

## Disappearing conglomerates

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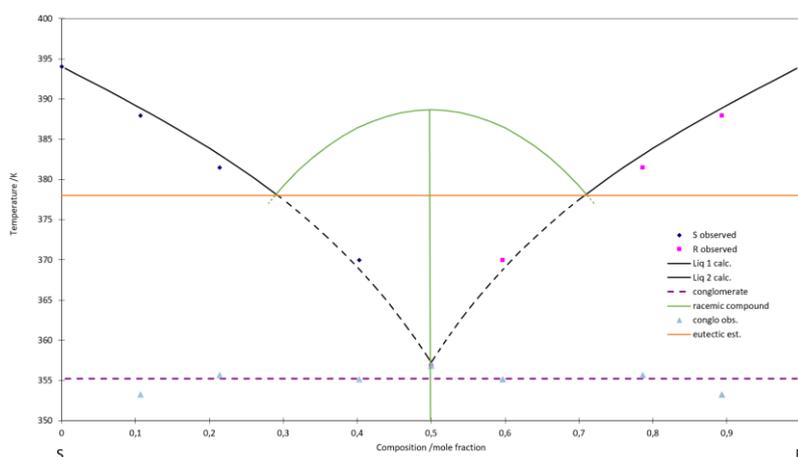
il ne faut pas souligner nos noms

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As the majority of active pharmaceutical ingredients are chiral, resolution methods to separate their enantiomers are of great importance for the pharmaceutical industry<sup>1</sup>. Preferential crystallisation, second order asymmetric transformation (SOAT) and deracemization are different processes for obtaining pure enantiomers;<sup>2</sup> however, these methods all have in common the need for a conglomerate forming system. The system discussed in this work is an atropisomer couple of enantiomers understood to be a conglomerate forming system<sup>3</sup>. Indeed, in the CSD, 2'-(phenylmethoxy)-[1,1'-Binaphthalen]-2-ol] (Binol-OBn) is reported with the space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub> (refcode UBULUB, CCDC 1443741) and the binary phase diagram with its two enantiomers possessing a 'stable' conglomerate has been established. However, upon crystallisation in our laboratory a stable racemic compound appeared. This new racemic compound was characterized by means of: Differential Scanning Calorimetry, IR spectroscopy, Second Harmonic Generation and single crystal X-ray diffraction.



**Figure 1** revisited binary system between enantiomers of 2'-(phenylmethoxy)-[1,1'-Binaphthalen]-2-ol]

### Discussion

The conglomerate melts about 30 degrees lower than the newly identified racemic compound. Therefore, the metastable conglomerate will be difficult to obtain again. With such a large difference in melting points, one can wonder how the conglomerate could have been observed in different laboratories. An explanation can be found in the complexity of the racemic compound structure which contains three molecules in the asymmetric unit, each of them with a different conformation. The structure of the racemic compound will be compared to that of the enantiomer. The following open question should now be carefully considered: how to predict the threat that such a case would occur in an industrial setting, while using a conglomerate forming system?

### References

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