

EXPERIMENT 6: Reactions of Carbonyl Compounds – Qualitative Reactions of Aldehydes and Ketones

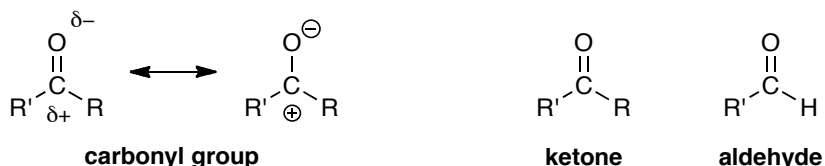
Relevant Sections in the text (Wade, 7th ed.) – Chapter 18: Ketones and Aldehydes

- 18.17 (p. 845) Condensations with hydroxylamine and hydrazines
- 18.20 (p. 854) Oxidation of aldehydes
- 22.1-2 (p. 1043) Condensations and α -substitutions of carbonyl compounds
- 22.5 (p. 1052) α -Halogenation of ketones

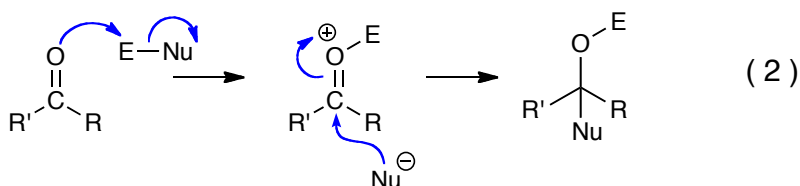
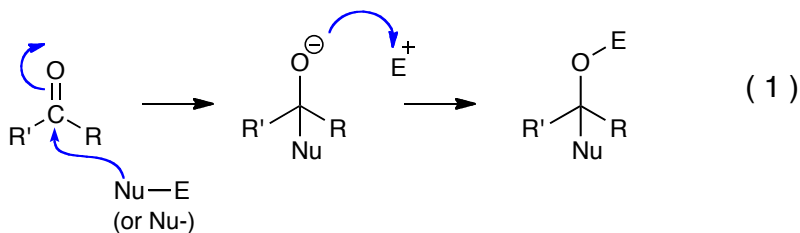
NOTE: The melting points of the derivatives can be measured in the second week of the experiment. The data sheet is due one week after completion of the laboratory.

General Concepts

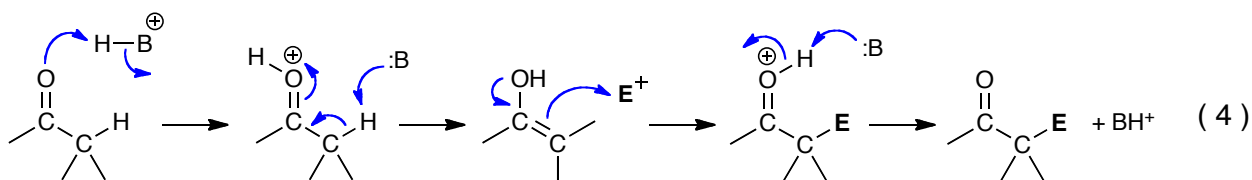
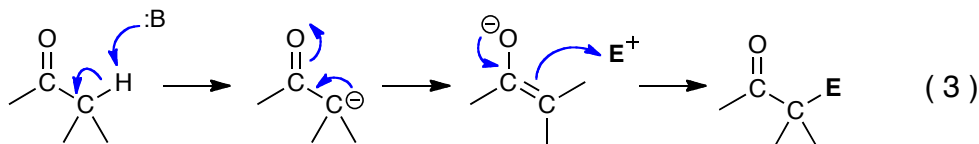
The carbonyl group (C=O) is a source of numerous important reactions in organic chemistry; mainly a result of the polarization of the carbon-oxygen- π bond due to the relatively high electronegativity of the oxygen atom. From what you have learned about resonance theory, this polarization arises from a contribution of the dipolar resonance structure for this functional group (C⁺-O⁻).



