17.8

Acetal Formation

Some reactions of aldehydes and ketones progress beyond the nucleophilic addition stage

Acetal formation

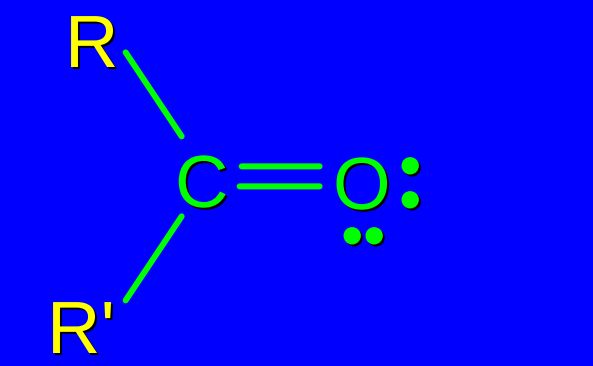
Imine formation

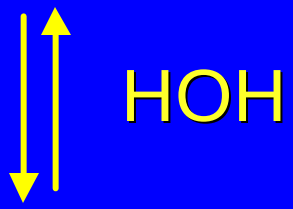
Enamine formation

Compounds related to imines

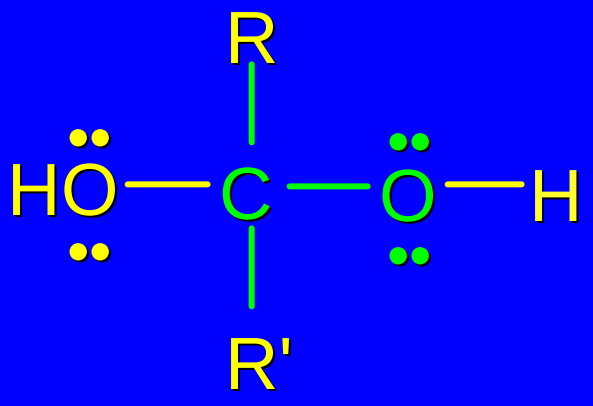
The Wittig reaction

Recall Hydration of Aldehydes and Ketones

