

# Chiral selectivity of the crystal packing in binary systems of enantiomers. A new way to quantify chirality

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The ability of a crystal lattice to differentiate the handedness of the constitutive molecules is a major issue when dealing with preparative enantiopurification via crystallization.

The chiral discrimination at the solid state can vary from 0 to 100 % . In the former case a complete solid solution exists between the enantiomers, in the latter case every lattice of a given enantiomer does not accept the intrusion of its antipode i.e. formation of a conglomerate. Polymorphism of these symmetrical components offers contrasted situations as depicted on the binary systems (1 to 4 ) below.

In practice, these phase diagrams show that when reaching high enantiomeric excess at a preparative scale is at stake , the management of the crystallization of a particular phase can dramatically improve the performance of the purification. Therefore, in order to set up a reliable enantiopurification both stable and metastable equilibria have to be carefully identified and the process (including nucleation, crystal growth, stirring mode and stirring rate, mode of filtration, etc.) has to be conducted accordingly (seeding, appropriate cooling rate, etc.).

At a given temperature a quantitative determination of the degrees of asymmetry of a molecule is proposed by using the stable (or metastable) binary heterogeneous equilibria with its antipode. For monophasic domains, this evaluation is based on the width in composition and on how far from the racemic mixture the boundaries are. For biphasic domains the evaluation corresponds to the algebraic departure in composition of the two co-existing phases. This quantification is shown to be temperature, composition and crystal lattice dependent. The assessment of the chiral character of an asymmetric molecule is therefore linked to the context in which the molecule is situated.

## References

1. Gallis, H., van Miltenburg, J.C., Oonk, H. (2000) *Phys. Chem. Chem.Phys.* **2**, 5619-5623.
2. Coquerel, G. (2000) *Enantiomer* **5**, 481-498.
3. Coquerel, G. (2004) *J. Phys. IV* **113**, 11-15.

Selected examples

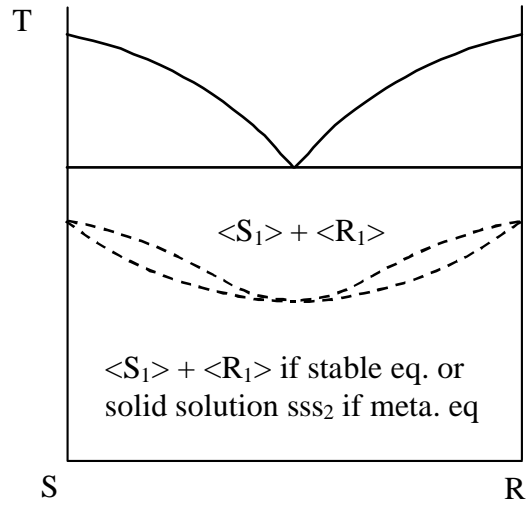


Figure 1

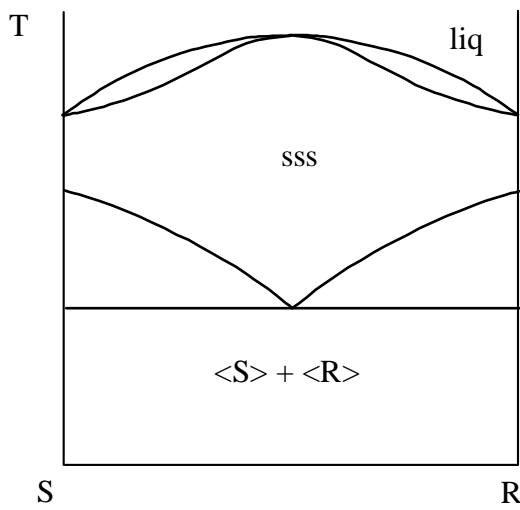


Figure 2

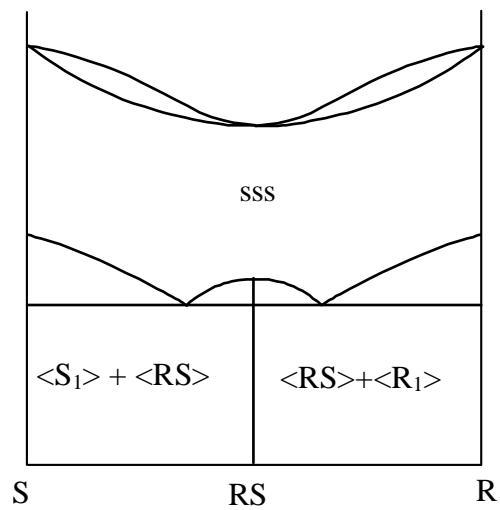


Figure 3

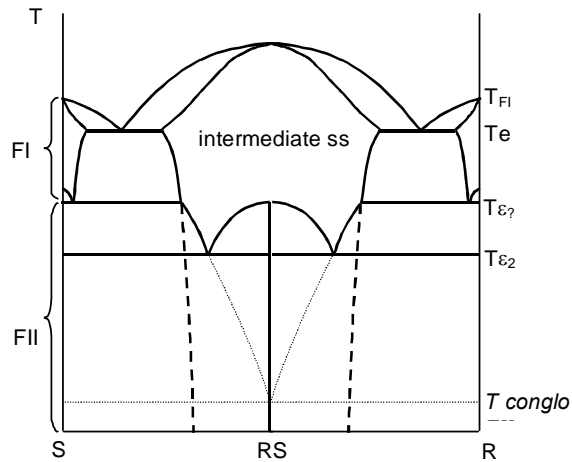


Figure 4