Scale-up of agrochemical urea-gypsum cocrystal synthesis using thermally-controlled mechanochemistry

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Abstract

Atom- and energy-efficient synthesis of crystalline calcium urea sulfate ($[Ca(urea)_4]SO_4$) cocrystal was explored using thermally-controlled mechanochemical methods with calcium sulfate compounds containing various amounts of crystalline water ($CaSO_4 \cdot xH_2O$, x=0, 0.5, 2). Small scale (200 mg) experiments in a shaker mill were first performed, and the progress was monitored by *in situ* Raman spectroscopy and *in situ* synchrotron PXRD. Time-resolved spectroscopy data revealed that the presence of water in the reagents' crystalline structure was essential to the reaction and largely determined the observed reactivity of different calcium sulfate forms. Reactions at elevated temperatures were shown to proceed significantly faster on all synthetic scales, while changes in rheology caused by adding external water hindered the reaction progress. The average yield of a 21-mm horizontal twin-screw extruder experiment was ~5.5 g/min of extrusion (~330 g/h). Energy consumption during the milling reactions required to achieve complete conversion ranged from 7.6 Wh/g at 70°C for a mixer mill to 3.0 Wh/g at 50 g scale and 4.0 Wh/g at 100 g scale for a planetary mill or 4.0 Wh/g at both 70°C and RT for a twin-screw extruder, showing significant improvement in energy efficiency at large-scale production. Obtained crystalline cocrystal exhibited significantly lower solubility in aqueous solutions, nearly 20 times lower per molar basis compared to urea. Further, reactive

nitrogen emissions in the air at 90% relative humidity, measured as NH_3, showed slow and nearly linear nitrogen loss for the cocrystal over 90 days, while the same level of emissions was achieved with urea after 1-2 weeks, showing the potential of this cocrystal material as a large scale nitrogen efficient fertilizer.

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Keywords: urea; mechanochemistry; cocrystal; gypsum

Introduction

Sustainable nitrogen cycle management is one of the 14 Grand Challenges for Engineering in the 21st Century.[1,2] Nitrogen is critical in food production, but its environmental cycling involves significant energy use to produce ammonia from stable dinitrogen molecules. For this reason, a recent emphasis at the forefront of academic research has been enabling low-temperature NH_3 synthesis *via* conventional catalyst design[3–5] as well as establishing its selective and energy-efficient electrochemical,[6–9] plasma-enhanced,[10,11] solid-solution based[12] and mechanochemical[13,14] synthesis routes. However, a deeper analysis of global nitrogen cycling reveals that a major nitrogen loss takes place when fertilizers are applied to the soil.[15–19] This results in a significant reactive nitrogen gas emission from non-point sources that are difficult to contain or remediate. While some technologies have been developed to control the release of the reactive nitrogen in the environment *via* better matching the plant uptake patterns by using physical slow-release coating materials – so-called enhanced efficiency fertilizers[20] – they often suffer from complex and expensive production processes and cannot be considered a panacea to the nitrogen cycle management.[21] Instead, very recent efforts have focused on the modification of the intrinsic properties of nitrogenous fertilizers, including their solubility or propensity to react in moist environments.[22–29]

In particular, a promising recent strategy to increase the soil retention time of urea (one of the common nitrogen fertilizers) has been cocrystallization.[30] To improve the performance of the fertilizer, urea is co-crystallized with co-formers that not only increase its stability and soil availability but also provide essential plant nutrients themselves. Examples are calcium urea phosphates and sulfates, which serve as a source of nitrogen, calcium, and phosphorus or sulfur, and were proposed to be significantly more stable in a moist environment than urea.

$CaSO_4 \cdot xH_2O$ ($x = 0, 0.5, 2$) + urea $\longrightarrow$ [Ca(urea)$_4$]SO$_4$ (CSD code: URCASU) + xH_2O
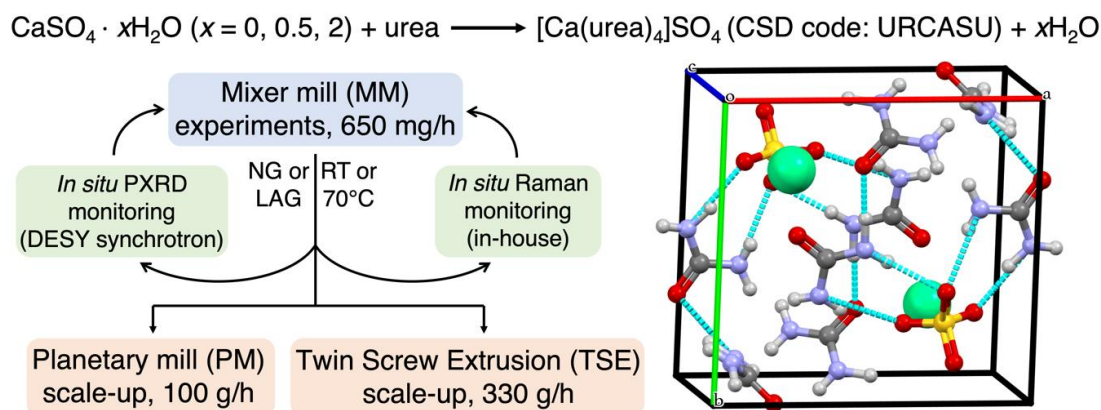
Figure 1. Reaction scheme for the small and large scale synthesis of calcium urea sulfate (URCASU, the crystal structure depicted on the right).

Crystalline calcium urea sulfate[31] ([Ca(urea)$_4$]SO$_4$, CSD code: URCASU,[32] Figure 1, right) is an excellent fertilizer candidate because it can be prepared from inexpensive gypsum (CaSO$_4$, most often as dihydrate) and urea, thus creating a value-added product from two ubiquitous and cheap starting materials. In addition, the use of waste drywall gypsum also helps in gypsum recycling, an important issue in today's booming building industry. Due to the low solubility of calcium sulfate, the preparation of URCASU by conventional solution methods is possible only from solutions containing a significant excess of urea. Unconverted urea remains in the mother liquor after the water reduction and crystallization of URCASU product, imposing complicated separation, waste management, and handling procedures with low atom economy.[33]

Recent studies have reported a novel and greener procedure for preparing calcium urea sulfate directly from gypsum and urea by mechanochemistry.[34] Mechanochemistry,[35] a branch of chemistry encompassing chemical reactions enabled through mechanical force, has lately been at the forefront of chemical synthesis due to its unusual reactivity and strong potential for sustainable production.[36–40] From a green chemistry perspective, mechanochemistry demonstrates many advantages;[41] it is fast, atom-economic, high-yielding, requires very little or no solvent, thus generating little waste, and it is capable of taking advantage of normally unusable starting reagents, such as poorly soluble metal oxides and carbonates. This makes mechanochemistry an intrinsically green synthetic method that is sustainable and environmentally beneficial. Early attempts at the mechanochemical preparation of calcium urea sulfate by Malinowski and coworkers found that calcium sulfate hemihydrate resulted in a slightly more facile conversion than gypsum. Still, neither provided complete conversion, even with very long grinding times.[42,43]