Consequently, the carbonyl group undergoes a variety of reactions in which the electrophilic carbon atom is attacked by nucleophiles (Lewis bases) and the oxygen atom, in turn, reacts with electrophiles (Lewis acids). The net result is the addition of a reagent Nu-E across the π -bond of the carbonyl group. The exact sequence of events for the addition of Nu-E across the carbonyl group varies according to the reagent and reaction conditions, but in general follows the pathway outlined in either equations 1 or 2.



The carbonyl functional group also acts to increase the acidity of any hydrogens on carbons directly attached to the carbonyl group (α -hydrogen atoms). This enhanced acidity means that the α - carbon atom can become nucleophilic, either through deprotonation reaction to form an enolate ion (eq. 3) or by keto-enol equilibration (tautomerization) to form the enol (eq. 4). Enolates or enols can then react with electrophiles at the α -carbon to give a net substitution reaction of the electrophile for the α - hydrogen.



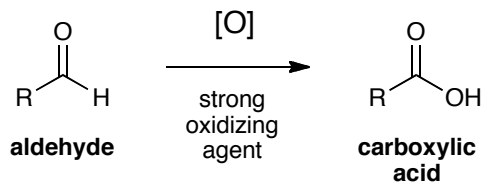
In this experiment you will explore some of the reactions of carbonyl groups by looking at a number of general reactions. In an aldehyde one of the bonds on the carbonyl carbon is to a hydrogen atom, whereas in ketones, both other atoms that are attached to the carbonyl carbon are carbons. Because the carbonyl group is present in both aldehydes and ketones, the two classes often react similarly. With the same reagent, aldehydes usually react faster than ketones, mainly because there is less crowding at the carbonyl carbon. Aldehydes are also more easily oxidized than ketones. In this experiment you will perform reactions that illustrate the similarities and differences between aldehydes and ketones and then use these tests to identify an unknown carbon

***GENERAL NOTE OF SAFETY*:** The ketones and aldehydes used in this laboratory may be harmful if inhaled or absorbed through the skin. Avoid contact, work in your fume hood and never transport any reagent without having the vessel corked or closed with a stopper.

PART A: OXIDATION

General Concepts

Aldehydes and ketones behave differently toward oxidizing agents. Because aldehydes have a hydrogen atom directly bonded to the carbonyl carbon it makes them more reactive to oxidation than ketones.

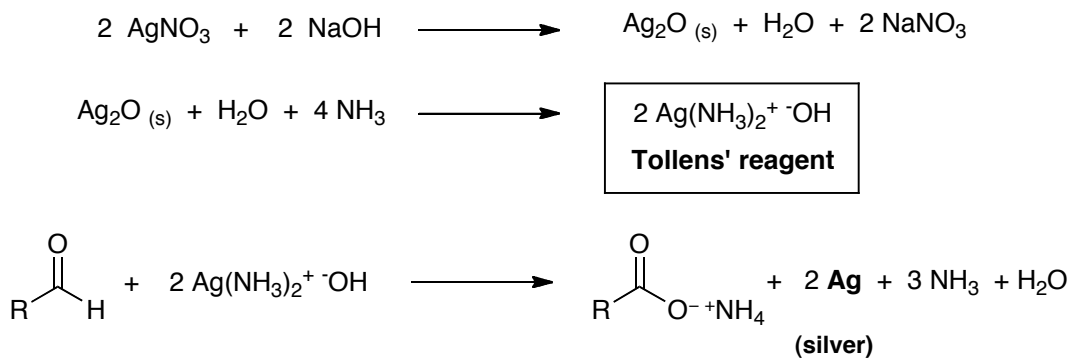


Ketones, which have no hydrogen attached to the carbonyl carbon atom, may be oxidized to a carboxylic acid only under more severe conditions (stronger reagents and higher temperatures), because their oxidation to an acid requires the rupture of a carbon-carbon bond. Under the usual oxidative conditions they will not oxidize. Several laboratory tests that distinguish aldehydes from ketones are based on the fact that the two classes of compounds are oxidized under different conditions.

