

EXPERIMENT B

Homogeneous Catalysis

Nickel-catalyzed isomerization of hept-3-ene.¹ Transition metal-catalyzed cross-coupling reactions.^{2,3}

In the first part of this experiment you will synthesize a nickel phosphite complex, tetrakis(triethylphosphite)nickel(0), that is a precatalyst for the isomerization of alkenes. The catalytic reaction is homogeneous and the active catalyst is prepared via protonation of the phosphite complex with H_2SO_4 in the presence of the substrate hept-1-ene. You will then monitor the isomerization of heptene by Gas Chromatography, under a variety of conditions. To further probe the mechanism of this reaction you will protonate the nickel complex with trifluoroacetic acid in an NMR tube and attempt to detect the hydride ligand.

The second part of this experiment involves a nickel-catalyzed coupling reaction between an aryl Grignard and an alkyl halide, commonly known as the Kumada coupling (Grignard cross-coupling). This reaction is one of a general class of reactions called cross-coupling reactions, and in this case you will synthesize an alkylthiophene, a common precursor for organic electronic materials.

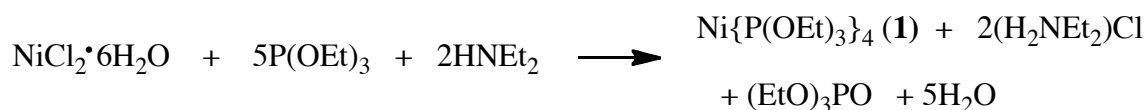
Both of these reactions introduce you to homogeneous catalysis and each involves a simple mechanism of a transition-metal catalyzed process.

INTRODUCTION.

Homogeneous catalytic reactions are those in which both the substrate and the catalyst are in the same phase, and although there are common examples of such processes in organic chemistry (e.g. acid catalysis), this experiment introduces transition-metal-catalyzed reactions. Transition-metal based homogeneous catalysts are often inorganic or organometallic compounds that can coordinate to the substrate and induce some change through bond forming or breaking reactions. In many cases the active catalyst is a coordinatively unsaturated species (often 16-electron) that is generated from a more stable precatalyst by loss of a ligand. Common steps in a catalytic cycle are coordination, oxidative addition, insertion, elimination, reductive elimination and decomplexation reactions. Many types of reactions now have efficient transition-metal based catalysts, for example hydrogenation, carbonylation, polymerization, and oxidation to name a few. In the first part of this experiment you will investigate alkene isomerization catalyzed by a nickel complex. Alkene isomerizations have a number of commercial applications one of the most important being the Shell SHOP process, which produces linear biodegradable

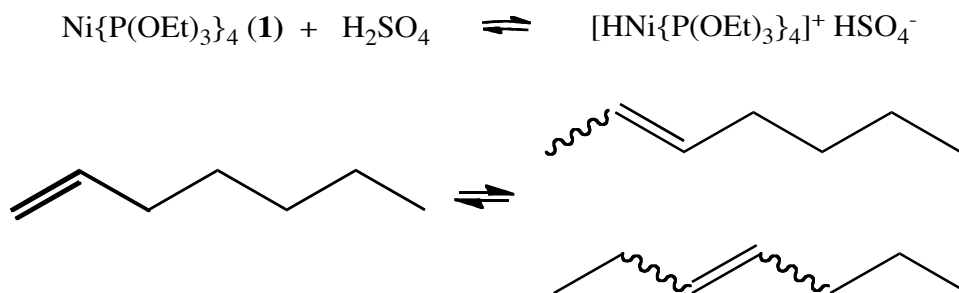
C11–C15 fatty alcohols for detergents.

The Nickel precatalyst used in the first part of this experiment $[\text{Ni}\{\text{P}(\text{OEt})_3\}_4]$ (**1**) is a tetrahedral d^{10} complex. It can be prepared by reduction of octahedral green nickel (II) with excess phosphite in the presence of diethylamine as shown below.



