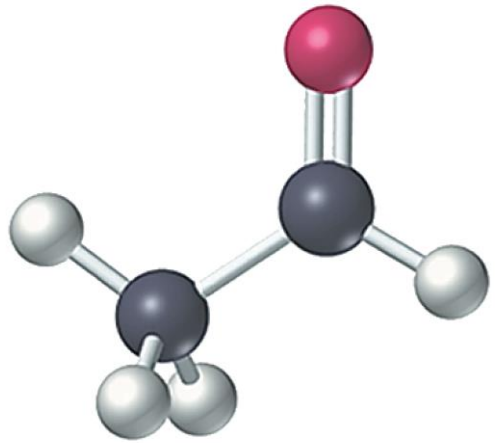
2302106 – Basic Organic Chemistry for ISE – Part II

Lecture 4-3

Aldehydes & Ketones – Nucleophilic addition-2



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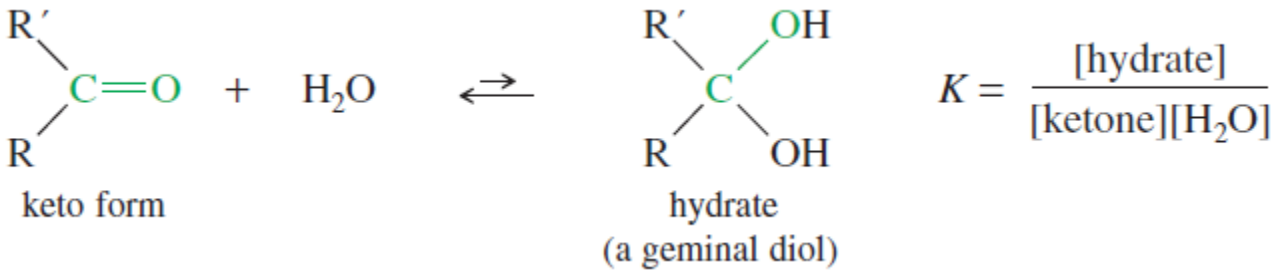
Recommended Textbook:

Chapter 18 in *Organic Chemistry*, 8th Edition, L. G. Wade, Jr., **2010**, Prentice Hall (Pearson Education)

Nucleophilic Addition with Weak Nucleophiles

1) Reaction with Water (Hydration)

- In an **aqueous** media, a ketone or an aldehyde is in equilibrium with a **geminal diol**



- The reaction is **very slow** because water is a **weak nucleophile**
- Either **activation** of the **nucleophile (the water)** or of the **electrophile (the carbonyl group)** is required

Nucleophilic Addition with Weak Nucleophiles

1) Reaction with Water (Hydration)

Base-catalysed hydration

Hydroxide is a much stronger nucleophile than water

Nucleophilic Addition with Weak Nucleophiles

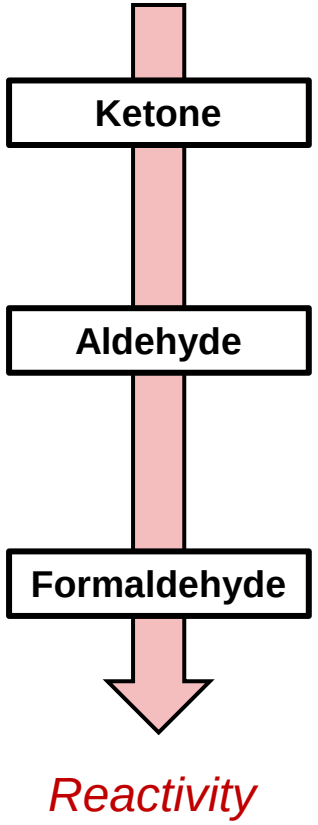
1) Reaction with Water (Hydration)