(i) Tollens' Test

Perhaps the most distinctive qualitative test for aldehydes is the Tollens' test in which silver ion [as the complex ion $\text{Ag}(\text{NH}_3)_2^+$] oxidizes the aldehyde to the corresponding carboxylic acid and, in turn, is reduced to metallic silver which is deposited on the walls of the test-tube as a mirror (hence, frequently referred to as the **Silver Mirror Test**). Tollens' reagent is reduced to metallic silver (Ag) by aldehydes. The aldehyde is oxidized to the corresponding acid as Tollens' reagent is reduced. *Ketones are not usually oxidized by the reagent.*

Tollens' reagent is an ammonia solution of silver ion prepared by dissolving silver oxide in ammonia:



When the test is carried out with dilute solutions of reagents and in *scrupulously clean* glassware, the silver deposits finely in the form of a mirror on the walls of the vessel. Otherwise the silver is deposited as a black precipitate.

TOLLENS' TEST PROCEDURE:

AS ALWAYS PERFORM ALL REACTIONS IN THE FUMEHOOD!
Stopper all test tubes when they are outside of the fumehood.

***CAUTION*:**

1. Avoid contact with the silver nitrate solution, which can form a dark, hard-to-remove stain on one's skin (it is unsightly, but not hazardous).
2. Tollens' reagent must be prepared immediately before use. When your tests are completed, immediately dispose all residues as specified under "Waste Disposal" below.
3. Ammonium hydroxide is a respiratory irritant. Prepare the reagent and perform the tests in a fumehood.

Prepare Tollens' reagent as follows:

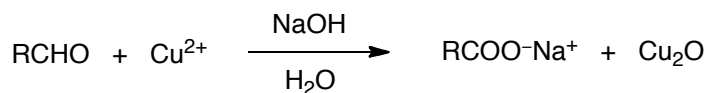
- Clean a large (18 x 150 mm) test tube thoroughly with soap and water, and rinse it with distilled water (the reaction works MUCH better with very clean test tubes!).
- To the CLEAN, large test tube add 2 mL of the silver nitrate solution provided. Add 10 drops of the sodium hydroxide solution provided and mix thoroughly (a solid black precipitate, Ag_2O , should form).
- Carefully, add the ammonium hydroxide solution provided to **just** dissolve the precipitate. **The test will fail if you add too much ammonium hydroxide.**
- Dilute the prepared mixture to about 6 mL with distilled water. Divide the Tollens' reagent equally among six CLEAN small test tubes, one of which is to serve as a comparison control.
- Add four drops of each of the carbonyl compounds to each test tube: **benzaldehyde**, **2-propionaldehyde**, **phenylethanone** (acetophenone), **cyclohexanone** and your **unknown**. (Obtain the unknown in a clean, dry 13 x 100 mm test tube from your demonstrator). As always, keep the test tube stoppered when outside of the fumehood.
- Shake each mixture, and then allow it to stand for 10 min. If no reaction occurs, place the tube in a beaker of warm water (35-50 °C) for 5 min. Record your observations.
- A **positive test** is denoted by the deposition of a silver mirror on the sides of the test tube.

Waste Disposal:

Place the content of all test tubes in the appropriate labeled container *Tollens' Waste Only*. Remove any silver mirror deposits with a few drops of 8 M nitric acid, and add the resulting solutions to the appropriate waste container.

(ii) Fehling's Test

A second test reagent, Fehling's solution, is restricted to the detection of *aliphatic* aldehydes. The reagent is a deep-blue, alkaline solution containing a complex cupric ion. Upon reaction with an aliphatic aldehyde, the cupric ion is reduced to form cuprous oxide which is deposited as an orange to red precipitate.



Aromatic aldehydes, because of additional resonance stabilization arising from conjugation of the carbonyl group with the benzene ring are insensitive to this reagent (the oxidation potential of cupric ion is less than that of silver ion). Simple ketones, alcohols, and alkenes are not affected by either of these reagents. Although simple ketones are not affected, compounds such as α -hydroxy ketones are oxidized almost as easily as aldehydes; both these tests find wide application in carbohydrate chemistry for the detection of reducing sugars. Fehling's test is the basis of a quantitative determination for "blood sugar" levels.

FEHLING'S TEST PROCEDURE:

**AS ALWAYS PERFORM ALL REACTIONS IN THE FUMEHOOD!
Stopper all test tubes when they are outside of the fumehood.**

- Prepare 10 mL of fresh Fehling's Reagent by mixing 5 mL of Fehling's Solution I (containing cupric sulfate) and 5 mL of Fehling's Solution II (containing sodium potassium tartrate and sodium hydroxide). Agitate the mixture briefly until the small quantity of precipitate formed initially redissolves.