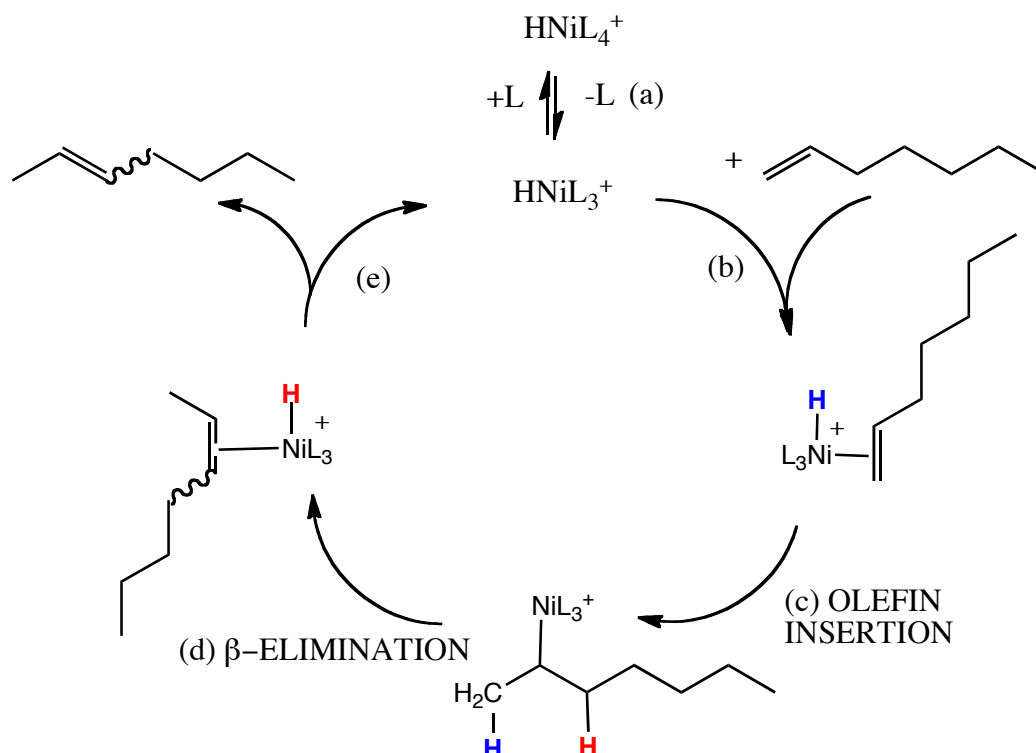
Q1. Why is the Ni(II) complex green yet the product is white?

The precatalyst is protonated to give the active catalyst $[\text{HNi}\{\text{P}(\text{OEt})_3\}_4]^+$ which catalyzes the isomerization of the substrate 1-heptene to an equilibrium mixture of 1-, 2- and 3-heptenes (1:20:78 ratio).



The mechanism of the isomerization is shown in the scheme below and involves the following steps: (a) reversible dissociation of a phosphite ligand; (b) addition (coordination) of the olefin; (c) insertion of the olefin into the metal-hydride; (d) beta-hydrogen elimination; (e) dissociation (decomplexation) of the isomerized olefin. All of these steps are reversible, however the reaction will proceed until an equilibrium mixture of the olefin isomers is formed.

Q2. The scheme shows the formation of 2-heptene, draw a scheme that would account for the formation of 3-heptene.



Q3. Give an electron count and oxidation state at the Ni center for all the nickel species shown in the cycle.

Catalyst Turnover Frequency (TOF)

TOF is the ratio of moles of product to moles of catalyst over time and gives the efficiency of the catalyst. Or, put another way, using the reaction in this experiment as an example, TOF indicates how many times a single nickel center catalyzes the isomerization of either hept-1-ene to hept-2-ene, or hept-2-ene to hept-3-ene per unit time (usually hr^{-1}).

If [P] is the concentration of product, and [B] is catalyst then

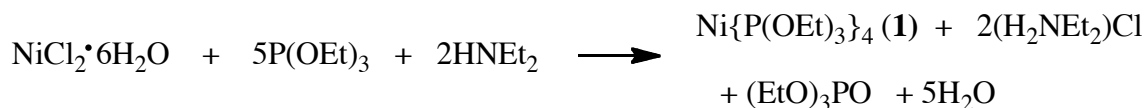
$$\text{TOF} = \frac{d[\text{P}]/dt}{[\text{B}]}$$

Using the data from the GC that you collected, TOF can be estimated. *Note that the mmol of hept-3-ene must be multiplied by 2 because it takes 2 catalyst cycles to produce one hept-3-ene molecule.*

Experimental Procedures

One of you should prepare compound 1, the other compound 2

Session 1a Preparation of tetrakis(triethylphosphite)nickel(0) $[\text{Ni}\{\text{P}(\text{OEt})_3\}_4]$ **1**.



