Mechanochemical metal-free transfer hydrogenation of carbonyls using polymethylhydrosiloxane as hydrogen source

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Abstract

We report herein a new methodology for the rapid and selective reduction of carbonyls in the solid phase. By exploiting mechanical energy and using a cheap and air-stable silane, polymethylhydrosiloxane (PMHS), we can reduce a variety of carbonyl compounds, with catalytic

amounts of fluorides. A scope of 19 substrates was explored to probe the generality of the method. In addition, an important biomass-based platform chemical, 5-hydroxymethylfurfural (5-HMF) and an insoluble polymer, polyketone, could be reduced with this methodology. A mechanistic study is also presented, suggesting the active role of volatile silane species. This method is particularly appealing to overcome substrate solubility issues and reduce solvent reliance in organic synthesis.

Introduction

The reduction of carbonyls to alcohols is a key reaction in the chemical industry, spanning from the production of commodity chemicals to pharmaceutical compounds.[1] On the lab scale, this is often done using stoichiometric amounts of hydrides, such as $NaBH_4$ or $LiAlH_4$.[2] Catalytic methods relying on transition metals allowed to unravel the potential of molecular hydrogen gas for this reaction, *via* the development of highly active and chemo-, regio- and enantioselective systems, with high atom-economy.[3] Alternatively, catalytic transfer hydrogenation reactions have been developed, whereby cheap and available hydrogen sources are selected, for instance alcohols, with the advantage of alleviating the need for high pressure.[4] Alternative reducing agents such as sodium formate,[5] Hantzch ester,[6] various isopropoxides,[7] or silanes[8] have been successfully reported. They also pave the way for hydrogen borrowing strategies, as green cascade methodology to build molecular complexity in one-pot. [9]

Polymethylhydrosiloxane (Me_3Si-$(OSiMeH)_nOSiMe_3$, abbreviated as PMHS) was first reported by Nitzsche and Wick in 1957 for the reductive silylation of carbonyls with organotin compounds. As a waste of the silicon industry, PMHS is an inexpensive and abundant chemical with reducing

abilities.[10] Contrary to other silanes, it benefits as well from its non-toxicity, moisture stability, and ability for its Si-H bonds to be easily activated under mild conditions.

Since then, it has been explored in solution phase with different activators such as titanium,[11] copper,[12] iron,[13] zinc,[14] TFA,[15] fluorides,[16] or bases. Typically, Kobayashi *et al.* used stoichiometric amounts of *tert*-butyl ammonium fluoride (TBAF) or KF, at -70 or 0°C, to perform both the hydrosilylation and the subsequent Si-O bond cleavage (**Scheme *1*A**).[17] Notably, this scheme based on silicon and fluoride chemistry is completely transition metal-free, and parts from the use of hazardous traditional hydrides. Further developments involved the use of potassium *tert*-butoxide and hydroxide to activate PMHS as shown by the Nikonov group.[18] Their mechanistic studies show a base-induced rearrangement of the polymer into shorter volatile hypervalent silicon species, highly active for carbonyl reduction. PMHS is also a suitable reagent for the chiral reduction of carbonyls.[19]

Beyond carbonyl reduction, silane chemistry has recently been highlighted as a powerful reagent to develop metal-free and non-toxic organic pathways. Cantat *et al.* reported the conversion of CO_2 to afford amine formylation products[20] or formamidine derivatives, using PMHS.[21] They also used Si-H bond as part of a frustrated Lewis Pair (FLP) scheme to reduce CO_2.[22] The Beller group showed as well the convenient conversion of amides into amines with PHMS.[23]
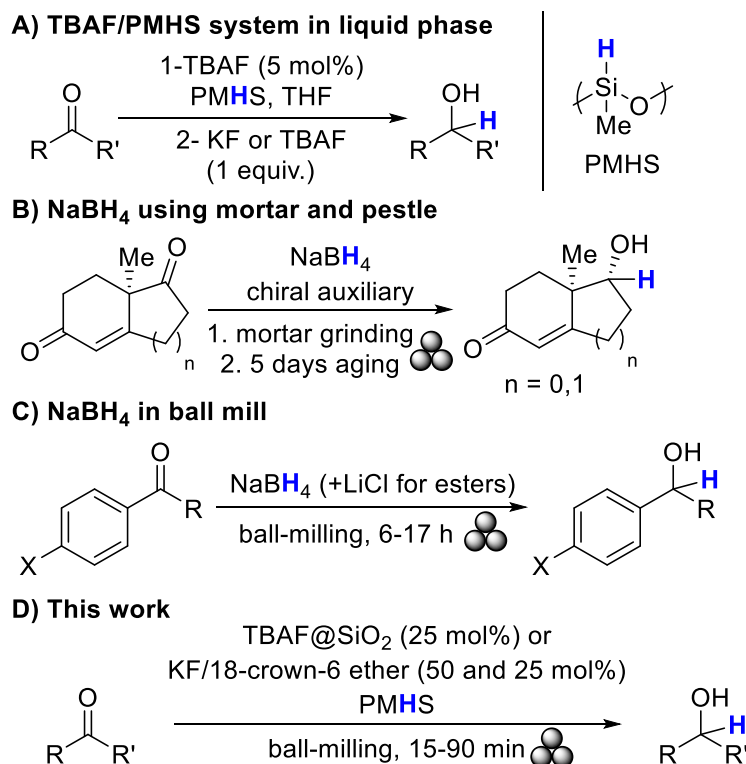
Scheme 1. Selected liquid phase and mechanochemical strategies for carbonyl reduction.