- Divide the Fehling's reagent equally in 2 mL portions among five CLEAN small test tubes. Add 2-3 drops of each of the carbonyl compounds to each test tube, shake well and warm in a gently boiling beaker of water for 3-5 minutes:
 - benzaldehyde (water insoluble)
 - D-glucose
 - your unknown.
 - propionaldehyde
 - cyclohexanone

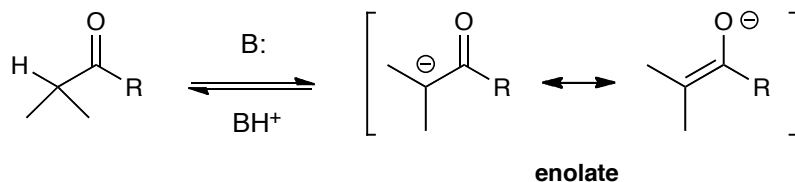
- A positive test is indicated by the gradual deposition of a yellow to orange-red precipitate of cuprous oxide. If sufficient additional carbonyl compound is added, the deep blue color due to the presence of cupric ion will be completely discharged.

Waste Disposal:

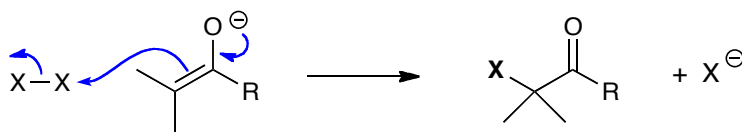
Place the content of all test tubes in the appropriate labeled container *Heavy Metal Waste Only*.

PART B: THE HALOFORM REACTION AND THE IODOFORM TEST

The haloform reaction differs from most reactions of carbonyl compounds, including those already described, by occurring at the α -carbon rather than the carbonyl carbon. This occurs because of the enhanced acidity of α -hydrogens which in turn is the consequence of resonance stabilization of the conjugate base, commonly referred to as the "enolate anion":

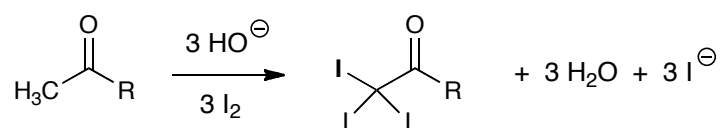


This enolate anion is also a good nucleophile and reacts rapidly with halogens to produce an α -halo substitution product:

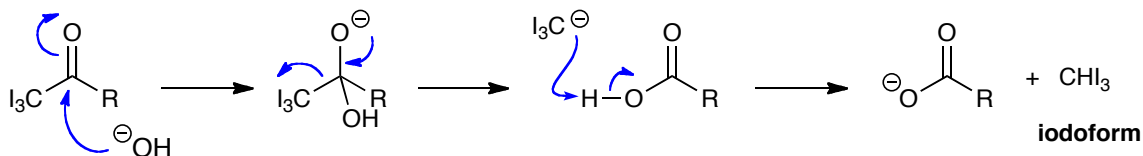


When an aldehyde or ketone that has α -H's is treated with a halogen in basic medium, halogenation occurs to give α -halocarbonyl compounds. The reaction involves the formation of the enolate ion, which reacts with the halogen to yield the substitution product. For iodine, the reaction is drawn below.

Because of the electron-withdrawing effect of the first halogen, any remaining hydrogens on the α -carbon become even **more** acidic and are rapidly replaced by halogens. In this way, a methyl group adjacent to a carbonyl group is rapidly converted to a trihalomethyl group by the halogen and base in a stepwise manner.



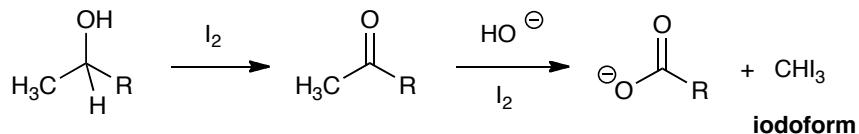
Because of the presence of strong electron-withdrawing groups on adjacent carbon atoms, the resulting trihalocompound is readily cleaved in the presence of excess base, a reaction that leads to **iodoform** (CHI_3), for $\text{R} = \text{H}$, alkyl, or aryl.



