October 2002

Organic Chemistry Cume

Department of Chemistry
University of Missouri—Columbia
Saturday, October 5th, 2002
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Announced Reading: **"Nobel Lectures 2001"**

Question 1. Asymmetric Hydrogenations. (30 points)

Based on the Nobel Lecture by Prof. Dr. William S. Knowles published in *Angew. Chem. Int. Ed.* **2002**, *41*, 1998-2007.

(a) Knowles performed the first asymmetric hydrogenation experiment using a strategy that combined _______________'s hydrogenation catalyst with the methods for the synthesis of chiral phosphanes by __________ and __________. Alpha-Phenylacrylic acid was reduced with 15% enantiomeric excess. Draw the substrate, the catalyst, the structure of the phosphane used (at least in principle), and the product (no need to show stereochemistry). (7 points)

(b) Draw perspective structures of (*S*)-PAMP and of (*R*)-CAMP (methylcyclohexyl-*o*-anisylphosphane). Do not use any abbreviations, draw complete line structures. (10 points)

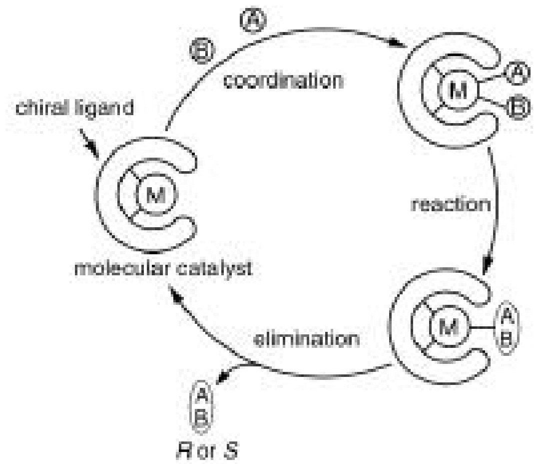
(*S*)-PAMP	(*R*)-CAMP

(c) Outline a synthesis of (*R*)-CAMP (methylcyclohexyl-*o*-anisylphosphane) starting from the chiral phosphinoxide with o-anisyl, methyl and OMen ligands. State what “OMen” stands for. Show how the cyclohexyl group is introduced. Show how the phosphinoxide is deoxygenated. (10 points)

(d) Knowles points out that the “inventive process is not clearly understood” and he offers various insights as to how inventions happen. Do you recall one of his philosophical tidbits? (3 points)

Question 2. Asymmetric Catalysis: Science and Opportunity. (35 points)

Based on the Nobel Lecture by Prof. Dr. Ryoji Noyori published in *Angew. Chem. Int. Ed.* **2002**, *41*, 2008-2022.



(a) The scheme shown on the left is a reproduction of Figure 1 of Noyori's review and illustrates the general principle of asymmetric catalysis. In your own words, explain the message this scheme is to convey. (5 points)

(b) The synthesis of BINAP was not easy and Noyori discusses it in some detail. One successful method involved the resolution of the corresponding bis-phosphinoxide of BINAP and its subsequent deoxygenation. The resolution was accomplished by fractional crystallization of the product formed by treatment of bis-phosphinoxide of BINAP with camphorsulfonic acid. Draw the structure of that product; use R*-SO_3H for camphorsulfonic acid. The deoxygenation was carried out with $SiHCl_3$ and NEt_3. What happens to the reagents in this process? (10 points)

Compound that is being resolved.	Fate of $SiHCl_3$ and NEt_3?