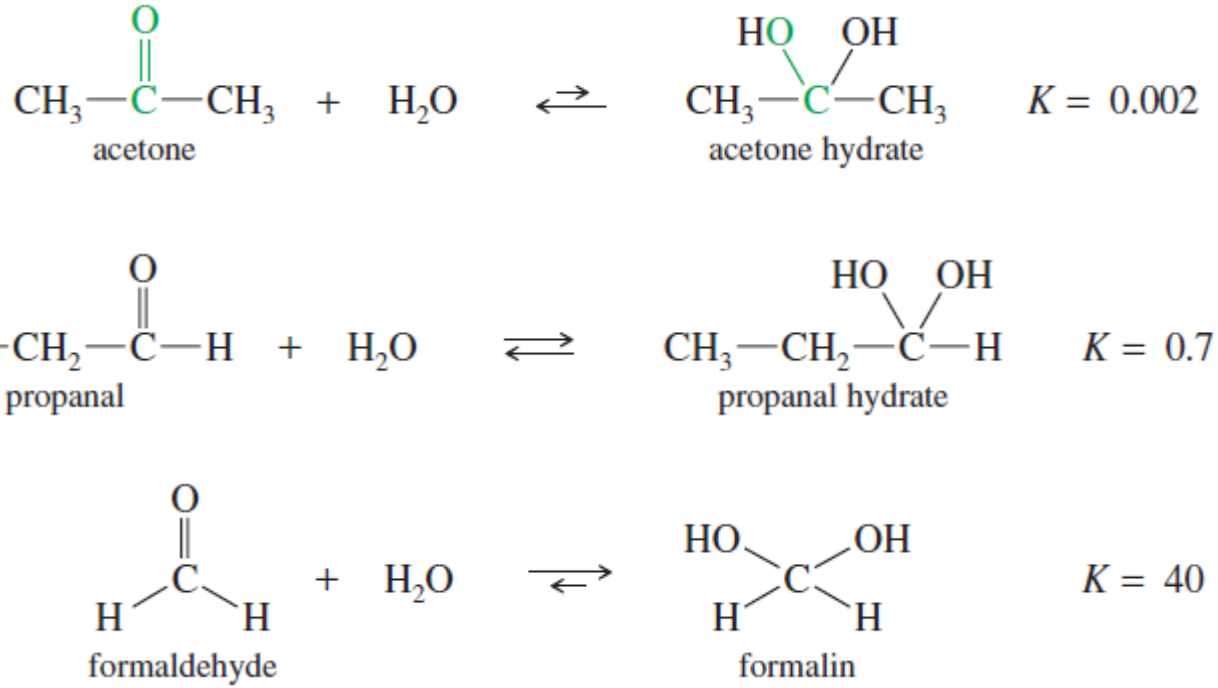
Acid-catalysed hydration

- A carbonyl group that is **protonated** (or bonded to some other electrophile) is **strongly electrophilic**, inviting attack by a weak nucleophile

Nucleophilic Addition with Weak Nucleophiles

1) Reaction with Water (Hydration)





Nucleophilic Addition with Weak Nucleophiles

2) Reaction with Alcohols (acetal formation)

Alcohol is a **weak nucleophile**

Base-catalysed

Nucleophilic Addition with Weak Nucleophiles

2) Reaction with Alcohols (acetal formation)

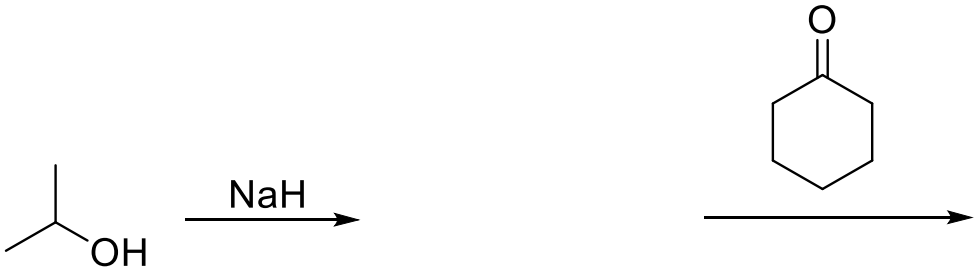
Acid-catalysed

Nucleophilic Addition with Weak Nucleophiles

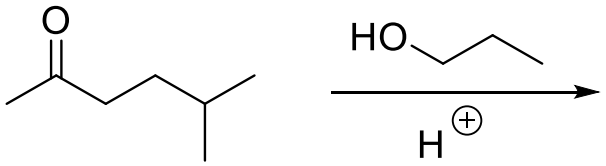
2) Reaction with Alcohols (acetal formation)

