(P3)

Mechanistic investigation of the enantioselective titaniumtartrate catalyst

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In 1980 Sharpless and Katsuki achieved a breakthrough in the enantioselective epoxidation of allylic alcohols. They showed that in the presence of tert-butyl hydroperoxide (TBHP) and a complex of titanium and a chiral tartrate ligand, an allylic alcohol could be converted into an epoxide with good yield and excellent enantioselectivity.[1] They achieved a selectivity that was, until then, only seen in enzymatic catalysis. Besides that, the reaction is chemoselective, it preferentially converts the allylic carbon-carbon double bound. This reaction is still significant for many processes in the production of fine chemicals where chiral intermediates are very valuable.

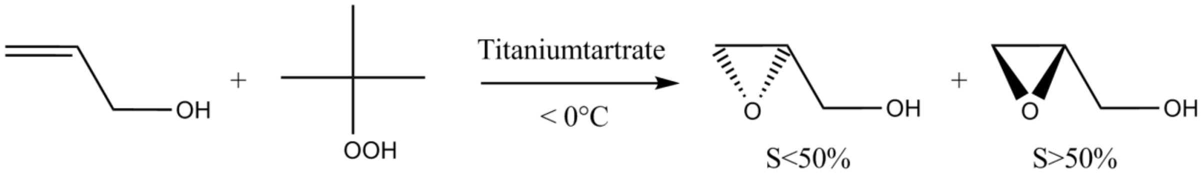

Figure 1: *The enantioselective Sharpless epoxidation, in the presence of a dimeric complex of titanium and a tartrate-ester, an allylic alcohol is epoxidized by TBHP with an excess towards a specific enantiomer.*

With recent advances in computational power it becomes possible to apply ab initio techniques to simulate the complete complex instead of using limited models as was done in earlier studies.[2] In this work a full model for the catalyst was used to predict the selectivity and kinetics of the Sharpless epoxidation. To accomplish this, a comparative study was made based on free energy instead of enthalpy to account for the significant influence of entropic contributions. With this approach it is possible to accurately predict the enantiomeric excess for a given substrate. Using the full structure as model also provides insight to the specific steric interactions leading to a certain selectivity revealing more details about the mechanism including accurate knowledge of the dimensions of every reaction step. With these dimensions a porous material can be searched in which the complex will be encapsulated thus designing a heterogeneous catalyst for the proposed reaction. Metal organic frameworks such as MIL-101[3] would be ideal for this task due to the possibility to have large cages with relatively small pores that can trap the complex. To model the behavior of the new catalyst, techniques that can take into account a large number of atoms are used, such as a QM/MM multilayer methodology.

References

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