Although all carbonyl compounds having hydrogens on the α -carbons undergo halogenation at these positions, **only those with α -methyl groups undergo the carbon-carbon cleavage to give haloform**

and the corresponding carboxylic acid. Presumably, this is because the activating influence of all three halogens attached to one carbon atom is necessary to weaken the bond to the point of rupture, or, in other terms, to produce a "leaving group" that is a sufficiently weak base.

The reaction is also shown by ethanol and all methyl secondary alcohols, which are easily and rapidly oxidized to the corresponding carbonyl compounds by aqueous solutions of halogens!



Iodoform, CHI_3 , is a highly insoluble crystalline solid, which, along with its distinctive yellow color and characteristic odor, make its formation in the reaction mixture easily detected. The conversion of a methyl ketone to a carboxylic acid with one less carbon atom is often useful in synthesis and this has become a second important application of this reaction. Most commonly, this reaction is used to test for the presence of compounds known as methyl ketones. However, qualitative tests for a methyl ketone uses iodine because it is safer to handle and because the product, iodoform, is a highly insoluble crystalline yellow solid that is readily observed and detected by its medicinal odor. **A positive test also results for alcohols having a hydroxymethyl group (-CHOHCH₃) as in ethanol and 2-propanol** and for acetaldehyde. Iodine is an oxidizing agent, and such alcohols are easily oxidized by it to methyl ketones, which then react further to yield iodoform.

IODOFORM TEST PROCEDURE:

**AS ALWAYS PERFORM ALL REACTIONS IN THE FUMEHOOD!
Stopper all test tubes when they are outside of the fumehood.**

- To four small clean, (not rinsed with acetone) but not dry, test tubes add the appropriate test compound (2-4 drops), about 2.5 mL of the base solution provided (NaOH) and then add in about 0.75 mL of the iodine solution provided. Shake well.
- Record your observations (you may have to cool the test tube in ice). The following compounds are to be tested:
 - 2-pentanone
 - 3-pentanone
 - cyclohexanone
 - phenylethanone (acetophenone)
 - your unknown.

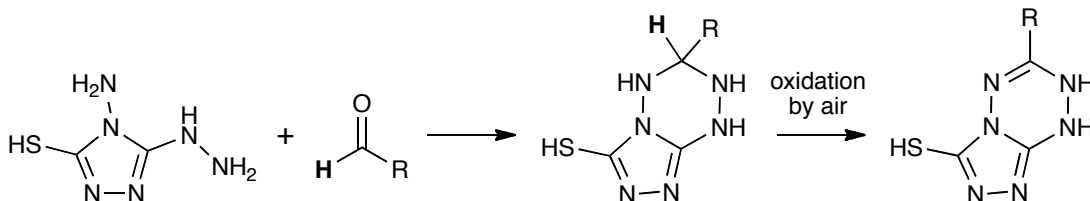
Waste Disposal: Dispose of the waste in the container labeled Haloform/ Iodoform Test Waste Only. (**DO NOT** place the waste in the halogenated waste container!)

PART C: ADDITION REACTIONS

As mentioned earlier, the most common reaction of carbonyl compounds involves the addition of various reagents to the carbon-oxygen double bond. This part of the experiment will illustrate several nucleophilic additions to the carbonyl group.

1. Purpald® Test for Aldehydes

The Purpald® reagent (the name of the reagent is a registered trademark of the Aldrich Chemical Company) reacts with aldehydes to form a cyclic derivative that, after air oxidation, forms a colored product, usually purple. The reagent is a heterocyclic compound 4-amino-3-hydrazion-5-mercapto-1, 2, 4-triazole, which reacts according to the reaction below.



Although both aldehydes and ketones react with the reagent to give the initial adduct, **only the aldehyde** adduct has a C-H bond in the six-membered ring and can be air oxidized to the final, intensely purple product.

