Crystal structure determination of 2 polymorphs of 1,3-diethylurea from X-ray powder data

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1,3-diethylurea of formula $C_5H_{12}N_2O$ is a small organic molecule (an urea derivative) that has been recently studied in our laboratory since it has been shown, as 1,3-dimethylurea before [1,2], to significantly increase the time persistence at room temperature of the metastable γ form of pyrazinamide [3] (of formula $C_5H_5N_3O$), an active pharmaceutical ingredient used in the treatment of tuberculosis. [4,5] Indeed, when pyrazinamide is crystallized in the presence of 1,3-diethylurea by spray drying for example, it shows only the γ polymorph that can be preserved for several months without any sign of conversion to the stable polymorph α while the latter occurs in a few weeks in the absence of 1,3-diethylurea. This result is of prime importance as the γ polymorph possesses superior solubility and dissolution rate performances compared to the other polymorphs of pyrazinamide, thus anticipating a potential higher bioavailability of the drug product that could be formulated from the γ form pyrazinamide. Therefore, several research works are curremtly carried out in our laboratory to understand the interactions between 1,3-diethylurea and pyrazinamide which are responsible of this long-lasting persistence of the γ polymorph at ambient conditions.

However, nothing is known on the crystal structure of 1,3-diethylurea. Furthermore, several attempts to grow single crystals of 1,3-diethylurea have been made but all resulted in soft and brittle crystals essentially composed of the agglomeration of small randomly oriented crystals. Thus, we present in this communication our first results on the crystal structure determination of 1,3-diethylurea from X-ray powder diffraction patterns measured at the CRISTAL beamline of SOLEIL synchrotron. A polymorphic transition has been revealed in the temperature range [355 K – 370 K], thus leading to the existence of 2 polymorphic forms named forms I and II for the low and high temperature forms, respectively (Figure 1). A crystal structure solution for both polymorphs will be detailed in this communication.

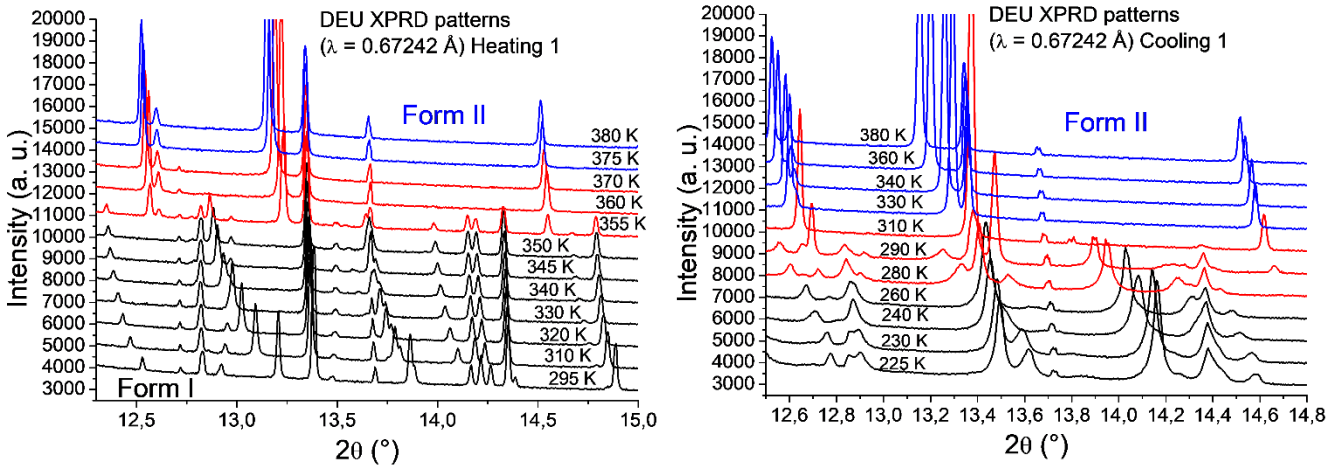

Figure 1. XRPD patterns of DEU measured (left) upon heating from 295 K to 380 K and (right) upon cooling from 380 K to 225 K..

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