More recently, Baltrusaitis and coworkers transformed not only chemically pure gypsum,[44] but also drywall waste[34] as well as calcium oxides, carbonates, and hydroxides[45] into crystalline urea cocrystals. Those were typically synthesized at small (mg) laboratory scales, and the in-depth information on these transformations that can facilitate the scale-up is lacking. Furthermore, the conversion was not always quantitative, and the procedure was quite time-consuming and energy-intensive.[34] For potential industrial applications, the process needs to be better defined and more energy-efficient. One of the solutions for improving mechanochemical reactivity would be the use of additives in the milling process, such as liquids (liquid-assisted grinding, LAG).[46–48] The mechanochemical synthesis of a related fertilizer, calcium urea phosphate, was significantly improved due to the autocatalytic action[49,50] of even small amounts of water produced during the reaction.[51] Additionally, recent work showed that milling under controllable temperature programs can lead to products not easily accessible by conventional milling procedures, a tremendous increase in the rate of product formation, and a reduction in energy requirements.[52]

Here, we combine these techniques and investigate the effects of temperature, different calcium sulfate source crystallinity, and different amounts of water in the reaction mixture on the URCASU formation (Figure 1). As calcium sulfate sources, anhydrous calcium sulfate, calcium sulfate hemihydrate, and calcium sulfate dihydrate (gypsum) were tested. The reactions were optimized on a small scale in a mixer mill (MM) with *in situ* monitoring using both Raman spectroscopy[53,54] and synchrotron powder X-ray diffraction (PXRD)[55,56] in a reactor that allowed monitoring of mechanochemical reactions at elevated temperatures. The optimized laboratory procedure was also transferred to larger scales, either a batch process (planetary mill - PM) or continuous mechanochemical processing (twin-screw extrusion – TSE). The energy consumption and space-time yield (STY) for all three methods established the most efficient synthetic method for preparing this important value-added product with increased stability and superior nitrogen release properties compared to urea.

Experiments and methods

Reactants and instrumental details: Full details of all instruments and reagents used are supplied in the *Supplementary Information* (SI). Mixer mill synthesis and reaction monitoring by Raman spectroscopy was performed on an InSolido Technologies IST-500 mixer mill. *In situ* monitoring by synchrotron PXRD was performed on an InSolido Technologies IST-636 mixer mill. High-temperature mixer mill experiments were performed using a setup described

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previously.[57] All small-scale high-temperature reactions were performed at 70 °C. Planetary mill synthesis was performed on a Fritsch Planetary Mono Mill Pulverisette 6. Twin-screw extrusion was performed on a Rondol 21mm LAB TWIN horizontal twin-screw extruder.

Laboratory PXRD patterns were collected on a Panalytical Aeris powder X-ray diffractometer with CuKα radiation (40 kV, 7.5 mA). FTIR spectra were collected on a PerkinElmer Fourier transform infrared spectrometer Spectrum Two (Section 2.3 in the SI). Raman spectra for *in situ* reaction monitoring were collected using a Maya 2000 Pro Raman spectroscopy probe made by Ocean Insight (Section 2.4 in SI). For consistency with scans taken during milling where the amount of material, jar background, etc., are ever-changing, *ex situ* Raman spectra were taken under the same conditions as the *in-situ* monitoring spectra. Consequently, all *ex situ* spectra also contain the background from the jar. Synchrotron PXRD *in situ* monitoring was performed at the P02.1. beamline of the Petra III facility of DESY synchrotron in Hamburg, Germany. Thermogravimetric experiments were performed on a Simultaneous Thermal Analyzer (STA) 6000 (PerkinElmer, Inc.). Monitoring of electric energy consumption for planetary and mixer mill experiments was performed by EMOS P5821 power consumption meter (Section 2.5 in SI). In the case of non-heated monitoring reactions, the mill was plugged directly into the measuring device, which was, in turn, plugged into the wall outlet, measuring the total power consumption of the mill. In the case of heated reactions, both the mill and the heater were plugged into the same extension cord, whose power consumption was then monitored by the same power consumption meter. In the case of twin-screw extruder experiments, the energy consumption of the screw motor was calculated from the strength of the electric current read directly from the TSE. The TSE has separate indicators showing when the section heaters turn on. Aside from the initial short temperature ramp, the heaters did not turn on during the extrusion at elevated temperatures. The friction generated by the screws was enough to maintain the temperature constant, and in a continuous process, the initial temperature ramp energy consumption would be negligible, so the heater energy was not taken into consideration.

Mixer mill (MM) synthesis: In all experiments, 300 mg (1.74 mmol) of calcium sulfate dihydrate, 252.6 mg (1.74 mmol) of calcium sulfate hemihydrate, or 237 mg (1.74 mmol) of anhydrous calcium sulfate were combined with 418.5 mg (6.97 mmol) of urea in a 14 mL milling jar. Aluminum jars with a sapphire window were used for Raman spectroscopy monitoring experiments, while poly(methylmethacrylate) (PMMA) jars were used for all other mixer mill syntheses. Two 7 mm (1.4 g) stainless steel balls were added, and the mixtures were

milled for 60 minutes at 30 Hz. In the case of LAG reactions, a small amount of water was added immediately before milling (10-100 μL depending on the type of experiment; details in SI 1.2.). Products were analyzed by *ex-situ* PXRD and FTIR-ATR after the reactions were completed.

Planetary mill (PM) synthesis: PM synthesis was performed by mixing a calcium sulfate source ($CaSO_4 \cdot xH_2O$, *x*=0, 0.5, 2, amounts listed below) with urea either in a 150 mL stainless steel jar along with ten 9 mm (3 g) and three 14.3 mm (11.7 g) stainless steel balls (35 g and 50 g scale), or in a 500 mL stainless steel jar along with twenty-six 9 mm (3 g), eight 10 mm (4 g), one 11 mm (5.4 g), one 12 mm (7 g), and three 14.3 mm (11.7 g) stainless steel balls (100 g scale). The reaction mixture was milled at 500 rpm for 60 minutes, and the product was then analyzed by PXRD and FTIR-ATR. The 35 g scale reaction was also milled at 300 rpm, and the resulting product mixture was divided into four parts and aged at ambient humidity at different temperatures (room temperature, 40°C, 70°C, and 135°C) to get the desired product. In LAG reactions, 5 mL of water was added to the reagent mixture immediately before milling. Reagent quantities are as listed: a) 35 g scale: 14.6 g (0.085 mol) of calcium sulfate dihydrate and 20.4 g (0.34 mol) of urea; b) 50 g scale: Calcium sulfate dihydrate (20.88 g, 0.12 mol), calcium sulfate hemihydrate (17.75 g, 0.12 mol), or anhydrous calcium sulfate (16.65 g, 0.12 mol) with urea (29.12 g, 0.48 mol); c) 100 g scale: Calcium sulfate dihydrate (41.75 g, 0.24 mol), or calcium sulfate hemihydrate (34.8 g, 0.24 mol) with urea (58.25 g, 0.97 mol). Details in the SI section 2.2.2 (Figures S7-S9).

Twin-screw extrusion (TSE) syntheses: Batches of reaction mixtures containing calcium sulfate dihydrate (41.76 g, 0.24 mol), calcium sulfate hemihydrate (35.5 g, 0.24 mol), or anhydrous calcium sulfate (33.3 g, 0.24 mol), and urea (58.25 g, 0.97 mol), as finely ground powders, were premixed and fed into the extruder turning at 90 rpm with the extruder sections non-heated or heated at 70°C. Reactions with anhydrous calcium sulfate as the starting material were performed as both neat grinding and with the addition of a small amount of water (~3 mL) into the chamber of the twin-screw extruder after the first kneading section. Details in the SI section 2.2.3 (Figure S10).