Examples

1)



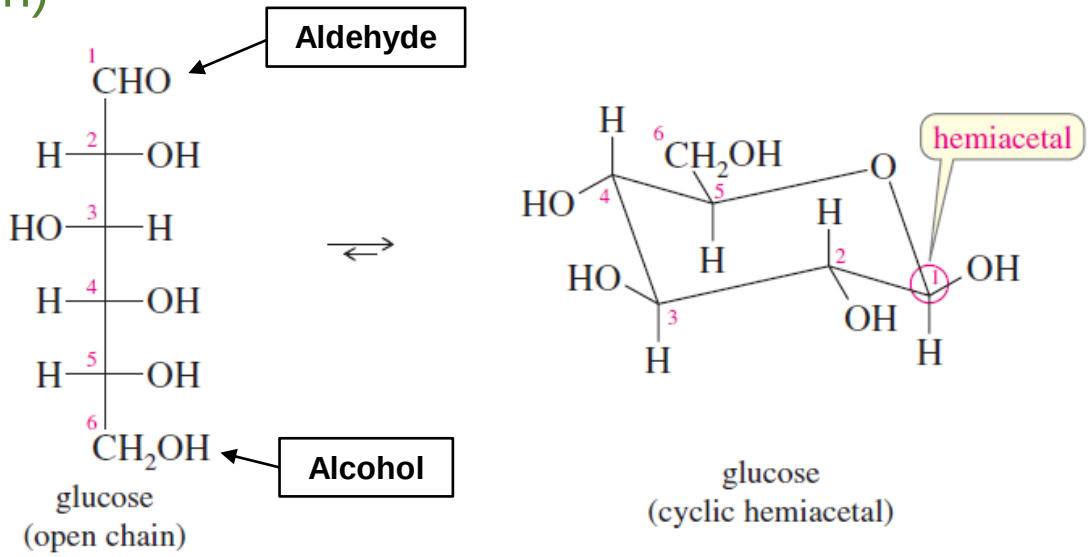
2)



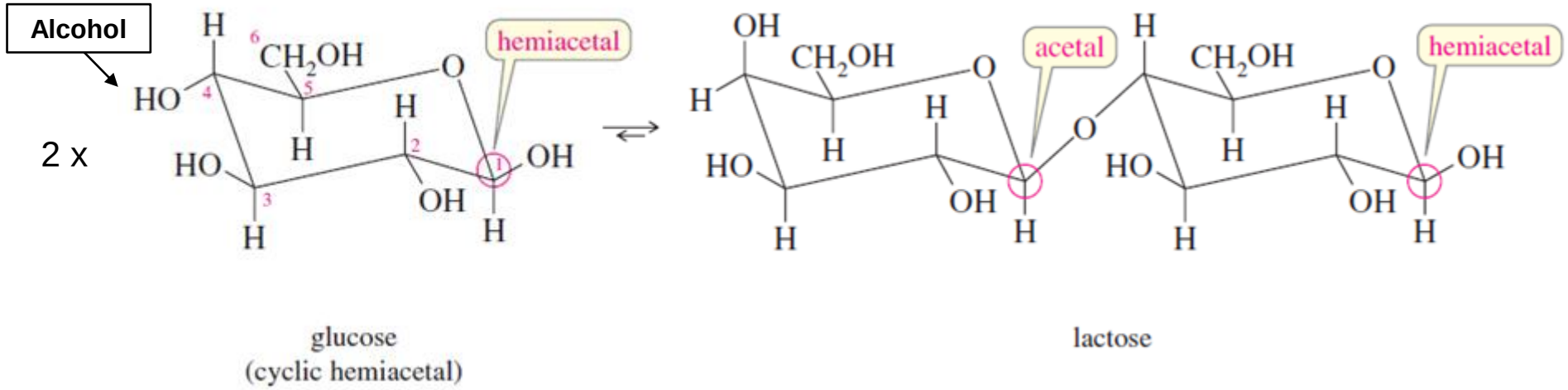
2) Reaction with Alcohols (acetal formation)

