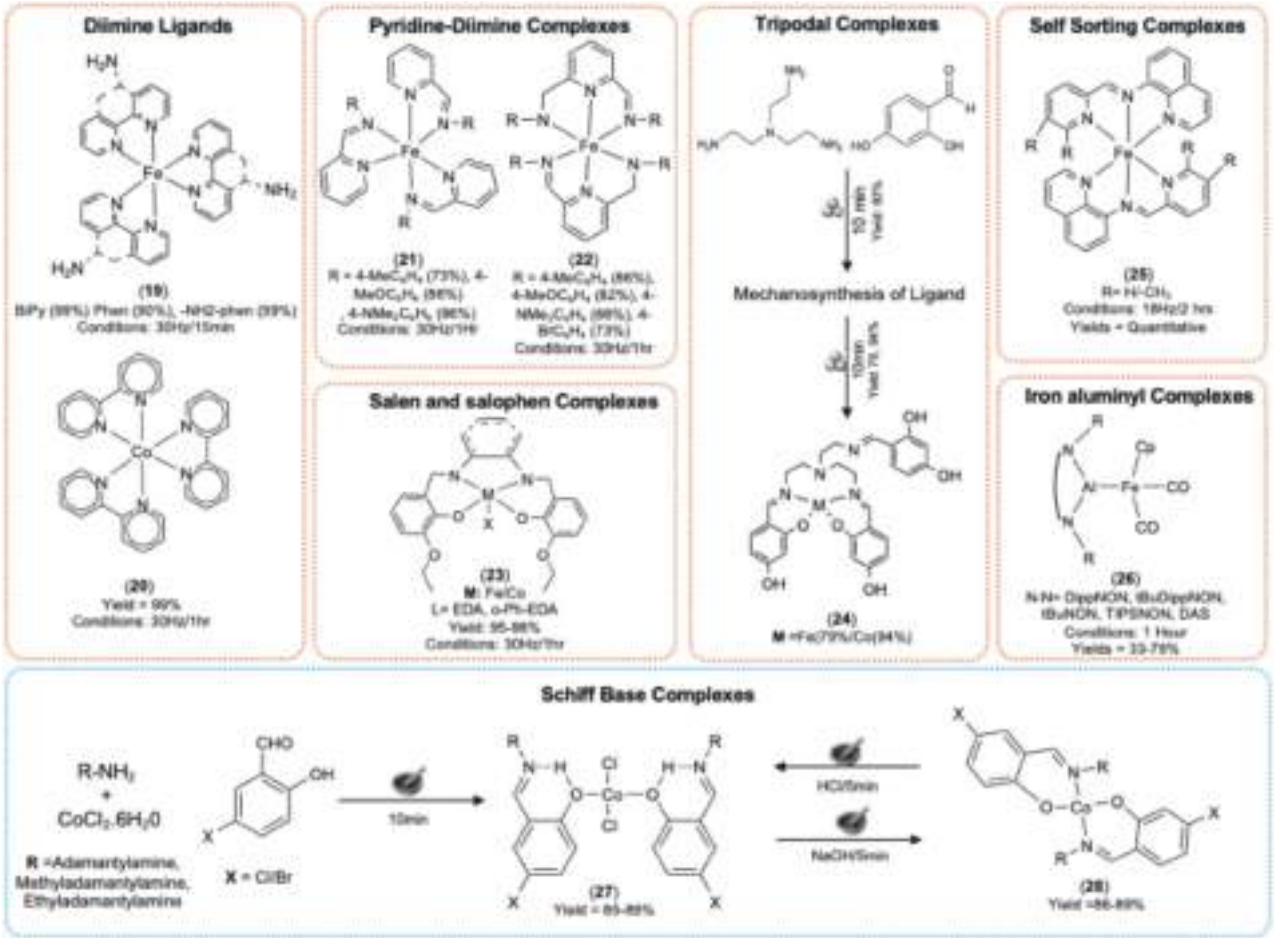
2.3.2. *Mechanochemical synthesis of Mn(I/II) and Re(I/III) complexes*

Several examples demonstrate the efficiency of mechanochemistry in Group 7 chemistry. Friščić and coworkers demonstrated that Rhenium complexes can be synthesized efficiently through mechanochemical oxidative addition [86] and multistep ligand exchange reaction [87]. Zero valent rhenium carbonyl [$Re_2(CO)_5$] and [$Mn(CO)_5$] were rapidly halogenated to corresponding pentacarbonyl halides [$M(CO)_5X$](**15**) under milling conditions using Oxone® and alkali metal halides (Scheme 3). Compared to classical solution-based protocols, often requiring halogenated solvents, elemental halogens or photochemical activation [88], the mechanochemical approach provided a solvent-free, rapid (≈ 5 min) and high-yielding (78–95%) alternative. These mechanochemically synthesized pentacarbonyl halides also serve as versatile intermediates for further ligand substitution reaction. Introduction of bidentate N-donor ligands afforded *fac*-[$Re(CO)_3$(N^N)X] (X = F, Cl) (**16**) species, highlighting the potential of stepwise carbonyl substitution under solvent-minimized conditions (Scheme 3). Similarly, $[Re(CO)_3Br_3]^{2-}$(**17**) complex (isolated as [TEA]$_2$ salts, where TEA = tetraethylammonium) was obtained *via* both one-pot and multistep milling approaches with comparable yields [87]. Friščić et al., also studied the cyclopentadienylrhenium(I) tricarbonyl [$ReCp(CO)_3$] complexes for oxidative addition of halogens (**18**) [86]. Beyond carbonyl derived systems of Re and Mn, several Mn(II) coordination polymers and phosphonate-based materials have also been accessed mechanochemically. For instance, Mn(II) phosphonates such us $MnNP_3$ and [$Mn(NP_2AH)_2$] were prepared *via* liquid assisted grinding of Mn$(OAc)_2{\cdot}4H_2O$ and corresponding phosphonic acids within 15 mins [89]. These studies demonstrate that mechanochemistry is particularly effective for oxidative and substitution processes involving carbonyl complexes, where solvent-free conditions can simplify multistep organometallic transformations.

The Mn(II)-bis(imino)pyridine complexes were obtained by a one-pot, one-step mechanochemical route, in which the N-donor ligand and the metal complex formed *in situ* during ball milling. Using MnX_2 (X = Cl, Br) and 2,6-diacetylpyridine, the method affords the species under solvent-free reaction conditions. These complexes feature a tridentate N,N,N-chelating ligand framework that stabilizes Mn(II) centers relevant to precatalyst design [90].

2.3.3. *Mechanochemical synthesis of Fe(II/III) and Co(II/III) complexes*

Mechanochemistry of iron complexes dates back to late 1990s when ferrocene was mechanochemically synthesized from $FeCl_2$ [91]. Subsequent studies expanded this approach to substituted ferrocenes and related systems [91–94]. After that, a lot of work has been published with the mechanochemistry of ferrocenes [92–94] and, more recently,



Scheme 4. Summary of Fe(II/III) and Co(II) complexes prepared by mechanochemical synthesis.

Fe(II) and Co(II) complexes bearing diimine and polypyridyl ligands such as 2,2-bipyridine (BiPy) or 1,10-phenanthroline (Phen) (**19**, **20**) were synthesized efficiently under milling conditions (Scheme 4), typically in short reaction times and good yields [95–97]. In some cases, condensation of primary amines and aldehydes (**21**,**22**) followed by *in situ* coordination to Fe(II) salts occurs in a single mechanochemical operation, streamlining processes that are less efficient in solution [96]. Direct milling of diamines, salicylaldehyde derivatives, and $FeCl_3$ or $CoCl_2$ yields the corresponding Fe(III) and Co(II) salen complexes (**23**) without prior ligand isolation [98]. Fe(II)- and Co(II)-bis(imino)pyridine complexes were prepared *via* a one-pot mechanochemical route, in which the N,N,N-donor ligand and metal complex formed *in situ* during ball milling (Scheme 4). Using FeX_2 or CoX_2 (X = Cl, Br) with 2,6-diacetylpyridine, the method affords the species under solvent-free reaction conditions, yielding precatalyst-relevant first-row transition-metal complexes [90]. Such transformations are comparatively rare under classical solution conditions, where hydrolysis and solubility issues frequently complicate the synthesis [99]. Tripodal Fe(III) and Co(II) complexes (**24**) have likewise obtained *via* one-pot, multistep mechanochemical sequences starting directly from aldehydes and amines, with subsequent application in catalytic oxidation of limonene in mechanochemical conditions [100]. Mechanochemistry also facilitates condensation metalation sequences that are often considered inefficient in solution [98]. Dynamic self-sorting of Fe(II) imine complexes (**25**) has also been achieved mechanochemically [97]. Whereas the analogous equilibrium in solution may require weeks (around 20 days) to reach completion [101], milling conditions provide the thermodynamically favored products within 2 h, demonstrating that mechanochemistry can reproduce solution-phase equilibria on significantly accelerated timescales. Heterobimetallic systems have also benefited from solid-state activation. Iron-aluminyl complexes (**26**), for example, were synthesized in approximately one hour under milling conditions (Scheme 4), compared to multiday protocols in solution [102]. Cobalt coordination chemistry under mechanochemical conditions reveals both similarities and divergences relative to solution behavior. Early studies demonstrated quantitative formation of [Co(α-diimine)Cl_2] complexes within minutes of grinding [103]. Related protocols afforded [$CoCl_2(H_2O)_2$(-amine)$_2$] species from primary aromatic amines [104]. Although steric effects influence product stability and lability, mechanochemical routes generally provide rapid and high-yielding access to Co(II) complexes. More recently, reversible coordination switching in cobalt Schiff-base systems has been demonstrated under ball-milling conditions [105]. Grinding amines with $CoCl_2{\cdot}6H_2O$ and salicylaldehyde derivatives yielded monodentate complexes [$CoCl_2(HL)_2$](**27**) (where L is the monodentate ligand) that could be transformed into bidentate analogues (**28**) through mechanochemically induced dehydrohalogenation, illustrating dynamic structural control in the solid-state. Finally, solvent-free one-pot protocols have enabled the conversion of [$Co_2(CO)_8$] to [Co(Cp*)(CO)I_2] complexes that are catalytically competent for C—H amidation directly in the mill [106]. Overall, Fe and Co systems exemplify how mechanochemistry can combine ligand formation, metalation, and even catalytic application within a unified solvent-free workflow, while often mitigating hydrolytic and solubility limitations encountered in solution chemistry.

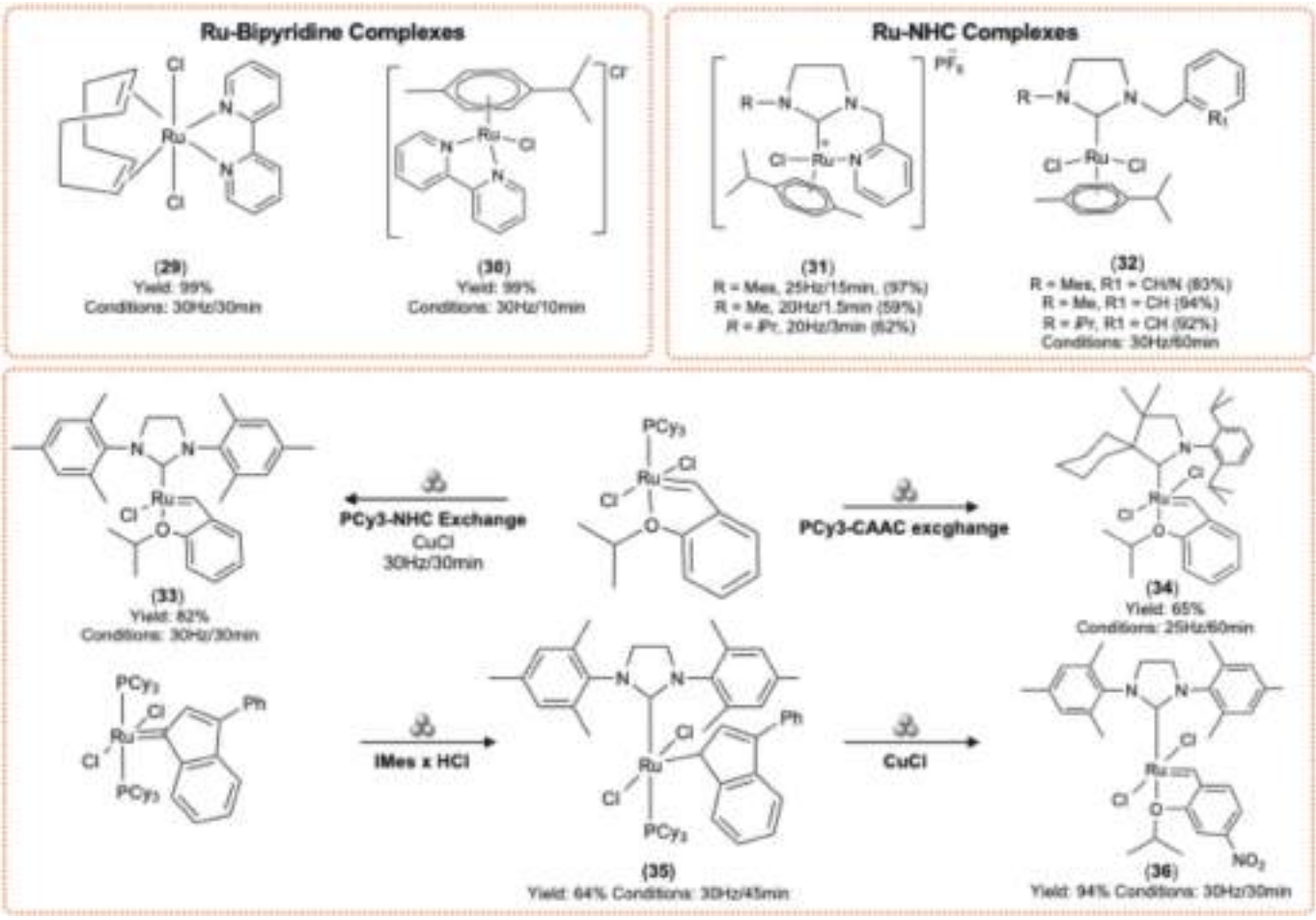
2.3.4. Mechanochemical synthesis of Ru(II), Rh(I/III) and Ir(III) complexes

Ruthenium carbene complexes bearing N-heterocyclic carbenes (NHC) remains of central interest for olefin metathesis [63,107–109]. Solid-state approaches have enabled the preparation of such catalysts (**31**,**32**) through ligand exchange and trans-metalation. In particular, different Noel type of Ru-arene-NHC complexes have been efficiently synthesized with ball milling conditions with high yields and shorter reaction time [110]. Furthermore, highly advance metathesis catalytic systems which include Hoveda, indenylidene and other third generation catalysts were also assembled by mechanochemistry by PCy_3 exchange with NHC and other ligand substitution pathways (for details see complexes **33**–**36**, Scheme 5) [111]. Solid-state synthesis of these catalysts ensures the high efficiency as well as it limits the side reactions possibility due to solution phase [63,107–109].

