Preparation of an Energetic-Energetic Cocrystal using Resonant Acoustic Mixing

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Abstract: Resonant acoustic mixing (RAM) was applied to the preparation of an energetic-energetic cocrystal comprised of CL-20 and HMX in a 2:1 mol ratio. We have prepared the cocrystal using the RAM technology in a re-source-efficient manner providing near quantitative yield. The cocrystalline product from the RAM preparation is consistent with the product from solution crystallization.

Keywords: LabRAM · Resonant acoustic mixing · Cocrystal · CL-20 · HMX · Energetic cocrystal

1 Introduction

We recently demonstrated and published our results for development and scale-up of cocrystals via resonant acoustic mixing (RAM) for non-energetic material [1,2]. Cocrystals comprised of two energetic coformers are now the current focus of our research using RAM methods. The aim is to discover new energetic forms of matter that significantly improve munitions sensitivity or physical properties while maintaining desired performance characteristics.

Cocrystals may have distinct physical and chemical properties and thus enable the development of poorly soluble or previously non-crystalline Active Pharmaceutical Ingredients (API). Cocrystals have developed a level of acceptance and maturity within the pharmaceutical industry.

While the energetics community has been seeking synthetic methods to alter various functional groups of existing materials to reduce various responses to stimuli, cocrystallization offers the technology to design materials with the desired responses using a less challenging approach with an infinite number of compound possibilities as targets. Cocrystals are a crystal engineering solution with possibilities to address Insensitive Munitions (IM) challenges through the formation of new energetic species using non-covalent bonds between energetic ingredients. Synthesis will always be play an important role as a means to produce and evaluate new target molecules, and cocrystallization is a complimentary technology suitable for generating a new class of novel materials for future testing. The opportunity to test these new materials in explosive and propellant formulations will answer the question regarding the viability of cocrystals for assisting in the all-important quest to solve IM challenges.

Cocrystallization has been utilized for decades in other communities [3,4]: many examples of energetic cocrystals can be found in literature. For example, Levinthal (Thiokol Corporation) utilized the cocrystallization technology to demonstrate an octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX) and ammonium perchlorate (AP) cocrystal. The HMX/AP cocrystal was not water soluble (the solubility of AP was altered by introducing it as a cocrystal with HMX) [5]. Zhou has been exploring energetic cocrystals of urea nitrate, 1,3,5-trinitroperhydro-1,3,5-triazine (RDX), 1,3,5-triamino-2,4,6-trinitrobenzene (TATB), and HMX. Zhou et al. published results for the production of urea nitrate/RDX and Jin et al. for TATB/HMX cocrystals [6,7]. In addition, Matzger (University of Michigan) has reported on the isolation of a cocrystal comprising 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane (CL-20). Matzger produced a 2CL-20:HMX cocrystal from solution phase that has been characterized and is the focus of the presented report [8].

There are several methods available for the formation of cocrystals, including solution cocrystallization, mechanochemical methods and ultrasound, each with their own strengths and weaknesses.

Solution cocrystallization processes require knowledge of each coformer's solubility in a variety of solvents and as a function of temperature. A significant amount of effort may be invested in searching for the optimal solvent system that provides acceptable solubility of the discrete ingredients (coformers) while avoiding the formation of un-

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desired solvates of coformers or the cocrystal product. Therefore traditional solution crystallization provides only a narrow scope for the scale-up of cocrystallization processes.

Mechanochemical methods such as solid-state grinding have been employed to induce a chemical or physical change and offer an advantage because of the ability to produce cocrystals that are unobtainable by other methods. Solid state grinding performed dry or with a small amount of solvent added (Liquid-Assisted Grinding, LAG) is typically achieved with a mortar and pestle or ball-mill grinding using grinding media made from stainless steel, ceramic, or Teflon. Solid-state grinding approaches are difficult to scale to multi-kilogram or larger quantities. Developing a scaleable mechanochemical process suitable for energetic materials necessitates the reduction of any components that could lead to potential hazards such as friction or impact. Grinding media could potentially initiate an energetic material and result in detonation or deflagration. Adopting the LAG method for energetics still presents potential friction and impact hazards and therefore care must be taken when designing each process.

