Study of solubility equilibria in the chiral malic acid system

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1. Introduction

The chiral malic acid system is inherently interesting in terms of solid/ liquid equilibria and polymorphism and in particular with regard to the remarkable diversity of interpretations in literature. Various authors report up to three intermediate compounds and polymorphism of the racemate as well as the formation of solid solutions [e.g. 1, 2].
A comprehensive approach to describe the behaviour of the malic acid system by Kuhnert-Brandstätter and Friedl [2] furnishes proof of dimorphism of the racemate and partial miscibility both for the enantiomers and the racemate. Nevertheless, inconsistencies within the literature could not be overcome completely.
Profound knowledge of phase equilibria including polymorphism is of crucial importance for the design of a separation process. This is in particular true for systems showing complex behaviour and narrow "areas of operation" within the ternary phase diagram. As a consequence we intended to intensively study the binary and corresponding ternary phase diagram of malic acid in order to specify the limits of miscibility in the solid state and to quantify the stability regions of the polymorphs.

2. Experimental work

It is known that the combined use of thermal- and lattice analysis techniques promises the best results. Therefore experimental work on the malic acid system is performed by means of XRPD, DSC, TG-DSC and thermooptical analysis (TOA). Within this work melting phase equilibria are investigated and discussed. In addition solubility measurements in different solvents/ solvent mixtures are conducted. Thus a classical isothermal method with equilibrium devices is used. Liquid and solid phase analyses are performed be means of HPLC and XRPD.

3. Results & Discussion

Figure 1 depicts first preliminary results for the melting point phase diagram of the chiral malic acid system, indicating the formation of a racemic compound and a region of solid solutions at the racemic compound side. We encountered polymorphism of the racemate, which can be seen from the two melting points of the racemate in figure 1.
Lines within the figure are just guide the eye and visualise the possible progressions of the liquidus, solidus and solvus curves related to each polymorphic form. A proper verification of the liquidus lines by the equations of Schröder-van-Laar and Prigogine-Defay fails due to the presence of mixed crystals and the distinctive non-ideality of the malic acid system. In the figure enantiotropy is assumed according to [2]. However, the melting point temperatures and melting enthalpy determined, indicate monotropy of the racemic phases.
Throughout our experiments a stable second polymorphic form could not be resolved. Further work to clarify this contradiction will be done.

As a result from the DSC measurements the eutectic composition is considered to be fairly close to the pure enantiomer side at 98.5 wt%. In literature a region of partial miscibility among the eutectic point and the malic acid enantiomer side is proposed. However, own investigations at the outer sides of the melting point diagram did not succeed neither in confirming nor denying the existence of partial miscibility close to the pure enantiomers sides. It is doubtable from the experimental background, if measurements in this narrow region can yield a reasonable contribution to this question.

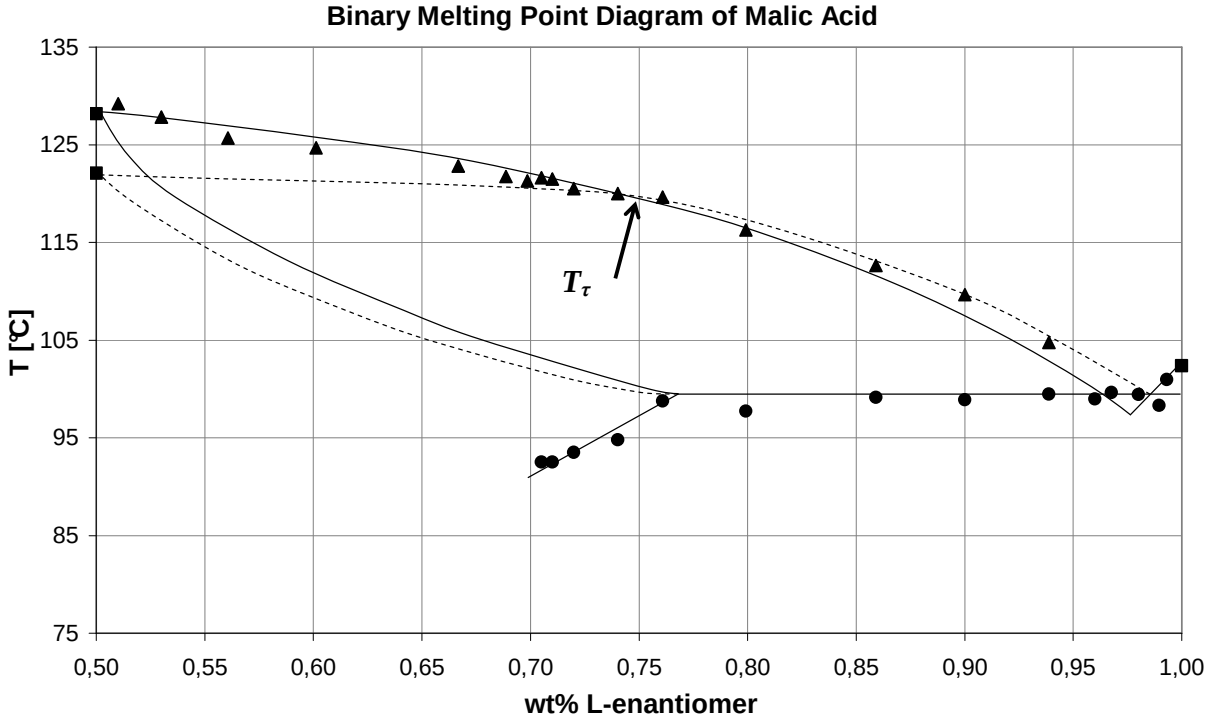

Fig. 1*: Preliminary melting-point diagram of malic acid enantiomer mixtures, as determined from DSC data. Lines are guides to the eye.* T_τ *indicates the temperature of polymorphic transition [2].*

4. Conclusion

The obtained results yield more detailed insight in the malic acid system. In our eyes the clear discrimination and determination of the existence of enantio- respectively monotropy is a key to understand the malic acid system more comprehensively.
Therefore further investigations will initially concentrate on the observed polymorphism and will be subsequently extended to the general influence of the solvent and solvent mixtures with respect to solubility equilibria of chiral substances on the basis of different types of phase diagrams.

5. References

[1] Ceolin R. and Szwarc H. and Lepage F.. On the Dimorphism of DL-malic acid. *Thermochim. Acta 158*, 1990, 347-352
[2] Kuhnert-Brandstätter M., Friedl L., Zur Frage der Existenz anomaler Racemate, *Mikrochim. Acta* II, 1997, 507-516