Cocrystal equilibrium solubility testing: The solubility of pure urea and its cocrystals was measured using the gravimetric method. A saturated solution of urea was prepared by dissolving a known amount of urea (6 g) in 5 mL of distilled water in a 25 mL beaker.[58] The beaker was sealed with parafilm and stirred in a water bath to maintain constant room temperature for 4 and 24 hours. After stirring, the remaining solid was filtered and dried

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overnight in the oven at 80 °C. The weight of the leftover solid was recorded. The average concentration was determined by the mass difference of either urea or URCASU in 5 mL of the water and leftover solid after stirring. Two replicates were performed at each time. The same procedure was used to determine the solubility of urea cocrystals. The determined average concentration g/mL was expressed as mol/L (M). The leftover solid residue was tested with Powder X-ray Diffraction to determine and verify that the correct equilibrium composition was used in all tests.

Kinetics of urea dissolution: 5 g of each sample (urea and cocrystal) was pelletized using Carver, Inc. hydraulic press and 25 mm dry pellet press die. The applied load was 2 tons, and the load was maintained for 5 min. In the static dissolution test, a single pellet was placed in a 250 mL Erlenmeyer flask with 50 mL of distilled water and kept at room temperature for 120 hr. As a control, a urea pellet was used. Three replicates were performed each time. To determine the percentage of urea dissolution, 0.5 mL of solution was measured every 10 min in the first hour, later after 24, 48, 72, and 120 hr. The samples were analyzed via HPLC (Agilent 1100 series) with a Diode Array Detector (DAD).

High-performance liquid chromatography: The amount of dissolved urea was measured using an 1100 series HPLC system with solvent degasser system, quaternary pump, autosampler, and diode array detector (Agilent Technologies, USA), following the method described in Babadi et al. [59] The Restek Pinnacle II C-18 column (250 mm × 4.6 mm ID, 5 μm) was used for separation. The column heater maintained a constant temperature of 30 °C. Mobile phases A (water) and B (acetonitrile) were mixed using the following LC gradient at 15A/85B with a flow rate of 1.00 mL/min; injection volume was 5 μL. Urea peak was identified on the absorption spectra at 195 nm wavelength. The stock solution of 10,000 ppm urea was made by adding 1 g urea powder to deionized water (Millipore) in a 100 mL volumetric flask. Calibration standards (100 ppm – 5000 ppm) were made from the stock solution.

Nitrogen volatilization experiments: About 0.004 grams of N per 1 gram of soil of either urea or URCASU were added into a 500 mL flask which also contained a 2.6 cm thick soil layer. Continuous airflow of moist air saturated at ~90 % relative humidity was passed through the bottle for the duration of up to 90 days. The evolved NH_3 was continually captured in 0.2 N H_2SO_4 solution and measured using a methyl red indicator. Mini prills of urea were used as a reference, while urea cocrystal was used in the powder form as synthesized mechanochemically using a planetary ball mill.

Results and Discussion

Mixer milling (small scale) experiments. The first set of experiments focused on determining the role of water contained in the starting materials used in synthesizing the URCASU product by using a small scale (<500 mg) mixer milling (Figures 2 and S3). Neat mixer milling (NG) experiments were performed using anhydrous calcium sulfate, calcium sulfate hemihydrate, or calcium sulfate dihydrate as the calcium source. In a typical mixer milling (MM) experiment, the calcium sulfate source $Ca(SO_4)\cdot xH_2O$ (x=0, 0.5, 2) was mixed with urea and milled for one hour at a frequency of 30 Hz. The progress of representative reactions was monitored separately by *in situ* Raman spectroscopy and *in situ* synchrotron PXRD. Notably, reactions monitored by Raman spectroscopy were performed in aluminum jars equipped with sapphire windows to ensure direct monitoring of milling at elevated temperatures, while all other MM reactions were performed in poly(methyl methacrylate) – PMMA – jars. The aluminum jars were also fitted with a temperature controller and heating device.[52] The vessels were insulated from the mill holders to prevent dissipation of energy and heating of the mill.

In the NG experiments (Figure 2), both hydrated calcium sulfates resulted in quantitative conversion (confirmed by PXRD) to the URCASU product after an hour of milling in a mixer mill at room temperature and 70 °C. This temperature was chosen as it is below the melting point of urea and is low enough not to dehydrate the hydrated calcium sulfate sources (see Figures S1 and S2). On the other hand, using anhydrous calcium sulfate at either temperature afforded little to no conversion (Figure 2, bottom). It can be concluded, therefore, that the presence of small amounts of water is crucial for the success of the reaction.
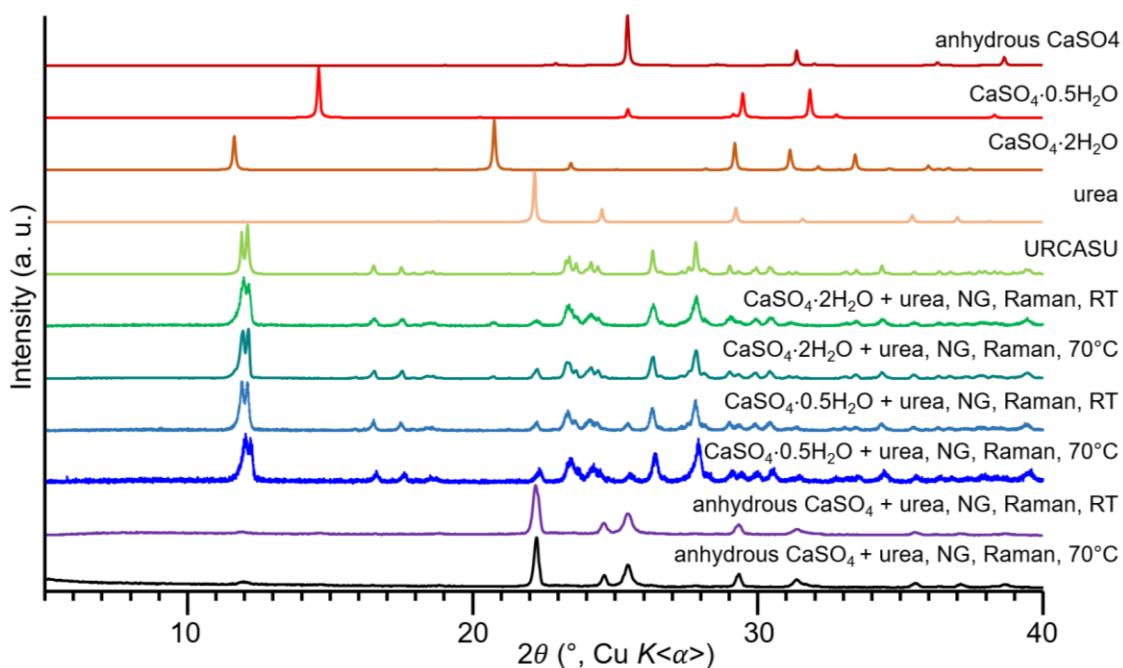
Figure 2. Experimental PXRD patterns of the reagents used and products obtained from small-scale MM mechanochemical synthesis of URCASU, using different calcium sulfate sources. The simulated PXRD pattern of calcium urea sulfate, URCASU. The MM syntheses were also monitored by Raman spectroscopy (Figure 3).

Next, LAG experiments were performed, with small amounts of water added to the reaction mixtures containing anhydrous calcium sulfate and urea (Figure S4). Interestingly, while some URCASU product was formed, the conversion in LAG was quite low, no matter what amount of water was added. Even adding more water than would be contained in an equimolar amount of calcium sulfate hemihydrate (15.8 μL) or calcium sulfate dihydrate (63 μL) still afforded very low conversion in all cases. Therefore, it appears that the presence of water directly in the crystal structures of the hydrated derivatives makes them more likely to react. Friščić and Baltrusaitis[27] have recently shown that the neat milling synthesis of calcium urea phosphate from urea, urea phosphate, and a calcium source proceeds significantly faster when calcium hydroxide, instead of calcium carbonate, is used as the source of calcium ions. They hypothesize this is due to the autocatalytic effect of water produced from the neutralization reaction between calcium hydroxide and urea phosphate. Their hypothesis is supported by the fact that externally added water accelerates the $CaCO_3$ reaction significantly and that changing the amount of water has a profound effect on the kinetics.

