Factors determining Polymorphism of Leflunomide

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Leflunomide is a medicament for the treatment of rheumatoid arthritis. The aim of this work was to explore its properties in the crystalline state. Single crystals of the two polymorphic modifications of leflunomide were grown by slow evaporation techniques from different solvents. The X-ray diffraction analysis revealed that forms I and II of leflunomide belong to space group $P2_1/c$ with two and one independent molecules per asymmetric unit, respectively. Two out of the three molecules are very similar in conformation whereas the third one differs in the orientation of the amide group. The molecules arrange in a chain which in the form I is organized by N-H..O and N-H..N hydrogen bonds, while that in the form II shows just the N-H..N interaction.This way, the choice of the solvent of crystallization appeared to be decisive to obtain the desired polymorphic modifications of the compound.

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