MS28 Navigating crystal forms in molecular and pharmaceutical materials

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Cocrystal polymorphs and mechanochemistry - mechanism and kinetics
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Abstract
Mechanochemistry is an effective, environmentally benign, and facile method for the synthesis of new crystal forms. Different milling parameters are known to affect the mechanisms and rates of product formation: milling frequency, milling time, filling degree of the milling jar, ball diameter and vessel size, degree of milling ball filling, and material of jars. The increasing interest in mechanochemistry is contrasted by a limited mechanistic understanding of mechanochemical reactivity and selectivity. Control over ball milling transformations is needed before the transformative potential of mechanochemical processing can be realized. Different analytical methods and their combinations have been developed for the time-resolved in situ monitoring of mechanochemical transformations, including powder X-ray diffraction, X-ray absorption spectroscopy, NMR, Raman spectroscopy, and thermography.[1] Here we will discuss our recent results investigating the formation of polymorphic cocrystals[2–3] thereby elucidating the influence of milling parameters (solvent, temperature, time) and reaction sequences on the formation mechanism and kinetics.[2-4] For the mechanochemical chlorination reaction of hydantoin normalizing the kinetic profiles to the volume of the milling ball showed clearly that milling reaction kinetics are conserved.[5] Here physical kinetics dominate reaction rates in a ball-milling transformation. Attempting to interpret such kinetics in purely chemical terms risk misinterpreting the results. Our results indicate that time-resolved in situ investigations of milling reactions offer a new approach to tune and optimize mechanochemical processes.

References

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