Carbohydrate Chemistry

- **Glucose** is a six-carbon sugar that is most stable as a **hemiacetal**



- **Lactose** is a disaccharide (composed of two sugar units) that has **one acetal** and **one hemiacetal**

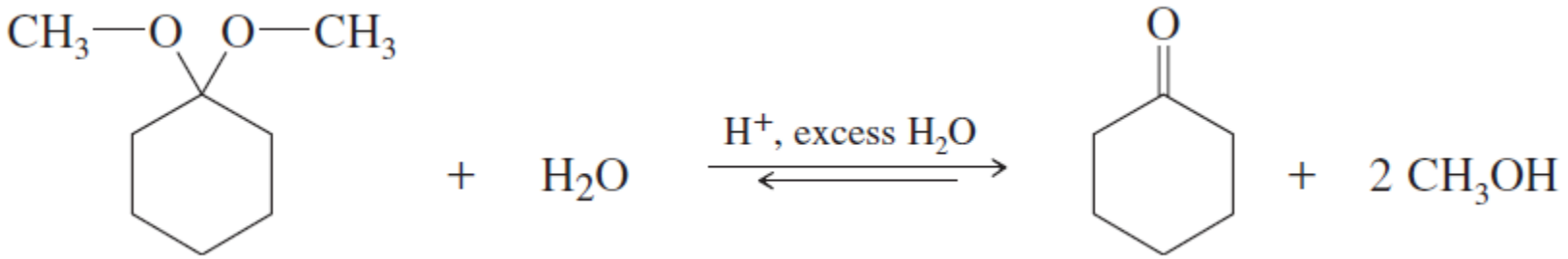


2) Reaction with Alcohols (acetal formation)

Equilibrium of Acetal Formation

- Acetal formation is **reversible**
- For simple **aldehydes**, equil. const. generally **favour the acetals**
- With **hindered aldehydes** and **most ketones**, equil. const. **favour the carbonyl**