In the case of URCASU product synthesis from differently hydrated calcium sulfates, no neutralization reaction would produce catalytic amounts of water. There is, however, the water included in the reagent crystal structure that could play a similar catalytic role when released during milling. In the case of calcium sulfate dihydrate, water molecules are directly

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coordinated to calcium atoms, while in the hemihydrate case, water molecules are crystallized in the structure's cavities. In both cases, water leaving the crystal structure would not only provide catalytic amounts of water and help the reaction (similar to the observations by Baltrusaitis and Friščić), but also mechanically disrupt the structure and crystallites of the calcium sulfate starting reagents, making them more likely to react. This disruption of structure and internal stress from water molecules may also be a part of the reason why water added directly into the reactions where anhydrous calcium sulfate is the reagent has a much weaker effect on reaction acceleration than crystalline water directly included in the reagents' crystal structures.

Control experiments, performed by milling anhydrous calcium sulfate with water in the absence of urea (Figure S5), showed that no matter the amount of water added, a large percentage of the anhydrous calcium sulfate remains even after an hour of milling. There was almost no conversion into the hemihydrate (detected only by FTIR), and transformation into the dihydrate started when 30 μL of water was added but never fully finished, even when 100 μL of water was added. On the other hand, milling calcium sulfate hemihydrate with water easily provides conversion into the dihydrate form (Figure S6). Looking at the Gibbs free energies of formation for the three calcium sulfate derivatives, the dihydrate is the most stable, followed by the more labile hemihydrate, and finally, the least stable anhydrous form.[60] It is therefore somewhat surprising that the thermodynamically least stable anhydrous calcium sulfate is at the same time very resistant to mechanochemical transformations. This further supports the hypothesis that water leaving the crystal structure of the hydrated forms during milling creates internal stress. That stress is only exacerbated by the harsh milling conditions and makes the hydrated forms reactive. On the other hand, it is known that milling and particle size comminution can drastically change the thermodynamic stabilities of materials, even reversing the relative stabilities of polymorphic phases.[61] It is likely that the observed trends in reactivity result from the complex interplay between these effects and the autocatalytic effect provided by the water included in the crystal structure of calcium sources.

In situ monitoring using Raman spectroscopy and PXRD was performed to explore the kinetics of these reactions. In the Raman monitoring experiments, for each of the three sources of calcium sulfate (anhydrous, hemihydrate, dihydrate) neat grinding reactions with urea at room temperature (RT) and 70 °C, and an RT LAG with urea using water were performed (Table S1 and Figures S22 – S30). In the case of a successful reaction, a new peak appears at 975 cm^{-1} due to the formation of the desired URCASU product.
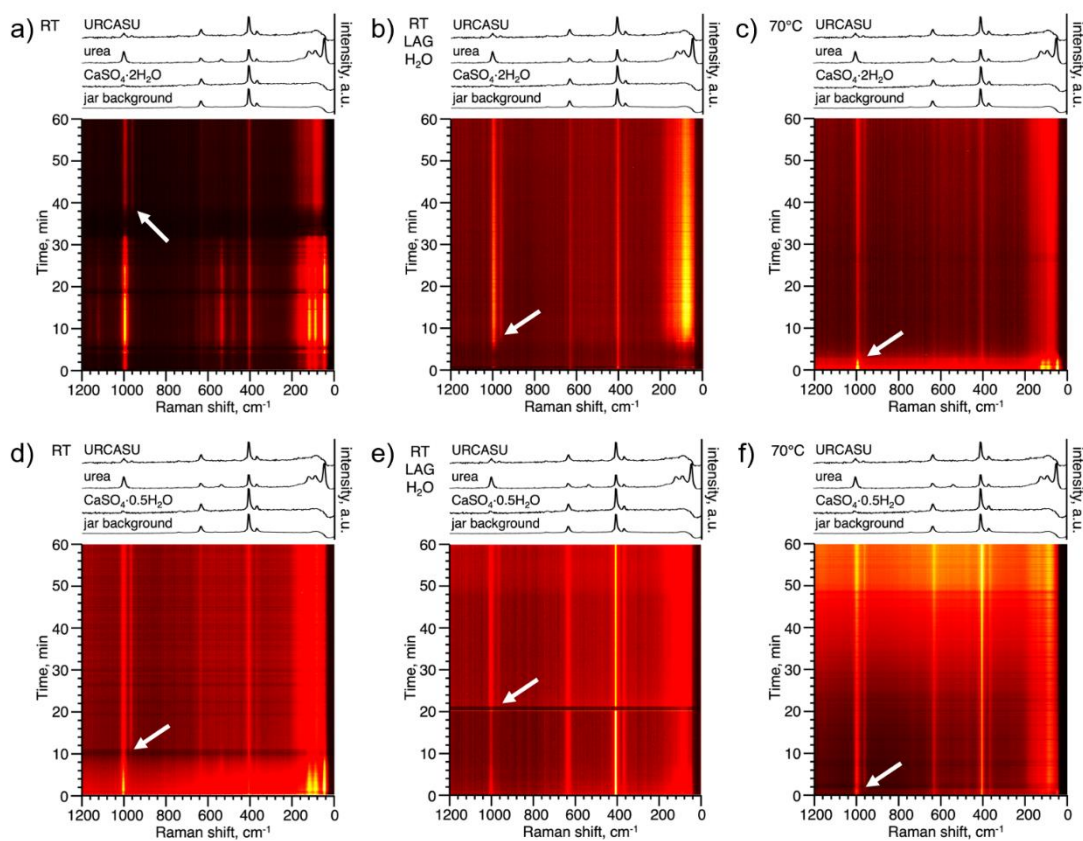
Figure 3. Experimental Raman spectra of $Ca(SO_4) \cdot xH_2O$ (x=0.5, 2), urea, the product of neat planetary milling of $Ca(SO_4) \cdot 2H_2O$ with urea at 500 rpm (URCASU), and the milling jar. *Ex situ* spectra all contain the jar background. *In situ* monitoring of the milling (30 Hz) of $Ca(SO_4) \cdot xH_2O$ (a-c: x=2, d-f: x=0.5) with urea by Raman spectroscopy at room temperature (NG: a, d; H_2O LAG: b, e) or 70°C (NG: c, f). White arrows indicate the appearance of the new product peak at 975 cm^{-1}.

