Synthesis of Chiral Vanadium Phosphonates and their Catalytic Activity

Robert Edgar Ellenwood Final Seminar September 17, 2004

Asymmetric catalytic reactions are some of the most interesting and fundamentally important processes in chemistry. Chiral chemistry is most impressively demonstrated by the interactions of enantiomeric molecules with biological systems. In this sense, it is extremely important to investigate catalytic processes and to continue searching for new and better catalysts and catalytic reactions. Several asymmetric processes are used in industry and these include key intermediate steps in the synthesis of pheromones, Vitamin E, aspartame, and several key therapeutic drugs (Figure 1).[1] Two significant asymmetric heterogeneous catalytic processes are the hydrogenation of an α-keto ester pril intermediate using a Pt / Al_2O_3 surface modified with cinchona alkaloids and the hydrogenation of a β-keto ester obesity drug using a Raney-Ni / NaBr surface modified with tartrate.

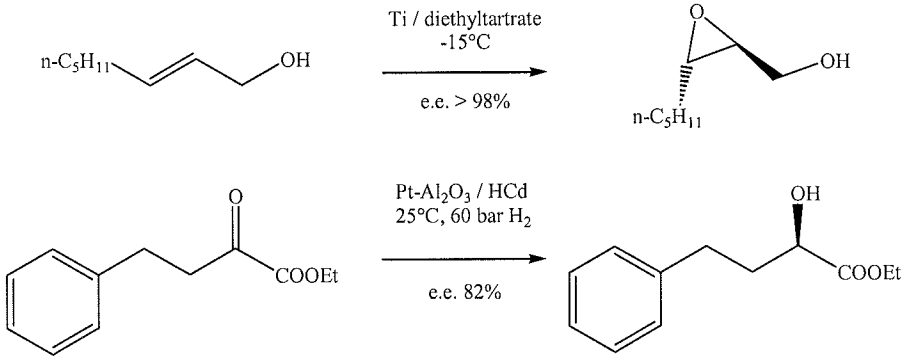


Figure 1: Two industrially important catalytic asymmetric reactions

Although most commercially significant asymmetric transformations use homogeneous catalysis, research in the past two decades has intensified in the area of asymmetric heterogeneous catalysis. The thrust behind this interest is to develop recyclable catalysts that reduce the costs of unrecoverable metals and ligands, that are easy to separate from product mixtures, and that improve the 'green-ness' of the industrial process. Heterogeneous catalysts are commonly prepared by 'heterogenizing' existing homogeneous catalysts or by altering catalytic materials with chiral modifiers.[2-4] Common 'heterogenization' techniques include tethering catalysts to insoluble supports, occluding catalysts in organic or inorganic polymeric supports, and using biphasic mixtures to separate the catalyst from the substrates and products.

A slightly different approach is to synthesize a catalytically active insoluble polymer from enantiopure molecular building blocks. In this approach, all of the metal

sites of the surface would be catalytically active and the use of chiral ligand building blocks would result in the formation of a chiral surface. Vanadium phosphonates could be useful for this approach and are prepared by treating vanadium starting materials with phosphonic acids. Vanadium phosphonates exist as soluble cage and cluster compounds, 1-dimensional chain structures, 2-dimensional layered structures, and 3-dimensional polymeric structures.[5-7] These structures have been studied for their interesting magnetic, sorptive, and potential catalytic properties as well as their structural diversity. To date, no reports of the synthesis of vanadium phosphonates with enantiopure phosphonic acids has been published.

The alkylation of lithium-stabilized alkyl phosphonates proceeds stereoselectively if the phosphonate is chelated with a chiral auxiliary (Figure 2). This lithium-stabilized alkylation reaction has been studied extensively and the most common chiral auxiliaries are *trans-N,N'*-dialkyl-1,2-diaminoalkanes,[8] (-) ephedrine,[9] and other substituted *N*-alkyl-β-amino alcohols.[10] Using these auxiliaries, chiral phosphonates are produced in high yields (> 90%) and with excellent diastereoselectivities (98 : 2). However, these chiral auxiliaries can be expensive, can take multiple steps to prepare, and can hydrolyze under humid conditions.

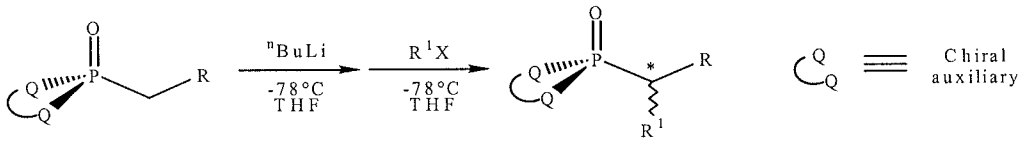
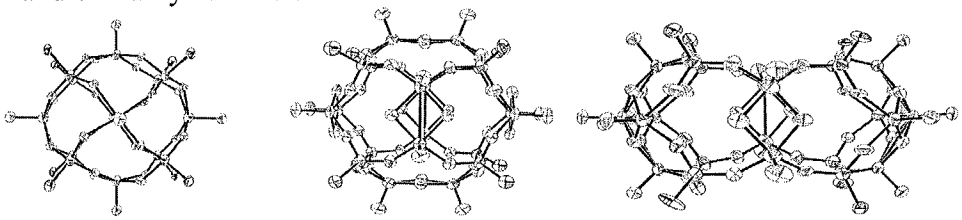