PURPALD® TEST PROCEDURE:

**AS ALWAYS PERFORM ALL REACTIONS IN THE FUMEHOOD!
Stopper all test tubes when they are outside of the fumehood.**

- To each of five clean, but not dry, small test tubes add about 10 drops of the Purpald reagent already prepared for you (*Note: it's important that your test tube **is not** rinsed with acetone – why?*).
- Return to your fumehood. Test the following components by adding ~4 drops of each compound:
 - benzaldehyde
 - propionaldehyde
 - cyclohexanone
 - phenylethanone (acetophenone)
 - your unknown.

Swirl gently and record your observation. (The purple color may be more easily observed by tapping the test tube and carefully observing the solution on the side)

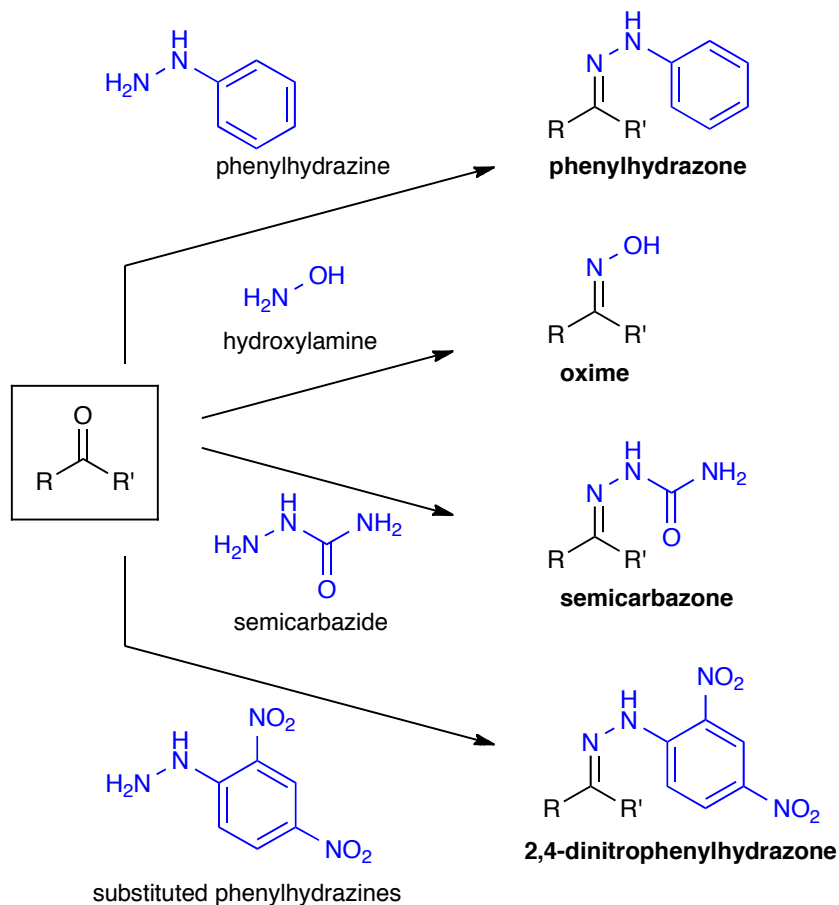
- A positive test is denoted by the formation of a deep purple colour upon oxidation by air.

Waste Disposal: Dispose of the waste in the waste container labeled *Purpald test Waste Only* before rinsing two times with acetone (*the rinses go in the waste container too*).

2. Reactions with Nitrogen Nucleophiles.

Many aldehydes and ketones are liquids at or near room temperature and it is often more convenient to convert these to solid derivatives for identification purposes. Solids are much easier to purify and identify than liquids and require much less material to do so. In some cases, the solid derivative is more stable than the parent carbonyl compound, aldehydes in particular, and consequently may be more readily stored in the solid form. When required, the carbonyl compound is regenerated by hydrolysis of the adduct, i.e., reversal of the original addition.

