Exp 3 – Oxidation of Benzhydrol

Reading Assignment
Review Mohrig Section 10 (Extraction) & 18 (TLC)

In this experiment, students will perform a simple oxidation reaction of a secondary alcohol. Recall that Oxidation Is a Loss of electrons while Reduction Is a Gain of electrons (OIL RIG). In order to apply this mnemonic, you must know the oxidation states of each atom within the compound, with particular interest on carbon. Carbon can carry oxidation states ranging from -4 to +4. A few examples are shown in **Figure 1** below. It is also common for carbon to carry an oxidation state of -3, -1, +1, and +3.

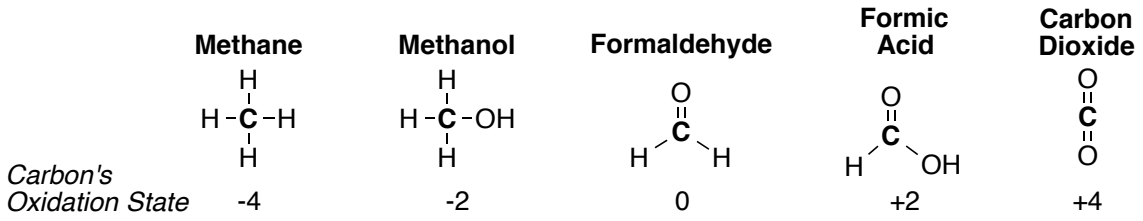
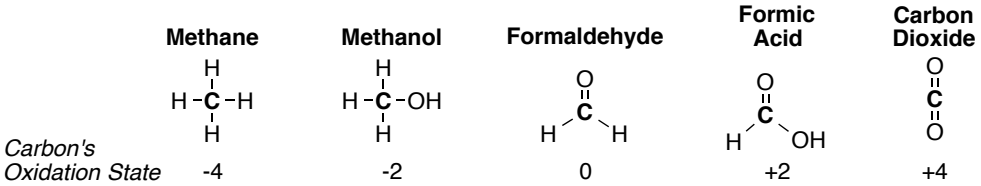
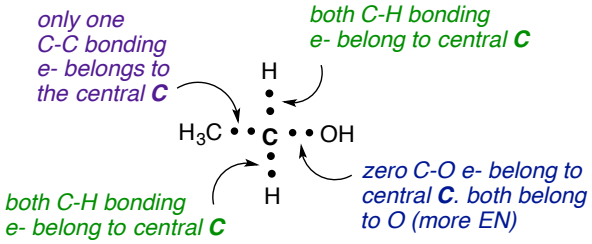


Figure 1. Examples of carbon's oxidation levels.

You may have noticed that all of the compounds in **Figure 1** are neutral and carbon has zero formal charge in each example. The concept of oxidation state and formal charge are similar with one important difference in the calculation. Both are calculated by taking the difference between the valence electrons (from the periodic table) and the number of electrons belonging to that atom within the molecule. For a given atom, the valence electrons will never change but the electrons 'belonging' the atom in the molecule will vary depending on number of lone pairs and attachments to more or less electronegative atoms. The important difference in the calculation of oxidation states and formal charge is based on the following assignment of bonding electrons (**Figure 2**). This is how the highlighted carbon in ethanol can have an oxidation state of -1 but a formal charge of zero.

- *Oxidation states assign bonding electrons to the more electronegative atom in a bond*, except when the two atoms are the same and the bonding electrons are split equally.





Ox St = (valence e-) - (atom's e- in molecule)

= 4 - 5

= -1

The oxidation state of the central **C** in ethanol is **-1**.

Formal Charge, all bonding e- split equally (50:50)...**FC = 4 - 4 = O**

The formal charge of the central **C** is ethanol is **zero**.

- *Formal charge splits bonding electrons equally between the two atoms*.

