Analysis of Asymmetric Reduction of Ketones Using Three-Dimensional Electronic States

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In this study, we introduced an approach combining transition state analysis and data-driven modeling that leverages the electronic states of ketone substrates to systematically analyze the selectivity of asymmetric reduction. Transition state analysis of the reduction of acetophenone and trifluoroacetophenone using the Corey–Bakshi–Shibata catalyst, B-chlorodiisopinocamphenylborane, and alpine borane successfully explained the reaction selectivity. Analysis was extended to a broader set of 315 asymmetric reduction reactions by incorporating the grid-based electronic and electrostatic features of the ketone substrates. The high predictive performance of the model (r2test = 0.82) confirms its generalizability and demonstrates its potential application in rational reaction design and catalyst development. Our method provides a comprehensive framework for analyzing and interpreting reaction mechanisms through the calculation of 3D electronic states, offering valuable insights into reaction pathways and selectivity.