The most common reagents for the formation of such derivatives are substituted amines the more important of which are: phenylhydrazine (Ph-NHNH₂), hydroxylamine (NH₂OH), semicarbazide (NH₂CONHNH₂), and substituted phenylhydrazines. The overall reaction with each of these is similar and can be written in general as:



These derivatives are usually crystalline solids, except frequently in the case of the lower molecular-weight oximes. 2,4-Dinitrophenylhydrazones are the most frequently employed for identification purposes since even the simple carbonyl compounds give highly crystalline solids, which are easily handled. Semicarbazones, on the other hand, are more commonly employed if the eventual aim is to regenerate

the parent carbonyl compound; steam distillation of the semicarbazone in the presence of dilute acid is generally used for the regeneration.

The great ease and rapidity with which 2,4-dinitrophenylhydrazones can be prepared, along with their *deep, distinctive colors (yellow-orange-red)* renders their formation an extremely useful qualitative test for the initial detection of the presence of a carbonyl function in an unknown compound. The preparation of a solid derivative of an "unknown" solid or liquid was the basis of a classical approach to structure elucidation. This method for the determination of an unknown is outdated, since most structural characterization is done by NMR spectroscopy. However, the formation of the derivatives illustrates the reactions of carbonyl compounds with nitrogen nucleophiles.

2,4-DINITROPHENYLHYDRAZONES: PROCEDURE FOR FORMATION OF A CRYSTALLINE DERIVATIVE

**AS ALWAYS PERFORM ALL REACTIONS IN THE FUMEHOOD!
Stopper all test tubes when they are outside of the fumehood.**

***CAUTION*:** 2,4-Dinitrophenylhydrazine is harmful if absorbed through your skin and will dye your hands yellow. Wear gloves and wash hands after using (you should wash your hands always before leaving the lab!).

(i) Qualitative analysis: Preparation of 2,4-DNPH derivatives

- To a large clean, but not dry test-tube dissolve 1-2 drops of the liquid compound (or an estimated 50 mg of a solid) in 1 mL of 95% ethanol (Conduct the test on each of the following: Acetone, Acetophenone, Benzaldehyde)
- Add 1 mL of the 2,4-dinitrophenylhydrazine reagent solution, shake well and allow to stand for a few minutes.
- In a positive test, a yellow to orange-red to red crystalline precipitate of the 2,4-dinitrophenylhydrazone derivative is deposited within a few minutes at room temperature. Occasionally, it may be necessary to warm the solution briefly to accelerate a slow reaction.
- Record your observations.

Waste Disposal: Dispose of the solid waste in the *Solid Waste Container*.

(ii) Preparation of Cyclohexanone 2,4-DNPH

You will also do this test with cyclohexanone, **but in this case you will collect the product:**

- Put **5 drops** of cyclohexanone in 2 mL of alcohol and add ~ 2mL of the 2,4- dinitrophenylhydrazine reagent.
- Collect the precipitate by suction filtration on a Hirsch funnel, wash with cold water and dry under the air vacuum. Recrystallize the 2,4-dinitrophenylhydrazone from 95% ethanol, dry in a 100-110 °C oven and determine its melting point. Use the melting point as a conformation of identity. Compare your results with the literature value and submit your product with your report.

(iii) Identification of an 'Unknown' Carbonyl Compound

- In the same way you did for cyclohexanone, prepare the 2,4-dinitrophenylhydrazone derivative with half of your unknown and isolate the derivative by suction filtration, recrystallize from ethanol (or alcohol/water), dry and determine its melting point.
- Note that in a few instances (higher MW compounds), the derivative is only very slightly soluble even in hot 95% ethanol; if your 2,4-dinitrophenylhydrazone derivative has not dissolved almost completely in 3-4 mL of boiling 95% ethanol, decant off the liquid from the remaining solid.
- After crystallization, isolate the solid by Hirsch filtration. Determine the mp of your unknown 2,4-DNPH-derivative. You should use the cyclohexanone 2,4-dinitrophenylhydrazone, prepared in part b) as a melting point standard.

BE SURE TO GET AN IR SPECTRUM OF YOUR UNKNOWN.