Ultrasonics (acoustic waves at ≥ 20 kHz) of powders have issues creating homogeneity across the sample or mixtures and are also not easily scaled for powder systems [9].

The approach we take to energetic cocrystal production in our laboratories at Nalas using RAM offers a safer option by elimination of grinding media while also providing a simpler alternative to solution-based processes. This approach is scalable and is supported by a commercial platform of RAM mixers available through the Resodyn Corporation.

Herein we use the 2CL-20:HMX cocrystal as a model system to demonstrate how RAM is used to generate energetic-energetic cocrystals. The production of the target 2CL-20:HMX cocrystal is confirmed by matching the powder X-ray diffraction data to the calculated powder pattern of the 2CL-20:HMX room temperature structure solved using a Rigaku R-AXIS RAPID-S diffractometer.

RAM may also be used as a screening method for the discovery of new forms or to extend the mechanical processing conditions. We employed similar conditions used for cocrystal preparation with variation in the solvent used for liquid assistance. One could also envision a system, wherein the coformer or discrete ingredient could be rendered amorphous or less ordered by application of the RAM technology.

2 Results and Discussion

2.1 Energetic Cocrystal Preparation

The 2CL-20:HMX cocrystal was initially prepared using a combined cooling and non-solvent crystallization. The crystallization can be accomplished with or without seeding with typical yield between 80% and 90%. The solution phase crystallization is complicated by the precipitation of the starting materials or a new solid form of CL-20. Solution crystallization is not trivial and care must be taken to ensure complete dissolution of the starting materials before non-solvent addition and cooling. Cooling rate and/ or the non-solvent addition rate can greatly influence formation of cocrystal or precipitation of discrete material from solution (e.g. HMX). CL-20 may also precipitate if the solvent composition is rich in non-solvent before the cocrystal begins to precipitate. The cocrystal stoichiometry was confirmed by ^{1}H NMR spectroscopy and by matching experimental powder diffraction pattern to the calculated powder diffraction pattern determined from the crystal structure [10].

The same cocrystal was prepared using RAM by accurately weighing stoichiometric quantities of CL-20 and HMX in specially prepared containers. The RAM operating conditions for the cocrystal preparation employed 33 μL of 30% acetonitrile/2-propanol to approximately 100 mg total solids and mixing for 1 h at approximately 80 G's acceleration. This method is superior with overall product yield at 100%. The powder diffraction pattern of cocrystal obtained through RAM matches that 2CL20:HMX cocrystal prepared from solution.

2.2 Energetic Cocrystal Characterization

The 2CL-20:HMX cocrystal prepared from solution was compared with that of material produced using RAM technology using PXRD. The two samples are compared with the calculated powder pattern in Figure 1. The patterns are consistent with the cocrystal.

The cocrystal's thermal properties were compared with a discrete mixture of CL-20 and HMX by differential scanning calorimetry (DSC). Two distinct changes can be noted in Figure 2. The cocrystal onset temperature (235.8 °C) is higher than the discrete mixture (232.9 °C) and the total in-
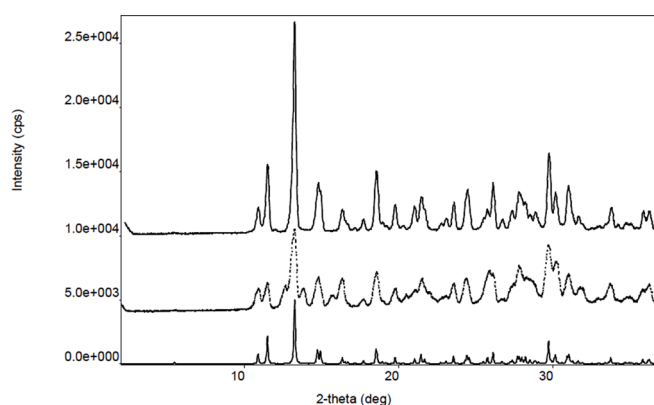

