

Supramolecular Entities in Chiral Recognition. Interpretation of Resolution Processes

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Chiral resolutions consist of the following general stages:

1. Reaction of the mixture of the two enantiomers with a proper, optically active resolving agent to form diastereomers,
2. Separation of the diastereomers, based on different distribution between phases,
3. Recovery of the enantiomer(s) from the diastereomer(s).

Although in Stage 1 usually diastereomeric salts are formed by an acidic racemate and a basic resolving agent (or vice versa), and Stage 2 is carried out by fractional crystallisation, other ways are available, as well. The diastereomers can also be coordination complexes (Mravik et al. 1997, *Angew. Chem. Int. Ed. Engl.* **36**, 1534) or supramolecular compounds without ionic building blocks (Illés et al. 2000, *J. Therm. Anal. Cal.* **61**, 745).

Usually, Stage 1 is explained as bimolecular reactions between the enantiomers and the resolving agent, resulting in two bimolecular associates, the diastereomers. These bimolecular associates are then distributed unequally between the two phases in Stage 2. Several observations, however, point to the fact that it may not be sufficient to take only bimolecular associates into account in the resolution. Larger entities, containing both of the enantiomers in a ratio different from 1:1, seem to be a part of the process.

Participation of a solid phase or solid phases (molecular crystals) brings about a supramolecular aspect itself. It is well-known that the type and structure of the resulting crystal(s) influence the possibilities of the intended resolution. That is why the solid-liquid phase diagrams are important tools in the design of optical resolutions.

The assumption of associates of several molecules seems essential in interpreting phenomena and processes in systems consisting of several components. In the so called Dutch resolutions better results were obtained with a mixture of two or more structurally related resolving agents than with any one of them (Vries et al. 1998, *Angew. Chem. Int. Ed. Engl.* **37**, 2349). On the other hand, the efficiency of resolution could be improved by starting from a mixture of racemates of similar structure, too (Bálint et al. 2000 *Tetrahedron Asymmetry* **11**, 809). A proper achiral additive can also enhance the efficiency.

Kinetic effects are also important. If one or more solid phases are involved, nucleation requires the formation of a larger associate anyway. Formation of mixed associates may be much faster than that of pure ones (even if the latter are more stable), so mixed structures may dominate first, then they may transform to more stable product. Growth of nuclei may also involve joining larger (and possibly mixed) associates to the growing new phase.

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