Figure 1: Asymmetric alkylation of lithium-stabilized phosphonates

To determine if 1,1'-binaphthyl-2,2'-diol, BINOL, could also serve as a chiral auxiliary, (*S*(-)BINOL)P(O)CH_2Ph was prepared by treatment of Cl_2P(O)CH_2Ph with *S*(-)BINOL in the presence of two equivalents of triethylamine. Resolved BINOL is commercially available, relatively inexpensive, and C_2-symmetric, and (BINOL)P(O)CH_2Ph was found to be stable under humid conditions. Further, treatment of (*S*(-)BINOL)P(O)CH_2Ph with butyllithium and alkyl halides (RX = MeI, EtI, allylBr, $PhCH_2Br$) was found to proceed with good yields (up to 94%) and good diastereoselectivities (up to 91 :9). Upon purification by column chromatography, the chiral auxiliary from (*S*(-)BINOL)P(O)CHMePh-*S* was cleaved under basic conditions and enantiopure $(HO)_2$P(O)CHMePh-*S* was isolated.

Treatment of vanadium starting materials with chiral and achiral phosphonic acids and phosphonates provided the soluble $[BuPPh_3]_4[(V_2O_2(OH)_2)_6(O_3PR)_8]$ R = CH(CH_2Ph)Pr and CH(Et)Pr, $[(VO)_6(O_3PR)_8\{Cl\}]$ R = CH_2Ph, CHMePh-*S*, and $[(V_{14}O_{22})(OH)_4(O_3PR)_8]^{6-}$ with R = CHEtPr, CH(CH_2Ph)Pr, and CH(Me)Ph-*S* cage complexes. These are the first reported examples of vanadium phosphonate cage molecules synthesized with racemic and enantiopure phosphonate starting materials. In addition, treatment of V_2O_5 with $(HO)_2$P(O)R in ethanol, where R = Ph and CHMePh-*S*, afforded (VO)(O_3PR)·yEtOH·xH_2O. (VO)(O_3PCHMePh-*S*)·H_2O is the first layered vanadium phosphonate material synthesized using an enantiopure phosphonic acid.

These materials were tested for catalytic activity in the asymmetric epoxidation of geraniol and cinnamyl alcohol.



a) b) c)

Figure 3: a) $[(VO)_6(O_3PR)_8\{Cl\}]$, b) $[(V_2O_2(OH)_2)_6(O_3PR)_8]^{4-}$, and c) $[(V_{14}O_{22})(OH)_4(O_3PR)_8]^{6-}$

References

1. Blaser, H. U.; Spindler, F.; Studer, M. "Enantioselective catalysis in fine chemicals production" *Appl. Catal.,* A **2001**, *221*, 119-143.

2. McMorn, P.; Hutchings, G. J. "Heterogeneous enantioselective catalysts: strategies for the immobilization of homogeneous catalysts" *Chem. Soc. Rev.* **2004**, *33*, 108-122.

3. Song, C. E.; Lee, S.-g. "Supported Chiral Catalysts on Inorganic Materials" *Chem. Rev.* **2002**, *102*, 3495-3524.

4. Saluzzo, C.; ter Halle, R.; Touchard, F.; Fache, F.; Schulz, E.; Lemaire, M. "Recent progress in asymmetric heterogeneous catalysis: use of polymer-supported catalysts" *J. Organomet. Chem.* **2000**, *603*, 30-39.

5. Clearfield, A. "Metal phosphonate chemistry" *Prog. Inorg. Chem.* **1998**, *47*, 371-510.

6. Khan, M. I.; Zubieta, J. "Oxovanadium and oxomolybdenum clusters and solids incorporating oxygen-donor ligands" *Prog. Inorg. Chem.* **1995**, *43,* 1-149.

7. Zubieta, J. "Clusters and solid phases of the oxovanadium-phosphate and -organophosphonate systems" *Comments Inorg. Chem.* **1994**, *16*, 153-183.

8. Bennani, Y. L.; Hanessian, S. "The asymmetric synthesis of α-Substituted α-Methyl and α-Phenyl Phosphonic Acids" *Tetrahedron* **1996**, *52*, 13837-13866.

9. Moody, C. J.; Morfitt, C. N.; Slawin, A. M. Z. "Preparation of chiral α-diazophosphonic acid derivatives" *Tetrahedron: Asymmetry* **2001**, *12,* 1657-1661.

10. Denmark, S. E.; Chen, C. T. "Alkylation of Chiral, Phosphorus-Stabilized Carbanions - Substituent Effects On the Alkylation Selectivity" *J. Org. Chem.* **1994**, *59*, 2922-2924.