On the other hand, Ru-Polypyridyl complexes are widely employed as starting precursors and also in the photo-redox catalysts [112,113], anti-cancer [114] and anti-bacterial agents [115]. Recently Bantreil and coworkers publish an interesting study in which they reported the direct transformation of $RuCl_3$ to Ru-polypyridal complexes of [Ru(BiPy)$_3$]$(PF_6)_2$ using a reducing agent directly in the mill [116]. Such transformation which involve direct reduction as well as coordination in one pot are quite rare in solution methodologies and also considered as inefficient as terms of high time and low yields [117–119]. Some of these type of Ru(II) complexes have been recently synthesized by us such as [Ru(*p*-Cym)(BiPy)Cl]Cl(**29**), [Ru(COD)(BiPy)Cl_2](**30**), [Ru$(PPh_3)_2$(BiPy)Cl_2], and [Ru$(OAc)_2(PPh_3)_2$] through ball milling [95] and manual grinding [120]. Details can be seen in Scheme 5.

As we have compatible experience with mechanosynthesis several Ru complexes, we tried to sketch out experimental design comparison between solution and mechanochemical approach. For that we choose [Ru(*p*-Cym)(BiPy)Cl]Cl(**29**), and both the approaches are described in Fig. 2. Clearly, mechanochemistry dominates classical solvothermal approaches by simpler/faster experimental design. Solution based approaches involves bulks solvents that after completion requires extensive workup procedures, further adding up to the total cost and time of reaction. On the other hand, mechanochemistry usually involve simpler setup, and most of the time no or less extensive workup procedure is required to isolate the product.

Mechanochemical approaches to the synthesis of Rh organometallic complexes is mainly focused on half sandwich type Rh(III)Cp*(**38**) derivatives and Rh(I)-NHC(**39**) complexes (Scheme 6). Mechanochemical implication of Rh(I)-NHC complexes have been achieved with both weak base and trans-metalation strategies that were observed to be quite useful in terms of eliminating bulk solvents and inert atmosphere. In this regard, Pisanò and Cazin reported a scalable route with weak bases in which azolium salts are milled with [RhCl(COD)]$_2$ and K_2CO_3, yielding Rh(I)-NHC complexes of the type [RhCl(COD)(NHC)](**40**) in good yields (Scheme 6) [122]. The reaction proceeds without the need for inert atmosphere that is quite necessary for the conventional free-carbene routes. Notably advanced mechanosynthesis route was reported by Udvardy, Czégéni and coworkers, describing the first ever mechanochemical synthesis of poly-Rh(I)-NHC(**39**) complexes [123]. Although the milling condition were quite same as the above ones, yet they reported to achieve the dinuclear bridging complexes in high yields and without the formation of macrocyclic byproducts which are often observed in solution strategies [124,125]. These synthesis of mono and dinuclear complexes of Rh(I) highlights the recurring prospect of mechanochemistry which enhances the selectivity as well as suppression of solution mediated equilibria. Hence solid-state synthesis of these complexes ensures the limited redistribution of ligands which helps in avoiding oligomerization pathways. Beyond these Rh-NHC complexes, Hernandez and coworkers reported the synthesis of Wilkinson catalysts (**37**) in mechanochemistry with quantitative yields [126]. Furthermore, mechanochemical methodologies have been also successfully used for the synthesis of half sandwich Cp* complexes of both rhodium and iridium due to their structural and electronic analogy between Rh(III)Cp* and Ir(III)Cp*(**42**) (Scheme 7). In this regard, Jia et al. reported the mechanochemical synthesis of [MCp*Cl(L)] type of complexes with Rh and Ir from direct grinding of the chlorine bridged dimers as precursors with hydroxyquinoline-2-carbaldehyde [127]. Mechanistic insights into such RhCp* mechanochemical transformations were later explored by Ardila-Fierro and co-workers. They demonstrated that C—H activation (assisted by acetate) progresses through the formation of metal-substrate cocrystals in the first step, followed by the dimer cleavage. Like the above discuses works, this study also reports the synthesis of six-membered rhodacycles that are usually considered inaccessible with



Scheme 5. Summary of Ru(II) complexes prepared by mechanochemical synthesis.

classical solution based routes [128].

Iridium mechanochemistry further extends to the to the cyclometalated Ir(III) complexes where a detailed mechanochemical exploration has been done by Kubota and coworkers. A two step, solid-state protocol was developed to synthesize various tris-cyclometalated iridium complexes starting from $IrCl_3$ and pyridyl ligands [129]. As compared with the conventional strategies which acquire high time (24–48 h) [129–131], this methodology offers quick formation of the targeted complexes and impressive values of green metrics. Furthermore, the intermediates (**43**) (Scheme 7) which are poorly soluble in solvents were also efficiently transformed to complexes (**44**) in solid-state which highlights the mechanistic advantage of mechanochemistry by overcoming the solubility constraints through solid-state grinding. In our very recent work, we have also observed that pentamethylcyclopentadienyl Iridium dichloride dimer was very prone to the reaction with dimine ligands such as BiPy (**41, 44**). The mechanochemical reaction affords quantitative yield in just 30 min, as compared to the 5 h of the reaction time in solution with limited yield [95].

2.4. Metals of groups 10 and 11

Coordination chemistry of Group 10 and 11 constitutes one of the most developed and application-driven areas of organometallic synthesis. In this context, mechanochemistry has evolved from a proof-of-concept methodology to a broadly applicable synthetic platform capable of addressing phosphine, polypyridyl, carbene and pincer ligand frameworks across Ni, Pd, Pt, Cu, Ag, and Au systems. Compared to others metal examples, these metal complexes more frequently involve soft-donor ligands, redox-sensitive metal centers, and catalytically active architectures, making them particularly informative for evaluating the scope and limitations of solvent-free coordination chemistry.

2.4.1. Mechanochemical synthesis of Ni(II) complexes

Nickel(II) coordination chemistry has proven particularly amenable to mechanochemical approaches, especially for phosphine- and diimine-supported systems relevant to catalysis. Solid-state synthesis of [Ni(P^P)X_2](**45**) (P^P = dppe, dppp, dppb, dppf, Xantphos; X = Cl, Br) has demonstrated that the energy delivered by the milling assembly is a decisive parameter, with higher-density stainless-steel media generally affording improved conversions relative to zirconia systems (Scheme 8) [132]. This dependence highlights how energy transfer efficiency and impact frequency can directly influence metal-ligand bond formation under solid-state conditions. Hydrated precursors such as $NiX_2{\cdot}6H_2O$ often facilitate product handling and recovery, although strictly anaerobic conditions are required to prevent phosphine oxidation and formation of phosphine oxide byproducts, as observed in NMR spectra. Solvent-free ball milling under argon affords Ni(II) diphosphine complexes that can be directly employed, without purification, as efficient catalysts for C—C, C—N, and C—P bond-forming reactions, with activities comparable to conventionally prepared analogues.

Ni(II) complexes bearing α-diimine ligands, important in olefin polymerization catalysis, have also been synthesized quantitatively by Gomes et al., milling [Ni(*DME*)Br_2] (DME = 1,2-dimethoxyethane) with the corresponding ligands under nitrogen [103]. In these systems, mechanochemistry circumvents solubility mismatches commonly encountered in solution and allows direct access to well-defined square-planar Ni(II) species. Notably, both solvated and anhydrous $NiBr_2$ can be employed, although the latter requires extended milling times,

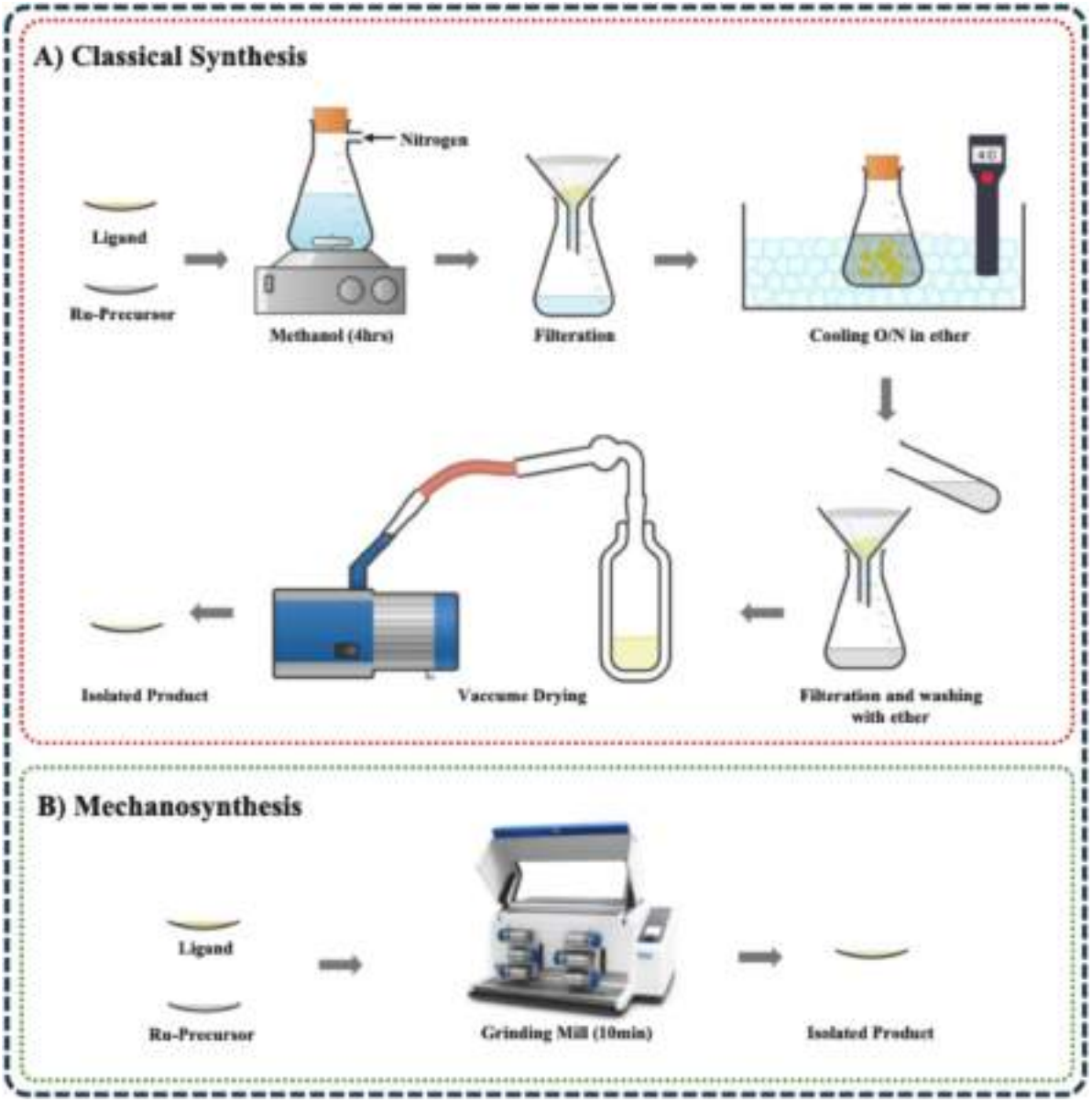
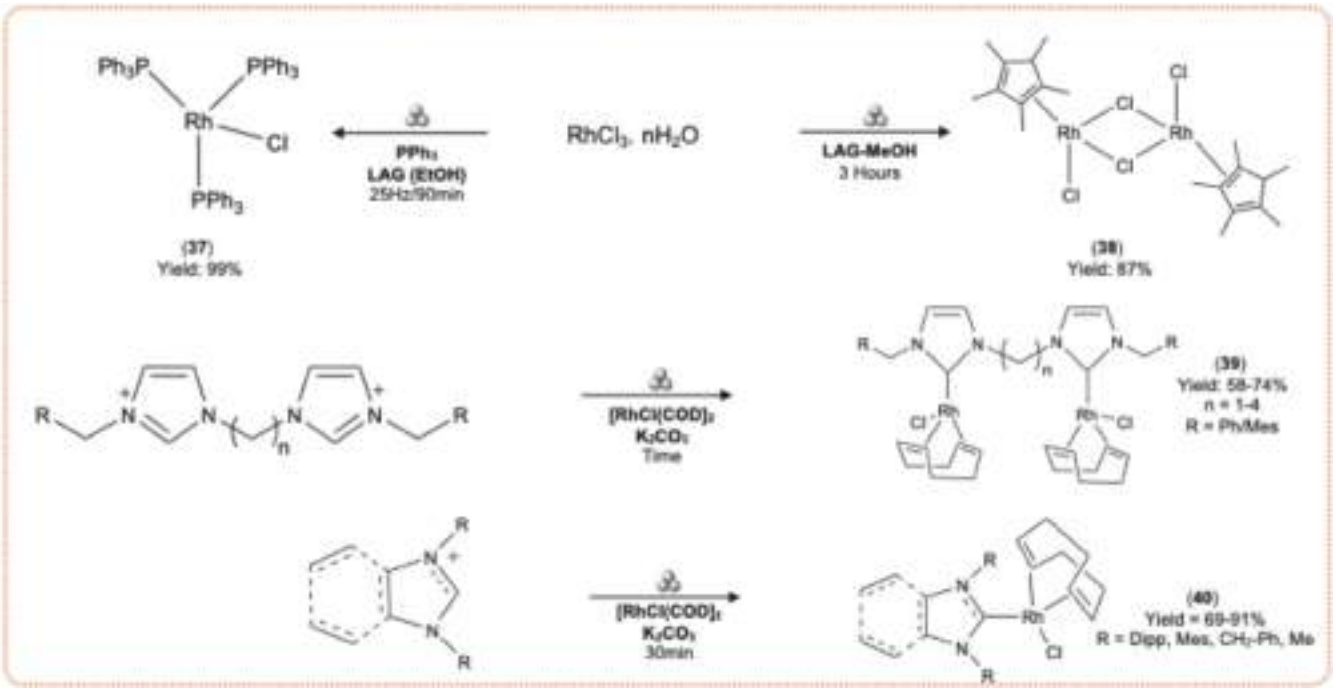


Fig. 2. Comparison of Classical solution based synthesis [121] with Mechanosynthesis [95]of [Ru(*p*-Cym)(BiPy)Cl]Cl(**29**).