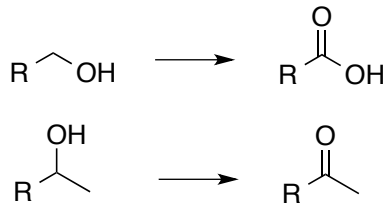
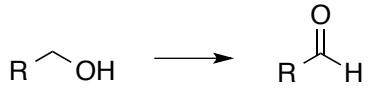
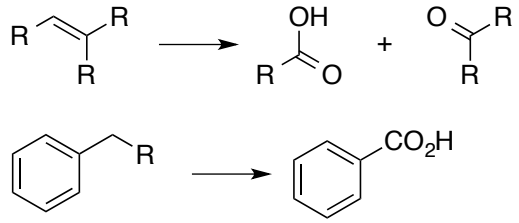
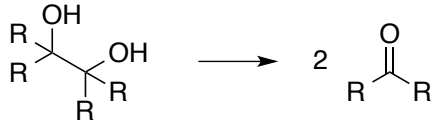
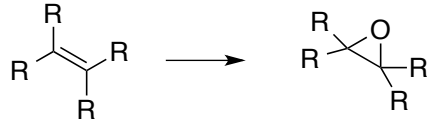
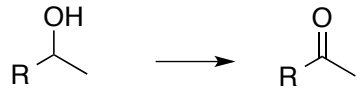
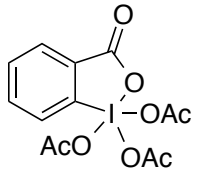
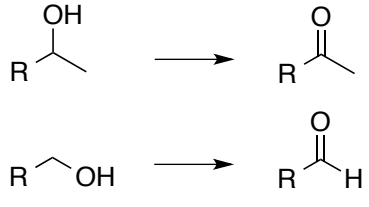
Figure 2. Calculation of oxidation state and formal charge of ethanol's central carbon.

As stated above, an oxidation reaction is one where an atom loses electrons. In other words, the atom gains a bond to a more electronegative atom (electron hogs!). The examples discussed in this experiment will involve oxygen-containing compounds (alcohols and carbonyl compounds) but there are many other examples of organic oxidation reactions that do not involve oxygen. You should be able to categorize whether the reactions learned in the 108 series qualify as oxidation or reduction based on the rules outlined above.

Table 1 below highlights common oxidizing agents and their applications. Selecting the proper oxidizing agent depends on several factors, the most important of which is "does it work?" In choosing the appropriate oxidizing agent, the following issues should be addressed…

…*Reactivity* – does it react with the starting material? Is it too reactive or not reactive enough for the desired transformation?
…*Selectivity* – will it also react with other functional groups in the molecule?
…*Ease of use* – is it toxic and/or does it require special equipment? How is waste handled?
…*Availability* – is it commercially available or does it need to be made separately? Is it cost-effective?

Table 1. Common oxidizing agents and applications

Oxidizing Agent	**Main Application(s)**	**Comments**
Jones Reagent: CrO_3, H_2SO_4		CrO_3 is highly toxic and a carcinogen. High waste disposal cost.
Pyridinium chlorochromate (PCC)		Suspected carcinogen, high waste disposal cost.
Potassium Permanganate ($KMnO_4$) with heat		Nonselective – many functional groups are oxidized (alkenes, alkynes, alcohols, etc.)
Periodic Acid (HIO_4)		N/A
Peroxyacids (RCO_3H)		Common peroxyacid: Meta-chloroperoxybenzoic acid (mCPBA)
Sodium Hypochlorite (bleach, NaClO)		Cheap and easy!
Dess-Martin Periodinane 		Easy to use but expensive reagent.

In this experiment, the oxidation of a secondary alcohol (benzhydrol) is achieved with commercially available bleach. This reagent is inexpensive and easy to handle with typical personal protective equipment (PPE) including goggles and gloves. Most importantly, it works! However, one issue is presented in using bleach: solubility. Bleach is an aqueous solution of NaClO but many organic compounds, including benzhydrol, are not water-soluble. Thus, a **phase transfer catalyst** (PTC) is employed to facilitate the reaction.

