

## **Progress in Crystal Structure Prediction for Diastereomeric Salts**

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The development of a methodology that will allow the prediction of the structure and relative stability of diastereomeric salt pairs could have an immense impact in the manufacture of chemical entities in optically pure form as it will assist the design of separation processes based on diastereomeric resolution. The solubility differences of the diastereomeric pair is an important determinant for the resolution efficiency of the resolving agent and can be estimated *via* lattice (free) energy calculations.

This paper develops an approach to the crystal structure prediction of such systems based on global lattice energy optimisation. To alleviate the mathematical complexity of the solution space due to the presence of two entities in the asymmetric unit, the search is guided by a statistical analysis of the Cambridge Structural Database for common coordination environments. A distributed multipole model for the dominant electrostatic interactions and high level *ab initio* calculations for the intramolecular contributions allow the quantitative calculation of the relative stabilities of the p- and n-salt for a given resolving agent.

The methodology is successfully applied in the case of 1-phenylethylammonium-2-phenylpropanoate. All experimentally determined known forms and their relative stabilities are predicted.

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