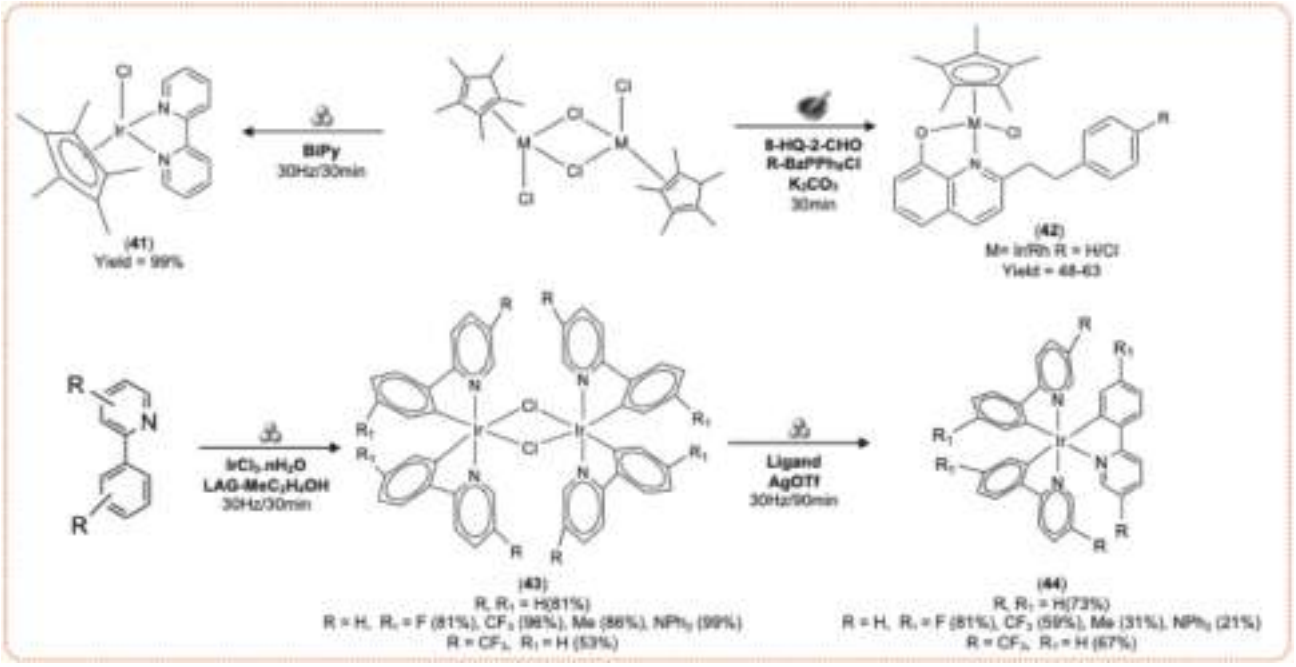
suggesting that lattice energy and precursor crystallinity can modulate the reaction. One-pot mechanochemical routes have further enabled the direct formation of Ni(II)-salophen complexes (**46**), without isolation of the ligand, Scheme 8. Milling *o*-phenylenediamine with $Ni(OAc)_2$ promotes *in situ* condensation and coordination, affording the target complexes in good yields [133]. The role of acetate is crucial, as substitution with $NiCl_2$ leads to incomplete reactions, underscoring how counterion basicity and internal proton transfer processes can determine success under solvent-free conditions. Ni(II)-bis(imino)pyridine complexes were obtained by one-pot mechanochemical synthesis, with the N,N,N-donor ligand and NiX_2 (X = Cl, Br) complex forming *in situ* during ball milling. This solvent-free route affords chelated bis(imino)pyridine species with coordination features relevant to precatalyst design [90].

Mechanochemical protocols have also been extended to Ni(II) dithiophosphonate complexes (**47**) generated *via in situ* activation of Lawesson's reagent (LR) with alcohols to generate dithiophosphonic acids in 5 min, followed by grinding generated acids with $NiCl_2{\cdot}6H_2O$ (Scheme 8) [134]. Cui et al. reported the stepwise mechanochemical synthesis of Ni(II) complexes with 1,1′-di(2-picolyl)-3,3′-methyl-enedibenzoimidazolium ($[H_2L]^{2+}$) as the ligand (**48**). The precursors $[H_2L]Br_2$ and $[H_2L](PF_6)_2$, were prepared *via* ball milling through alkylation and subsequent anion metathesis. Then the coordination was performed by grinding the ligand salts with $Ni(OAc)_2$ using LAG with methanol, acetonitrile or water (Scheme 8). This procedure afforded the tetra-coordinated species $[NiL]Br_2{\cdot}CH_3OH$, $[NiL]Br_2{\cdot}2H_2O$ and $[NiL](PF_6)_2{\cdot}0.5CH_3CN$. A structural transformation to a five-coordinated $[NiLBr](PF_6)$, was achieved by further grinding. This complex was synthesized *via* three routes: grinding $[NiL]Br_2{\cdot}CH_3OH$ with $(NH_4)(PF_6)$, grinding $[NiL]Br_2{\cdot}2H_2O$ with KBr, or directly grinding the bromide and hexafluorophosphate complexes, together, to induce an anion exchange [135]. Such mechanically driven structural rearrangements emphasize that coordination number and geometry can remain dynamic even in the absence of bulk solvent.

Collectively, Ni(II) systems highlight how mechanochemistry can integrate ligand synthesis, coordination, and structural reorganization within a single operational platform, while offering insight into how precursor hydration, counterions, and milling energetics govern reactivity.



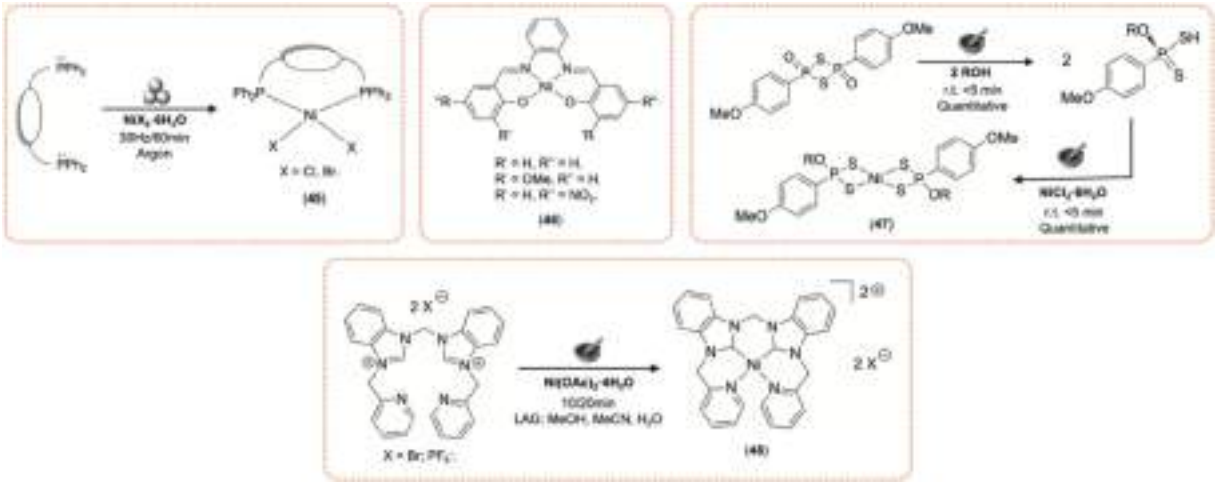
Scheme 6. Summary of Rh(I/III) complexes prepared by mechanochemical synthesis.



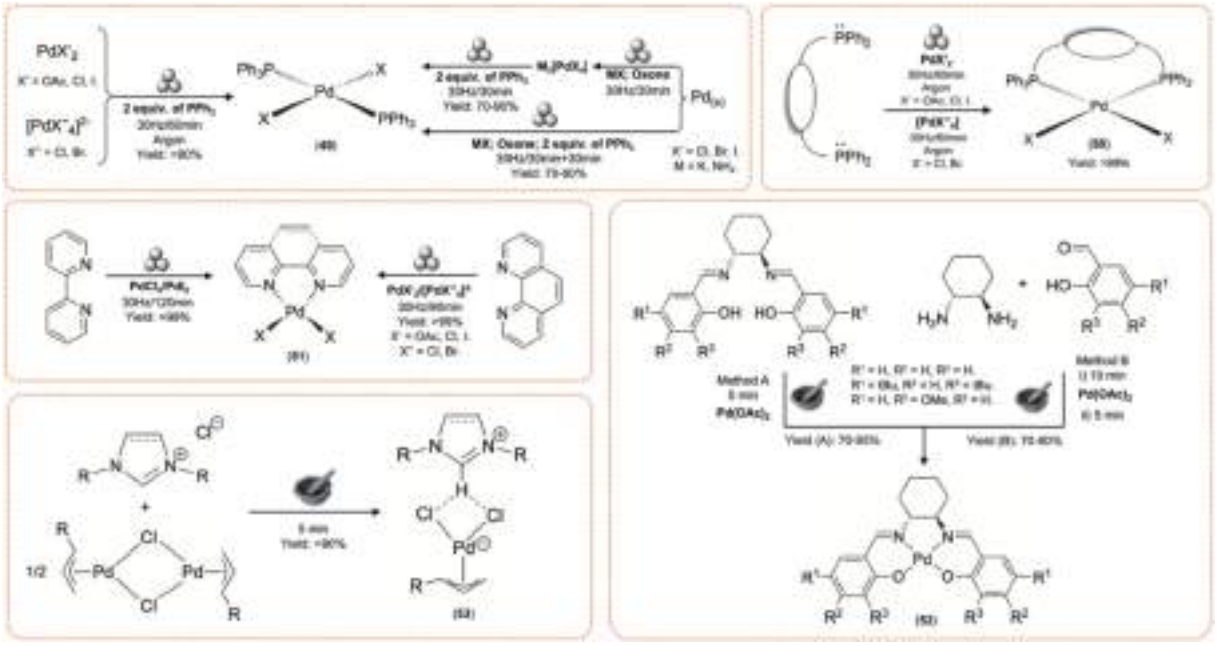
Scheme 7. Summary Ir(III) complexes prepared by mechanochemical synthesis.

2.4.2. Mechanochemical synthesis of Pd(II) complexes

Palladium(II) complexes represent one of the most extensively explored classes in mechanochemical organometallic chemistry. Given their central role in cross-coupling and C—H functionalization catalysis, Pd(II) systems provide an ideal testing ground for evaluating selectivity, robustness, and scalability under solvent-free conditions. Two complementary strategies have emerged: direct complexation from Pd(II) precursors [136] and oxidative mechanochemical activation of elemental Pd(0), followed by ligand coordination (Scheme 9) [137]. The reactivity of commercially available Pd(II) precursors with PPh_3 has been studied extensively. It is known that the reaction of PdX'_2 (X' = OAc, Cl, I) or $[PdX''_4]^{2-}$ (X'' = Cl, Br) with 2 equiv. of PPh_3 is highly sensitive to milling conditions. Under air, prolonged milling resulted in the quantitative oxidation of the ligand to triphenylphosphine oxide (PPh_3O) rather than complex formation. However, by reducing the reaction time and operating also in Eppendorf under argon atmosphere, the desired complex $[Pd(PPh_3)_2\ X\ _2]$(**49**) was obtained with high selectivity. Additionally, for halide precursors of Pd(II), the mechanochemical reaction works better. This distinct strategy allows the synthesis of these complexes directly from elemental Pd(0), avoiding the need for pre-synthesized precursors (Scheme 9). Using this method, **49** were isolated in yields ranging from 69% to 87%. Mechanochemical oxidative



Scheme 8. Summary of Ni(II) complexes prepared by mechanochemical synthesis.



Scheme 9. Summary of Pd(II) complexes prepared by mechanochemical synthesis.

activation of Pd metal enables the solvent-free, room-temperature formation of the catalytically active complex **49** with chlorine which promotes Suzuki coupling reactions in yields comparable to literature protocols. This oxidative methodology proved versatile for other monodentate phosphines, complexes with tricyclohexylphosphine and tris (pentafluorophenyl)phosphine ($PPFP_3$) were successfully synthesized [137].

The mechanosynthesis of complexes with bis(diphenylphosphino) methane (dppm), −ethane (dppe), −propane (dppp) and -butane (dppb) has recently been reported by us. Reactions utilizing halide precursors of Pd(II) proceeds quantitatively, yielding [Pd(P^P)X_2] (X = Cl, Br, I) (**50**). However, when $Pd(OAc)_2$ is used as precursor, the stability of the product varied significantly depending on the ligand used. While [Pd (dppe)$(OAc)_2$] was obtained stably, reactions with other diphosphines often led to degradation or the formation of phosphine oxides, necessitating careful handling or argon atmospheres during the reactions (Scheme 9). Ferrocenyl ligands, 1,1′-bis(diphenylphosphino)ferrocene (dppf) and its di-isopropyl analogue (dippf), were also compatible with mechanochemical conditions. High yielding syntheses of [Pd(dppf)X_2] and [Pd(dippf)X_2] were achieved for above mentioned complexes. Furthermore, the oxidative mechanochemical route starting from Pd(0) was successfully applied to synthesize [Pd(dppf)X_2] in a one-pot procedure. This strategy couples mechanical oxidation with *in situ* complexation, demonstrating that redox processes and coordination events can be seamlessly integrated in a single milling operation [137]. The synthesis of chiral diphosphines complexes, crucial for asymmetric catalysis, has been demonstrated with (*R*)-BINAP. Quantitative yields of [Pd((*R*)-BINAP)X_2] were obtained using $[PdX_4]^{2-}$ or PdI_2 precursors, although the reactivity of $PdCl_2$ was notably lower compared to tetrachloroplatinate [136]. Xantphos, a wide-bite-angle ligand, presents specific challenges in solution synthesis, primarily the formation of catalytically inactive bis-ligated species [Pd(Xantphos)$_2$] [138]. In mechanochemistry, the outcome of the reaction depends greatly on the precursor used. In the case of halide precursors $[PdX_4]^{2-}$, the monoligated species [Pd(Xantphos)X_2] were obtained in high yields and selectivities. A significant advancement was reported by Takahashi et al., who developed a solvent-free route to the dialkyl complex [(Xantphos) Pd$(CH_2TMS)_2$] (TMS = trimethylsilyl), by milling the precursor [(COD)

$Pd(CH_2TMS)_2$] with Xantphos for just 5 min, the desired pre-catalyst was obtained in 97% yield on a gram scale [139].