The mechanism employed by a PTC is similar to that used in soaps. Soaps contain both non-polar and polar (typically ionic) regions so they can absorb grease and also be washed away with water. Quaternary alkylammonium salts such as tetrabutylammonium hydrogen sulfate ($Bu_4N^+HSO_4^-$) are common examples of PTCs. For the remainder of this discussion, this salt will be abbreviated by Q^+X^-. These salts are soluble in both water and organic solvents. When $NaClO_{(aq)}$ is mixed with an immiscible organic solvent such at ethyl acetate (EtOAc), little to none of the NaClO enters the organic phase. However, once a small amount of Q^+X^- is added, the salts participate in the following equilibrium (**eq. 1**).

$$Q^+X^- + Na^+ClO^- \rightleftharpoons Q^+ClO^- + Na^+X^- \qquad \textbf{(1)}$$

Some of the hypochlorite (ClO^-) ion, the active oxidizing agent, is paired with the tetrabutylammonium cation Q^+. Because Q^+ is soluble in organic solvents, it can carry the ClO^- ion from the aqueous to the organic phase where the reaction can occur (**Figure 3**). As the ClO^- reacts in the organic phase, the equilibrium shifts to transport more ClO^- from the aqueous phase to reestablish equilibrium. It is important to note that the salts do not instantly transport from one layer to another. *Vigorous stirring is required to facilitate phase transfer.* This continues until the reaction is complete and the solubility issue is resolved! The applications of PTC are widespread to many other types of reactions, not just oxidations.

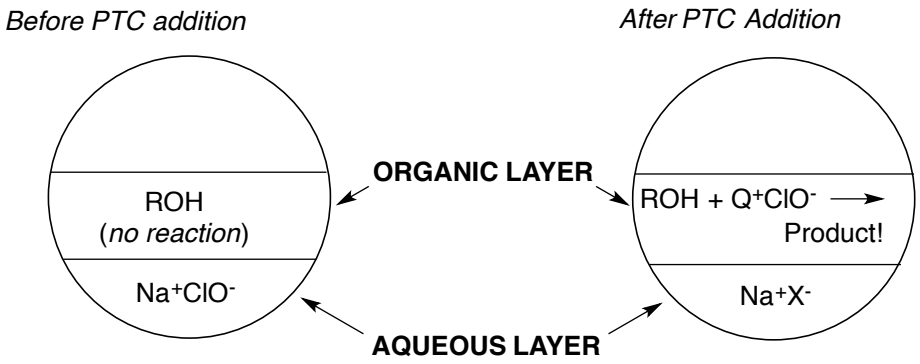
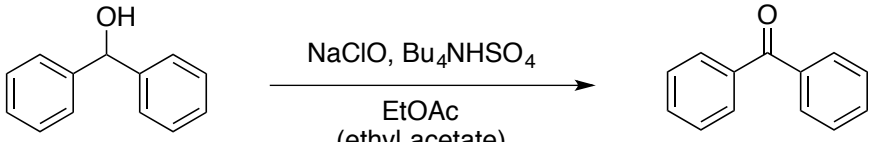


Figure 3. Phase-transfer catalysis (PTC) in an oxidation reaction.

Notebook Preparation

- *Purpose* – one-sentence description of the purpose in addition to the following scheme:



Benzhydrol **Benzophenone**

- *Reagent table* – amount (mg or mL), mmol, equiv*, MW, bp or mp, density, and one-word hazards for each of the chemicals in the scheme above. Leave space in the table to write the actual amounts of starting materials used.

  ** equiv = molar equivalents as defined by the limiting reagent (in this case benzhydrol). After calculating moles of each reagent, indicate the mole ratio of each relative to benzhydrol.*
- *Procedure* – hand-written, step-by-step procedure. Reproduce **Tables 2 and bring the lecture handout for Tables 3 & 4**.
- *Safety & Clean-up* – copy **Table 5** into your notebook.

EXPERIMENTAL PROCEDURE - *Students work individually on this experiment.*

Reaction Preparation and Set-up: TLC will be used to monitor reaction progress. Prepare TLC standards and plates before setting up the reaction. Make solutions of the standards (benzhydrol and benzophenone) in small test tubes. This doesn't require careful measuring, but do be conservative. Dissolve a small amount of the compound (microspatula tip) in ethyl acetate (EtOAc, 1 mL or less). Obtain three TLC plates, carefully handling by the edges without bending, and gently spot the plate at the origin with a capillary tube (not a melting point capillary). Create one lane for benzhydrol, another for benzophenone, and leave a space for the reaction mixture to be spotted later. Be sure to record which lane is which in your notebook. Take note of the solvent in the TLC chambers.