In the case of the calcium sulfate dihydrate, the neat reaction at RT (Figure 3.a) is somewhat slow, only starting after 30 minutes of milling, while adding water accelerates the reaction (Figure 3.b) so that the product formation in RT LAG with dihydrate starts after 8 minutes of milling. *Ex situ* PXRD analysis (Figure S3) of the product shows that the reaction is not complete, and the material looks "sticky", and "caked" to the inside of the vessel. This is likely due to a change in rheology caused by both the added and released water, wherein the mixture adheres to the vessel walls and milling balls, so inadequate mixing and lowered impact occur. Elevating the temperature of the milling setup to 70 °C has a significant effect on URCASU formation; the neat grinding reaction at 70 °C (Figure 3.c) starts after mere 3 minutes of milling. This is consistent with our hypothesis that dehydration increases the reaction rate, as water will more easily leave at higher temperatures. The hemihydrate reaction shows a similar acceleration at a higher temperature. The room temperature neat milling reaction (Figure 3.d) starts after 10 minutes of milling, but at 70 °C, the product peaks appear already within the first

minute (Figure 3.f). The LAG reaction (Figure 3.e) is, however, hard to interpret due to the weak signal of both reagents and products in the first 20 min of the reaction, most likely due to inadequate mixing and sticking of the reaction mixture to the balls and the milling vessel walls, which likely also contributed to a delay in reaction start. However, the *ex situ* PXRD analysis of the product (Figure S3) shows that the reaction is complete, despite the initial change in rheology, and the final product is not "sticky" anymore, unlike the dihydrate LAG reaction, where more water is released from the crystal structure during the reaction. Interestingly, the neat milling of urea with calcium sulfate hemihydrate appears to proceed much more quickly than the dihydrate reaction, both at room temperature and 70 °C (See Table S1). This is consistent with the previously mentioned MM experiments of milling anhydrous calcium sulfate and calcium sulfate hemihydrate with water, where the hemihydrate demonstrated significantly lower kinetic stability under mechanochemical conditions compared to the dihydrate, and especially anhydrous calcium sulfate. Water molecules in the dihydrate structure are directly coordinated to calcium ions and thus harder to dissociate than those in hemihydrate, which are crystallized inside cavities in the structure, and, therefore, easier to release. TGA analysis reveals that the hemihydrate starts releasing water at temperatures as low as 70 °C, whereas the dihydrate is stable up to 110 °C (Figure S1). This can explain both the difference in reactivity between the dihydrate and hemihydrate, as well as the significant increase in the reactivity of both starting materials at higher temperatures, where the release of water is much faster.

In all cases when anhydrous calcium sulfate was used, the results were somewhat hard to interpret due to the strong luminescence of the starting material (Figures S22-S24.). However, it can be seen that in all three cases, there was little to no conversion into the final product, as evidenced by the absence of the new peak at 975 cm^{-1}. This is consistent with the PXRD analysis of the milling product after the reaction was finished (Figure 2, S3), where only the LAG reaction shows small amounts of URCASU product, along with significant remaining reagents (Figure S3).

While the Raman monitoring data for milling the anhydrous calcium sulfate and urea was ambiguous due to the strong luminescence of the reaction mixture, in *situ* monitoring of the same reactions by using synchrotron PXRD (Figures 4a and d) provided much clearer results and confirmed the conclusions drawn from Raman spectroscopy. Neither reaction shows any signs of product formation, and the only visible Bragg reflections throughout are those of the reagents. In the case of calcium sulfate hemihydrate (Figure 4.b), the reactants persist in a significant amount for about 7-8 minutes after the product peaks appear, and a small amount

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of urea is visible throughout the reaction. This is consistent with *ex situ* PXRD analysis of the analogous reaction, where traces of the reagents are visible after the end of milling.
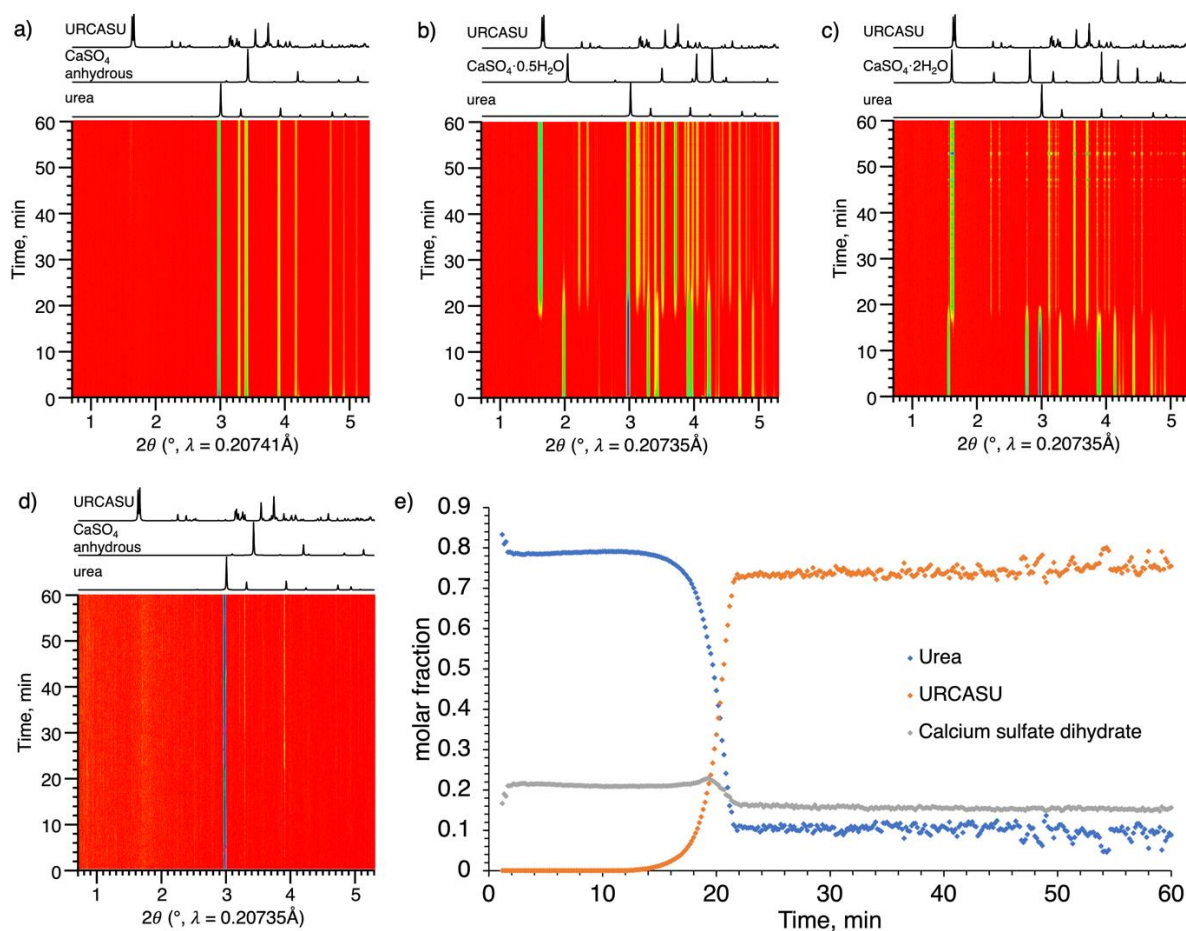

Figure 4. *In situ* monitoring of the room temperature neat milling of anhydrous calcium sulfate (a), calcium sulfate hemihydrate (b), or calcium sulfate dihydrate (c) with urea by using synchrotron PXRD. d) *In situ* monitoring of the room temperature liquid-assisted milling of anhydrous calcium sulfate with urea by using synchrotron PXRD. The simulated PXRD patterns of URCASU, $Ca(SO_4) \cdot xH_2O$ (x=0, 0.5, 2), and urea are included above every *in situ* monitoring plot. e) Rietveld analysis of the *in situ* monitoring of the room temperature neat milling of calcium sulfate dihydrate with urea by using synchrotron PXRD. Mole fractions of urea (blue circles), $Ca(urea)_4SO_4$ (URCASU, orange circles), and calcium sulfate dihydrate (grey circles) are plotted over time.