Mechanochemistry has proven particularly powerful for N-donor ligands. Elemental Pd(0), Oxone®, and a chloride salt were directly milled in the presence of acetonitrile results in the quantitative formation of targeted $[Pd(MeCN)_2Cl_2]$. This high conversion demonstrates that liquid ligands, (N-donor ligands) can be effectively introduced as additives during the milling process to serve as reagents and milling auxiliaries [137]. The mechanochemical reaction of Pd(II) precursors with bidentate N-donor ligands, such as BiPy and Phen, has been reported in Scheme 9. For BiPy, the synthesis of $[Pd(BiPy)X_2]$(**51**) was achieved successfully by milling $PdCl_2$ and PdI_2 [95]. After BiPy, the mechanochemical kinetics of Pd(II) coordination with functionalized bipyridines, specifically dialkyl 2,2′-bipyridine-4,4′-dicarboxylates (L^n) were investigated. Formation of $[PdL^nX_2]$ (X = Cl, I) complexes demonstrated that the physical state of the reaction mixture plays a critical role in reaction kinetics. For instance, the synthesis of $[PdL^{\alpha 14}Cl_2]$ (where $L^{\alpha 14}$ is the di-tetradecyl ester) exhibited a sticky rheology in the grinding vessel, requiring periodic interruptions and manual mixing to achieve complete conversion. In particular, the formation of a liquid-crystalline product phase during the synthesis was found to increase the reaction rate by facilitating diffusion [140]. Subsequently, the mechanochemical synthesis of Pd(II)-BiPy complexes was significantly improved with LAG. The addition of small amounts of DMSO markedly accelerated complex formation. Importantly, DMSO was shown to be a non-innocent additive, forming transient Pd(II)-DMSO species that facilitate ligand substitution and coordination [141]. Such findings illustrate that small amounts of liquid can dramatically alter reaction kinetics and even influence intermediate speciation without reintroducing bulk solvent behavior. It has recently been expanded the scope of mechanosynthesis to include Pd(II)-Phen complexes. Using a ball mill, quantitative yields of $[Pd(Phen)X_2]$ (X = Cl, Br, I) (**51**) are reported (Scheme 9). The acetate complex [Pd(Phen)$(OAc)_2$] was also accessible *via* milling $Pd(OAc)_2$ with 1 equiv. of Phen [136]. The synthesis of cationic palladium 2,2′:6′,2″-terpyridine (terpy) complexes of the type [Pd(terpy)X]X (X = OAc, Cl, Br, I) has been comprehensively reported. Milling of terpy with various previously mentioned Pd(II) precursors produced quantitative targeted complexes. For instance, [Pd(terpy)Cl]Cl was obtained quantitatively from $Na_2[PdCl_4]$ in 60 min, whereas the use of the less reactive precursor $PdCl_2$ required 75 min to reach completion [136]. The formation of Schiff base ligands is a key preliminary step in the synthesis of Pd(II)-Salen complexes, and mechanochemical approaches have proven particularly effective for this purpose. It is reported that manual grinding of *trans*-cyclohexane-1,2-diamine with aromatic aldehydes enables rapid ligand formation, affording moderate to excellent yields and allowing the synthesis of a diverse library of eleven Salen ligands. This strategy was extended to Pd(II)-Salen complexes (**52**) through a two-step milling protocol: ligand formation followed by the addition of $Pd(OAc)_2$ (Scheme 9) [142]. Similarly, Leoni et al. employed automated ball milling to synthesize Salophen ligands from *o*-phenylenediamine and salicylaldehyde derivatives, obtaining good yields. While dry grinding was sufficient for unsubstituted ligands, LAG with methanol improved the synthesis of substituted analogues. In several cases, mechanochemical protocols suppress oligomerization or competing coordination pathways observed in solution, likely due to the absence of dilution-driven equilibria. Mechanochemical coordination with Pd(II) is very sensitive to the metal precursor: $PdCl_2$ was ineffective, whereas Pd(II) acetylacetonate proved to be the most suitable source [133]. The solid-phase synthesis of non-classical N-metalated Pd(II) pincer complexes *via* the direct cyclopalladation of functionalized monothiooxamides has been reported. The reaction employed $[PdCl_2(NCPh)_2]$ and was conducted using both manual grinding and vibration ball milling, achieving the formation of N,N,S- and N,S,S-palladacycles in the absence of additives [65].

Recent studies have established protocols for the cyclopalladation of symmetrical and unsymmetrical S-donor pincer ligands bearing thione sulfur donors, which had previously synthesized in solution. Two mechanochemical approaches were reported: a two-component and a three-component system. In the two-component approach, bis(benzonitrile)Pd(II)chloride was grinded with 1 equiv. of either symmetrical bis(thiocarbamate) ligands or unsymmetrical analogues, using a mortar or a ball mill. This procedure affords the desired cyclopalladated complexes in quantitative yield. To enhance sustainability and cost efficiency, a three-component strategy was subsequently developed (employing the ligand with $PdCl_2$ as precursor and DMSO as LAG additive). This method demonstrated under mortar conditions, requiring 15 min of reaction time and providing yields exceeding 80% [143].

The synthesis of Pd(II) diene complexes, specifically with COD, represents a foundational aspect of organometallic chemistry. The investigation in the solid-state of $[PdX_4]^{2-}$ (X = Cl, Br) and $PdCl_2$ with COD, revealed that $[Pd(COD)X_2]$ can be synthesized efficiently. The optimization of milling parameters is crucial, using $Na_2[PdX_4]$ with 1 equiv. of COD yielded the target complex quantitatively after 20 min of mill at 15 Hz. It was observed that higher frequencies led to product degradation, proven by a transition of the powder from yellow to grey, suggesting that lower energy input is preferable for this reaction. The protocol demonstrated excellent versatility also for the less reactive $PdCl_2$, afforded the complex in 98% yield, although it requires slightly more vigorous conditions. However, it is not possible to synthesize the iodine and acetate analogues using this methodology [136].

A prominent class of Pd(II) complexes accessible *via* mechanochemistry consists of imidazolium palladates of the general formula $[NHC{\cdot}H][PdCl_2(\eta^3\text{-}R)]$(**53**). A general solvent-free protocol is based on grinding $[Pd(\eta^3\text{-indenyl})Cl]_2$ with 2 equiv. of the appropriate azolium salt in a mortar, as reported in Scheme 9. The versatility of this approach was demonstrated by varying the NHC ligands (IPr = *N*,*N*′-bis(2,6-diisopropylphenyl)imidazol-2-ylidene, IPent = 1,3-Bis(2,6-bis(1-ethylpropyl)phenyl)imidazol-2-ylidene, IPr* = N,N′-1,3-bis[2,6-bis(diphenylmethyl)-4-methylphenyl]imidazole) and the allyl fragments (allyl, 2-methyl-allyl, crotyl, cinnamyl, tBu-indenyl). This methodology has also proven suitable for the synthesis of complexes with other more sterically hindered NHC ligands, such as IPr* and IHept (1,3-bis(2,6-di-4-heptylphenyl)imidazol-2-ylidene). The synthesis of these Pd(II) complexes was achieved by grinding the NHC salts with $[Pd(\eta^3\text{-cinnamyl})Cl]_2$, yielding stable solids that exhibited high microanalytical purity [144]. The mechanochemical assembly of $[Pd(\eta^3\text{-R-allyl})(Cl)(NHC)]$ rely on the straightforward milling of an azolium chloride salt with $[Pd(\eta^3\text{-allyl})Cl]_2$ as metal precursor and a weak base (K_2CO_3), with high yield. Mechanistically, the cleavage of the Pd-dimer and subsequent carbene coordination is presumed to proceed through the formation of a palladate intermediate. Interestingly, this intermediate can be physically isolated if the mechanochemical milling is conducted in the absence of K_2CO_3 [122]. More recently, this grinding technique was applied to synthesize a series of indenyl-palladate complexes. By reacting $[Pd(\eta^3\text{-indenyl})Cl]_2$ with a range of imidazolium salts, including IPrCl and IPr* derivatives, afforded the corresponding indenyl palladate complexes in quantitative yields [145]. While the direct grinding of Pd(II) precursors yields ionic palladate species, mechanochemistry were applied to generate neutral Pd(II)-NHC *via* transmetalation. It is reported a mill strategy to synthesize Pd(II)-NHC complexes from imidazolium salts and Ag_2O. These Ag(I) complexes subsequently served as trans-metalating agents: milling [AgCl(IMes)] (IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene) with $[Pd(\eta^3\text{-allyl})Cl]_2$ afforded the complex $[Pd(IMes)(\eta^3\text{-allyl})Cl]$. Furthermore, a one-pot and two-step procedure was developed, allowing the synthesis of Pd(II)-NHC directly from the imidazolium salt, Ag_2O and Pd(II) precursor without isolating the silver intermediate, achieving high yields [146]. A two-step method involving the grinding $[PdCl_4]^{2-}$ with 1,3-dibenzylimidazolium chloride (HIBz·HCl) to form a hydrogen-bonded intermediate $[HIBz]_2[PdCl_4]$ has been established [147]. Expanding on the utility of solid-state ion-pairing, it is recently reported the rapid

mechanochemical assembly of air-stable ionic palladates of the type [NHC·H][Pd(NH_2)(C^C)Cl_2] (where C^C is biphenyl). By grinding the precursor [Pd(NH_2)(C^C)Cl]$_2$ with various imidazolium salts for 5 min under air, the corresponding complexes were obtained in quantitative yields [148].

Overall, Pd(II) systems illustrate how mechanochemistry can deliver high selectivity, short reaction times and access to reactive intermediates that are challenging to observe under conventional solution conditions, while simultaneously offering improved green metrics and operational simplicity.

2.4.3. Mechanochemical synthesis of Pt(II) complexes

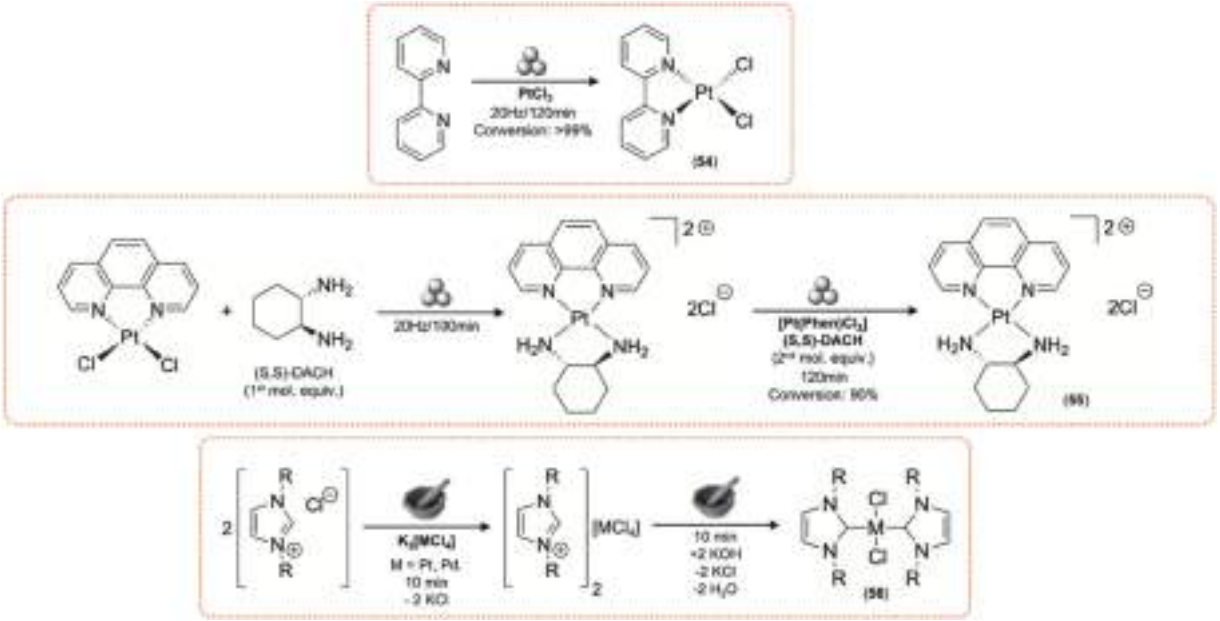
Platinum(II) coordination chemistry under mechanochemical conditions parallels that of general palladium reactivity in several respects yet exhibits distinct kinetic and aggregation behavior. Quantitative conversion to [Pt(BiPy)Cl_2](**54**) can be achieved by ball milling, although spectroscopic analysis often reveals minor secondary species which are consistent with partial dimerization [Pt(BiPy)(Cl_2)Pt(BiPy)]Cl_2 or alternative aggregation states under solid-state conditions [95]. It was recently published a mechanochemical synthesis of Pt(II) heteroleptic complexes (**55**) for cancer treatment with Phen derivative and a chiral diamine (1*S*,2*S*)-diaminocyclohexane (*S*,*S*-DACH). The optimized method is reported in Scheme 10 and involves a milling and mixing approach, where (*S*,*S*)-DACH is added in two steps to manage the rheological transformation of the reaction mixture from a powder to a paste. This protocol was applied to synthesize six derivatives of Phen, with the reaction times varied significantly based on steric hindrance. The purification has done *via* precipitation using water and THF or acetone, yielding the complexes in high purity [149]. Such operational considerations emphasize that physical properties, powder flow, paste formation and localized heating, can significantly influence mechanochemical outcomes. In this respect, late-transition metal systems provide valuable insight into the interplay between chemical reactivity and mechanical processing parameters.