In a 25-mL Erlenmeyer flask equipped with a magnetic stir bar, add 0.37 g (± 0.01 g)[*] of benzhydrol, 5 mL of commercial bleach (approximately 0.7 M NaClO), 5 mL of ethyl acetate (EtOAc), and 40 mg (± 5 mg)[*] of tetrabutylammonium hydrogen sulfate (Q^+X^- or $Bu_4N^+HSO_4^-$). Secure the flask to a ring stand, loosely stopper, and *stir vigorously on a stir plate without heat*.

Monitoring Reaction Progress: After about 10 minutes, stop stirring to allow phase separation and remove a small aliquot of the upper layer of the reaction by dipping the tip of a pipet into the reaction. Obtaining one drop of a liquid does not require a pluringe or pipet bulb! Carefully dip the tip of the pipet into the reaction then place that pipet into an empty test tube. Apply a little pressure to the top of the pipet with your thumb to transfer the solution. Spot the TLC plate with this aliquot using a capillary tube alongside the standards. Run the TLC plate using the chambers provided in the fume hood. *Do not remove the chambers from the fume hood!* Develop the plate with a UV or fluorescence light after evaporating the solvent from the plate in the fume hood.

If starting material is still present in the reaction, continue stirring for another 10 minutes and take another TLC aliquot. A faint spot for benzhydrol may still appear on a visualized plate, even when the reaction is complete. When there is no *dark* spot for benzhydrol in the reaction mixture, you may consider the reaction to be complete. The 10 minutes is counted from the first aliquot (20 min total). By the time you run the first TLC plate, it's probably time to run the second! Continue taking aliquots at 10-minute intervals until the reaction is complete. If the reaction is taking longer than 40 minutes, you may stop the reaction and proceed. Time permitting, obtain the IR of benzhydrol during the reaction, but this can also be done later.

[*] It is acceptable to obtain 10 mg more or less benzhydrol and 5 mg more of less Q^+X^-. Record the exact mass obtained, including the uncertainty of the balance used.

Reaction Work-up: Transfer the completed reaction mixture to a screw-cap test tube and remove the aqueous layer with a pipet. Wash the organic layer with 3 mL of brine (sat. NaCl) followed by a wash with 2 mL of water – mix, invert, then remove the aqueous layer after each portion of brine or water is added. Dry the organic layer over $MgSO_4$, gravity filter using a pipet with cotton plug, and collect the filtrate in a pre-weighed 25-mL round-bottom flask (RBF). Concentrate using a rota-vap and weigh the product. Pro-tip: the product rarely crystallizes on the rota-vap. When the solvent appears to have evaporated, take the flask off the rota-vap and swirl in the ice bath to crystallize. You can still proceed with the product in liquid form.

Analysis: Obtain the IR of the starting material and product. Record the identifying peaks in your notebook. Sketch the final TLC plate into your notebook and calculate the R_f values for each spot. Report your data in table format (on the next page). Analyze the sample ^{1}H NMR spectra of benzhydrol and benzophenone (provided in lecture) using the following table format (adjust the Table numbers). **Reproduce at least Table 2 into your notebook. Tables 3 & 4 are part of the benzhydrol NMR handout from lecture – you may bring this handout to lab instead of reproducing Tables 3 & 4 in the notebook.**

Table 2. TLC Results

Sample	**R_f**	**Identity**
Benzhydrol		--
Benzophenone		--
Reaction Mixture (x minutes)		Benzhydrol (if present)
* add more rows as needed		Benzophenone

Table 3. ^{1}H NMR Analysis of Benzhydrol (include the structure with H's labeled)

Signal	**Integration (# of H's)**	**Expected Chemical Shift (ppm)**	**Observed Chemical Shift (ppm)**
A			
B			
C			
D			
E			

Table 4. ^{1}H NMR Analysis of Benzophenone (include the structure with H's labeled)

Signal	**Integration (# of H's)**	**Expected Chemical Shift (ppm)**	**Observed Chemical Shift (ppm)**
A'			
B'			
C'			

Table 5. Clean-up & Safety

Clean-up	**Safety**
Liquid waste: aqueous layers and contents of rota-vap trap	Ethyl acetate is flammable.
Solid waste: $MgSO_4$, pipets, filter pipets, capillary tubes, and TLC plates	Benzophenone, benzhydrol, and Bu_4NHSO_4 are irritants.
After analysis, dispose of your product in the liquid waste using a *very small amount* of ethanol from a wash bottle to aid the transfer.	Sodium hypochlorite is an oxidizer. It will bleach your clothes so consider your wardrobe for the day!
Wash all glassware and wipe down counters.	Wear gloves & goggles throughout the experiment.