All these methods however call for the use of solvents, either to ensure good gas miscibility, since gas-liquid mixing is often rate-determining,[24] or as the "hydrogen" provider itself.[25] Yet, solvents contribute significantly to waste generation in the chemical enterprise. For instance, an estimation published by Glaxo-Smith-Kline revealed that solvents represented 85% of the total mass of chemicals used in pharmaceutical manufacture.[26] Recently, mechanochemistry, a method enabling reactions in solid phase, with limited amounts or no solvents, and using mechanical energy emerged as an interesting alternative to liquid-phase methodologies.[27] It also offers new solutions for addressing issues related to recalcitrant or insoluble substrates.[28]

Despite the rising popularity of ball-milling, it has been seldom investigated for carbonyl reduction methodology. Toda *et al.* reported the reduction of ketones using NaBH$_4$ by mortar grinding and

aging in a dry atmosphere for 5 days.[29] They could synthesize a range of chiral hydroxyketones of synthetic interest with 100% *ee* using (+)-taddol as a chiral auxiliary **Scheme 1B**). Mack and co-authors reported the use of NaBH4 in ball milling to reduce a wide range of aromatic carbonyls.[30] By adding LiCl, they could generate LiBH4 *in situ* and reduce esters, although after several hours of milling (**Scheme 1C**). This system was further studied by Naimi-Jamal *et al.*,[31] who analyzed the sodium tetraalkoxyborate intermediates as well as the selectivity of the reaction. Alternatively, Wang *et al.* performed the reductive amination of aromatic aldehydes, using Hantzch ester as a reductant and zinc chloride as a catalyst.[32] These examples are, to the best of our knowledge, the only examples of solid-state reduction of carbonyls and imines.[33] Although NaBH4 and the Hantzch ester are highly popular, they suffer from safety issues for the former,[34] and toxicity issues for the latter, including the generation of pyridine derivative as byproducts.[35]

In our continued efforts to develop greener chemical reductions, we herein present the reduction of carbonyls using ball milling, with catalytic amounts of solid fluorides to activate polymethylhydrosiloxane, as an industrial waste, stable and non-toxic hydrogen source. The method afforded moderate to excellent yields on a range of substrates, in short reaction times. Importantly, it opened avenues to address separation issues in the context of 5-hydroxymethylfurfural (5-HMF) hydrogenation and solubility issues for a polyketone reduction.
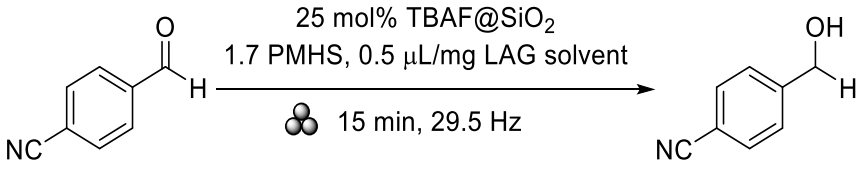
Results and discussion

In this study, we used a mixer mill operating 2 Teflon jars at 29.5 Hz, each equipped with 1 zirconium oxide ball. To develop the methodology, we first focused on 4-formylbenzonitrile as a model substrate. Indeed, as a solid electron-poor aromatic aldehyde, it is expected to be reactive

5

under reduction conditions. Several fluoride salts, including KF, LiF and TBAF@SiO$_2$, were examined. We found that TBAF@SiO$_2$, a silica-supported fluoride source, was the most successful to activate PMHS with the model substrate. It is a less hygroscopic fluoride source than its liquid counterparts, which we reasoned could prevent any potential water-quenching of the activated silane. As reaction conditions were optimized, we realized that 0.25 equivalent of TBAF@SiO$_2$ was sufficient in activating PHMS, which is an improvement compared to the Kobayashi's solution methodology relying on stoichiometric amounts of fluoride.[17] We had initially conducted the optimization phase using stainless steel jars and a stainless ball for milling. Eventually, we moved to the current apparatus due to their lower price and similar performance. Furthermore, we had concerns that stainless steel could react with the mixture, as had been reported previously by our group.[36] We used ZrO balls as they were more durable on the long run than Teflon balls. After optimizing quantity of reagents and milling time, the corresponding alcohol, 4-(hydroxymethyl)benzonitrile, was obtained in 82% yield within 15 minutes of milling, using 25% TBAF@SiO$_2$ and 1.7 equivalents of PMHS (Table 1, entry 1).