Mechanochemical strategies provide a rapid, solvent-free and environmentally friendly route to PEPPSI complexes. These highly stable catalysts, with a Pt(II) (or Pd(II)) center coordinated to an NHC carbene, a pyridine ligand and two chlorides, can be prepared practically quantitatively in the solid-state. The synthesis of these complexes relies on a two-step solid-state methodology utilizing manual grinding in an agate mortar. This rapidly generates a mixed-cation intermediate salt with the formula [HL][HPy][$PtCl_4$]. In this intermediate, charge-assisted hydrogen bonding pre-organizes the acidic protons of the cations near the negatively charged chloride ligands on the metal. The intermediate mixed salt is then ground with 2 equiv. of KOH. The base readily deprotonates the pre-organized cations, eliminating KCl and H_2O and facilitating the direct coordination of the resulting N-heterocyclic carbene and pyridine ligands to Pt(II). The solid-state reaction rapidly generates the target [$PtCl_2$(Py)(NHC)]-PEPPSI-type complexes in quantitative yield [150]. More recent, a study on the synthesis of Pt(II) complexes with NHC carbenes has been reported (Scheme 10). Grinding K_2[$PtCl_4$] with HIBz·HCl affords the intermediate [HIBz]$_2$[$PtCl_4$]. It was observed that the milling of the Pt(II) precursor required longer times than the Pd(II) analogues to achieve complete conversion. The second step involves the dehydrochlorination of [HIBz]$_2$[$PtCl_4$] by grinding with KOH to generate the target complex [$PtCl_2$(IBz)$_2$](**56**) [147].

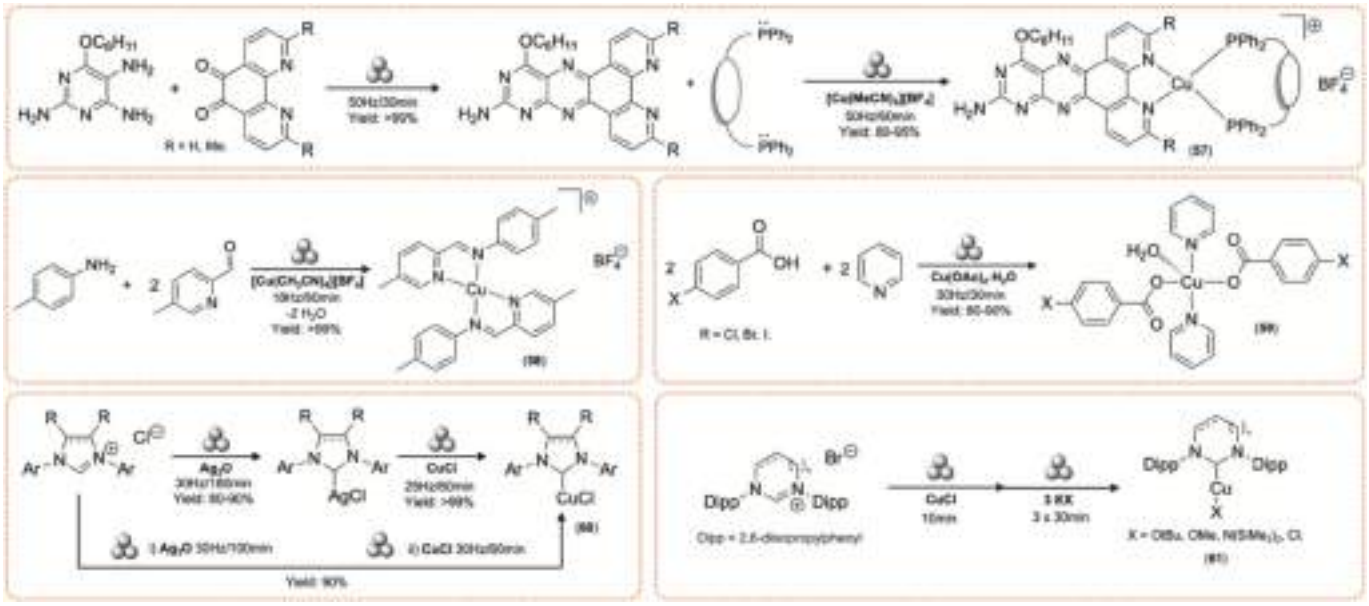
These examples demonstrate that even relatively inert Pt(II)-Cl frameworks can be transformed under mechanical activation, provided that proton transfer and carbene generation are effectively coupled to coordination.

2.4.4. Mechanochemical synthesis of Cu(I/II) complexes

Copper coordination chemistry has benefitted extensively from mechanochemical methodologies, particularly for phosphine, polypyridyl, Schiff-base and NHC ligands. Manual grinding with LAG has been employed to access cost-effective Cu(I) complexes bearing monodentate phosphines. Garra and coworkers reported the synthesis of complexes [CuX(PPh_3)$_2$(Py)] (X = Cl, Br, I) by grinding CuX, PPh_3, and pyridine derivatives in a mortar. This approach has produced species important for redox polymerization applications without the need for large amounts of solvents or extensive purification steps [151]. To access more structurally complex heteroleptic systems, Bandaru et al. utilized a ball milling to synthesize [Cu(N^N)(P^P)]$^+$(**57**) with chelating bisphosphines. The solvent-free reaction, summarized in Scheme 11, allows to obtain high yields of Cu(I) complexes. Solution NMR spectroscopic studies indicate that dissolution may trigger ligand redistribution equilibria not necessarily present in the solid-state. Such observations highlight that mechanochemically generated solids can display distinct coordination environments relative to their solution counterparts [152]. Mononuclear [CuI(PPh_3)$_2$L] (where L = pyridine,



Scheme 10. Summary of Pt(II) complexes prepared by mechanochemical synthesis.



Scheme 11. Summary of Cu(I/II) complexes prepared by mechanochemical synthesis.

isoquinoline, 1,6-naphthyridine, 2,2′-(phenylphosphinediyl)dipyridine) complexes were obtained mechanochemically by manual grinding only in the presence of a small amount of benzonitrile as LAG agent. In the other hand, neat grinding was effective only for the parent isoquinoline complex, highlighting the key role of ligand melting point and solvent assistance in promoting complex formation [51].

The use of naturally chiral pool molecules was successfully applied to the construction of metalloligands through mechanochemistry. A strategy for synthesizing chiral N,N-ditopic metalloligands based on the reaction between CuX (X = Cl, Br, I) and quinine (QN) has been reported. The grinding of CuX with QN in a 1:1 ratio, in LAG of acetonitrile, facilitated the formation of green powders identified as $[CuX(\mu\text{-QN})]_2$. This process promoted the oxidation of Cu(I) to Cu(II), a transformation not typically observed in mechanochemistry. Structural analysis confirmed that these dimeric complexes adopting a distorted square planar geometry. The QN moieties within these dimers are oriented in a nearly parallel fashion, establishing them as effective chiral N,N-ditopic metalloligands capable of further coordination [153]. The chiral copper complexes $[XCu(\mu\text{-QN})]_2$ (X = Cl, Br) were obtained by LAG grinding of CuX and quinine in acetonitrile under air, producing dark-green powders whose PXRD patterns matched the single-crystal structures. This mechanochemical route enabled the oxygenation of Cu(I) to Cu(II) and afforded N,N-ditopic metalloligands with potential for further coordination-driven assembly [153].

The mechanochemical synthesis, summarized in Scheme 11, of Schiff base ligands and subsequently coordination to $[Cu(CH_3CN)_4][BF_4]$ is reported. The reaction led to the selective formation of homoleptic Cu(I) complexes (**58**). This protocol is described as a clean milling process that evolves into LAG due to the *in situ* release of water from the condensation reactions [97]. Cu(II)-bis(imino)pyridine complexes were synthesized by a one-pot mechanochemical route. Using CuX_2 (X = Cl, Br), this solvent-free approach affords the species, where copper is present in the +2 oxidation state and it is stabilized by the chelating N-donor ligand framework [90].

Recent advancements expands mechanochemical Cu coordination chemistry to C-scorpionates (tris-(pyrazol-1-yl)methanes) functionalized with oxime moieties. The synthesis of these Cu(II) complexes followed the mechanochemical preparation of the ligands *via* the 1,4-addition of pyrazoles to conjugated α-halogenated nitrosoalkenes. Subsequent solvent-free ball milling 2,2,2-tris(1H-pyrazol-1-yl)acetaldehyde oxime (L), with stoichiometric amounts of $Cu(OAc)_2{\cdot}H_2O$ or $CuCl_2{\cdot}2H_2O$, afford $[Cu(OAc)_2L]$ and $[CuCl_2L]$ in high yields. These Cu(II)-scorpionate compounds efficiently catalyze Azide-Alkyne Cycloaddition under mechanochemical conditions. The ball mill conditions facilitated *in situ* reduction of Cu(II) to the catalytically active Cu(I) species without external reducing agents, yielding 1,2,3-triazoles with yields up to 78% [154]. The selectivity of mechanochemistry is evident in the synthesis of heteroleptic complexes where multiple coordination geometries are possible. Mechanochemical reaction of $Cu(OAc)_2{\cdot}H_2O$ with pyridine and *p*-halogenated benzoic acids has been investigated. The mechanochemical approach enables access to hydrated pentacoordinate complexes (**59**), reported in Scheme 11, with quantitative yields. Structural analysis confirmed that the metal adopts a square pyramidal coordination geometry defined by two *trans*-κ^1-carboxylate anions, two pyridines and an apical H_2O. Despite the potential for the carboxylate group to act as a chelating ligand, no traces of the alternative bis-chelate octahedral complexes were observed in the products [155]. The synthesis of Cu(II) complexes featuring BiPy and nonpolar amino acids (L-Ala, L-Val, L-Phe) has been explored. Using LAG with water or methanol, the authors successfully synthesized a series of ternary complexes, including polymeric and monomeric species. The study highlighted that while solution-based outcomes for L-Phe and L-Ala were highly dependent on unidentified external factors, making pure bulk products difficult to isolate, the mechanochemical synthesis provided a reliable route to obtain pure bulk materials. Structural characterization revealed that these complexes with Cu(II) in penta- or hexacoordinated, exhibiting distorted square-pyramidal or octahedral geometries due to the Jahn-Teller effect. The supramolecular architecture of these mechanochemically derived solids is stabilized by extensive hydrogen bonding and π stacking interactions between the aromatic bipyridine rings. In these systems, the suppression of competitive solvation and hydrolysis appears to play a decisive role in directing product formation [156].

Mechanochemical synthesis successfully accessed novel coordination geometries of Cu(II) complexes utilizing the non-steroidal anti-inflammatory drug meloxicam (H_2Mel as 4-Hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide). Through LAG in DMF with $Cu(OAc)_2{\cdot}H_2O$, a new octahedral complex $[Cu(HMel)_2(DMF)]$, was isolated. This distinct phase, confirmed *via* PXRD, exhibited enhanced cytotoxic properties against ovarian cancer. Furthermore, the versatility of this solvent-free protocol allowed for the substitution of toxic organic solvents with water. The resulting

biocompatible complex $[Cu(HMel)_2(H_2O)_x]$, maintained significant cytotoxic efficacy, highlighting the potential of mechanochemistry in generating potent, green metallodrugs [157].

The versatility of mechanochemistry extends to the multi-step synthesis of ligands and their subsequent metalation. The mechanosynthesis of *N*-phenyl-4-(2-pyridinyl)sydnone (L) and its coordination to Cu(II) has been investigated. Following the mechanochemical synthesis of the sydnone, the ligand reacted with $CuCl_2$ or $Cu(OTf)_2$ in a mill. Within 1 h, the reaction yielded the complexes $[CuCl_2(L)_2]$ and $[Cu(OTf)_2(L)_2]$ in good yields. SCXRD diffraction experiments of the chloride complex revealed an octahedral geometry where the Cu(II) is coordinated by two sydnone ligands and two chlorines. A distinctive structural feature of these complexes is the *trans*-arrangement of the anionic ligands, with the sydnone ligand acting as a bidentate N,O-donor [158].

A manual grinding protocol to synthesize Cu(II)-Salen complexes derived from *trans*-cyclohexane-1,2-diamine has been developed. Two strategies were employed using $Cu(OAc)_2$ and 2 equiv. of methanol for LAG. The first method is a two-step milling process involving the isolation of intermediate Salen ligands, and the second is a one-pot procedure where the metal precursor is added directly to the unpurified ligand mixture. Both methods afforded *trans*-[*N*,*N*-Bis(2-hydroxybenzylidene)cyclohexane-1,2-diamino]Cu(II) in high yields. The first method showing slightly higher efficiency. The complexes were applied to the oxidative aromatization of methyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylates to α-naphthols [142].

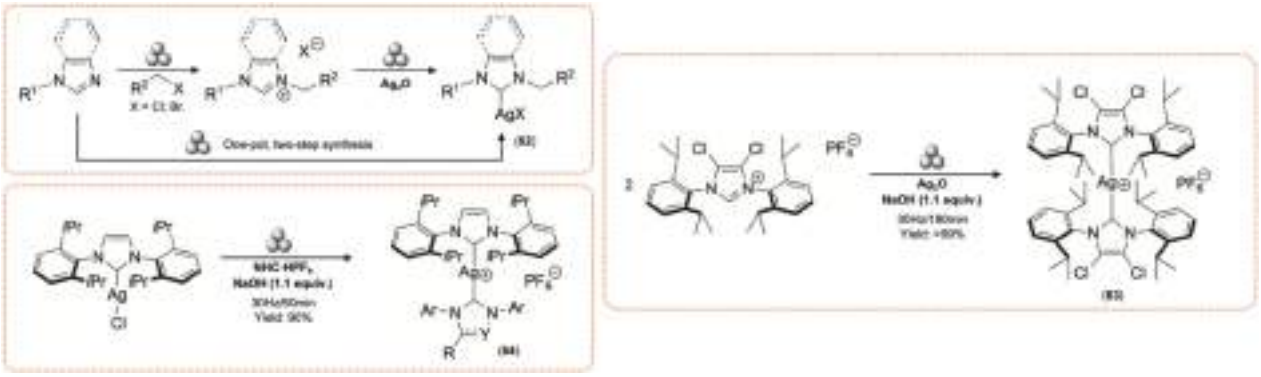
The mechanochemical synthesis of Cu(II) complexes with metronidazole (MET) and salicylate anions yields the penta-coordinated species $[Cu(Sal)_2(MET)_2(H_2O)]$. The stability of this coordination sphere is influenced by the mechanochemical precursors employed. LAG of MET with the pre-assembled metal precursor $[Cu(Sal)_2(H_2O)_2]$ facilitates the quantitative formation of the thermodynamically stable form. Conversely, attempts to assemble the coordination sphere starting from $CuCl_2$ and free salicylic acid results in amorphous products, highlighting the advantage of using pre-organized metal-salicylate molecules in solid-state reactions. The thermal profile of the complex correlates with its coordination environment, where the removal of the coordinated H_2O occurs between 343 and 373 K, leaving a stable anhydrous $[Cu(Sal)_2(MET)_2]$ up to 433 K [159].

