

## Colloque VIA : Composés d'intérêts pharmacologiques

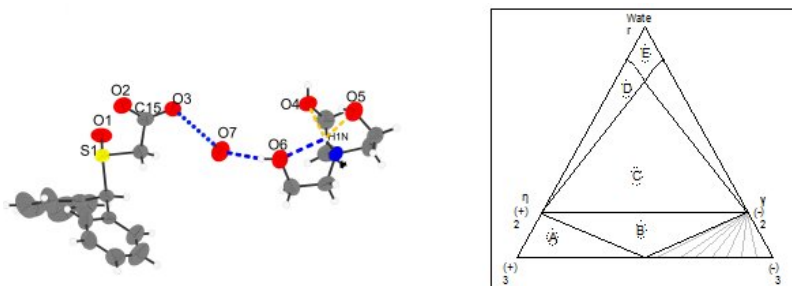
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### The Different Roles of Water Molecules in Chiral Discrimination in the Solid State

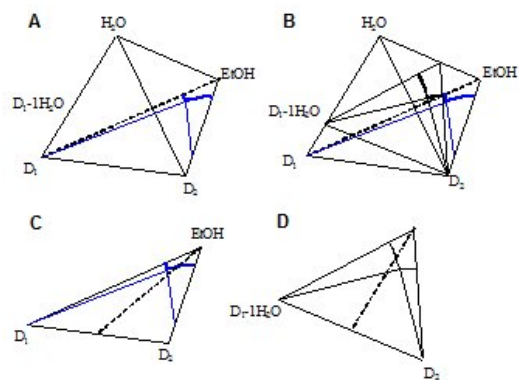
It is sometimes desirable to have a high degree of chiral discrimination in the solid state so that a quantitative enantio-purification can be achieved through a crystallisation process. Indeed, it can be necessary to overcome various problems such as : non selective asymmetric synthesis or partial racemisation. In addition to this recurrent problem, a classical pasteurian resolution remains also an economical way to access to a particular chiral molecule. Once again the chiral recognition in the solid state is thus at stake.

A single water molecule as detailed in the following example[1] can be the necessary key to open the chiral discrimination gate. R and S triethanolammonium modafinate form a complete solid solution when anhydrous components are considered. By contrast, when the R and S monohydrates are analysed a stable conglomerate is obtained without any detectable solid solution. A sharp difference is then obtained in the chiral discrimination in the solid state with or without water molecule.



Left : Visualisation of hydrogen bonds between modafinate anion and triethanolammonium cation through the bridging water molecule (O7). Right : Isothermal section of the ternary phase diagram [R and S triethanolammonium modafinate- water].  $\gamma$  and the  $\eta$  represent the R and S monohydrate salts.

The phase diagrams on the left hand side show the possible inversion of the nature of the less soluble salt when a hydrate crystallizes. In ethanol rich composition D2 is obtained. In the water rich region D1-1H<sub>2</sub>O is obtained.



This general example illustrates the usual strong impact of water molecules on molecular recognition in the solid state. It shows that the water molecules are most of the time an active partner in the chiral discrimination rather than just a space filler inside the crystal lattice.

[1] N. Wermester, O. Lambert ; G. Coquerel ; Cryst.Eng. Comm. ; in Press 2008-10, 724-733