In situ monitoring of the room temperature neat milling of calcium sulfate hemihydrate or dihydrate with urea shows that in both cases, the products start forming around 18 minutes after the start of milling. In the case of calcium sulfate dihydrate, the reaction is finished after an additional 2 minutes milling (Figure 4.c), evidenced by the complete disappearance of both the urea and calcium sulfate dihydrate peaks. The precise Rietveld quantitative phase-analysis is made difficult by the sizeable amorphous background stemming from the presence of the PMMA jar (Figure S32), and carries inherent – and hard to estimate – error due to peaks being obscured by the background. However, the general trend of the kinetics shows sigmoidal behavior typical of autocatalysis, similar to that reported by Baltrusaitis and Friščić. [27]. There

is an induction period of 12 min, followed by a rapid transformation that finishes by the 22nd minute of milling. Such induction periods are standard in mechanochemical reactions and indicate a positive feedback mechanism.[62] The phenomenon often stems from either autocatalysis (as mentioned before), an initial period of particle size diminishment up to a critical point when the reaction quickly occurs, or internal heating driven by a reaction isotherm.[62] While all three of these could be contributing, the fact that using thermodynamically least stable calcium source, anhydrous calcium sulfate, leads to no conversion supports the autocatalytic mechanism the most.

Interestingly, these results are somewhat different from those observed in the Raman monitoring of the reactions when the two hydrated calcium sulfates are used. There, the hemihydrate RT reaction appeared to proceed faster (starting within 10 minutes) than the dihydrate one (starting within 32 minutes). The reasons for these differences are still being elucidated but could potentially be ascribed to the differences in milling vessels used.[63] In Raman monitoring, aluminum vessels with a sapphire window were used, providing higher impact energy, whereas plastic PMMA vessels were used at the synchrotron, resulting in milder milling conditions.

Ex-situ FTIR data of the products of MM are consistent with PXRD and Raman data. The products have bands very similar to those of the reactants, but some broaden or slightly shift due to hydrogen bonding between urea nitrogen and sulfate oxygen. Namely, bands ascribed to urea N-H stretching (3430 cm^{-1} and 3330 cm^{-1}) and bending (1590 cm^{-1}) along with calcium sulfate asymmetric stretching (1096, 1089, and 1094 cm^{-1}) and bending (around 670-600 cm^{-1}) vibration modes of SO$_4$ tetrahedron (Figures S11-S21).[64,65]

Overall, it can be seen that the URCASU product can be synthesized on a small scale (~0.65 g) from two different calcium sulfate sources, the hemihydrate and the dihydrate, with the hemihydrate reactions being generally faster but affording incomplete conversion. In contrast, the dihydrate reactions are slightly slower but result in full completion. Notably, the anhydrous calcium sulfate provides little to no conversion into the desired product, even when water is added as a LAG liquid. This indicates that water needs to be incorporated into the crystal structure of the calcium sulfate source for optimal effect. The mechanism of reaction acceleration is presumably twofold: (1) due to autocatalysis in the mechanochemical process,consistent with the shape of the kinetic curves obtained through *in situ* monitoring,[50] and previous studies on similar materials[27], and (2) due to internal stress built up in the structure of the hydrates when water is leaving the structure. The results particularly emphasize the

strong impact of temperature control in the laboratory milling formation of URCASU, as reactions at elevated temperature (70 °C) are all significantly faster and more efficient than those at room temperature.

Large-scale experiments. With the small-scale data in hand, a scale-up of the synthesis was performed to obtain larger quantities of the product. Two scale-up methods were used: batch processing by planetary milling (PM) and a continuous flow method by twin-screw extrusion (TSE).

Planetary milling was performed on a 35 g, 50 g, and 100 g scale. First, calcium sulfate dihydrate and urea were milled neat in a planetary mill on a 35 g scale at 300 rpm for 1 hour. The reaction mixture shows no conversion immediately after milling. Still, it is known in the mechanochemical community that accelerated aging - leaving the milled reaction mixture undisturbed for a time, especially at elevated temperatures and higher - can result in reactivity even if there is no immediate conversion.[66] Here, leaving the milled reaction mixture for three days at room temperature in the closed milling jar shows partial conversion, with leftover urea and calcium sulfate dihydrate (Figure S7). The three-days aged mixture was divided into four parts and left to further age at RT, 40°C, 70°C, and 135°C. While the RT portion showed no further conversion after another day of aging, all three remaining parts achieved fairly high conversion (based on PXRD) into the desired product after only one hour of aging at 40°C, 70°C, or 135°C, with the 135°C part reaching near completion (Figure S7). Notably, a slight odor of ammonia could be felt from the reaction mixture aged at 135 °C, indicating some degree of urea decomposition (urea melting temperature is 133 °C; the decomposition temperature is 350 °C).

Further optimization showed that judicial choice of planetary milling frequency and milling media can provide full conversion (Figure S8) of starting materials to the desired product after only one hour of neat milling at the 35 g scale (500 rpm, addition of larger milling media). Interestingly, liquid-assisted milling using water showed no advantage to dry milling, leading to incomplete conversion as seen by leftover urea peaks in the PXRD pattern (Figure S8). This could be due to water preventing the binding of urea to calcium ions by coordination to the calcium, rheological changes in the reaction mixture resulting in less efficient mixing of starting materials ("caking" of the reaction mixture), or due to the shifting of reaction equilibrium.

Next, larger scale (50 and 100 g) planetary milling of urea with different sources of calcium sulfate (anhydrous, hemihydrate, dihydrate) was performed using the optimized procedure (Figure 5). Unlike the small-scale experiments, reactions using anhydrous calcium sulfate as the starting reagent show partial conversion into the URCASU product, especially when water is added to accelerate the reaction. Still, the reaction is far from complete, and a significant amount of starting materials is left in the product mixture. On the other hand, both the 50 and 100 g scale reactions with calcium sulfate dihydrate as the starting reagent show full conversion to the URCASU product, while the reactions using calcium sulfate hemihydrate show a minute amount of residual starting reagents. Interestingly, these reaction mixtures all appear to change rheology during milling so that they are "caked "to the jar's walls, resulting in one solid chunk of URCASU material. Such a change in rheology could easily result in insufficient mixing and incomplete conversion, but the exact opposite is true. Seeing the strong influence of temperature on reaction conversion in Raman-monitored mixer mill experiments, we hypothesized that the elevation of milling vessel temperature due to friction might be (at least partially) responsible for the success of the reaction after the reagents have been well mixed in the first, free-flowing phase, of milling. While it is not possible to attach a temperature-controlling device to the milling vessel in a planetary mill due to the type of oscillations of the milling stage, measuring the temperature of the milling vessel immediately after milling completion shows a temperature of 55°C, which may be an explanation for high formation yields despite the rheological changes and caking of reaction mixtures.
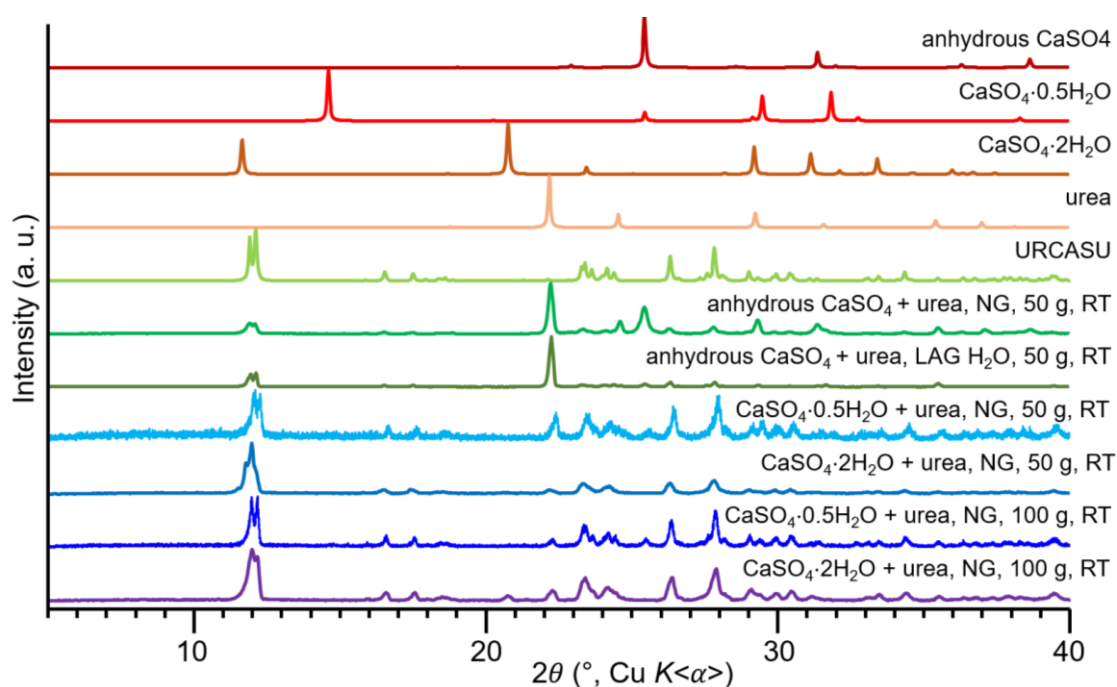
Figure 5. Experimental PXRD patterns of $Ca(SO_4) \cdot xH_2O$ (x=0, 0.5, 2) and urea. The products of neat planetary milling of $Ca(SO_4) \cdot xH_2O$ (x=0, 0.5, 2) with urea at 500 rpm on a 50 g scale, and of $Ca(SO_4) \cdot xH_2O$ (x=0.5, 2) with urea at 500 rpm on a 100 g scale. The product of liquid assisted planetary milling of anhydrous $CaSO_4$ with urea at 500 rpm on a 50 g scale, with the addition of 5 mL water. The simulated PXRD pattern of $Ca(urea)_4SO_4$ (CSD code URCASU).

