# Chiral Interactions at the Molecular Level: Insights from NMR and Computational Studies

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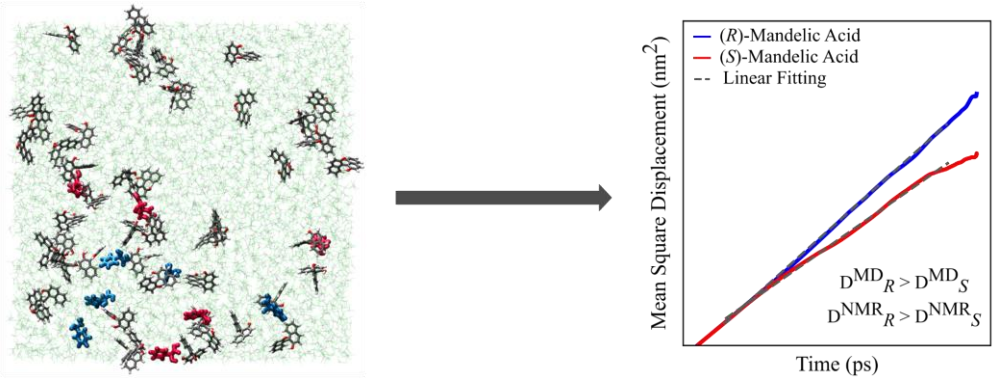
The separation and identification of enantiomers is critical for the pharmaceutical, agricultural, and food industries. The matrix-assisted diffusion-ordered spectroscopy (DOSY) approach is emerging to evaluate chiral molecules employing a chiral matrix to separate enantiomeric mixtures via Nuclear Magnetic Resonance (NMR) spectroscopy. However, this method needs detailed insight into the chiral recognition modes and the complexation process at the molecular level.[1] Here, we integrate computational methods with experimental investigations to explain the differences in complexation between mandelic acid enantiomers and (*R*)-BINOL as a chiral matrix. $^{1}$H and diffusion NMR measurements in $CDCl_3$ were carried out using the *Oneshot* pulse sequence.[2] at 25 °C on a 600 MHz spectrometer. DFT and molecular dynamics (MD) studies were performed to support experimental findings.[3] The experimental results reveal that the mandelic acid enantiomer exhibiting the highest shielding effect in the NMR spectrum shares the same chirality as the employed BINOL. On the other hand, it was observed that the enantiomer interacting more strongly (with a lower diffusion coefficient) has the opposite stereochemistry to the BINOL. DFT studies at the *M06-2x*/*cc-pVTZ* level confirm the preferred formation of enantioselective binding and emphasize the role of intermolecular hydrogen bonding to explain the observed shielding effect in the NMR spectrum. The MD simulations are able to give dynamic properties such as diffusion coefficients in good agreement with the experimental data. Additionally, the classical simulations offer valuable insights into the complexation process between (*R*)- and (*S*)-mandelic acid and BINOL over time, enhancing our understanding of experimental observations. This integrated approach illustrates the feasibility of enantiodiscrimination through NMR and underscores the indispensable role of theoretical studies in unveiling molecular recognition processes.

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