In an effort to improve the reaction rates, addition of stoichiometric amounts of solvent was tested (typically 0.5 µL per mg of substrate). This method, also known as liquid-assisted grinding (LAG),[37] has been successful, for instance in the synthesis of metal organic frameworks,[38] co-crystallizations,[39] or selective fluorination.[40] Adding ethyl acetate increased the yield to 94% (Table 1, entry 2). Addition of toluene afforded a moderate yield improvement to 87%, while with THF and notably water, the reaction performance was unchanged (Table 1, entries 3 to 5). As we will discuss below, the effect of the choice of LAG solvent greatly varied depending on the substrate. Control experiments were conducted to ascertain the role of each component in the

system. Replacing TBAF@SiO$_2$ with KF or LiF (Table 1, entries 6 and 7) or removing either the fluoride source or the PMHS (Table 1, entries 8 and 9) totally disabled the reaction.

Entry	Modification	Alcohol yield (%)
1	-	82
2	LAG solvent: EtOAc	94
3	LAG solvent: Toluene	87
4	LAG solvent: THF	83
5	LAG solvent: H$_2$O	82
6	KF as a fluoride source	NR
7	LiF as a fluoride source	NR
8	No TBAF@SiO$_2$	NR
9	No PMHS	NR

Reaction conditions: 4-formylbenzonitrile, 1.7 PMHS, 25 mol% TBAF@SiO$_2$, LAG solvent (0.5 µL/mg substrate). Ball milling (Teflon jar, 1 ZrO ball) 29.5 Hz, 200 mg total chemical products weight.
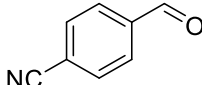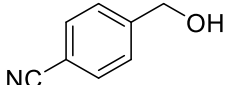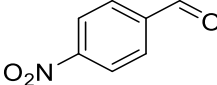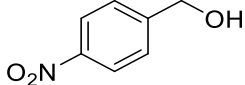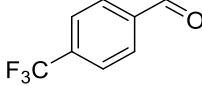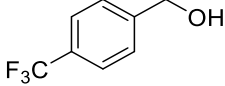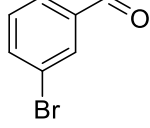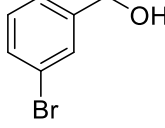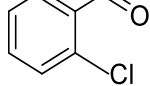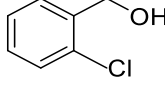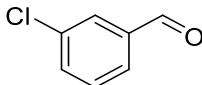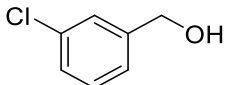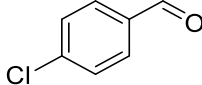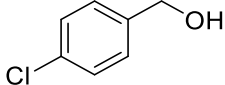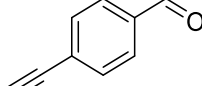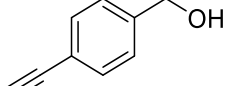
Table 1. Control experiments.
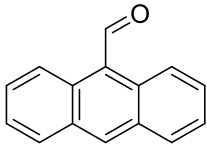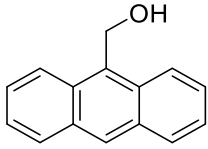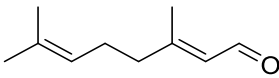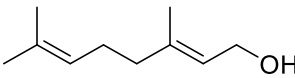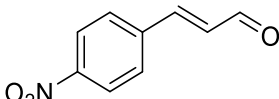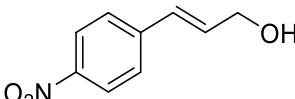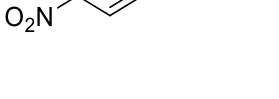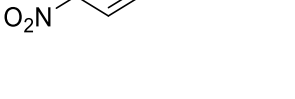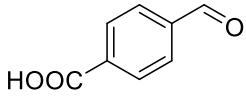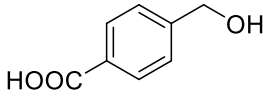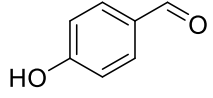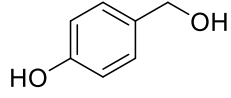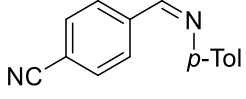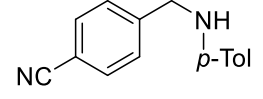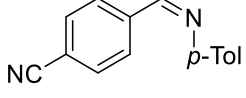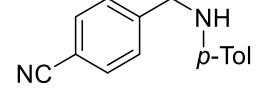
Next were investigated benzaldehyde derivatives. Milling time, fluoride source, and choice of LAG solvent were optimized for each substrate. Electron-poor benzaldehydes such as 4-formylbenzonitrile, 4-nitrobenzaldehyde, 4-(trifluoromethyl)benzaldehyde and 3-bromobenzaldehyde (Table 2, entries 1 to 4) gave high yields between 78% to quantitative. Ethyl acetate was the best LAG solvent there, except for 4-nitrobenzaldehyde, which worked better in

