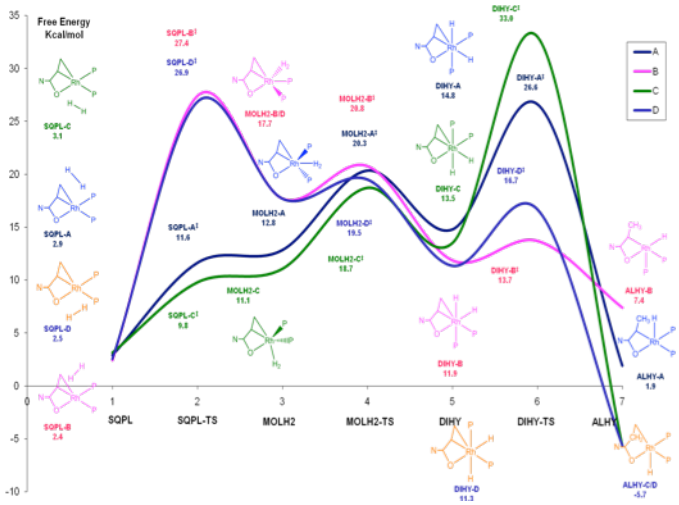
The earlier stages of this research provided a new computational tool for the accurate prediction of enantiomeric excesses for a reaction that is widely used in basic research and industrial processes, namely the rhodium-catalyzed enantioselective hydrogenation of enamide-based dehydroamino ester derivatives. This computational method, based upon an implementation of the Norrby Q2MM protocol, is now being extended to other classes of hydrogenation substrates, including acrylate derivatives, carbonyl compounds, and imines. The first stage of such an investigation is a detailed quantum mechanical study of the mechanism of the desired reaction.



Pathways for Rh(I) catalyzed hydrogenation of acrylamides

In the case of acrylic acid derivatives, the QM investigation revealed subtle differences in the mechanism compared to the previously more widely studied enamides. The main differences in the structures and energetics of the acrylate hydrogenation can be traced to the smaller ring size of a chelate, which leads to a weaker coordination of the alkene double bond to the rhodium, and the absence of a second acceptor that was provided in the enamide/ester substrates. Together, these differences lead to higher relative free energies of the species involved in the pathway. These results have important consequences for the overall reaction because an isomerization between competing pathways now becomes energetically competitive.