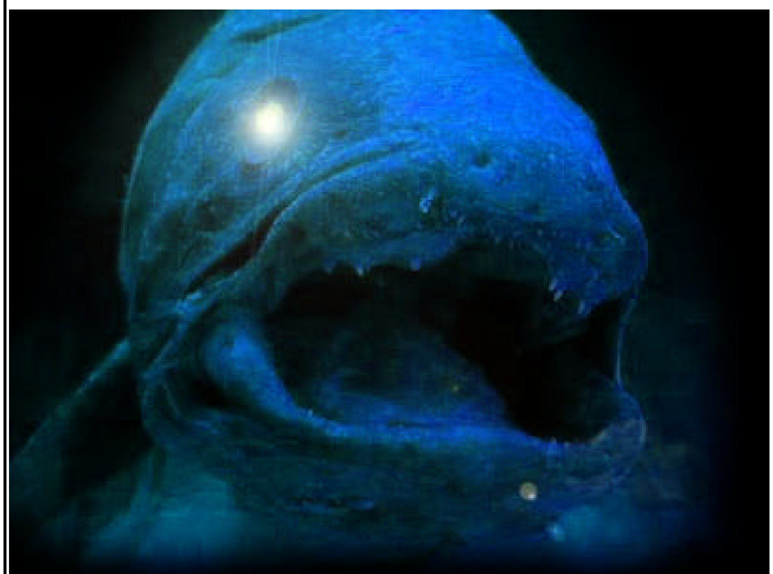
(c) In 1986, a major breakthrough occurred with the discovery that asymmetric catalytic hydrogenation of a variety of functionalized alkenes can be accomplished with BINAP-Ru(II) dicarboxylate complexes. The review shows molecular models of these complexes in Figure 5. What is the coordination number of Ru(II) in these complexes? How are the carboxylates bonded to Ru(II)? Are the carboxylates *cis* or *trans* with respect to each other? Answer these questions and then draw either the (*R*)- or the (*S*)-BINAP-Ru(II) diacetate complex as best as you can (e.g. draw one of them and write whether it is *R* or *S*). This complexes break the H-H bond by way of _______________ (heterolysis or homolysis). (10 points)

(d) A general method for the asymmetric catalytic hydrogenation of simple ketones was discovered in 1995. This method involves catalysts of the type [RuX_2(phosphane)$_2$(diamine)] and the presence of ____________________________. What is X? Give an example of a diphosphane (with stereochemistry) used for the "(phosphane)$_2$" unit. For <u>one</u> of the three diamines discussed in the review, provide the structure (with stereochemistry) and the name. (10 points)

Question 3. Searching for New Reactivity. (35 points)

Based on the Nobel Lecture by Prof. Dr. K. Barry Sharpless published in *Angew. Chem. Int. Ed.* **2002**, *41*, 2024-2032.

(a) What is the name of this creature? And what does this dinofish have to do with Dr. Sharpless search for new reactivity? (6 points)



(b) While many chemists like to employ the terms "clever", "elegant" or "novel" to celebrate chemical milestones, Sharpless writes how his Quaker upbringing made him value "useful" chemistry the most. With respect to the chemical reactions, what does Sharpless want to imply with "useful"? (6 points)

(c) Mechanistic studies showed that $[Ti(dipt)(O\text{-}i\text{Pr})_2]_2$ (dipt = diisopropyl tartrate) is the most reactive species in the titanium-tartrate catalyzed asymmetric epoxidation of allylic alcohols. Draw the structure of this reactive species as best as you can (and draw the dipt structure in full). (8 points)

(d) Name five metals other than titanium that catalyze the epoxidation of allylic alcohols by TBHP. These metals feature "ligand-decelerated" catalysis. Briefly explain the meaning of the term "ligand-deceleration." (7 points)

(e) The catalytic asymmetric dihydroxylation employs osmium tetroxide and “cinchona” alkaloids. Sharpless refers to the cinchona alkaloids as substituted **quinuclidines**. Draw the structure of quinuclidine. The actual catalyst actually is an ammonium salt of quinuclidine. Any idea what R-groups are attached to make the ammonium salt? The cinchona alkaloids also contain a **quinoline** moiety. Draw the structure of quinoline. Do you remember how the quinuclidine and the quinoline are connected? Draw the structure of a cinchona alkaloid as best as possible. (8 points)

Quinuclidine	**Ammonium salt of quinuclidine**
Quinoline	**Cinchona alkaloid**