absence of such an additive. Notably 4-(trifluoromethyl)benzaldehyde worked well under milling conditions despite being a liquid at room temperature. Chloride-substituted benzaldehydes proved to give different optimal results depending on the position of the substituent, ranging from 56% for 2-chlorobenzaldehyde to 73% for 4-chlorobenzaldehyde and 96% for 3-chlorobenzaldehyde, with the optimal LAG solvent being none, toluene and ethyl acetate respectively (Table 2, entries 5 to 7). 4-Ethynylbenzaldehyde and 9-anthracenecarboxaldehyde, as electron-rich substrates, were successfully reduced at yields of 84% and 72%, respectively, with no LAG solvent and ethyl acetate respectively (Table 2, entries 8 and 9). 1,2-conjugated unsaturated carbonyls, such as citral, were successfully reduced in moderate yields of 65% with toluene as LAG solvent, despite its lower reactivity due to the absence of a benzylic position (Table 2, entry 10). No trace of the C=C reduction product was detected, showing excellent selectivity. For 4-nitrocinnamaldehyde, initial results gave 28% yield after 15 minutes of milling (Table 2, entry 11). Extending reaction time did not significantly alter the reaction progress. We reasoned that catalysts was likely degrading under the milling conditions. Inspired by the approach of the Friscic group, [41] we fractioned the addition of PMHS into three portions of 1 equivalent each, followed by 10 minutes of milling and successfully increased the yield from 28% to 63% (Table 2, entry 12, with 50 mol% TBAF@SiO$_2$ added once at the beginning of the reaction). Protic aldehydes and imines showed no reactivity to the reaction (Table 2, entries 13 to 15). Most examples in the literature seem to indicate that imine hydrosilylation does not seem to proceed under fluoride activation unless a Lewis acid or a transition metal catalyst is added. We attempted to use Zn(OTf)$_2$ as a Lewis acid to activate the imine, unfortunately to no avail (Table 2, entry 14). With our system, the reaction proceeded very fast, with 15 minutes being the optimal reaction time. Prolonging the reaction for longer than 15 minutes usually does not improve the yield, pointing towards the fast degradation of the active

species. In comparison, the reaction times in the carbonyl reduction with $NaBH_4$ was longer, with milling between 6 and 17 hours,[30] while reduction by the Hantzch ester proceeded within 90 minutes of milling. [32]
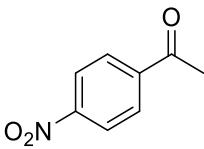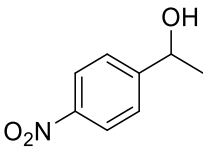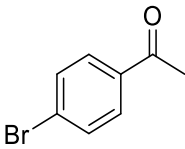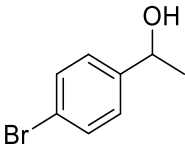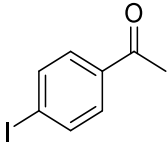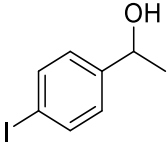
Entry	Substrate	Product	LAG solvent	Time (min)	Yield (%)
1			EtOAc	15	94
2			-	15	86
3			EtOAc	15	78
4			EtOAc	15	quantitative
5			-	15	56
6			EtOAc	15	96
7			Toluene	15	73
8			-	15	85

9			EtOAc	30	72
10			Toluene	15	65[b]
11			-	15	29
12				3*10	63[a,b]
13			-	90	NR
14			-	90	NR
15			-	90	NR
16			-	90[c]	NR

Reaction conditions: Substrate, 1.7 PMHS, 25 mol% TBAF@SiO$_2$, LAG solvent (0.5 µL/mg substrate). Ball milling (Teflon jar, 1 ZrO ball) 29.5 Hz, 200 mg total material weight. [a]PMHS was added in three portions consisting of 10 minutes of milling, one equivalent each. 100% selectivity to the C=O reduction product. [b]50 mol% TBAF@SiO$_2$ was used. [c]25 mol% Zn(OTf)$_2$ was added to the mixture

Table 2. Scope of aldehydes.

