Poster

Unveiling dehydration and solid-solid phase transition through single crystal-to-single crystal transformation: A case study of AZD9898

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Understanding the structural properties is crucial before exploring into the mechanistic aspects of dehydration of pharmaceutical hydrates and polymorphic transformations, such as solid-solid phase transitions. While various techniques exist for determining crystal structures, X-ray diffraction—encompassing powder and single crystal structure determination—stands out as the most commonly used method. In cases where single crystals of the initially hydrated phase transition to a polycrystalline phase, structure determination using powder methods becomes essential for establishing the dehydration mechanism of hydrated pharmaceuticals. Systems in which the hydrated phase retains its single-crystallinity upon dehydration pose experimental challenges, and only a few examples have reported the dehydration mechanism using single crystal X-ray structure determination. In this study, we present one such rare system involving AZD9898, which undergoes single-crystal-to-single-crystal dehydration and solid-solid phase transition.

Previously considered as a potential active pharmaceutical ingredient, AZD9898 Form A hydrate was discovered during development and undergoes dehydration upon heating to yield anhydrous Form B. Further heating triggers a solid-solid phase transition to a new anhydrous phase, Form C. This study provides crystal structures of Form A, B, and C, obtained by heating the single crystal of Form A in situ on the diffractometer, thus establishing the dehydration and solid-solid phase transition mechanisms. The dehydration from Form A hydrate to Form B anhydrous represents an isostructural process, while the solid-solid phase transition from Form B to Form C necessitates significant structural changes. Additionally, this study reports the correlation with relevant thermal profiles and vapor sorption behavior of these forms [1].

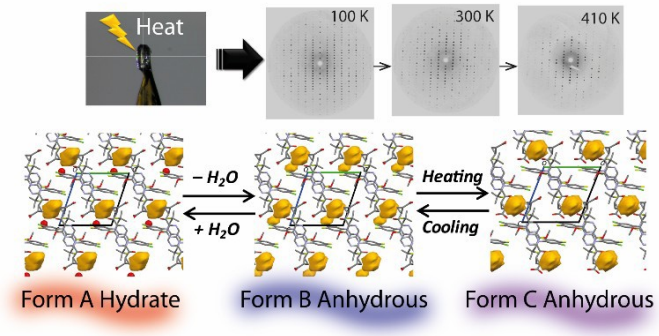

Figure 1. Isostructural dehydration from Form A hydrate to Form B, and solid-solid phase transition from Form B to C of AZD9898 were revealed by in situ single crystal-to-single crystal transformations.

[1] Pettersen, A., Putra, O.D., Light, M.E. & Namatane, Y. (2020). *CrystEngComm*, **22**, 7280.

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