Finally, twin-screw extrusion (TSE)[67] experiments at 90 rpm were performed with all three sources of calcium sulfate at room temperature and 70 °C (Figure 6). Analogous to the planetary mill experiments, reactions using calcium sulfate dihydrate reach complete conversion at both temperatures. At the same time, those with the hemihydrate show a small amount of residual hemihydrate starting reagent at both temperatures. Similarly to the planetary milling experiments, room temperature TSE enables low conversion of anhydrous calcium sulfate into URCASU, especially when water is added. Even in this liquid-assisted extrusion, the conversion was once again incomplete, and there is a significant amount of starting reagents leftover. The 70 °C TSE experiments using anhydrous calcium sulfate show minimal conversion. This is likely due to insufficient mixing and "caking" of the reagent mixture, which was sometimes quite severe, to the point of blocking the extruder operation. The average yield of a typical TSE experiment was ~5.5 g/min of extrusion (~330 g/h).
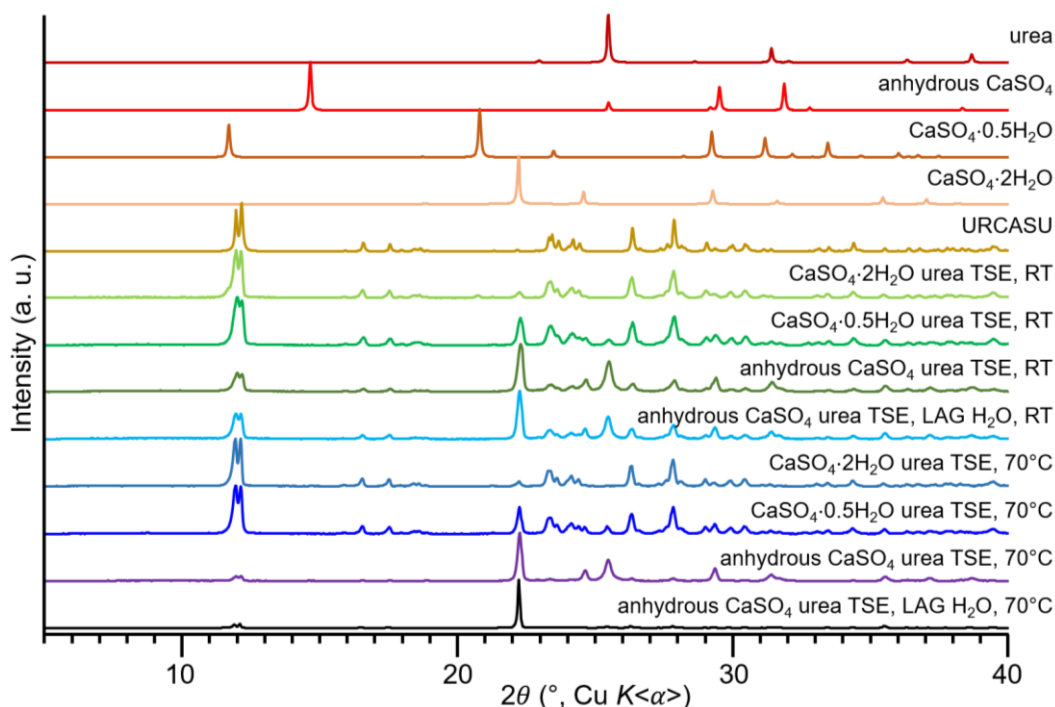

Figure 6. Experimental PXRD patterns of $Ca(SO_4) \cdot xH_2O$ (x=0, 0.5, 2), urea, and the products of twin-screw extrusion (TSE) of $Ca(SO_4) \cdot xH_2O$ (x=0, 0.5, 2) with urea at 90 rpm. Products of reactions at room temperature (RT) or 70°C, and neat (x= 0, 0.5, 2) or with the addition of water (x=0) are shown. The simulated PXRD pattern of $Ca(urea)_4SO_4$ (CSD code URCASU).

Energy monitoring during the milling reactions shows that scaling up from a mixer mill (7.6 Wh/g at 70°C, 6.5 Wh/g at RT) to a planetary mill (3.0 Wh/g at 50 g scale, 4.0 Wh/g at 100 g scale) or twin-screw extruder (4.0 Wh/g at both 70°C and RT) significantly reduces the energy consumption per gram of produced material (Table S2). TSE shows no difference in energy consumption between the heated and unheated reactions since – after an initial temperature ramp – the energy of friction is enough to maintain the desired temperature of 70 °C. Interestingly, the energy consumption of the twin-screw extruder per gram of produced material is very similar to that of the planetary mill. Still, the larger amount processed per hour of operation and the ability of continuous processing allows for much faster bulk synthesis. With the throughput of 330 g/h, the space-time yield of TSE is estimated at 169,900 $kg/m^3 \cdot d$, which is orders of magnitude more than the most productive batch process (4,800 $kg/m^3 \cdot d$ for the planetary mill at the 100 g scale). Once started, the extrusion process can run uninterrupted between planned or emergency shutdowns, whereas in the batch process, the time required for filling, emptying, and cleaning the reactor after each batch must also be taken into account.

Urea and URCASU solubility and reactivity property testing. Measured equilibrium solubility data of urea and URCASU are shown in Table 1**.** The solubility of urea at room temperature varies from 1.1 to 1.2 g/mL or approximately 19 M in water, consistent with previous gravimetric measurements.[29] The solubility of URCASU ranged from 0.221±0.001 g/mL to 0.259±0.0018 g/mL after 4 and 24 hours, respectively. It varied little with time and was consistently lower than the solubility of pure urea. Dissolution measurements were performed to evaluate the propensity of URCASU to dissolve, and the initial kinetics are shown in Figure 7.a. It can be seen that urea dissolves much faster; more than 90% is dissolved after 30 minutes of the experiment. URCASU exhibited slower dissolution kinetics, with the corresponding urea content entirely dissolving only after about two days of experiments, indicating enhanced stability in an aqueous solution.