Ketones were then investigated. Electron-poor acetophenones such as 4'-nitroacetophenone, 4'-bromoacetophenone, and 4'-iodoacetophenone (Table 3, entries 1 to 3) gave high yields,[42] following a similar trend to previously reported. With 4'-nitroacetophenone, using 25% TBAF@SiO$_2$ gave a 71% yield after 90 minutes of milling. In an effort to improve this reaction, we screened again fluorides. While KF gave no reaction, the addition of 25% 18-crown-6 ether in conjunction with 50% KF increased the yield to 81% after only 15 minutes of milling (Table 3,

entry 1). The crown ether is known to coordinate with the K^+ cation to enhance the reactivity of the F- anion, as previously applied by Goldberg et *al.* in solution phase.[43] Similarly to aldehydes, electron-rich or sterically hindered ketones such as 2',6'-dimethoxyacetophenone, 4'-methoxyacetophenone, 4-methylbenzophenone and 4-bromobenzophenone proved to be more challenging, giving no reaction to low yields (Table 3, entries 4 to 7). In the case of 4-methylbenzophenone, increasing the milling time from 30 minutes to 90 minutes decreased the yield from 59% to 44% (Table 3, entry 6), hinting at a possible degradation of the product. 2-bromo-4'-nitroacetophenone was reduced in moderate yield (46 %) with 25% TBAF@SiO$_2$, while preserving the reactive bromine functionality (Table 3, entry 8). Our system proved completely inactive on aliphatic ketones such as cyclopentanone and camphor (Table 3, entries 9 to 10).

Entry	Substrate	Product	Fluoride	LAG solvent	Time (min)	Yield (%)
1			KF/18-crown-6 ether	Toluene	15(90)	86(71[a])
2			TBAF@SiO$_2$	Toluene	15	82
3			TBAF@SiO$_2$	-	15	quantitative

Reaction scheme (header of table): R-C(=O)-R' → R-CH(OH)-R', Fluoride source, 1.7 PMHS, 0.5µL/mg solvent, 29.5 Hz

	Substrate	Product	Catalyst	Solvent	Time	Yield
4			TBAF@SiO$_2$	-	90	NR
5			TBAF@SiO$_2$	EtOAc	15	47
6			TBAF@SiO$_2$	-	30(90)	59(44)[b]
7			KF/18-crown-6 ether	Toluene	15	40
8			TBAF@SiO$_2$	EtOAc	15	46
9			TBAF@SiO$_2$	-	90	NR
10			TBAF@SiO$_2$	-	90	NR

Reaction conditions: Ketone, 1.7 PMHS, 25 mol% TBAF@SiO$_2$ or 50 mol% KF/25 mol% 18-crown-6 ether, LAG solvent (0.5 µL/mg substrate). Ball milling (Teflon jar, 1 ZrO ball) 29.5 Hz, 200 mg total material weight. [a]Yield in parentheses: TBAF@SiO$_2$ 25 mol%, 90 minutes of milling. [b]Yield in parentheses: TBAF@SiO$_2$ 25 mol%, 90 minutes of milling.

Table 3. Scope of ketones.

To prove the feasibility of the process on the gram scale, the reaction was tested in a planetary mill (Scheme 2). After 30 mins of milling at 500 rotations per minute, an isolated yield of 78% was afforded.
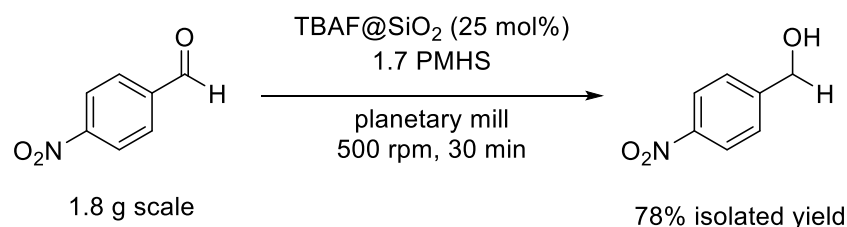
Scheme 2. Gram scale reduction of 4-nitrobenzaldehyde.

In an effort to showcase the intrinsic advantages of our system, we investigated specific substrates, where the liquid phase reaction shows limitations. 5-hydroxymethylfurfural (HMF) is a platform biomass-based chemical that can be produced from the triple dehydration of hexoses.[44] It can be used as a starting material to access a wide range of furan-type compounds. For instance, the aldehyde function can be reduced to obtain 2,5-dihydroxymethylfurfural (DHMF). However, both HMF and DHMF are difficult to extract from water due to their low partition coefficient.[45] Liu et *al.* reported 2-butanol/THF 1:4 ratio as an efficient mixture for HMF extraction.[46] Continuous extraction in biphasic systems such as water/methyl isobutyl ketone (MIBK) mixtures was also reported.[47] All these methods are intricate and require complicated solvent mixtures. Under our standard conditions, with 25 mol% TBAF@SiO$_2$, 1.7 equivalents of PMHS, and milling for 15 min at 29.5 Hz, only 36% of the product was obtained (Table 4, entry 1). Adding toluene as a LAG solvent only afforded a minor yield increase to 41% (Table 4, entry 2) and increasing the milling time did not change the yield (Table 4, entry 3). Varying milling times between 15 and 90

minutes with or without a LAG solvent afforded at the best a 50% yield (Table S3). Again, by fractioning the addition of PMHS to the reaction mixture into three equal portions of one equivalent each with 10 minutes of milling upon each addition, the yield could be increased to 69% (Table 4, entry 4). Interestingly, after reaction, both the product and the starting material were easily extracted with ethyl acetate, and a simple filtration. As no water was introduced during either the reaction or the work-up, this procedure solves very simply the challenge of separating HMF and its products from reaction mixtures. To the best of our knowledge, this constitutes the first example of HMF reduction to DHMF in ball-milling.[48] A more thorough comparison to other reports in liquid phase is provided in supporting information, as well as a further investigation on carbon mass balance (Table S4).

