Reduction of Carbonyl Compounds

Characteristics of Reduction Reactions
1. A gain of hydrogen, $H_2$
2. A loss of oxygen, O

- Reduction of a carbonyl compound in general gives an alcohol
- Note that organic reduction reactions add the equivalent of $H_2$ to a molecule

\[
\text{R} -\text{C} - \text{H} \quad \xrightarrow{[\text{H}]} \quad \text{R} -\text{C} - \text{H}^\text{OH}
\]

A carbonyl compound
an alcohol

where $[\text{H}]$ is a generalized reducing agent

- Aldehydes gives primary alcohols
- Ketones gives secondary alcohols

\[
\text{R} -\text{C} - \text{H} \quad \xrightarrow{[\text{H}]} \quad \text{R} -\text{C} - \text{H}^\text{OH}
\]

Aldehyde
1° Alcohol

\[
\text{R} -\text{C} - \text{R}' \quad \xrightarrow{[\text{H}]} \quad \text{R} -\text{C} - \text{R}'^\text{OH}
\]

Ketone
2° Alcohol
ALDEHYDES/KETONES

Reduction by Hydride Reducing Agents

\[
\text{Borane} + \text{Sodium Hydride} \rightarrow \text{Sodium Borohydride (NaBH}_4\text{)}
\]
- used in water and alcohol solvents
- reduces aldehydes and ketones

Nucleophilic Addition to C=O (Convert C=O to CH-OH)

NaBH\(_4\) reacts as donor of hydride ion (H:\(\cdot\))
- Attack of H:\(\cdot\) at sp\(^2\) carbon of carbonyl leading to sp\(^3\) TI
- Protonation (H\(^+\)) of resulting alkoxide then affords alcohol

Tetrahedral Intermediate

\[
\text{then } H_3\text{O}^+ \rightarrow R-CR'
\]
Sodium Borohydride Reduction

Advantages to using NaBH₄
• Safe and relatively stable to water
• Sodium borohydride is chemoselective for the carbonyl in an aldehyde or ketone, does not react with other reducible functionality
Selectivity

A reaction is said to be *regioselective* if it might produce two or more structural isomers but in fact yields one of the preferentially.

A reaction is said to be *stereoselective* if it might produce two or more stereoisomers but in fact yields mainly (or entirely) one of them.

A *chemoselective* reaction is a reaction in which a reagent reacts with one functional group in preference to another.
Sodium Borohydride Reduction

Mechanism
Sodium Borohydride Reduction

Procedure
1. Dissolve 4-nitrobenzaldehyde (1.5 g) in ethanol (15 mL)
2. Warm the solution (hot plate setting of 1)
3. Add NaBH₄ (0.75 g) in increments over 5 min
4. Warm for 30 min (Do not allow the ethanol to evaporate, an orange smoke will be produced)
5. Slowly pour the mixture into cold water (30 mL). Product a yellow precipitate
6. Collect precipitate and recrystallize from 50:50 ethanol:water (~ 6 mL).
7. Determine percent yield, melting point, IR (KBr)
8. Perform a TLC on the product using CH₂Cl₂ at eluent; compare with starting material
**Sodium Borohydride Reduction**

**IR**
Look for the absence of a peak at $\sim 1700 \text{ cm}^{-1}$ due to carbonyl
Look for a peak at $\sim 3350 \text{ cm}^{-1}$ due to an O-H stretch (broad, intense, not sharp)
Look for peaks $\sim 2850 – 2950 \text{ cm}^{-1}$ due to aliphatic C-H stretch
Look for absorptions due to N—O stretch
  - Asymmetric stretch at $\sim 1520 \text{ cm}^{-1}$
  - Symmetric stretch at $\sim 1350 \text{ cm}^{-1}$

**Report:**
Give $R_f$ value for the product and compare with starting material commenting the completeness of reaction and on the role of hydrogen bonding. $R_f$ values are unitless. Indicate how IR allows you to assess the expected conversion, include units for IR absorptions.