3-Ethyl-3-phenylpyrrolidin-2-one (EPP) is an experimental anticonvulsant based on the newly proposed α-substituted amide group pharmacophore. These compounds show robust activity in animal models of drug-resistant epilepsy and are thus promising for clinical development. In order to understand pharmaceutically relevant properties of such compounds, we are conducting an extensive investigation of their structures in the solid state. In this article, we report chiral high-performance liquid chromatography (HPLC) separation, determination of absolute configuration of enantiomers, and crystal structures of EPP. Preparative resolution of EPP enantiomers by chiral HPLC was accomplished on the Chiralcel OJ stationary phase in the polar-organic mode. Using a combination of electronic CD spectroscopy and anomalous dispersion of X-rays we established that the first-eluted enantiomer corresponds to (+)-(R)-EPP, while the second-eluted enantiomer corresponds to (-)-(S)-EPP. We also demonstrated that, in the crystalline state, enantiopure and racemic forms of this anticonvulsant have considerable differences in their supramolecular organization and patterns of hydrogen bonding. These stereospecific structural differences can be related to the differences in melting points and, correspondingly, solubility and bioavailability.