

TITLE: SEPARATION OF RACEMIC MANDELIC ACID BY ENANTIOSELECTIVE PRECIPITATION USING CHIRAL IONIC LIQUIDS

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ABSTRACT: In spite of sharing the same physical and chemical properties (excepting for their optical rotation), the two enantiomers of a drug can be discriminated by biological systems. While one of the enantiomers exerts the desired pharmacological effect, the other may be inert, less potent or even toxic. Under this scenario, pharma industry is constantly searching for efficient methods to obtain enantiopure drugs. The direct synthesis of the desired enantiomer represents the most widely used route; yet, its high cost and operational complexity are restricting substantial progress in the development of enantiopure drugs. As a simpler, cheaper and more flexible alternative, the chiral resolution of racemates emerged.

In this work, the enantiomeric precipitation of racemic drugs is proposed as a simple and low-cost enantioseparation technique. To this aim, chiral ionic liquids (CILs) were applied as chiral selectors in the selective precipitation of mandelic acid (MA) enantiomers (here used as model drug). Aqueous solutions of CILs bearing chirality on the cation or the anion were evaluated regarding their capacity to selectively precipitate one enantiomer. The precipitation studies were performed using different CILs' aqueous solutions, where the impact of the CIL structure and chirality was investigated. The influence of different operational conditions (e.g., time, agitation speed, CIL concentration and MA concentration) on the formed precipitate was additionally appraised. Remarkably, the developed CIL-based precipitation approach led to c.a. 49% of enantiomeric excess in a single-step and without further additives.

Keywords: Chiral ionic liquids, Enantioseparation, Precipitation, Mandelic acid

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