- Most acetals are **hydrolysed** by shaking with **dilute acid in water**

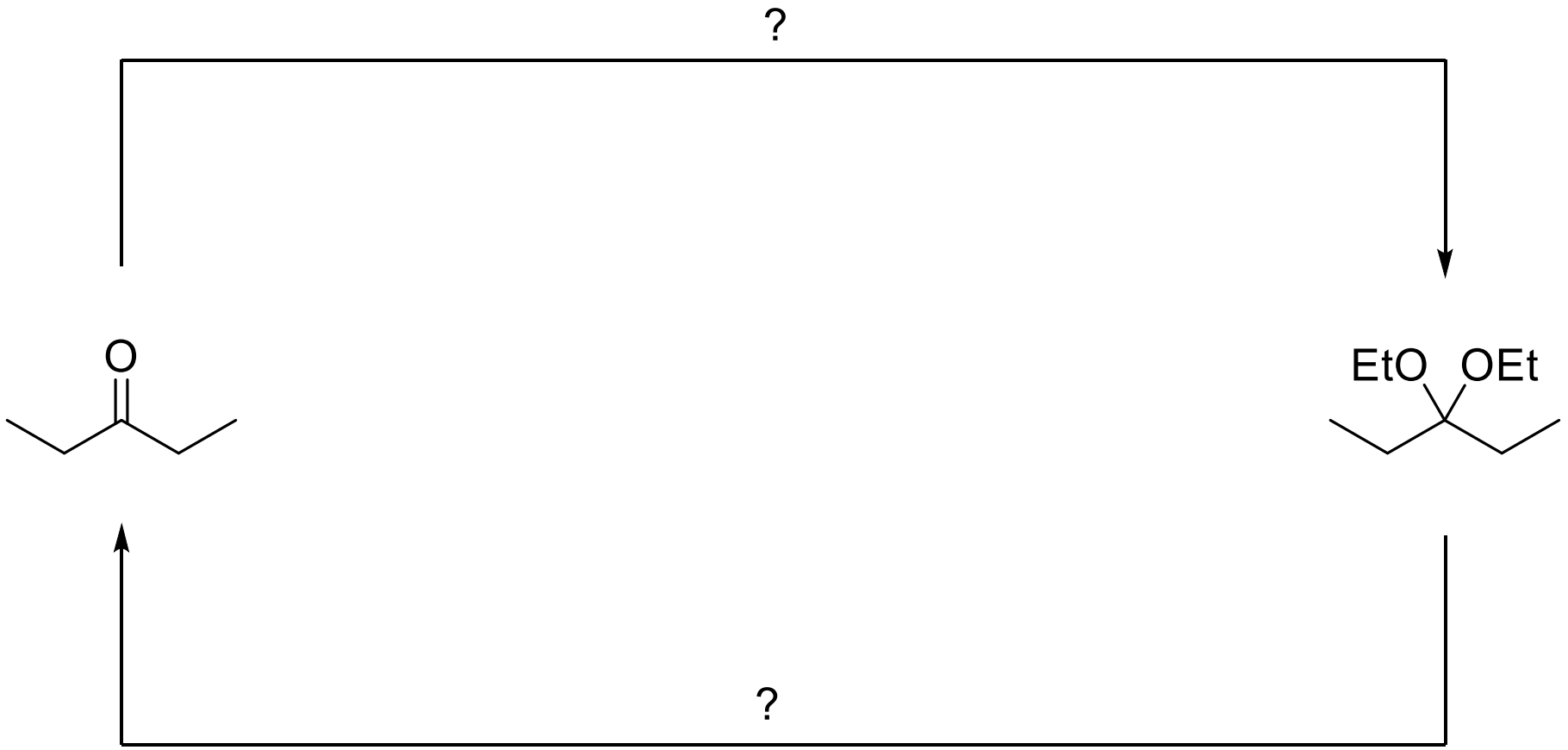


- Large **excess** of water drives acetals back to C=O

Nucleophilic Addition with Weak Nucleophiles

2) Reaction with Alcohols

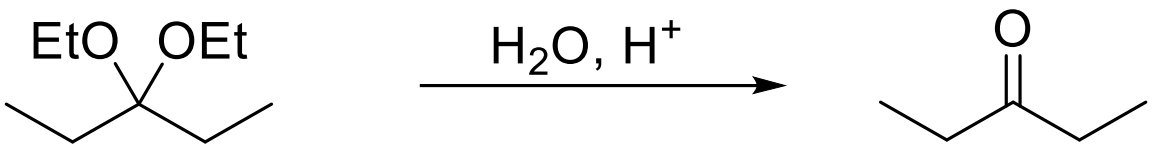
Examples



Nucleophilic Addition with Weak Nucleophiles

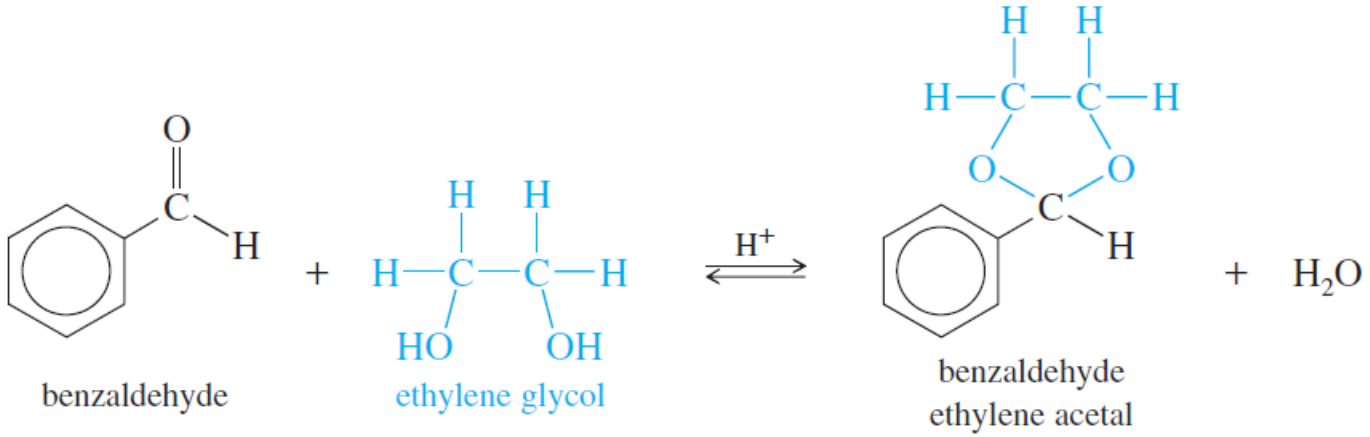
2) Reaction with Alcohols

Mechanism:



2) Reaction with **Alcohols** (acetal formation)

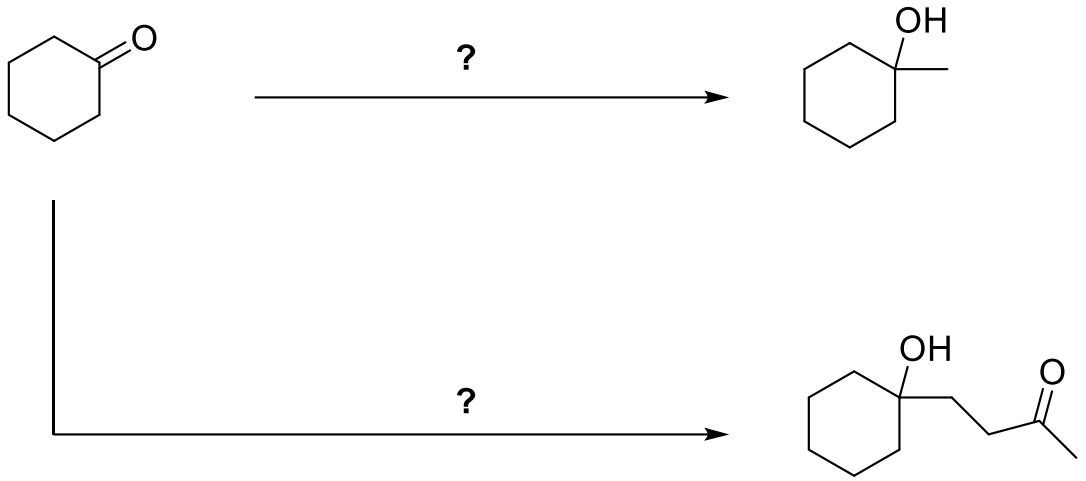
Cyclic Acetals • Formation of an acetal using a **diol** as the alcohol gives a **cyclic acetal**

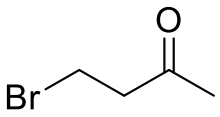


- Cyclic acetals often have **more favourable** equilibrium constants, since there is a **smaller entropy loss** (2 molecules condense instead of 3 for normal alcohol)

2) Reaction with Alcohols (acetal formation)

Acetals as Protecting Groups





- Acetals are **stable** to **strong bases** and **nucleophiles**

2) Reaction with Alcohols (acetal formation)

Acetals as Protecting Groups

Examples