Introduction: Pre-Lab Questions

1. Which atom is oxidized in the reaction of benzhydrol with bleach? Redraw the structures and indicate the oxidation number of that atom in the starting material and product.

2. What are the main differences you expect to find between the IR of the starting material and product?

3. Briefly explain how phase transfer catalysts work and why one is necessary in this experiment.

4. What is the advantage of using bleach as an oxidizing agent? What other oxidizing agents could be used to carry out the same transformation?

5. What are the two solvents used in the reaction? Will the aqueous layer be on the top or bottom in the extraction?

6. Calculate the moles of each reagent used, identify the limiting reagent, and calculate the theoretical yield of benzophenone (recall that catalysts cannot be limiting). Show your work.

Results: In-Lab Questions

1. (*5 points*) Report the yield of product (mg and %). Briefly discuss any parts of the procedure that may have caused the yield to be lower than 100%. Be specific. List sources of intrinsic error (ILE's of measuring tools used).

2. (*5 points*) Report the TLC results (mobile phase, R_f values, and identification) of TLC analysis in table format and explain how you decided to stop the reaction. Briefly explain why the separation was successful by comparing the polarity of the sample and mobile phase.

3. (*5 points*) Compare the IR of the starting material and product. Briefly explain which peaks signify reaction completion, including functional group, bond, and stretching frequency. Attach the IR spectra to the back of the report. No IR table is necessary for this experiment.

4. (*10 points*) Interpret the ^{1}H NMR spectra of benzhydrol and benzophenone by completing the tables in the lecture handout (attach to the report) and answer the following in one sentence: **Which NMR peak(s) best distinguish starting material from product?**

5. (*5 points*) Perform a literature search to find a journal article from *Tetrahedron Letters* (*Tet. Lett.)* with "benzophenone" in the title. Web of Science is an excellent search tool and requires on-campus access. Give a one-to-two sentence explanation of the role of benzophenone role in this publication and provide a proper citation to follow your answer (Technical Writing Guidelines, Part E).

Experimental Methods

See Technical Writing Guidelines, Part D for content and format. A sample experimental section is posted online that contains much more detail than 108M students will need to provide! Do include TLC conditions ["reaction progress was monitored by TLC (solvent)"] but do not include NMR data in this section.

Experiment adapted from…

Palleros, D. R. *Experimental Organic Chemistry*, Wiley: New York, **2000**; pp. 255-257.

Exp 3 - Oxidation of Benzhydrol Name _____

Section Day _____ Time _____ TA Name _____

CHEM 108M GRADING RUBRIC - Use as cover page for report

SECTION	INSTRUCTOR COMMENTS	POINTS ASSIGNED
IN-LAB QUIZ		**/ 10**
LAB REPORT – Staple the report together in this order before coming to lab:		
ABSTRACT One paragraph, four sentences: Purpose, procedure, main result(s), and conclusion(s).	NONE	0 / 0
INTRODUCTION Original responses to pre-lab questions with TA initials		/ **30**
RESULTS The main results are stated, as outlined in the in-lab questions, using complete sentences.		/ **30**
EXPERIMENTAL METHODS The experimental details (including final amount used and obtained) are *briefly* described in a few sentences.		**/ 20**
NOTEBOOK PAGES Proper format: reaction scheme, chemical info table, procedure, safety, waste, and clean up notes		/ **20**
NEATNESS, ORGANIZATION, & LAB TECHNQIUE Proper order and format (see syllabus for full descriptions of each section), spelling & grammar. Safety rules followed, equipment handled properly.		/ **15**
	LAB REPORT TOTAL	**/ 125**