Entry	PMHS (eq.)	LAG solvent	Time (min)	Yield (%)
1	1.7	-	15	36
2	1.7	Toluene	15	41
3[a]	1.7	-	90	27
4	3 in 3 equal portions	-	10, 3 times	69

Reaction conditions: HMF, PMHS, 25 mol% TBAF@SiO$_2$, LAG solvent (0.5 µL/mg substrate). Ball milling (Teflon jar, 1 ZrO ball) 29.5 Hz, 200 mg total material weight. [a]PMHS was added in three portions followed by 10 minutes of milling each.

Table 4. HMF reduction.

Finally, we explored the opposite side of the solubility issue. Polyketones are a class of thermoplastic polymers developed by Shell Chemicals (under the name of Carilon) and produced

now by Hyosung. Among other interesting properties, they possess a significantly higher melting point than their polyethylene counterparts, and a low solubility in most solvents. They are produced from CO/olefin copolymerization.[49] Polyketones have a very poor solubility in most solvents. The hydrogenation of their carbonyl functionality has been investigated as a means to improve their ability to dissolve in protic media. In this scheme, even partial reduction can be beneficial. The reduction of polyketones has been reported by Milani and co-workers with the transfer hydrogenation of atactic CO/4-Me-styrene polyketones in liquid phase.[50] Using a 2-propanol/dioxane 5:3 mixture and [Ir(cod)(Me$_2$bipy)Cl] as a catalyst, they obtained a 70% conversion of the polymer into the corresponding polyalcohol. To the best of our knowledge, this is the sole example of polyketone reduction in the literature. We were interested in exploring this reaction by mechanochemistry, as this methodology has been shown in recent examples to afford sustainable solutions for polymer functionalization and deconstruction challenges.[28, 51] We also saw an opportunity to perform this reaction without relying on any metal. For this reaction, we synthesized polyketone, using Pd catalyzed styrene and carbon monoxide copolymerization with a procedure adapted from Guo et al.[52] In this fashion, we obtained a polyketone sample of featuring a number average molecular weight of 2200 g/mol and weight average molecular weight of 2400 g/mol, as determined by matrix-assisted laser desorption/ionization – time of flight (MALDI-TOF). The complete insolubility of polyketone in common solvents, prevented any further characterization by gel permeation chromatography (GPC). We then loaded this sample in a stainless steel jar with 2 balls to increase the impact energy, compared to the small molecule substrates. The conversion of C=O into C-O was monitored by X-ray photoelectron spectroscopy (XPS). After 90 mins of milling and 2 days of aging 54% of the C=O bonds were converted to C-O bonds (Scheme *3*).
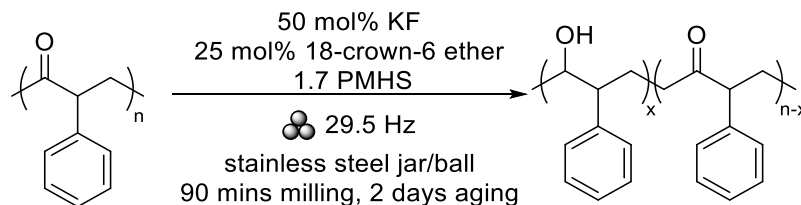
Scheme 3. *Polyketone reduction*

Mechanism

The reaction of reduction of carbonyls in the solution phase by PMHS has been studied by other researchers. Lawrence originally proposed a 'zipper' mechanism where the fluoride migrates from one monomer to another, activating several Si-H bonds in the process (**Scheme 4**).[10]

a) Lawrence's 'zipper' mechanism
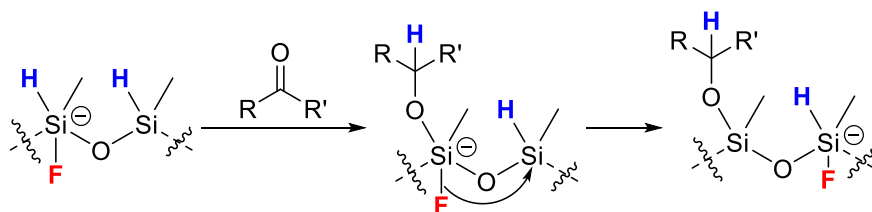
b) Nikonov's re-arrangement mechanism
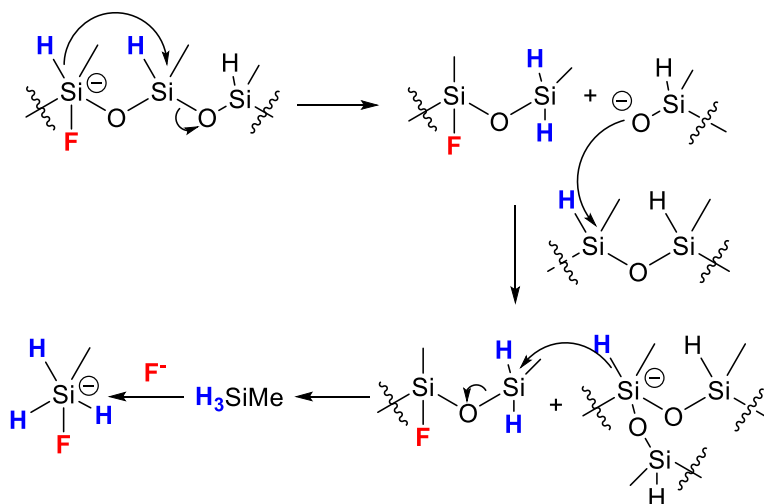
Scheme 4. Proposed mechanisms for the activation of PMHS with fluoride. For clarity, fluoride and active hydrides are highlighted in red and blue, respectively.