Figure 1. Powder X-ray diffraction patterns for the 2CL20:HMX cocrystal produced from RAM (2:1) at 100 mg scale (middle) compared with co-crystal produced from solution 40 g scale (top) (2 to 37° 2-theta) and the calculated powder pattern from the crystal structure (bottom).
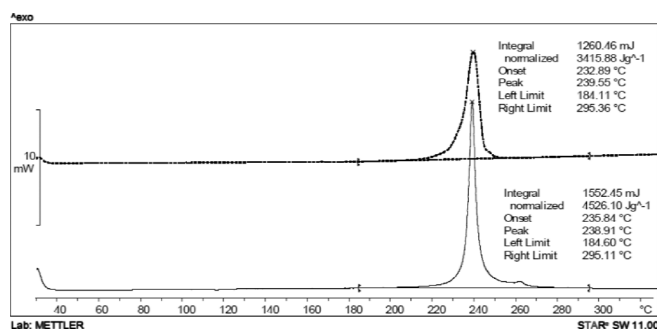
Figure 2. DSC of 2CL-20 : HMX cocrystal (bottom) and a physical mixture (top) of CL-20 and HMX (2 : 1) run at 4 °C min⁻¹ in a high-pressure gold pan. The cocrystal onset of decomposition by the tangent method is 236 °C.

tegrated heat evolved is significantly higher for the cocrystal.

It is interesting to note that the cocrystal produces greater energy during decomposition than the physical mixture of discrete CL-20 and HMX at the same stoichiometric ratio (i.e. 4526 J g⁻¹ compared to 3415 J g⁻¹). These data indicate that cocrystallization results in a crystal packing arrangement with stronger non-bonded interactions amongst the constituent coformers. A focus of our ongoing research is the relative contribution of different non-bonded interactions (hydrogen bond, van der Waals interactions) to the total energy evolved during decomposition events [11].

Small scale sensitivity testing was completed at ARDEC using ERL impact, BAM friction and measured response to electrostatic discharge (ESD). The cocrystal is compared with the discrete materials as well as an RDX standard in Table 1. It should be noted that the sensitivity data does not correlate with previously reported values in the literature [8]. We bring attention to this detail for safety concerns; previously reported data suggest the cocrystal was less sensitive than ε-CL-20, which was not validated under this effort. The cocrystal exhibited higher sensitivity to impact when compared with ε-CL-20. Although this increased sensitivity was not desired, it demonstrated that the cocrystal sensitivity is different from the discrete materials.

Table 1. Sensitivity of cocrystal compared with known energetic materials.

Material	ERL Impact (50 %) [cm]	BAM Friction (10 no go) [N]	ESD (go/no go [0.25 J])
ε-CL-20	26	72	go
HMX (class 5)	28	80	no go
RDX (type II, Class 5)	18	168	go
2CL-20 : HMX cocrystal	17	72	go

3 Experimental Section

3.1 100-mg Scale (Solution Phase)

Initial scale-up experiments were conducted at the 100-mg scale to generate enough of the new cocrystal to run DSC, TGA, PXRD, NMR, and HPLC to confirm the stoichiometry and properties.

A cocrystal between CL-20 and HMX was first prepared for initial screening experiments from a mixture of ethanol and DMSO. Equimolar quantities (0.5 mM) of CL-20 and HMX were combined and the cocrystal was precipitated by slow evaporation at room temperature. Clusters of needles were observed after the evaporation of a significant portion of the solvent over a 10-day period.

A more suitable solvent system (acetonitrile and 2-propanol) was employed at the 100-mg scale. This involved the dissolution of CL-20 and HMX in acetonitrile at room temperature. The reaction solution was allowed to concentrate by evaporating approximately 70 % of the acetonitrile and adding 2-propanol to crystallize the cocrystal.