NOTE: triethylphosphite and diethylamine are extremely noxious (these compounds stink!), all waste including syringes and needles from this experiment must be placed in the appropriate waste containers in the hood. ABSOLUTELY ALL ASPECTS OF THIS EXPERIMENT MUST BE DONE IN A HOOD! WEAR GLOVES FOR ALL MANIPULATIONS.

Preparation of tetrakis(triethylphosphite)nickel(0) $[\text{Ni}\{\text{P}(\text{OEt})_3\}_4]$ **1**

Weigh 2.6 g (11 mmol) of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ and place it in a 100 mL Erlenmeyer flask containing a stir bar. Add 50 mL of methanol and stir for 5 minutes to dissolve the nickel (II) chloride. Cool the emerald green solution in an ice bath and carefully add 9.4 mL (9.1 g, 55 mmol) of triethylphosphite over a 2 minute period via syringe. The solution should turn blood red. After stirring for 5 minutes, carefully add diethylamine dropwise via syringe (2.5 mL, 1.8 g, 24 mmol). After half the amine has been added a white precipitate of product should begin to form. Continue the addition very slowly until the deep red solution just begins to fade (*addition of too much amine will result in a light green impurity, it is better to sacrifice yield and obtain pure product by stopping the addition of amine early*). Stir for a further 10 minutes in the ice bath and then filter off the white precipitate in air and wash with 3 x 10 mL portions of ice cold methanol. Transfer the white solid using a powder funnel to a pre-weighed dry Schlenk flask and dry under high vacuum for at least 30 minutes or until no significant weight loss occurs, then calculate the % yield. The product, $[\text{Ni}\{\text{P}(\text{OEt})_3\}_4]$ **1**, is sensitive and it must be stored under nitrogen away from sunlight between lab periods. Measure the IR spectrum as a KBr pellet and set aside at least 50 mg of product under nitrogen in a vial for a protonation study with CF_3COOH in the dry box. The ^1H , ^{13}C and ^{31}P NMR spectra of compound **1** are provided (Figures B4-6). These should ALL be assigned and compared to those of the protonated species (see below) and of free triethylphosphite (Figures B1-B3).

Q4. *What is the red-colored intermediate in the reaction ?*

Protonation of 1 with trifluoroacetic acid.

NOTE: arrange with the NMR staff to run this sample as soon as it has been prepared.

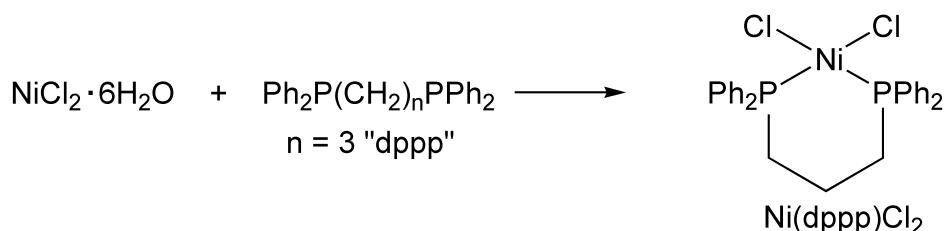
The NMR sample should be prepared in the dry box in CDCl_3 in a vial. Transfer the solution to

the NMR tube and carefully add one drop of CF_3COOH to the tube and place the cap on the tube. Measure the ^1H and ^{31}P NMR spectra of this sample immediately, be sure that the ^1H NMR spectrum is measured from -20 p.p.m. to $+20$ p.p.m. Assign as many peaks as you can, it is often a mixture.

Q5. What is the structure of the cation formed by protonation of **1**.

Q6. Calculate the $^2J_{\text{HP}}$ coupling constant.

Session 1b Preparation of bis(diphenylphosphinopropane)nickel(II) chloride, $\text{Ni}(\text{dppp})\text{Cl}_2$ **2**.