Table 1. The equilibrium solubility of urea and URCASU

Name	Solubility, g/ml (4 hr)	Solubility, g/ml (24 hr)	Solubility, M (4 hr)	Solubility, M (24 hr)
Urea	1.152±0.006	1.153±0.013	19.18±0.096	19.19±0.213
URCASU	0.221±0.001	0.259±0.002	0.587±0.002	0.687±0.004

While solubility measurements in an aqueous solution can be viewed as an extreme case of the fertilizer materials exposed to the environment, a more realistic measure of performance in real-world conditions is to study the stability of both fertilizers in contact with soil and

humidity. To that end, the emission of reactive nitrogen gas - NH_3 (a decomposition product of urea released in moist air) was measured to ascertain reactivity when materials are dispersed over moist soil. Relative humidity of 90% was maintained for up to 90 days. The emitted NH_3 was periodically sampled, and the results are shown in Figure 7.b. When using pure urea, up to 70 % of the nitrogen was emitted as NH_3 already after 20 days of the experiment, with the release pattern increasing almost linearly within the first few days of the experiment. Very differently, the same released NH_3 amount from URCASU was measured only after more than 90 days, showing an unprecedented nitrogen economy of URCASU. While the underlying mechanisms for this phenomenon are unknown and under investigation, data in Figure 7.b indicate that cocrystal materials containing urea and widely abundant calcium sulfate compounds can result in significantly altered nitrogen release patterns, potentially leading to more sustainable and controlled nitrogen release.
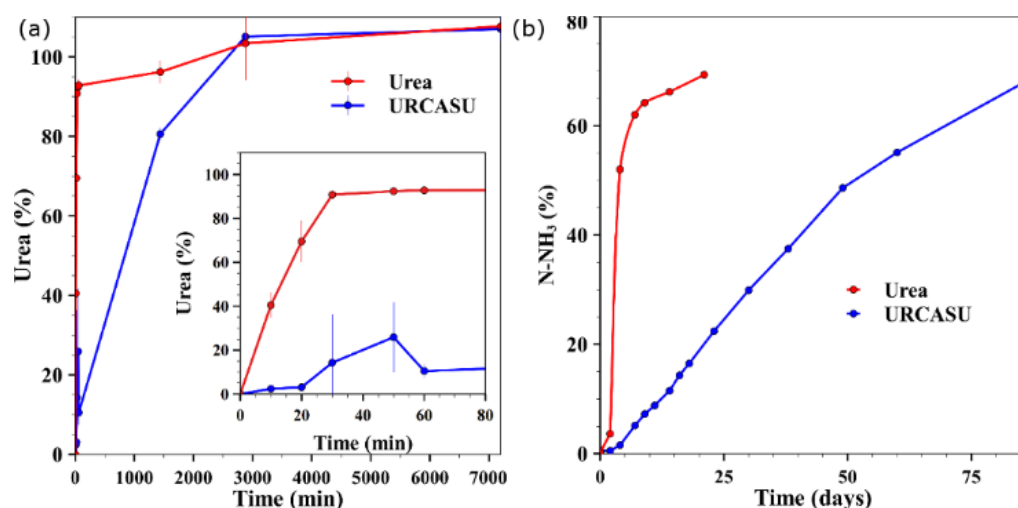

Figure 7. (a) Kinetic dissolution experiments of urea and URCASU pellets and (b) gas-phase ammonia measurements evolved from urea and URCASU with the applied loading of 0.004 mg N/gram of soil.

Conclusions

In this work, we have demonstrated the green, efficient, and scalable synthesis of a valuable fertilizer product, calcium urea sulfate (URCASU), by mechanochemistry at elevated temperatures. URCASU shows superior stability and nitrogen release properties compared to urea, and its mechanochemical synthesis is possible directly from cheap and abundant starting reagents, urea, and two different hydrated calcium sulfate sources, including gypsum, a

common industrial/building waste product. The presence of crystallized water in the two hydrated calcium sulfate sources proved crucial for the success of mechanochemical synthesis, likely through a dual effect of the reagents' dehydration. Water leaving the reagents catalyzes the reaction with urea through partial dissolution and enhanced diffusion of the particles. At the same time, it creates internal stress in the structure of the hydrated calcium sulfates, making them more reactive. Consequently, anhydrous calcium sulfate shows the lowest reactivity. Calcium sulfate hemihydrate, where the water is loosely bound in its structure, shows the highest reactivity, and calcium sulfate dihydrate, with coordinated, tightly bound, two water molecules per formula unit, shows medium reactivity.

Interestingly, in some cases, when the water was added externally to LAG processing, the URCASU product formation was hindered, likely due to rheological changes that impeded the movement of milling media and prevented efficient mixing and mechanical impact. In other words, added water, alongside the water released from the reagents, made the mixture into a very dense mass that adhered to the sides of the milling vessel and the milling media ("caking" of the mixture). Increasing the milling temperature to 70 °C leads to a significant acceleration of product formation and highly crystalline URCASU product, both due to inherent kinetic acceleration at higher temperatures and easier dehydration of the hydrated calcium sulfates. The mechanochemical processing can be readily transferred to larger scales using planetary milling and twin-screw extrusion. Planetary milling at high frequencies provides complete conversion into the products within an hour. Even milling at low frequencies, followed by aging at elevated temperatures (below 100 °C), provides substantial conversion into the URCASU product. In a continuous production mode by twin-screw extrusion, the space-time yield is orders of magnitude greater than laboratory processing, with similar overall energy consumption for all tested methods. Further scale-up in industrial conditions (e.g., larger twin-screw extruders, cement mixers, etc.) would likely be more efficient. The results of this work show promise for future use of this process in the remediation of building waste, providing a high-added-value product from waste material in a simple, energy-efficient, and atom economic process.

Supporting Information

The Supporting Information (SI) is available online. SI contains detailed information on all instruments and methods, detailed descriptions of all experiments, full PXRD diffractograms, TGA thermograms, IR spectra, and *in situ* Raman and PXRD monitoring results, as well as energy monitoring details and data.

Acknowledgments

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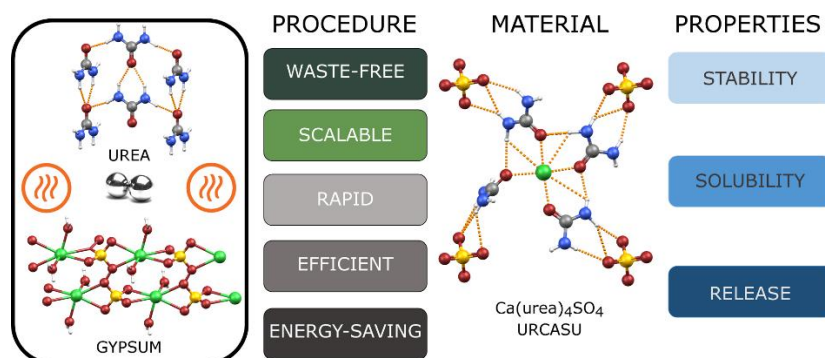
SYNOPSIS:

Thermally-controlled mechanochemistry enabled scalable, efficient, and waste-free synthesis of calcium-urea fertilizer with advantageous stability and nitrogen release properties.