

Oral Contributions

[MS25 - 03] **Chiral Discrimination in the Solid State-Molecular Interactions in Inclusion Compounds and Diastereomeric Salts of Cinchona Alkaloids.** Nikoletta B. Báthori, Luigi R. Nassimbeni,

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The enantiomeric purity of a chemical entity is important in various industries, such as analytical, food, pesticide and pharmaceutical. When a compound is produced as a racemic modification typically only one of the enantiomers exhibits the required biological effect. The main resolution methods include spontaneous resolution by crystallization, enzymatic transformations and chromatographic methods. Inclusion formation of chiral host compounds, such as cyclodextrins or deoxycholic acid derivatives is also a constructive technique for resolving enantiomers. In addition, formation of diastereomeric salts is also a widely used practice. An example is the employment of cinchona alkaloids in the separation of racemic modifications of carboxylic acids.[1] Interestingly we still do not fully understand the mechanism of chiral discrimination and the lack of this knowledge limits our ability of designing the 'perfect' resolving agent for a given racemic modification.

In order to understand the molecular recognition during the resolution process we have studied a series of inclusion compounds [2] and diastereomeric salt formations [3] to map the correlation between structure and the success of the enantiomeric resolution. A series of competition experiments were set up to measure the selectivity profile of a given host compound (resolving agent) towards a pair of guests A and B (enantiomers). Crystals were harvested and the selectivity coefficient was defined at each step to describe the efficacy of the discrimination of

the host for a given guest. In case of inclusion compounds correlation has been found between selectivity, the torsional flexibility of the host, and the concomitant remaining volume in the crystal structure that accommodates the guest. This was confirmed by employing the 'Dutch Resolution method' for the same racemic modification when the combination of two (occasionally three) generally homochiral, structurally related resolving agents was used to improve the enantiomeric excess of the targeted racemate. [4]

[1] Toda, F., Ed. *Enantiomer Separation. Fundamentals and Practical, Methods*; Kluwer: Norwell, MA, 2004.

[2] a) Báthori, N. B., Nassimbeni, L. R. (2010). *Cryst. Growth & Des.*, 10, 1782-1787.

[3] a) Báthori, N. B. Nassimbeni, L. R. Oliver, C. L. (2011) *Chem. Commun.*, 47, 2670–2672. b) Nassimbeni, L. R, Báthori, N. B., Curtin, T.-L. (2012) *Cryst. Growth & Des.*, 12, 4144–4148.

[4] Báthori, N. B., Nassimbeni, L. R. (2012) *Cryst. Growth & Des.*, 12, 2502–2507.

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