MELTING POINTS: (For Unknown)	Aldehyde or Ketone	m.p. of 2,4-DNPH derivative
	Propanal (propionaldehyde)	154
	Butanal (butyraldehyde)	123
	Buten-2-al (crotonaldehyde)	190
	<i>p</i> -Tolualdehyde (4-methylbenzaldehyde)	233
	Benzaldehyde	237
	<i>p</i> -Anisaldehyde (4-methoxybenzaldehyde)	254 (decomp)
	2-Propanone (acetone)	126
	2-Pentanone	144
	3-Pentanone	156
	2-Hexanone	106
	2-Heptanone	89
	2-Octanone	58
	Acetophenone (phenylethanone)	238
	Propiophenone (1-phenylpropanone)	191
	Benzophenone	238
	Cyclopentanone	146
	Cyclohexanone	162

EXPERIMENT 6: Reactions of Carbonyl Compounds: Aldehydes and Ketones – DATA SHEET

NAME:	
LAB SECTION:	
DEMONSTRATOR(S):	

DUE DATE: _____

PART A: OXIDATION

Tollens' Silver Mirror Test – Basic Reaction Equation:

COMPOUND	STRUCTURE	RESULT AND CONCLUSION
Benzaldehyde (phenylmethanal)		
Propionaldehyde (propanal)		
1-Phenylethanone (acetophenone)		
Cyclohexanone		
Your unknown		

Fehling's Test – Basic Reaction Equation:

COMPOUND	STRUCTURE OF COMPOUND	RESULT AND CONCLUSION
Benzaldehyde		
Propionaldehyde (propanal)		
D-Glucose		
Cyclohexanone		
Your unknown		

PART B: REACTIONS OF ENOLATE ANIONS

Iodoform Test – Basic Reaction Equation:

COMPOUND	STRUCTURE OF COMPOUND	RESULT AND CONCLUSION
2-Pentanone		
3-Pentanone		
Cyclohexanone		
1-Phenylethanone (acetophenone)		
Your unknown		

PART C: ADDITION REACTIONSPurpald[®] Aldehyde Test – Basic Reaction Equation:

COMPOUND	COLOR IN TEST	CONCLUSION
Benzaldehyde		
Propionaldehyde (propanal)		
Cyclohexanone		
1-Phenylethanone (acetophenone)		
Your unknown		

2,4-DNP Derivatives – Basic Reaction Equation:

COMPOUND	DESCRIPTION OF SOLID	OBSERVATIONS
2-Propanone		
Benzaldehyde		
Cyclohexanone		m.p. _____
1-Phenylethanone (acetophenone)		
Your unknown		m.p. _____

PART C: UNKNOWN**OBTAIN AN IR OF YOUR UNKNOWN****UNKNOWN NUMBER:** _____

Summary:

TEST	RESULT	CONCLUSION
Tollens'		
Fehling's		
Purpald		
Iodoform		
2,4-DNP Derivative		

2,4-DNP derivative melting point: _____ °C

Literature melting point (from table in laboratory procedure): _____ °C

Melting point of cyclohexanone derivative: _____ °C

Literature melting point (from table in laboratory procedure): 162 °C**NAME AND STRUCTURE OF UNKNOWN IS:**

Questions:

- 1) Discuss briefly your IR Spectrum and summarize how you concluded your unknown's identity.
- 2) Sketch what you think the NMR spectra of your unknown would look like.
- 3) Imagine you are Gil Grissom (or Catherine Willows) (a.k.a. –CSI) and you have been called as a forensic scientist (Chemist!) to help investigate a fire at a local drinking establishment (*The Ceeps*) that the police suspect to be arson. Residue found at the scene was found to contain traces of MEK (methyl ethyl ketone or 2-butanone). One of the key suspects of the case is a rowdy patron who was recently barred from ever entering the premise over an unpaid bar bills and he has been threatening the owners of the establishment. The suspect, in his spare time, likes to tinker on cars as a hobby in his home garage and would use MEK, which is a degreasing agent. Since they were in sight police find two unlabelled cans containing flammable liquids in the suspect's garage. The suspect claims that one can is fuel for his lawn mower and the other is BBQ starter. Of course as a chemist you know that fuels are mostly mixtures of hydrocarbons. In an attempt to get a full search-warrant the police require two quick test results that would provide evidence that one or both of the unknown containers could possibly contain MEK (and not fuel). What two quick tests could you perform?

Once you were given more time, how could you definitively match one of the samples found to the solvent recovered at the scene and therefore discredit the suspect's claim and thus help in conviction?