The foundational entry to Cu(I)-NHC chemistry is [Cu(Cl)(NHC)] (**60**). Two mechanochemical approaches have been reported: transmetalation *via* Ag(I) intermediates and a direct route employing weak bases (Scheme 11). Notably, the direct strategy demonstrated the feasibility of multistep mechanochemical organometallic synthesis without intermediate purification [146]. To enhance sustainability by avoiding silver and reducing waste, a direct protocol was developed in which NHC·HCl salts react with CuCl and excess K_2CO_3 under air. Optimization with IPr·HCl showed rapid formation of $[NHC{\cdot}H][CuCl_2]$, while longer milling times were required for deprotonation and metalation. The method proved broadly applicable to sterically and electronically diverse NHC ligands, including IPr-type (IPr, IPr*) and mesityl-substituted systems (IMes, SIMes) [160]. This methodology relies on direct reaction between the imidazolium salt and CuCl. Depending on the intermediate formed, *in situ* chloride substitution can be achieved by affording the complexes summarized as **61** (Scheme 11). A related one-pot protocol involves mechanochemical reaction of the imidazolium salt with CuCl followed by treatment with an organolithium reagent to yield organocopper species [161]. Tzouras et al. have further extended the Cu-NHC mechanochemistry to complexes relevant for luminescent and photocatalytic applications. Although these complexes are mainly investigated in solution, a solvent-free protocol was achieved with [CuCl(IPr)], carbazole and K_2CO_3 to obtain [Cu(Cbz)(IPr)] (Cbz = carbazolyl). These results highlights the robustness of the mild-base mechanochemical approach, enabling carbazole deprotonation and providing a greener route to photoactive materials [162]. It has been reported a solvent-free mechanochemical route to the [CuCl(IPr)]-NHC complex by grinding IPr·HCl, CuCl, and K_2CO_3 in a ball mill or mortar and pestle, highlighting this approach as a greener alternative to solution-based syntheses due to reduced solvent use, shorter reaction times, and comparable yields [163].

2.4.5. Mechanochemical synthesis of Ag(I) complexes

Silver(I)-NHC chemistry advanced significantly through ball-milling techniques. Recent investigations into crystal engineering strategies for antimicrobial development have successfully employed mechanochemistry to synthesize mixed-ligand Ag(I) complexes containing O-donor salicylate ligands. The synthesis of [Ag(Sal)(MET)] (where Sal = salicylate, MET = metronidazole) using LAG (water) has been reported. Alternatively, the same crystalline product was obtained *via* a one-pot mechanochemical reaction starting from raw precursors, the salicylic acid (HSal), $AgNO_3$ and MET, demonstrating the versatility of the mechanochemical approach. Structurally, SCXRD confirms the mechanochemically complex has a linear coordination geometry [159].

The application of ball-milling to Ag(I)-NHC synthesis was reported by Beillard and coworkers, who demonstrated the efficiency of this method over solution-based protocols. The synthetic strategy is reported in Scheme 12 and involves the reaction of imidazolium salts with Ag_2O in a ball mill using steel jars affording the corresponding [Ag(*NHC*)X] (X = Cl, Br) (**62**) complexes up to 93% of yield. This enhanced reactivity is attributed to the efficient macroscopic mixing and the continuous regeneration of reactive surfaces on the Ag_2O particles due to shear stress and impact during milling. This method was extended to various ligands, including bis-imidazolium and pyridine-functionalized imidazolium. While sterically hindered ligands or those containing pyridine moieties required slightly longer milling times, the procedure remained robust. This approach allowed for the isolation of unprecedented complexes, such as specific bis-NHC species $[\{Ag(NHC)_2\}^+AgBr_2^-]_2$, which were structurally confirmed *via* X-ray diffraction to contain a dimeric $[AgBr_2]^-$ as counter-anion. In the same work, an efficient one-pot two-step procedures (where the imidazolium salt is generated *in situ* from imidazole and alkyl halides, followed by the direct addition of Ag_2O to form the complex without isolating the intermediate salt) was reported (Scheme 12). This sequential alkylation or metalation strategy was successfully applied to synthesize various complexes like **62** [164]. Still in the synthesis of Ag(I)-NHC complexes, Bantreil et al. reported the synthesis of numerous compounds [AgCl(NHC)] obtained mechanochemically by the simple milling of imidazolium salts with Ag_2O (Scheme 12). This approach proved superior respect to solution approach for accessing complexes with electron-deficient or sterically hindered ligands allowing their isolation in high yields. The solid-state environment appears to reduce ligand scrambling and disproportionation processes commonly encountered in solution. The protocol was further extended to the synthesis of $[Ag(NHC)_2](PF_6)$ complexes (**63**) *via* a one-pot milling of imidazolium hexafluorophosphate salts, Ag_2O and NaOH. Additionally, the study reported the unprecedented mechanochemical synthesis of heteroleptic cationic bis-NHC complexes (**64**) by reacting pre-formed [AgCl(IPr)] with distinct imidazolium salts. These mechanochemically generated complexes exhibited significant biological activity, with cationic derivatives showing cytotoxicity against cancer cells [165]. A highly efficient mechanochemical methodology utilizing a weak base has been established for the synthesis of [Ag(Cl)(NHC)] complexes. This approach relies on the treatment of an azolium chloride salt with AgCl, in the presence of an excess of K_2CO_3. The ball milling protocol yields various [Ag(Cl)(NHC)] complexes in good to excellent yields. Notably, the methodology demonstrates high functional tolerance with no restriction regarding the steric bulkiness of the corresponding NHC ligand salt employed [122]. Ryzhakov coworkers reported the synthesis of Ag(I)-NHC thioglycosides, a class of compounds combining the pharmacophore properties of both carbenes and carbohydrates. Grinding the thioglycosylated imidazolium salts with a slight excess of Ag_2O in a ball mill resulted in full conversion to the target Ag(I)-NHC thioglycosides compounds [166]. Wróblewska et al. extended mechanochemical protocols to the synthesis of N-oxy-

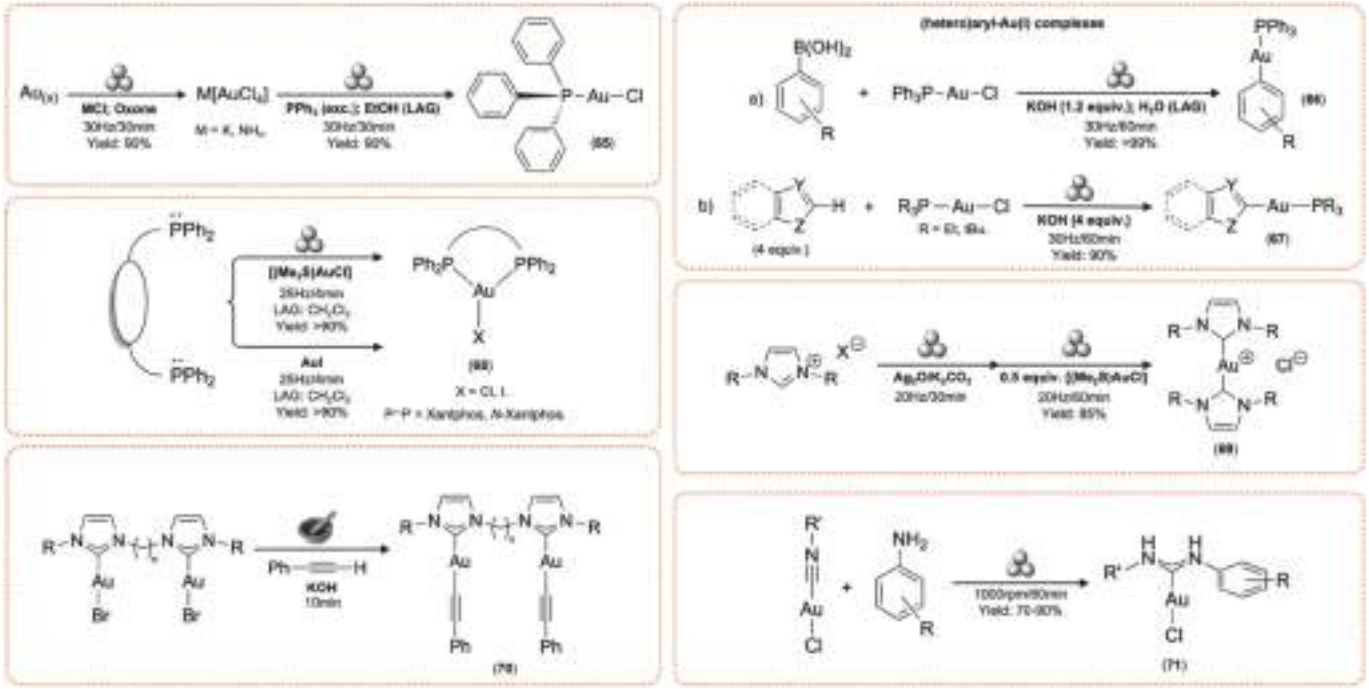


Scheme 12. Summary of Ag(I) complexes prepared by mechanochemical synthesis.

heterocyclic carbenes (NOHCs). Using a ball mill, 1,3-di(benzyloxy)imidazolium bromides were reacted with Ag_2O to yield monodentate [Ag(NOHC)Br]. This represents the first synthesis of monodentate 1,3-di(benzyloxy)imidazol-2-ylidene Ag(I) complexes. The solid state environment facilitated the synthesis of light-sensitive materials that required storage in the dark. The versatility of this method was further demonstrated in the synthesis of homoleptic cationic complexes. A stepwise mechanochemical procedure involving bromide to hexafluorophosphate anions followed by reaction with Ag_2O afforded the bis-carbene complex $[Ag(NOHC)_2](PF_6)$ [167]. These examples further reinforce the versatility of mechanical activation in carbene transfer chemistry.

2.4.6. *Mechanochemical synthesis of Au(I/III) complexes*

Mechanochemical activation of elemental gold represents a landmark development in oxidative organometallic synthesis. A mechanochemical route for the direct, r.t. activation of elemental Au into soluble salts and subsequent in coordination complexes (as reported in Scheme 13) has been established. After the initial oxidative milling, the addition of excess PPh_3 and ethanol as a LAG agent facilitated both the reduction of Au(III) to Au(I) and the complexation of the metal center, producing $[Au(PPh_3)Cl]$(**65**) [137]. This strategy demonstrates that even noble metals can undergo efficient redox activation through mechanical force. Mechanochemical protocol for synthesizing (hetero)aryl-Au(I) complexes *via* two pathways (trans-metalation from organoboron reagents and direct C—H activation) has been reported (Scheme 13). The mechanochemical trans-metalation of aryl groups from boronic acids to Au(I) precursors proved highly efficient. Using $[Au(PPh_3)Cl]$ as the precursor and phenylboronic acid, quantitative conversion to the organogold product (**66**) was achieved by milling in the presence of KOH in LAG of water. This protocol demonstrated broad tolerance of aryl groups. An advancement reported was the direct C—H auration of arenes under mechanochemical conditions. This approach utilized $[Au(PR_3)Cl]$ precursors and a base to activate C—H bonds in polyfluoroarenes and heteroarenes to obtain organogold complexes (**67**). For polyhaloarenes, this method facilitated the synthesis of various polyfluoro- and polychloro-phenyl Au(I) complexes with ligands such as PEt_3 and $P(tBu)_3$. In contrast to haloarenes, the C—H auration of heteroarenes such as benzothiazole and benzoxazole proceeded efficiently using KOH as the base. The mechanochemical C—H activation strategy was robust enough to functionalize complex bioactive molecules. Both protocols are suitable for the synthesis of Au(I)-NHC carbenes with aryl functionality, directly bonded to the metal center [168]. These solvent-free transformations expand the scope of organogold chemistry beyond



Scheme 13. Summary of Au(I/III) complexes prepared by mechanochemical synthesis.

traditional solution-phase protocols and illustrate how mechanical energy can facilitate both oxidative addition and metal–carbon bond formation. Beyond monodentate phosphines, mechanochemistry has been applied to the synthesis of Au(I) halide complexes with chelating diphosphine ligands. Deák et al. reported the synthesis of luminescent complexes of [Au(P^P)X] (X = Cl, I) (**68**), as reported in Scheme 13. A key finding was the polymorphism-dependent luminescence of the complex [Au(Xantphos)I]. Recrystallization yielded two concomitant solvates: a blue-emitting and a bluish-green emitting form [169].

The mechanochemical synthesis of [$AuCl_2(\kappa^2$-Tpm)]Cl (Tpm = hydrotris(pyrazol-1-yl)methane) involves the neat grinding of H[$AuCl_4$]·3H_2O and Tpm. The study highlighted the critical influence of mill energetics and jar material on the integrity of the final complex. This procedure yielded a bright yellow powder with an isolated yield of 90%. Beyond the synthesis of the molecular complex, mechanochemistry was also successfully employed for the heterogenization of [$AuCl_2(\kappa^2$-Tpm)]Cl in graphene supports. Among the tested immobilization methods (including wet impregnation and microwave irradiation), LAG proved to be the most effective. Using minimal volume of water, LAG facilitated a homogeneous dispersion of energy, resulting in small particle sizes and high gold loading efficiencies on the graphene support [170].

Recent advancements in the synthesis of Au(III) complexes have established planetary ball milling as a robust method for the direct functionalization of [AuCl(C^N^C)] pincer complexes. Hashmi and coworkers demonstrated this protocol using the methoxy-substituted precursor [AuCl(C^N^C^{OMe})]. The synthesis is conducted in a stainless-steel jar with the Au(III) chloride complex, KOtBu, and an aryl coupling partner. In the specific arylation with 1,5-dibromo-2,4-difluorobenzene, after optimization studies, the product was to isolate the arylated product, [(1,5-dibromo-2,4-difluorobenzene)Au(C^N^C^{OMe})], in high yield. This solid-state technique verified the formation of the Au (III)-C bond without the need for pre-functionalized boronic acids or organometallic reagents. Solid state protocol proved versatile for activating C—H bonds across different hybridizations and this mechanochemical strategy was further extended to [$AuCl_2$(terpy)]. While arylation with electron-deficient arenes resulted in a mixture of mono- and di-arylated products with a low yield, the mechanochemical method proved highly efficient for alkynylation. The reaction with (4-chlorophenyl)-acetylene and KOtBu carried out the two-fold alkynylated product in high yield [171,172].

