Dehydration as a Preparative Tool in the Crystal Structure Landscape Investigations of Tenofovir

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Streszczenie

In this work, we present the use of diffraction-guided dehydration and the complementary use of various diffraction techniques (including X-ray and electron diffraction) to fully explore the crystal landscape of the antiviral drug tenofovir (TEN). Thermally induced transformations of eight forms of TEN were described. The crystal structures of two polymorphs (orthorhombic α-TEN·H_2O and monoclinic β-TEN·H_2O), a series of hydrates (TEN·$x$$H_2O$, x = 5.5, 4.5, 3.8, 3.5, 3), as well an anhydrous form of TEN were described. Polycrystalline anhydrous TEN was obtained by dehydration of β-TEN·H_2O, and its crystal structure was determined by continuous rotation 3D electron diffraction (3D ED). It was shown that the crystal architecture and the location of water molecules have a significant impact on the behavior of crystals during dehydration, and it was indicated which ones are crucial for durability of obtained hydrates. The most important types of intermolecular interactions were described, including hydrogen bonds and π···π stacking. The dehydrations were tested using X-ray diffraction methods, such as variable-temperature single-crystal X-ray diffraction (VT SC-XRD) and variable-temperature micropowder diffraction (VT micro-PXRD), as well as 3D ED. It was demonstrated that the gradual temperature-/humidity-induced transformations between hydrates with high water content and anhydrous TEN [TEN·$x$$H_2O$ (x = 5.5–3) → α-TEN·H_2O → β-TEN·H_2O → TEN] are associated with the significant reconstruction of the crystal architecture from a planar hydrate (loose) to a compact (dense) one, and that this phenomenon is related to an irreversible phase transition between the two monohydrates α-TEN·H_2O → β-TEN·H_2O. Individual dehydrations were shown to occur as single-crystal-to-single-crystal or as single-crystal-to-powder transformations. The results obtained using X-ray and electron diffraction methods were supplemented with thermal (TGA/DTA) and spectroscopic (FT-IR) analyses.

Słowa kluczowe

Crystal structure, Crystals, Dehydration, Diffraction, Solvates

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