Preparation

- To 1.2 g (5.0 mmol) $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ in an Erlenmeyer flask, add enough 5:2 (v/v) 2-propanol:methanol to make a 0.2 M solution (_____ mL). Heat the mixture on a hot plate to just below boiling.
- In a separate vessel, prepare a solution of 0.90 equiv. diphenylphosphinopropane (dppp; 1.86 g) in just enough 2-propanol to get almost all of the phosphine into solution (keep the mixture hot on the hot plate during this process).
- Add the hot phosphine solution dropwise to the $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ solution while stirring. Allow to stir, heated, for thirty minutes, then

Workup

- Cool the reaction mixture to room temperature,
- Filter the precipitate, and wash the product several times with small portions of methanol.
- Remove all residual solvent under high vacuum ($50\text{ }^\circ\text{C}$, 30 min). Characterize the product by IR spectroscopy and take a melting point (once completely free of solvent).
- Determine the percent yield for the Ni catalyst and save it for the Kumada cross-coupling during the final period of these experiments and for the GRIM polymerization later in the semester.

Session 2 Catalytic Isomerization of 1-heptene by a nickel hydride complex.

Set up **all** the apparatus before initiating the reaction, you will be required to extract samples every 2 minutes initially and transfer them to test tubes, if you are not set and ready you will miss an extraction and have to start over. ***This reaction is air sensitive, the catalyst is pale yellow when active, if the solution goes colorless the catalyst has likely been exposed to air.***

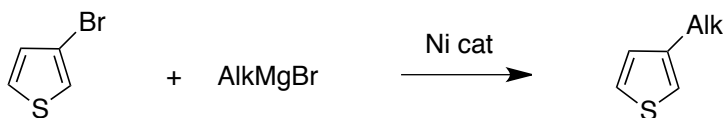
RUN 1. Add 71 mg of the nickel complex **1** to a 100 mL Schlenk flask equipped with a stir bar and evacuate and refill the flask with nitrogen three times on the Schlenk line. Add 30 mL of diethyl ether by syringe through the septum and immediately purge the solution gently with nitrogen, do not purge too vigorously or the ether solvent will completely evaporate. After 5 minutes purge remove the needle and seal the flask under a positive pressure of nitrogen. Using a 1 mL syringe, add 0.30 mL of hept-1-ene to the flask and then extract a 1.0 mL sample for GC analysis (inject a 1 microliter sample into the GC or GCMS, this may be automated), this will be time zero GC. Get the timer ready (practice using it first!). Now add 1.0 mL of 0.1 M H₂SO₄ in methanol via syringe to initiate the isomerization and start the timer. Make careful observations and extract 1.5 mL samples at 5, 10, 20, 40 and 60 mins. These samples should be syringed into test tubes and shaken in air immediately to quench the reaction. Measure the GC of each sample starting with the last that was extracted, if the reaction has failed the last sample will show no isomerization and you must repeat the reaction. If the reaction shows some progress continue to monitor the reaction at 30 minute intervals up to 180 minutes.

RUN 2. If your reaction above proceeded very quickly (finished within less than 60 minutes), in a clean dry flask, repeat the conditions in run 1 but at 0 °C in an ice bath and extract samples at 10, 20, 30 and 45 minutes. Measure the GC of the last sample first but do not stop the timer or wash the flask yet, if the reaction is not complete continue measurements every 20 minutes up to 180 mins if needed. Calculate the TOF at the fastest part of the reaction from your GC data.

Analysis of the GC data: The relative amounts of each of the isomers can be determined from the areas under the peaks in the GC. Plot a graph of mol % heptenes vs. time for each of the runs and calculate the TOF at the fastest part of each run from your GC data.

Q.7 Discuss how you would expect addition of 10 mol% triethylphosphite affect the nickel-catalyzed isomerization reaction.

