Reactions of Aldehydes and Ketones

Structure Deduction using Classification Tests
Determination of Structure

Determining the structure of an unknown organic compound is an exercise in deductive reasoning. (Hello, Sherlock!)

In modern chemical laboratories, this process primarily involves analysis of data from modern analytical instruments – GC, FTIR, MS, and NMR are the most important.

For many decades, the primary method for structure deduction involved reactions characteristic for a limited number of functional groups – Classification Tests.

Classification Tests

Studying classification tests can help you understand the relationship of structure to reactivity. That is why we continue to use them in organic teaching laboratories.

Today, you will use characteristic reactions of aldehydes and ketones to determine the structure of an unknown sample.

You will work with a partner in this experiment. Which one will be Sherlock and which Watson?
Classical Structure Determination
(of a previously known compound)

1. Separation and Purification
2. Physical Properties
   a. Melting Point
   b. Boiling Point
   c. Refractive Index
3. Chemical Classification Tests
4. Preparation of Solid Derivatives

Today’s Experiment - Identification of an Unknown Aldehyde or Ketone

7 Distillation
   – Boiling point
7 Classification Tests
   – Functional group (aldehyde or ketone?)
   – Partial structure
7 Solid Derivatives
   – Comparison of m.p. to knowns
7 Infrared Spectrum
Classification Tests

7 Tollen’s Test
   – Positive with aldehydes

7 Schiff’s Test
   – Rapid color change with aliphatic aldehydes

7 Iodoform Test
   – Yellow ppt. with methyl carbonyls or methyl 2° alcohols

\[
\begin{align*}
    \text{H}_3\text{C} - & \text{C} - \\
    \text{H}_3\text{C} & \text{O} \\
\end{align*}
\]

Derivative Formation

7 2,4-DNP formation
   – Colored solid with aldehydes and ketones
   – Useful solid derivative (color variation can indicate structural features)

7 Semicarbazone derivative
   – Useful solid derivative (more difficult to get good mp than DNP)
**Tollen’s test - Reaction**

\[ R-\text{CHO} + \text{Ag}^+ (\text{NH}_3)_2 \xrightarrow{\text{OH}^{-}} R-\text{COOH} + \text{Ag} \downarrow \]

1. In this reaction, the aldehyde is oxidized to the carboxylic acid while the Ag(I) ion is reduced to metallic silver which forms a black precipitate or a silver mirror on clean glass surfaces.
2. The test is negative with other O-containing functional groups.

**Schiff’s test - Reaction**

1. Aldehydes undergo addition to the carbonyl group much more readily than ketones. One such addition is the reaction with sodium bisulfite. This reaction is not often used synthetically, but is the basis for the Schiff’s test.
Schiff’s test - Reaction

Bisulfite also adds to the dye, rosaniline hydrochloride, to give a colorless adduct that is called Schiff’s reagent.

\[
\begin{align*}
\text{aldehyde} & \quad \text{bisulfite} \\
\text{ROS} & \quad \text{HSO}_3^- \\
\end{align*}
\]

When Schiff’s reagent is added to an aldehyde, the equilibrium of these two reactions favors the free dye and the aldehyde adduct. Aliphatic aldehydes (R = alkyl) give a intense color almost instantaneously. Aromatic aldehydes and ketones will give the color change at a much slower rate.
Iodoform Reaction

7 Iodine in a basic solution gives hypoiodite ion, an oxidant like hypochlorite in chlorine bleach. Hypoiodite will oxidize $2^\circ$ alcohols to ketones. This oxidation results in no visible change – it is not useful as a classification test.

7 However, iodine in base also leads to substitution of hydrogens $\alpha$ to carbonyl groups by iodine.

\[
\begin{align*}
\text{H}_3\text{C} &= \text{C} = \text{CH}_2 \\
\text{HO}^- &\rightarrow \\
\text{I}_3\text{C} &= \text{C} = \text{CH}_2
\end{align*}
\]

Iodoform reactions

7 In the case of carbonyl groups with a methyl group on one side, the substitution reaction occurs almost exclusively on the methyl group.

7 This substitution reaction results in a triiodomethyl group attached to the carbonyl. Again, no visible change to this point.
Iodoform Reaction

7 Under the basic conditions, hydroxide anion can attack the carbonyl group giving a tetrahedral intermediate, which can collapse to $I_3C^-$ anion and a carboxylic acid.

Iodoform Reaction

7 The $I_3C^-$ anion is a reasonable leaving group because of the delocalization onto the iodine atoms. A proton transfer then gives iodoform ($CHI_3$) as a yellow precipitate.
Iodoform Reaction

Thus, this test gives a yellow precipitate from the reaction solution if either of the following structural features are present in the molecule:

\[
\begin{align*}
\text{H}_3\text{C}-\text{C} & \quad \text{H}_3\text{C}-\text{C} \\
\text{O} & \quad \text{OH}
\end{align*}
\]

Derivatives

Both the 2,4-DNP and semicarbazone derivatives are stable imine-type derivatives of aldehydes and ketones.

\[
\begin{align*}
\text{R} & \quad \text{R(H)} \quad \text{H}_2\text{N} - \text{Y} \\
\text{2,4-DNP} & \quad \text{Y} = \text{OH} \\
\text{Semicarbazone} & \quad \text{Y} = \text{OH}
\end{align*}
\]
Derivatives - Mechanism

\[ R'\overset{\text{C}}{\text{R(H)}} \overset{\text{H}_2\text{N-Y}}{\rightleftharpoons} R'\overset{\text{C}}{\text{N-R(H)}} + \overset{\text{Y}}{\text{N}} + \overset{\text{H}_2\text{O}}{\text{H}_3\text{O}^+} \]

7 The reaction medium must be slightly acidic for the dehydration step to occur, but not too acidic that the nucleophilic amine derivative is totally protonated.

Hints

7 Make sure your glassware for classification tests is not contaminated with wash acetone. Water, however, does not complicate these tests.

7 Make sure to distill your unknown rapidly enough to get a good boiling point – a major hint in deducing your structure.

7 Make your solid derivatives first. These solids need to dry before taking m.p.
Procedure

7 You MUST complete the derivative formation this lab period. Other classification tests, melting points and the infrared spectrum will be completed NEXT WEEK.

7 You will need to store both your distilled unknown and the solid derivatives.

Procedure – Next Week

7 Obtain m.p. values for your derivatives and complete classification tests. Use this data to determine the most likely structure of your unknown.

7 You need to write this structure in your lab note-book and get your TA to initial it before you take your infrared spectrum.

7 Obtain an infrared spectrum of your unknown.
Structure Deduction

7 Reference spectra for the unknowns will be posted on the webpage for this experiment after next week’s lab.

7 Use all of your data to deduce the structure that best matches your data. Explain your reasoning and any data that might be inconsistent with your conclusion in your laboratory report.

Safety

7 All reagents and unknowns used in the experiment are, at least, irritants. Try to avoid spills and exposure to skin. Read Safety info at end of each Classification Test in the Techniques section.

7 The 2,4-DNP reagent, Tollén’s reagent, and iodoform reagents will stain and injure skin.

7 Dispose of all used and unused reagents in the appropriate waste bottle.