Building upon established protocols for N,N-dialkyl NHC ligands, it was successfully extended the application of solvent-free mechanochemistry to the synthesis of Au(I) complexes bearing sterically hindered NHC ligands. It has been demonstrated that ball milling is a highly efficient method for performing trans-metalation reactions to [AuCl (NHC)] species, specifically utilizing the mesityl-substituted ligand. Two distinct mechanochemical strategies were developed, the first approach involved the mechanochemical trans-metalation of a pre-isolated Ag(I) intermediate. Reacting [AgCl(IMes)] with [AuCl(DMSO)] in a steel jar yields quantitatively [AuCl(IMes)] with the same procedure used for **60** in Scheme 11. To further enhance the utility of the protocol, a one-pot two-step procedure was established, eliminating the need to isolate light-sensitive Ag(I) intermediates. This process started directly from the imidazolium salt (IMes·HCl) and was milled with Ag_2O to generate the Ag(I) carbene species *in situ*. Then, [AuCl(DMSO)] was added directly to the milling jar, followed by grinding. This streamlined methodology afforded the [AuCl(IMes)] complex in good yield [146]. The same approach, involving trans-metalation from Ag(I) intermediates or by direct metalation, has been proposed for the synthesis of [AuCl(NHC)] complexes, with great heterogeneity of the NHC carbenes employed. The synthesis of $[Au(NHC)_2]^+$(**69**) complexes is also reported which are obtainable by appropriately varying the reaction conditions as shown in Scheme 13 [62]. The mechanochemical synthesis of [AuCl(NHC)] is achieved through a user-friendly and highly efficient strategy under aerobic conditions. This methodology employs a weak base route, utilizing K_2CO_3 to facilitate the reaction. Experimental observations indicate that the mechanochemical synthesis involves an intermediate aurate species, which is subsequently converted to the final Au(I) complex in the presence of K_2CO_3 [122]. Advancements in the solid-state derivatization of Au complexes have demonstrated the efficacy of mechanochemistry for accessing luminescent dinuclear Au(I) alkynyl complexes. A synthetic protocol to synthetize species as [(diNHC)(Au-C ≡ CPh)$_2$](**70**), has reported (Scheme 13). The success of this mechanochemical route is strictly correlated to the topology of the diNHC ligand and the stoichiometry of the reaction allows for structural tunability. By reducing the equivalent ratio of phenylacetylene, the authors successfully isolated a desymmetrized monosubstituted [(diNHC)(Au-C ≡ CPh)(AuBr)]. NMR characterization studies that are widely employed to probe coordination environments in Au(I) complexes have been proven highly valuable for understanding these systems [173]. Hence, indicate distinct coordination environments for the two metal centers, supporting a structure with one terminal acetylide and one bromide ligand. The fully substituted dinuclear complexes exhibit solid-state phosphorescence in the blue-white region [174]. The isonitrile route, involving the nucleophilic attack of an amine on a coordinated isocyanide, is a well-established method for synthesizing N-acyclic carbene Au(I)-NAC complexes (**71**). While solvent-free thermal melt procedures were employed for this transformation, they are often limited by the melting points and thermal instability of the amine precursors. To address these limitations, it has been reported a mechanochemical protocol (shown in Scheme 13) using ball milling to access unsymmetrically substituted diaryl **71**. By increasing the milling speed, were successfully synthesized **71** complexes derived from *p*-chloroaniline and *p*-phenoxyaniline in good yields. Furthermore, the protocol tolerated *p*-halogenated anilines bearing additional methyl substituents. However, steric limitations were observed, the reaction with the bulky aliphatic amine resulted in a diminished yield, suggesting that excessive steric bulkiness hinders the efficiency of the solid-state nucleophilic addition [175]. Taken together, these Au systems demonstrate that mechanochemistry can accommodate a broad spectrum of ligand classes and oxidation states, while enabling oxidative activation, ligand exchange, and bond-forming processes within a unified solvent-free paradigm. The cumulative evidence indicates that, for many Au complexes, mechanochemical synthesis is no longer merely an alternative route but a competitive and, in selected cases, strategically advantageous methodology.

2.5. Comparison with solution-based coordination chemistry: Green chemistry and sustainability considerations

Mechanochemical coordination chemistry is most meaningfully assessed in direct comparison with conventional solution-based methodologies. Such comparison must extend beyond solvent elimination and consider structural divergence, mechanistic transferability, kinetic behavior, and quantitative sustainability metrics. In this section, we critically analyze when mechanochemistry provides genuinely distinct chemical outcomes and when it represents a solvent-minimized analogue of established synthetic routes

2.5.1. Phase behavior and structural divergence

In the field of synthetic chemistry, mechanochemical synthesis has been shown to exert a significant influence on the phase identity, polymorphism, coordination mode and geometric outcome of metal complexes when compared to conventional solution methodologies. In the domain of solution synthesis, the identity of the product is typically governed by thermodynamic equilibria in the presence of coordinating solvents, solvation effects and crystallization conditions. Consequently, the presence of solvates, polymorphic mixtures, or kinetically trapped species is frequently observed. In contrast, mechanochemical synthesis occurs under conditions that are solvent free or minimize the use of solvent. In these cases, phase formation is controlled by direct solid-solid

contact and localized energy input. This approach frequently results in the formation of single crystalline phases, without the need for solvent inclusion, thereby facilitating access to non-solvated or less-solvated forms and enabling the selective isolation of specific polymorphs. For instance, Pd(II) and Pt(II) NHC complexes prepared by ball milling were obtained as isomerically and polymorphically pure, whereas solution synthesis produced mixtures of species [147]. Consequently, mechanochemistry can function as a phase-selective synthetic instrument, especially in systems that are susceptible to solvent coordination or crystallization dynamics.

Solution synthesis frequently involves the phenomenon of ligand exchange equilibria, which are influenced by solvent donor strength, dilution effects and temperature-dependent thermodynamic control. Consequently, solution products may reflect solvent-stabilized geometries, mixed coordination environments or equilibrating species. In contrast, mechanochemical synthesis has been shown to promote direct metal-ligand bond formation without competitive solvation, alternative coordination modes and different stereochemical outcomes. A notable example of this phenomenon is observed in the oxidative halogenation of Re(I) complexes, where solvent-free mechanochemistry yields products with controlled stereochemical outcomes [86]. In dynamic multicomponent systems, solid-state milling accelerates self-sorting while preserving preferred geometric outcomes [97]. More broadly, solvent-free environments can unlock coordination pathways that are suppressed in coordinating solvents [40]. However, it is important to emphasize that mechanochemistry does not inherently generate new geometries in every case. In numerous systems, both approaches ultimately result in the same thermodynamically stable structure, with the primary distinction lying in the purity of the phase or the solvation state [95,136].

2.5.2. Transferability between solution and mechanochemical synthesis

A fundamental question in mechanochemical organometallic synthesis concerns the direct transferability of a transformation developed in solution to a solvent-free mechanochemical protocol. Generally, transferability is frequent, though not invariable. Its occurrence is contingent on the mechanistic role of the solvent, behavior of the reactants, and the nature of the steps involved. In essence, simple coordination reactions (*i.e.* direct metal-ligand bond formation) exhibit a high degree of probability in terms of their transformation in mechanochemical protocols (see above sections for evidence of this, with several metal-ligand bonds being formed efficiently). Indeed, within such systems, the solution merely serves as a medium, thereby facilitating the contact between the reactants, a process that is typically achieved through grinding in mechanochemical conditions.

In a similar manner, it is conceivable that several of the reactions may necessitate specific modifications prior to progression through mechanochemical pathways. For instance, the sequential oxidative addition and ligand substitution with Re and Mn were successfully accomplished in a single vessel under mechanochemical conditions [86,122,129]. In addition, tris cyclometallated complexes were prepared through a two-step mechanochemical methodology involving LAG. This methodology facilitates the execution of these transformations and replicates the solvation effects under solvent-minimized conditions [40,129]. Nevertheless, it should be noted that not all solution-based reactions can be directly transferred to mechanochemical conditions. The primary limitation is observed when the solvent actively participates in the reaction, whether as a reactant, a coordinating ligand, a proton shuttle or a stabilizer for reactive intermediates. In such cases, transitioning to neat mechanochemical conditions often proves unsuccessful or necessitates LAG instead of a fully solvent-free approach. For instance, systems reliant upon the coordination of solvents to stabilize low-coordinate intermediates may yield different species or fail to proceed at all under neat grinding conditions. It can thus be concluded that reactions which are intrinsically dependent on solvents for solvation equilibria may pose significant challenges in terms of replicating their effectiveness in the grinding approach.

2.5.3. Reactivity differences

As previously discussed, it is evident that a significant proportion of organometallic transformations can be transferred from solution to mechanochemical conditions. However, it should be noted that the reaction pathways and intermediates may differ from those observed in classical approaches. Solution-based approaches are characterized by the progression of intermediates through a series of solvent-coordinated processes, culminating in the occurrence of dissociative ligand exchange equilibria. However, the presence of such intermediates has not been observed under mechanochemical conditions. For instance, the solution synthesis of Pd(II)/Pt(II) NHC systems results in the generation of isomeric mixtures due to solvent-mediated equilibria. Nevertheless, mechanochemical routes result in the formation of single isomeric products [147]. This finding indicates that mechanochemical pathways circumvent the utilization of solvent-stabilized intermediates, thereby promoting direct solid-solid reactions. Furthermore, in solid-state synthesis, reactions usually take place at crystal interfaces, grain boundaries, or defect sites, which can suppress side reactions and prevent the scrambling of the ligands [89]. For example, Ni(II) diphosphine complexes and Cr(III) PN/PNP complexes were obtained in a clean manner, with no evidence of solvent-coordinated intermediates being present [81,132]. Mechanochemistry also opens the doorways to the new reactivity patterns of the same reactants that were explored in solution. For instance, in recent studies, the formation of $[Ru(COD)(BiPy)Cl_2]$ and *trans*-$[Ru(PPh_3)_2(BiPy)Cl_2]$ species has been explored, as these species are not yet well-known in the field of solution chemistry due to the aforementioned constraints [95].

2.5.4. Reaction kinetics and green metrics

Mechanochemical protocols have been shown to outperform classical solution methods in terms of reaction kinetics, while often delivering comparable or higher yields and improved (or altered) selectivity. The fundamental operational premise is predicated on the integration of elevated effective reactant concentrations, efficient mixing, mass transfer, and solubility independence. Collectively, these factors serve to mitigate diffusion and dissolution limitations that frequently manifest in the context of solution-state complex formation [40,136,155]. A recurrent theme in extant literature pertains to the substantial decrease of the reaction time; processes that necessitate several hours or days in solution often occur within minutes to a few hours under mechanochemical conditions. To illustrate, Co(II) Schiff-base complexes attain full conversion within 10 min under mechanochemical one-pot conditions. These conditions are otherwise considered inaccessible in conventional solution-based methodologies [105]. In addition, the synthesis of Au(I) diphosphine halides is accomplished within a span of four minutes under milling conditions [169]. A clear illustration is provided by the dynamic self-sorting Cu(I) and Fe(II) imine-based system, which requires 20 days to reach equilibrium in solution but achieves similar thermodynamically favored products within 24 h in mechanochemistry [97]. Moreover, mechanochemistry has demonstrated to exceed solution methodologies with regard to reaction yields. For instance, the synthesis of several metal complexes was achieved with higher or comparable yields with respect to those obtained in solution methodologies, which typically require several hours [81,96,103,122,136].

The utilization of mechanochemistry has been demonstrated to frequently yield optimal sustainability performance regarding green metrics, reaction efficiency and process simplicity. A central argument in favor of mechanochemical synthesis concerns the quantification of environmental impact through established green metrics such as the *E*-factor, Effective Mass Yield (EMY) and others. The metrics thus provide an objective basis for comparison between mechanochemical and solution pathways. A recent comprehensive review by Fantozzi et al. systematically applied a set of green metrics to a range of chemical reactions [176]. In the majority of instances, mechanochemical

procedures demonstrate a reduced environmental impact in comparison to analogous solution-based reactions. This is attributable to the absence of bulk solvents, diminished stoichiometric excesses and, frequently, streamlined work-up procedures. The mechanochemical synthesis of organometallic complexes frequently yields significantly lower *E*-factors and higher EMYs in comparison to conventional syntheses. A considerable body of research utilizing green metrics has evidenced that mechanochemistry exhibits superior performance in comparison to conventional solvothermal methodologies for the synthesis of organometallic complexes [95,120,136]. In order to obtain a more comprehensive perspective on the subject, a comparison was made between the syntheses of a multitude of metal complexes, both those reported through solution and those achieved by mechanochemical means (see Table 2). The focus of this study was two parameters, the E-factor and the EMY. The values of these parameters were calculated according to well-established expressions [176]. The low waste production inherent in mechanochemical syntheses is the foundation for these values. Conversely, as previously outlined, solution methodologies predominantly depend on bulk solvent during synthesis and purification, consequently yielding suboptimal values for green metrics, along with extended duration and diminished yield. Further details can be found in Table 2 and Fig. 3.

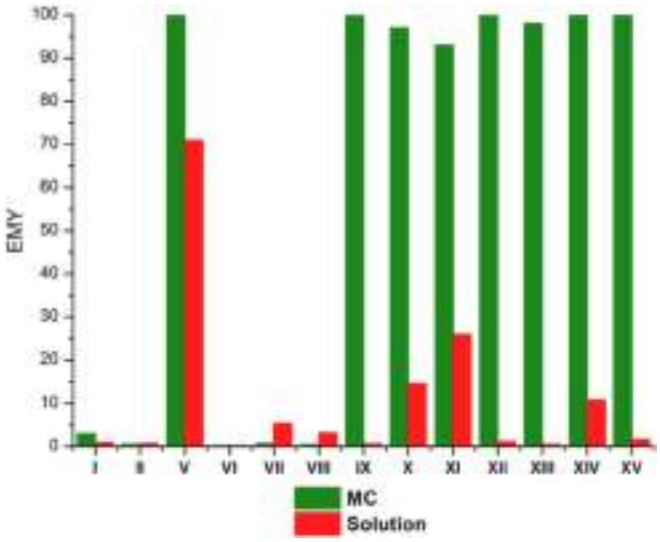


Fig. 3. Comparison of EMY in mechanochemistry and solution.