3.2 One and Five Gram Scale (Solution Phase)

Subsequent batches were prepared without evaporation by minimizing the initial charge of acetonitrile and running at higher temperature. Scale batches with 1 g (prepared in 25 mL test tubes with magnetic stirring) and 5 g (prepared in 100 mL glass reactor) were prepared in the Mettler Toledo EasyMax™. Overhead stirring was used for the 5 g scale.

The PXRD pattern of these batches and subsequent 1 g and 5 g scale crystallizations were consistent with the material described in Bolton and Matzger, wherein the authors note the cocrystal is a 2 : 1 ratio of CL-20 to HMX [8].

3.3 100 mg Scale Using RAM

Mechanochemical cocrystallization studies were performed in a LabRAM® resonant acoustic mixer (Resodyn™ Acoustic Mixers, Inc., Butte, MT).

The LabRAM experiments were carried out as follows: CL-20 (80.1 mg, 0.1826 mmol) was placed into a small vial followed by HMX (27.03 mg, 0.0913 mmol) in a 2 : 1 CL20:HMX molar ratio. 33 µL of the solvent mixture (30 : 70 v : v of acetonitrile : 2-propanol) was added to the vial using a calibrated pipette (approximately 30 µL per 100 mg of solids). The LabRAM® was adjusted to 80 % intensity (near 80 G's, where G = acceleration of gravity), in auto-resonance mode (typically near 60 Hz).

3.4 Safety Concerns when Working with Energetics on the LabRAM

An Electrostatic Fieldmeter (Digital Stat-Arc-3, Monroe Electronics, Lyndonville NY) was used prior to handling ener-

getic solids. Bonding and grounding of all equipment, as well as personnel handling energetic materials, is critical to avoid static discharge.

A tested explosive safety shield (when appropriate) and Kevlar gloves should be used when handling sensitive energetic materials including the 2CL-20:HMX cocrystal.

3.5 Small Scale Safety Testing

The ERL Type 12 impact tester, utilizing a 2.5 kg drop weight, was used to determine the impact sensitivity. The drop height corresponding to the 50% probability of initiation was used to measure impact sensitivity. The ERL Type 12 Impact Test Method is described in STANAG 4489 Ed.1 "Explosives, Impact Sensitivity Tests". All impact tests were conducted using 180A garnet sandpaper and the test procedures given in AOP-7, 201.01.001. Bruceton method of statistical analysis was used to determine the 50% point.

The Large BAM Friction Test Method is described in AOP-7, 201.02.006, "BAM Friction Test". The porcelain pin was lowered onto the sample and a weight was placed on the arm to produce the desired load. The tester was activated and the porcelain plate was reciprocated once to and fro. The results were observed as either a reaction (i.e. flash, smoke, and/or audible report) or no reaction. Testing was begun at the maximum load of the apparatus (360 N) or lower if experience warrants it. If a reaction occurred in ten trials, the load was reduced until no reactions were observed in ten trials.

The ABL ESD test procedure is described in AOP-7, "Electrostatic Discharge Sensitivity Test". This test determines the energy threshold required to ignite explosives by electrostatic stimuli of varying intensities.

3.6 Differential Scanning Calorimetry

Differential Scanning Calorimetry data was measured with a Mettler Toledo Model 822e instrument calibrated with indium and tin reference standards. Samples ($0.350\,mg \pm 0.02\,mg$) were scanned in high pressure gold pans at a heating rate $4\,°C\,min^{-1}$.

4 Conclusions

The CL20:HMX (2:1 molar ratio) energetic-energetic cocrystal was successfully prepared in LabRAM using a liquid-assisted method. A minimal amount of solvent was added to the mixture of energetic materials and processed for 1 h at approximately 80 G's acceleration without additional processing. Future work includes evaluating various new

cocrystals as potential solutions to IM challenges. The novel RAM method of producing energetic materials greatly increases safety and is scalable for manufacturing of large quantities of energetic cocrystals and their formulations.

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