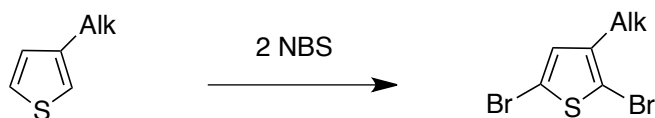
Session 3. Grignard Cross-Coupling (Kumada Coupling). Synthesis of 3-Alkylthiophenes.²



Right at the beginning of the session place a 250 mL 2-neck Schlenk flask, a reflux condenser, and an addition funnel into the oven. Weigh out magnesium (1.94 g, 0.080 mol) using a weighing paper or weighing boat. Take the 2-neck flask out of the oven while it is still hot, add the Mg filings and an egg-shaped stir bar, and then place the addition funnel in the center and the reflux condenser on one of the sides (remember to grease the joints!). Close off the joints with 24/40 septa, evacuate the assembly on the vacuum line and backfill with nitrogen. Add anhydrous THF (100 mL, provided by the TA) via a cannula through the septum. Under nitrogen flow, switch the rubber septum on the top of the condenser for a T-shape connector that is attached to the vacuum line. Close the stopcock on the addition funnel and add the specific alkyl bromide that has been provided (___ g, ___ mL, 0.080 mol) through the septum. Add the alkyl bromide dropwise to the Mg suspension while refluxing the mixture until all (or almost all) of the Mg has reacted (ca. 1-2 h; make sure the side-arm stopcock is closed !). Let the mixture cool to room temperature and then place it in an ice bath while continuing to stir. Remove the addition funnel and add 1,3-bis(diphenylphosphino)propane nickel(II) chloride synthesized during the earlier session ($\text{Ni}(\text{dppp})\text{Cl}_2$, 0.33 g, 0.61 mmol) under a flow of nitrogen. Close the joint with a septum and then add 3-bromothiophene (10.0 g, 0.061 mol) dropwise by syringe to the solution at 0 °C (ice bath). Allow the reaction to proceed under nitrogen at room temperature until the next period.

Q8. Draw a catalytic cycle using the exact components of your reaction.

Q9. The 2010 Nobel Prize for Chemistry was awarded for the discovery of a series of closely related reactions (Kumada had already passed away). Who were the awardees and how do their discoveries differ from Kumada's?

Session 4. Isolation of 3-Alkylthiophene and Electrophilic Bromination.

Part 1. Quench the reaction mixture from the last period by addition of 5 mL of a 1 M HCl solution, dilute with a small amount of water, extract with ether using a separatory funnel, and wash with water. Collect the organic phase, filter under vacuum using a Buchner funnel and then remove the solvent using a rotary evaporator. Perform a (quick) fractional distillation under high vacuum at elevated temperature (use a heat gun; record the boiling point). Weigh the product into a vial, acquire ^1H , ^{13}C NMR and GC-MS data. Also acquire ^1H , ^{13}C NMR and GC-MS data for 3-bromothiophene and compare them.

Part 2. Into a vial with a micro stir bar add the 3-alkylthiophene (1.0 g, _____ mol) and then 5 mL of distilled THF (provided by the TA) and 5 mL of glacial acetic acid. Wrap the flask with tin foil. Then add 2.0 equiv *N*-bromosuccinimide (NBS) (_____ g, _____ mol) and stir for 1 h. Dilute the mixture with distilled water (ca. 20 mL) and diethyl ether (ca. 40 mL). Separate the layers in a small separatory funnel and wash with (i) dilute aqueous KOH (20 mL), (ii) dilute aqueous $\text{Na}_2\text{S}_2\text{O}_3$, (iii) distilled water (20 mL). Remove the solvent on a rotary evaporator and transfer the remaining oil to a pre-weighed labeled vial. Weigh the product, acquire ^1H , ^{13}C NMR and GC-MS data (compare to the data for the precursor and assess the selectivity of the bromination), and then tightly close the lid and store the product in the dark in your locker or in the fridge. We will use this compound as a precursor to a conducting polymer in Experiment D.

Q10. *What is the reaction type? Propose a mechanism and explain why the Br ends up in the 2,5-positions of thiophene.*

Literature Cited

1. "Simple Synthesis and Use of a Nickel Alkene Isomerization Catalyst"; Kurt R. Birdwhistell and Joann Lanza, *J. Chem. Educ.*, **1997**, *74*, 581.
2. Tamao, K.; Kodama, S.; Nakajima, I; Kumada, M. *Tetrahedron* **1982**, *38*, 3347.
3. Ted M. Pappenfus, David L. Hermanson, Stuart G. Kohl, Jacob H. Melby, Laura M. Thoma, and Nancy E. Carpenter, Demetrio A. da Silva Filho and Jean-Luc Bredas *J. Chem. Educ.* **2010**, *87*, 522-525.