Nikonov and coworker revised the mechanism considering that the hydride may migrate along the PMHS chain and between ones, before the insertion of the carbonyl occurs. [18] This leads to the rearrangement of the PMHS chain into oligomers and eventually monomeric, volatile H_3SiMe (**Error! Reference source not found.Scheme 4**). H_3SiMe can further react with fluoride to form $[H_3SiFMe]^-$, an hypercoordinate species. Nikonov was able to rationalize their observation that reactivity would drop in an open vessel in solution. In our case, such a mechanism can explain that we would observe gas pressure build-up in the jars when they were opened after the milling.

In order to verify if the mechanochemical reduction reaction relied on the generation of reaction silicon volatiles, we performed a test experiment. Replicating the optimal conditions for the reduction of 4-formylnitrile (Table 2, entry 2), we first milled the PMHS and the TBAF@SiO$_2$ for 15 minutes alone, carefully opened the jar under the fumehood, and then added the aldehyde to be milled again for 15 minutes(**Scheme 5**). Only traces amount of product was formed, hinting at the active species are gaseous and easily escape the reaction vessel upon its opening.

Two step test

Canula experiment

A=TBAF@SiO$_2$	87% conversion
A=nothing	no conversion
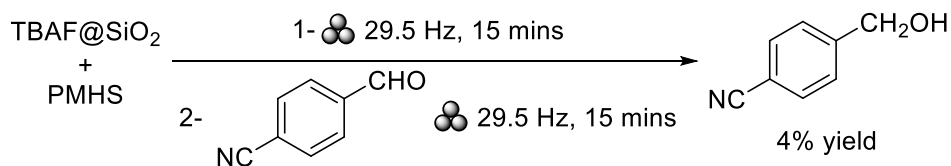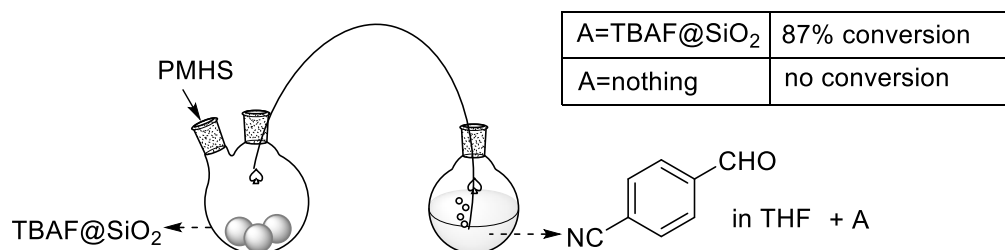
Scheme 5 Two-steps milling and canula experiments.

To further explore the possibility of a volatile active species, another experiment was designed. A 250 mL round-bottom flask containing TBAF@SiO$_2$ was sealed with 3 ZrO balls to replicate ball milling conditions under stirring. It was connected to another sealed flask through a cannula immersed into a solution of 4-formylnitrile in THF (**Scheme 5**, Figure S2). Upon injecting PMHS in the first flask, we observed bubbling in the solution of the second flask, and interpreted this as formation of H$_3$SiMe. The set-up was left for 2 h under vigorous stirring for both flasks, resulting in no conversion of the aldehyde. In a second experiment, TBAF@SiO$_2$ was added also to the

second flask. This time, after 2 hours, 87% of the alcohol product was measured. This result is consistent with the reaction of gaseous H_3SiMe formed in flask 1, with the fluoride source in flask 2 to afford $[H_3SiFMe]^-$ *in situ*, and this the alcohol, as Nikonov reported.

Finally, the role of water in the mechanism is worth mentioning. To our surprise, its presence totally shut down the reduction of 4-nitrobenzaldehyde or 4'-nitroacetophenone while it did not affect 4-formylbenzonitrile (Table 1, entry 5). we expect nitro-substituted compounds to favor the formation of acetals by hydrogen-bonding stabilization.[53] A more detailed study on the influence of water on 4-formylbenzonitrile and 4-nitrobenzaldehyde reduction is provided in the supporting information.

