**Course Code: MSCH6002** 

**Course Name: Reagents and Heterocyclic Chemistry** 

Complex metal hydride reductions: LiAlH4 and NaBH4

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### **TOPICS COVERED**

- ➤ Lithium Aluinium Hydride (LAH)
- > Mechanism of Reduction using LAH
- Reduction of carbonyl compounds, carboxylic acid using LAH
- Reduction of amides, esters, epoxides using LAH
- Comparative analysis of LiAlH4 and NaBH4
- >Stereochemistry of Ketone Reduction and Problems

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#### Lithium Aluminum Hydride (LAH)

Lithium aluminum hydride (LAH) is a strong reducing agent with chemical formula LiAlH<sub>4</sub>. It can reduce a variety of functional groups such as aldehydes, esters, acids, ketones, nitriles, epoxides and azides. It vigorously reacts with water and all the reactions are performed in polar aprotic solvents.

### Preparation

It was first prepared by treating lithium hydride (LiH) with aluminum chloride (AlCl<sub>3</sub>)

$$4LiH + AlCl3$$

$$LiAlH_4 + 3LiCl$$

In industrial scale, it is prepared from sodium aluminum hydride which is prepared by reaction of sodium, aluminum and hydrogen at high temperature and pressure

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## **Mechanism of Ketone Reduction Using LAH**

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## Functional group reduced by LAH

Functional group	Reduction product
RCHO	RCH <sub>2</sub> OH
$R_2C=O$	RCH(OH)R
$RCO_2R'$	$RCH_2OH + R'OH$
RCO <sub>2</sub> H	$RCH_2OH$
RCONHR'	RCH <sub>2</sub> NHR'
RCONR′ <sub>2</sub>	RCH <sub>2</sub> NR' <sub>2</sub> or RCH(OH)NR' <sub>2</sub> ( $\rightarrow$ RCHO + R' <sub>2</sub> NH)
RC≡N	$RCH_2NH_2$ or $RCH=NH (\rightarrow RCHO)$
RCH=NOH	$RCH_2NH_2$
$RNO_2$	$RNH_2$
ArNO <sub>2</sub>	ArNHNHAr or ArN=NAr
RCH <sub>2</sub> Br	$RCH_3$
RCH <sub>2</sub> OSO <sub>2</sub> Ar	RCH <sub>3</sub>
R C CH <sub>2</sub>	OH C C C C C C C C C C

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LiAlH<sub>4</sub> is a stronger reducing agent than NaBH<sub>4</sub>

LiAlH<sub>4</sub> is used to reduce compounds that are nonreactive toward NaBH<sub>4</sub>

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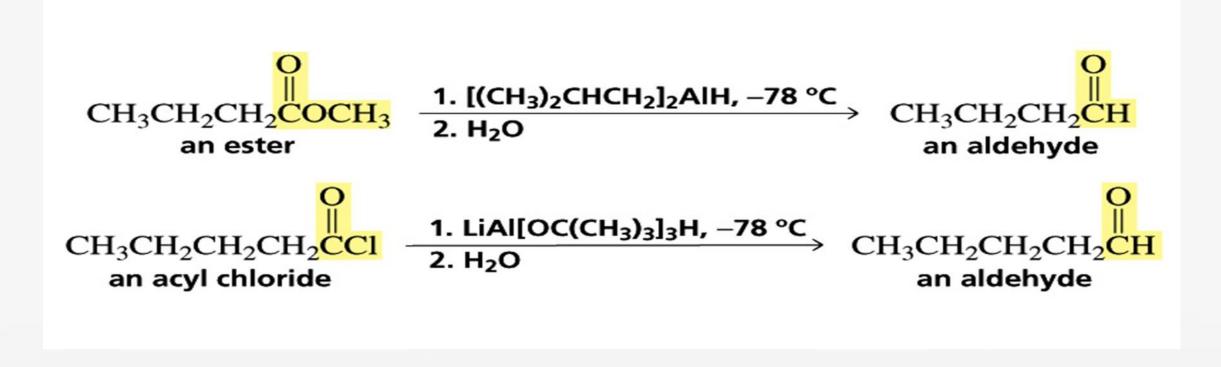
# Formation of Amines by Reduction

$$CH_{3}CH_{2}CH_{2}CNH_{2} \xrightarrow{ \textbf{1. LiAlH}_{4} } CH_{3}CH_{2}CH_{2}CH_{2}CH_{2}CH_{2}NH_{2}$$
 a primary amine 
$$CH_{3}CH_{2}CH_{2}CH_{2}CNHCH_{3} \xrightarrow{ \textbf{1. LiAlH}_{4} } CH_{3}CH_{2}CH_{2}CH_{2}CH_{2}NHCH_{3}$$
 a secondary amine 
$$CH_{3}CH_{2}CH_{2}CH_{2}CH_{2}CH_{3} \xrightarrow{ \textbf{1. LiAlH}_{4} } CH_{3}CH_{2}CH_{2}CH_{2}CH_{2}NCH_{3}$$
 a tertiary amine 
$$CH_{3}CH_{2}CH_{2}CH_{2}CH_{2}CH_{2}NCH_{3} \xrightarrow{ \textbf{2. H}_{2}O} CH_{3}CH_{2}CH_{2}CH_{2}NCH_{3}$$
 a tertiary amine

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DIBAL allows the addition of one equivalent of hydride to an ester Replacing some of hydrogens of LiAlH<sub>4</sub> with OR groups decreases the reactivity of the metal hydride



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NaBH<sub>4</sub> can be used to selectively reduce an aldehyde or a keto group in a compound

$$CH_{3}CCH_{2}CCH_{2}CCCH_{3} \xrightarrow{\textbf{1. NaBH}_{4}} CH_{3}CHCH_{2}CH_{2}CCCH_{3}$$

CH<sub>3</sub>CH=CHCH<sub>2</sub>CCH<sub>3</sub> 
$$\xrightarrow{\text{1. NaBH}_4}$$
 CH<sub>3</sub>CH=CHCH<sub>2</sub>CHCH<sub>3</sub>

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# Reduction of Epoxides

The epoxides are reduced to the corresponding alcohols. The hydride ion is transferred to the less hindered side of the epoxides.

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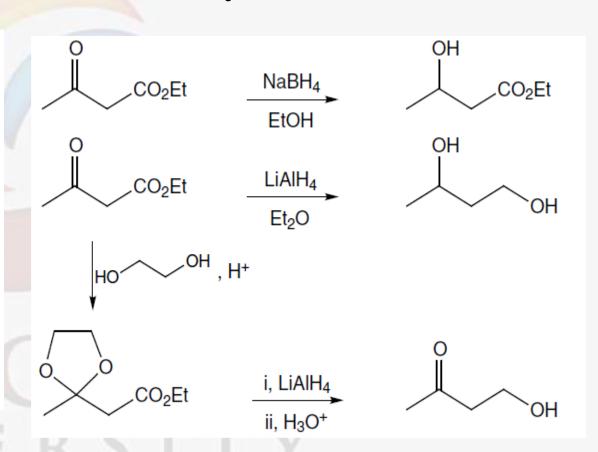
#### **More Examples of Reduction by LAH**

Ph CHO 
$$\frac{\text{LiAlH}_4}{\text{Et}_2\text{O}, 35 \,^{\circ}\text{C}}$$
 Ph OH

Ph CHO  $\frac{\text{LiAlH}_4}{\text{Et}_2\text{O}, -10 \,^{\circ}\text{C}}$  Ph OH

Ph OH

Ph OH



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