One of the inherent limitations of mechanochemical synthesis is that it is not always possible to synthesize large amounts of the complex in a comparable milling container. This is due to the fact that it can limit the energy dissipation inside the system. Furthermore, in instances where a minimal purification step is necessary, there is no substantial discrepancy between the green metrics of solution and mechanochemistry. This is exemplified by complex **II**, for which solid-state synthesis requires 0.31 g, in contrast to 1.89 g required for solution-based purification using hexane [178,191].

A salient feature of mechanochemical techniques is the substantial decrease in reaction time. In contrast to classical solution reactions, which often necessitate prolonged heating, reflux, and extensive stirring, mechanochemical reactions under solid-state grinding frequently attain completion within minutes. A comparable tendency was observed in relation to mechanochemistry for the complexes in question, regarding both yield and duration (Fig. 4).

Notwithstanding the demonstration of mechanochemistry as an efficient methodology for organometallic synthesis, there are several limitations associated with mechanochemistry, which are primarily due to its intrinsic features of solid-state reactivity, mechanical energy input and the design of equipment. The material of the grinding jar and ball has the potential to interfere with the reaction. Indeed, a critical, often under-reported challenge in mechanochemical synthesis is the attrition of milling media. In the synthesis of d-block complexes, the leaching of Cr, Ni, or Fe from stainless-steel jars can lead to more than just physical impurities; these trace metals may act as adventitious catalysts, potentially misrepresenting the reactivity of the primary metal center. While ZrO_2 or PTFE vessels mitigate this risk, they introduce a trade-off in terms of lower energy transfer due to their reduced density, a factor that must be systematically quantified when reporting yields and reaction rates.

For instance, the utilization of steel balls during the synthesis of Ru (II) complexes resulted in the unintended formation of $[Fe(BiPy)_3](PF_6)_2$ through a redox reaction with iron in the jar [116]. In a similar manner, stainless-steel jars and balls present certain challenges when employed in reactions with acid media, due to the occurrence of surface corrosion [111]. Conversely, the transition to low-density materials has the potential to influence reaction time and efficiency [132]. A number of studies have been conducted that provide support for the assertion that the corrosion of milling auxiliaries is an inevitable occurrence within the context of mechanochemistry [192,193]. Moreover, it was determined that the reacted species can undergo decomposition during extended reaction times, primarily as a consequence of the high energetic impact and the generation of heat during milling [95]. Conversely, there are numerous organometallic reactions that necessitate elevated temperatures, even within the mill itself. The synthesis of such complexes is only possible if the reaction is carried out at elevated temperatures and with milling. Ambient conditions are incompatible with this process [129].

On the other hand, mechanochemistry has the capacity to cleave weak bonds selectively and spontaneously, as evidenced by the cleavage

Table 2
Green metrics comparison between mechano- and solution-synthesis.

Complex	Mechanochemical Synthesis				Solution Synthesis				
	E-factor	EMY	Time [hrs]	Ref.	E-factor	EMY	Temp [°C]	Time [hrs]	Ref.
Na[VO_2(N,O^N,O)] (I)	32	3	1	[79]	106	0.94	reflux, r.t.	26	[177]
[Zr(N,O^N,O)Cl_2] (II)	193	0.52	2	[76]	141	0.70	reflux, r.t.	17	[178]
[Cr(P-NH-P)Cl_3] (III)	0.28	71	0.08	[81]	–	–	–	–	[82]
[Fe(BiPy)$_3$](BF_4) (IV)	0	100	0.25	[95]	–	–	r.t.	3	[179]
[Ru(*p*-Cym)(BiPy)Cl]Cl (V)	0	100	0.17	[95]	0.4	71	25	4	[180]
[Ru(BiPy)(PPh_3)$_2Cl_2$] (VI)	534	0.18	0.50	[95]	569	0.17	r.t.	0.75	[181]
[Co(Cp*)(CO)I_2] (VII)	142	0.70	2	[106]	18	5.4	reflux, r.t.	7	[182]
[RhCl(PPh_3)$_3$] (VIII)	21	0.45	1.5	[126]	31	3.13	reflux, r.t.	0.1	[183]
[Ir(Cp*)(BiPy)Cl]Cl (IX)	0	100	0.5	[95]	162	0.6	50	5	[184]
[Ni(dppe)Cl_2] (X)	0.03	97	1	[132]	5.7	14.5	80, 0	1	[185]
[Pd(PPh_3)$_2Cl_2$] (XI)	0.08	93	1	[136]	2.8	26	80	2	[186]
[Pd(Phen)Cl_2] (XII)	0	100	1	[136]	79	1.25	r.t.	3	[187]
[Pd(COD)Cl_2] (XIII)	0.02	98	0.5	[136]	194	0.51	r.t.	1	[188]
[Pt(BiPy)Cl_2] (XIV)	0	100	2	[95]	8.2	10.7	60	12	[189]
AgBr(iPr,NHC,Bz) (XV)	0	100	0.17	[164]	59	1.66	r.t.	24	[190]

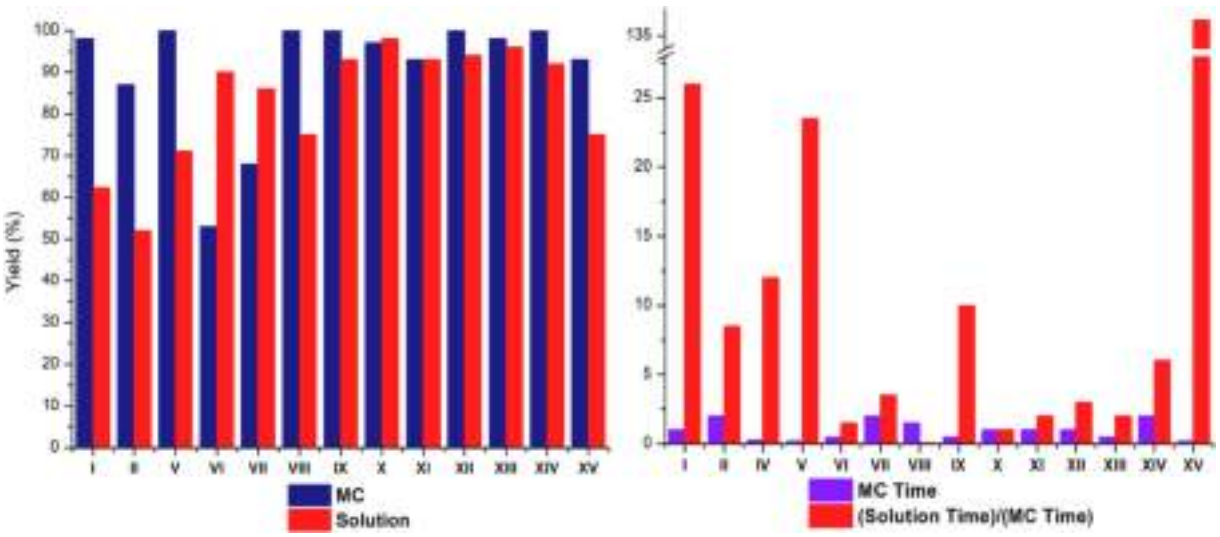


Fig. 4. Comparison of Time (on the left) and Yield (on the right) in mechanochemistry and solution. In the comparison of time, the violet bars represent the reaction time under mechanochemical conditions (in hours). The red bars indicate the ratio of solution reaction time to mechanochemical reaction time. For clarity and generality, solution reaction times are expressed as multiples relative to the corresponding mechanochemical times. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

of Mo-ROH bonds [85]. This makes the mechanochemical synthesis of such systems impossible to achieve. Likewise, the use of excessively bulky ligands, such as substituted anilines has been observed to show no product formation. Some mechanochemically synthesized complexes were found to be highly labile or amorphous [111], making the isolation and characterization impossible [87,147].

Despite the prevailing designation of mechanochemistry as a solvent-free or minimized methodology, the purification process entails the utilization of organic solvents for extraction. The utilization of these solvents, which are restricted, has the potential to influence green parameters and the standards established by mechanochemistry itself. It should be noted that there are several limitations that are inherent to the design and environmental control systems of the milling containers. For instance, the isolation of the jar is occasionally imperative to circumvent the oxidation of the contents. This necessitates either the enclosure of the jar within a glove box or the continuous purging of inert gases, with a view to averting oxidation and hydrolysis.

Despite the sustainability and efficiency benefits offered by mechanochemistry in many contexts, it cannot be considered a universal replacement for solution-based synthesis. It is evident that certain transformations continue to necessitate homogeneous reaction environments, particularly in the context of substrates that are not readily activated by mechanical force or where solvent effects play a pivotal role in the reaction pathways and selectivity. As both the mechanochemistry literature and recent articles have highlighted, mechanical activation delivers several key benefits, including greater sustainability, reduced waste, faster reactions and often improved yields. However, it is important to note that, despite these advantages, mechanical activation remains a complementary approach rather than a wholesale substitute for solution chemistry. Mechanochemistry has been demonstrated to expand the synthetic toolbox by enabling greener alternatives where applicable. However, solution-phase methodologies will remain indispensable for reactions that depend on solvation, catalysts active in solution, or where mechanical activation is impractical.

3. Summary and perspectives

Mechanochemistry has evolved into a powerful and increasingly mature platform for the synthesis of d-block metals coordination and organometallic complexes. As illustrated across early-, middle-, and late-transition metals, mechanical activation enables the efficient formation of metal-ligand bonds under solvent-free or solvent-minimized conditions, frequently delivering high yields, reduced reaction times and simplified work-up procedures. In many systems, mechanochemical protocols reproduce coordinations already known from solution chemistry, demonstrating a high degree of transferability for direct metal-ligand bond forming.

At the same time, this Review highlights that mechanochemistry is not merely a solvent-free or solvent-reduced analogue of classical synthesis. The absence of bulk solvent fundamentally alters the coordination, suppresses solvation-driven stabilization of intermediates and modifying the reaction in its entirety. These effects can translate into enhanced phase selectivity, access to unsolved species, altered stereochemical outcomes and, in selected cases, coordination geometries that diverge from solution-derived products. Particularly in late-transition-metal systems, mechanochemistry enables the rapid assembly of catalytically relevant phosphine, NHC, polypyridyl and pincer complexes, often integrating oxidative activation, ligand formation and metalation within a single operational workflow.

Quantitative comparison with solution-based methodologies further confirms that mechanochemical approaches frequently outperform classical protocols in terms of green metrics such as *E*-factor, EMY and reaction time. The elimination of bulk solvents and the reduction of purification steps are decisive contributors to improved sustainability performance, especially if the mechanochemical protocol is scalable, allowing for more eco-sustainable syntheses. Nevertheless, mechanochemistry is not universally superior. Certain transformations remain intrinsically dependent on homogeneous environments, solvent-mediated stabilization, or large-scale heat transfer. Moreover, practical considerations, such as equipment material, abrasion phenomena, energy input, scale limitations and occasional need for extraction, must be carefully accounted for when evaluating overall environmental impact.

From a conceptual standpoint, the most significant development in recent years is the transition from empirical protocol optimization toward mechanistic and physical rationalization. The increasing availability of real-time *in situ* techniques has fundamentally changed how mechanochemical coordination reactions can be investigated [194–197]. Time-resolved diffraction and spectroscopic methods have revealed that solid-state transformations may proceed through transient crystalline intermediates, short-lived amorphous phases, or rapid reorganization processes that are inaccessible to *ex situ* analysis. Such

approaches are expected to become central tools for clarifying reaction pathways in coordination and organometallic systems.

Looking forward, the transition of mechanochemistry from a 'black-box' empirical method to a precision synthetic tool will be driven by the integration of *in situ* monitoring techniques. The deployment of time-resolved X-ray diffraction (PXRD) and Raman spectroscopy directly within the milling jar is beginning to reveal the transient intermediates of d-block complexes that are otherwise invisible in solution. Future research should prioritize the correlation between these kinetic observations and the mechanical energy dose, moving beyond 'milling time' as the sole reaction parameter.

Equally important is the emerging recognition that the physical description of energy transfer in ball milling requires deeper refinement. Recent experimental studies have demonstrated that milling ball trajectories, ball-to-vessel ratios, filling degree, and contact dynamics critically determine not only the magnitude but also the quality of energy input. Simplified correlations between milling frequency and reactivity are therefore insufficient. A trajectory-informed and experimentally grounded understanding of impact dynamics will be essential for improving reproducibility, comparability and rational optimization in mechanochemical coordination chemistry [193,198–200].

Furthermore, the increasing understanding of LAG underscores that minimal amounts of solvent can profoundly alter reaction mechanisms, supramolecular organization and even the chemical identity of the resulting phase. Rather than acting as passive dispersants, liquid additives may function as competitive agents, templating species, or structure-directing components whose influence depends sensitively on their physicochemical properties and amounts [201–203]. The development of predictive frameworks that integrate liquid descriptors, surface chemistry and milling parameters represents one of the major challenges for future research.

Looking forward, several directions appear particularly promising. The integration of *in situ* monitoring, quantitative energy modeling, and computational approaches capable of estimating mechanical work along reaction coordinates opens the possibility of transforming mechanochemical coordination chemistry into a predictive discipline. At the same time, improved reactor design and a more rigorous treatment of equipment-related effects, including abrasion and unintended catalytic contributions, will be necessary to disentangle intrinsic chemical reactivity from mechanical artefacts.

In conclusion, mechanochemistry should be regarded neither as a universal replacement for solution chemistry nor as a niche green alternative. Rather, it constitutes a complementary and conceptually distinct synthetic framework that expands the coordination chemist's toolbox. By combining sustainability advantages with controlled solid-state activation, refined reactor engineering, advanced *in situ* monitoring, and emerging predictive models, mechanochemical methodologies are poised to assume an increasingly strategic role in the future development of organometallic and coordination chemistry across the d-block.

CRediT authorship contribution statement

Conceptualization, Supervision, writing-original draft, Daniele Zuccaccia; writing-original draft, Leonardo Genesin; writing-original draft, Talha Munir; writing-original draft, Fabio Trigatti; writing-original draft, Review and editing, Eleonora Aneggi.

Fundings

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare that they have no known competing financial interest or personal relationship that could have influenced the work reported in this study.

Data availability

No data was used for the research described in the article.

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