In conclusion, we have developed a ball-milling approach for the selective reduction of a wide range of carbonyl compounds in the absence of any metal catalyst and using an inexpensive and easy-to-handle silane, PMHS. Ball-milling not only enabled a higher reaction rate than solution-based reactions, with typical reaction times of 15 minutes, but it also allowed insoluble substrates to be reduced. We also confirmed that the reaction mechanism proceeded through the *in situ* formation of volatile silicon species, consistent with past accounts. Future studies will focus on removing solvents from the work-up as well, with solvent-free extraction methods such as supercritical carbon dioxide (sCO_2).[54-55] With this system, we hope to expand the carbonyl reduction toolbox in mechanochemistry.

Experimental

All chemicals and solvents were purchased from commercial sources and used without purification unless noted. TBAF@SiO_2 (1.5 mmol/g) was purchased from Sigma and was freeze-dried before use and stored in a desiccator. Alternatively, it can be made from TBAF in THF

solution. The procedure is given in the supporting information. The molecular weight of PMHS was taken to be 65 g/mol for calculations of stoichiometry. A Retsch MixerMill MM 400 was used to perform milling experiments. NMR spectra were recorded on a Bruker AV500 spectrometer operating at 500 MHz for ^{1}H acquisitions and on a Varian VNMRS operating at 400 MHz for the solid state ^{13}C acquisition. Chemical shifts are reported in ppm with a solvent resonance as an internal standard (^{1}H NMR; chloroform as internal standards, indicating 7.26 ppm). Mesitylene was used as an internal NMR standard. Yields were an average of a minimum of two different experiments. XPS was performed on a VG ESCALAB 3 MKII spectrometer (VG, Thermo Electron Corporation, UK) equipped with an Mg Kα source. Polyketone copolymerization with carbon monoxide were carried out in a Parr Instruments 5000 Series Multiple Reactor System. MALDI-TOF measurement was taken on a MALDI Autoflex III- TOF-(BRUKER).

Typical procedure.

In a typical reaction, one zirconium oxide ball (10 mm, 3.24 g weight) was added in a 10 mL Teflon milling jar. It was then filled with a total of 200 mg of solid reagent material on one side, and liquids on the other. The jar was carefully closed, wrapped with parafilm and loaded onto the Retsch MM-400 mixer mill. The reactions were conducted over 15 minutes, milling at a frequency of 29.5 Hz. At the end of the reaction, the jar was opened under a fumehood, 5 mL of ethyl acetate were added to the jar, and was manually shaken with the balls for 20 seconds to scrape off the solid content. This operation was done three times to ensure a full product recovery. The three fractions were combined, sonicated for 10 seconds, and then concentrated *in vacuo*. To remove the PMHS byproducts and the activator, the mixture can be recrystallized or dissolved in an EtOAc/hexanes mixture and filtered through a silica plug. The imines were prepared by milling the corresponding aldehydes and amines in presence of Na_2SO_4.

ASSOCIATED CONTENT

Details on the closed-flask experiments, planetary mill experiment, influence of water on the reduction of 4-nitrobenzaldehyde and 4-formylbenzonitrile, optimization details for the reduction of 5-HMF and the rest of the scope, comparison of 5-HMF reduction to other examples in the literature, discussion on the polyketone synthesis and characterization, and NMR of the model reaction product, comparison with the product made by $NaBH_4$ reduction.

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Author Contributions

The paper was written through contributions of all authors. All authors have given approval to the final version of the paper.

Table of contents artwork

A mechanochemical method for carbonyl reduction is reported, using an inexpensive waste from the silicon industry as a reductant.
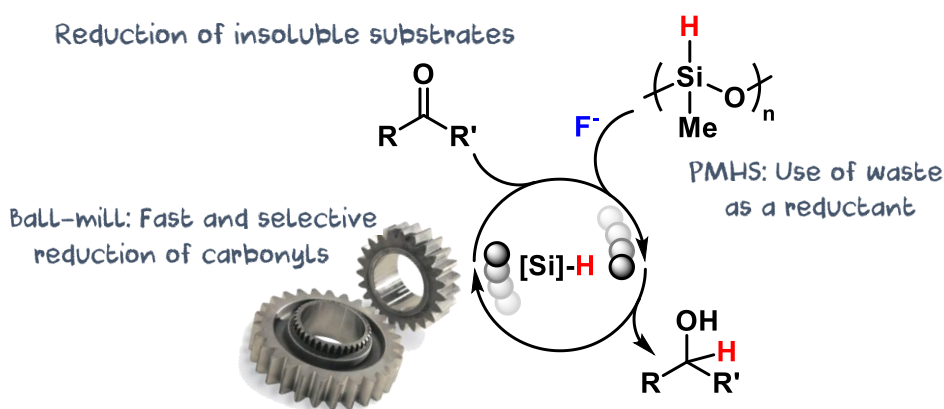
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ABSTRACT GRAPHIC