Application of Thermal Analysis and X-Ray Diffraction Methods in the Study of Resolutions *via* Derivatives

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Thermoanalytical and X-ray diffraction methods were used in the study of molecular recognition processes during optical resolutions *via* diastereomeric salt formation.

The studied model compound was α-phenylethylamine, a basic resolving agent widely used in pharmaceutical industry. The efficiency of its resolutions by derivatives made of dicarboxylic acids with different chain lengths is generally quite high. For our studies, we used the derivatives made by dicarboxylic acid with the shortest carbon chain (oxalic aid) and a relatively long chained dicarboxylic acid (glutaric acid).

The chain lengths of the dicarboxylic acids and the size of the aromatic ring of the model compound were changed. The effects caused by structural changes were studied by thermoanalytical and single crystal X-ray diffraction methods. We found that the chain length has determining effect in the resolution processes. The thermoanalytical data were used to calculate solid-liquid binary phase diagrams. Depending on the chain length of the derivatizing dicarboxylic acid the thermoanalytical properties of the compounds and the phase diagrams show significant differences.

The effects of the methyl-substitution and the change of the phenyl ring to naphthyl ring in α-phenylethylamine were studied using the oxalic acid derivative. Calculated solid-liquid binary phase diagrams and single crystal X-ray diffraction structures were compared. The substitution of the aromatic ring, although it doesn't take part in the formation of the H-bond network, has a determining role in the resolution process. The thermoanalytical properties depend on the size of the aromatic part of the molecules.

The efficiency of the resolution was low using the derivative made by glutaric acid. Notwithstanding, in this case the use of achiral additives increased the efficiency to a high level. The additives were urea and its derivatives: N-methyl-urea, N,N'-dimethyl-urea and thiourea. X-ray powder diagrams and solid-liquid phase diagrams were calculated and measured. The studies show that urea increases the efficiency of the resolution by forming an eutectic with the crystallizing diastereomeric salt with 1:2 ratio, while the derivatives of urea act in a different way and they aren't detectable in the crystalline material.

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