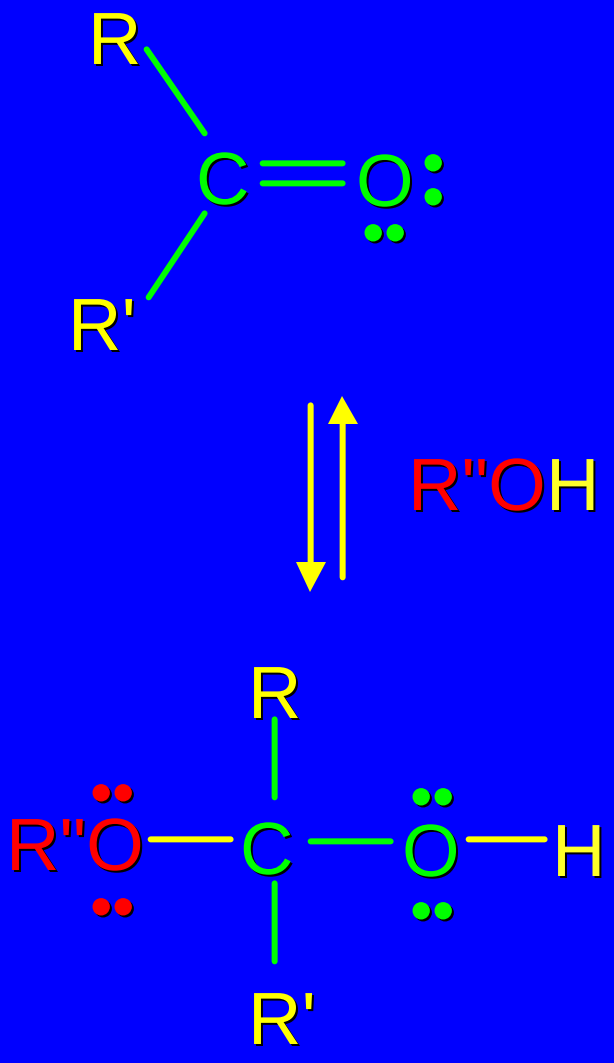




HOH

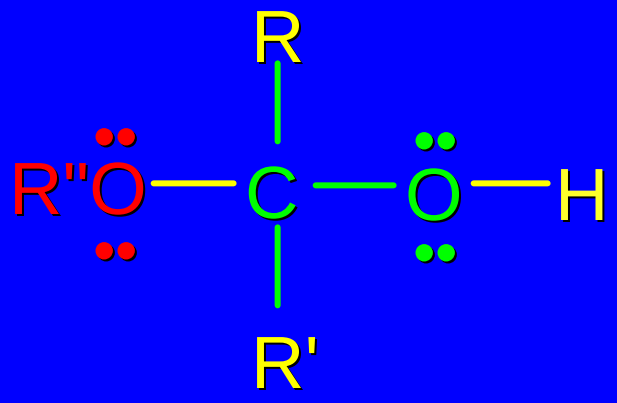


Alcohols Under Analogous Reaction with Aldehydes and Ketones



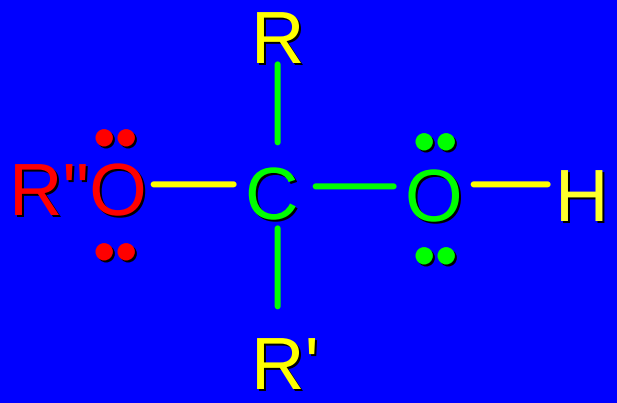
Product is called a *hemiacetal*.

Hemiacetal reacts further in acid to yield an acetal



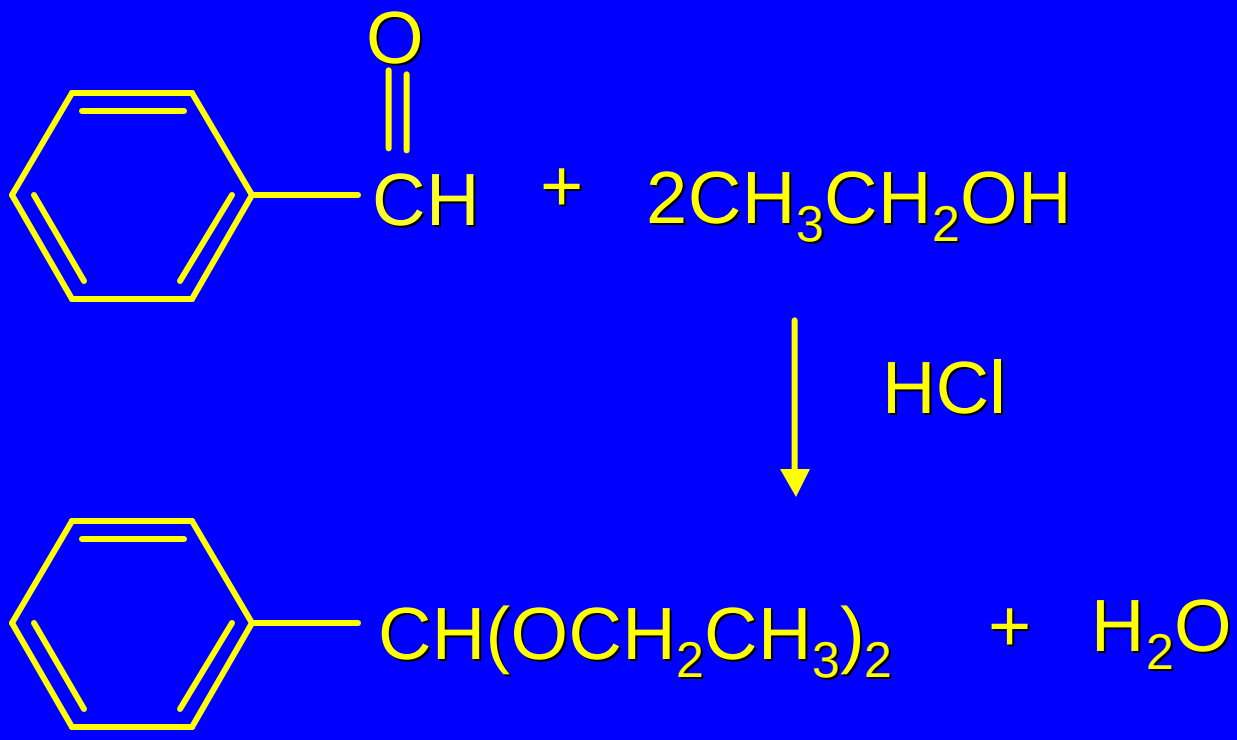
Product is called an *acetal*.

ROH, H^+



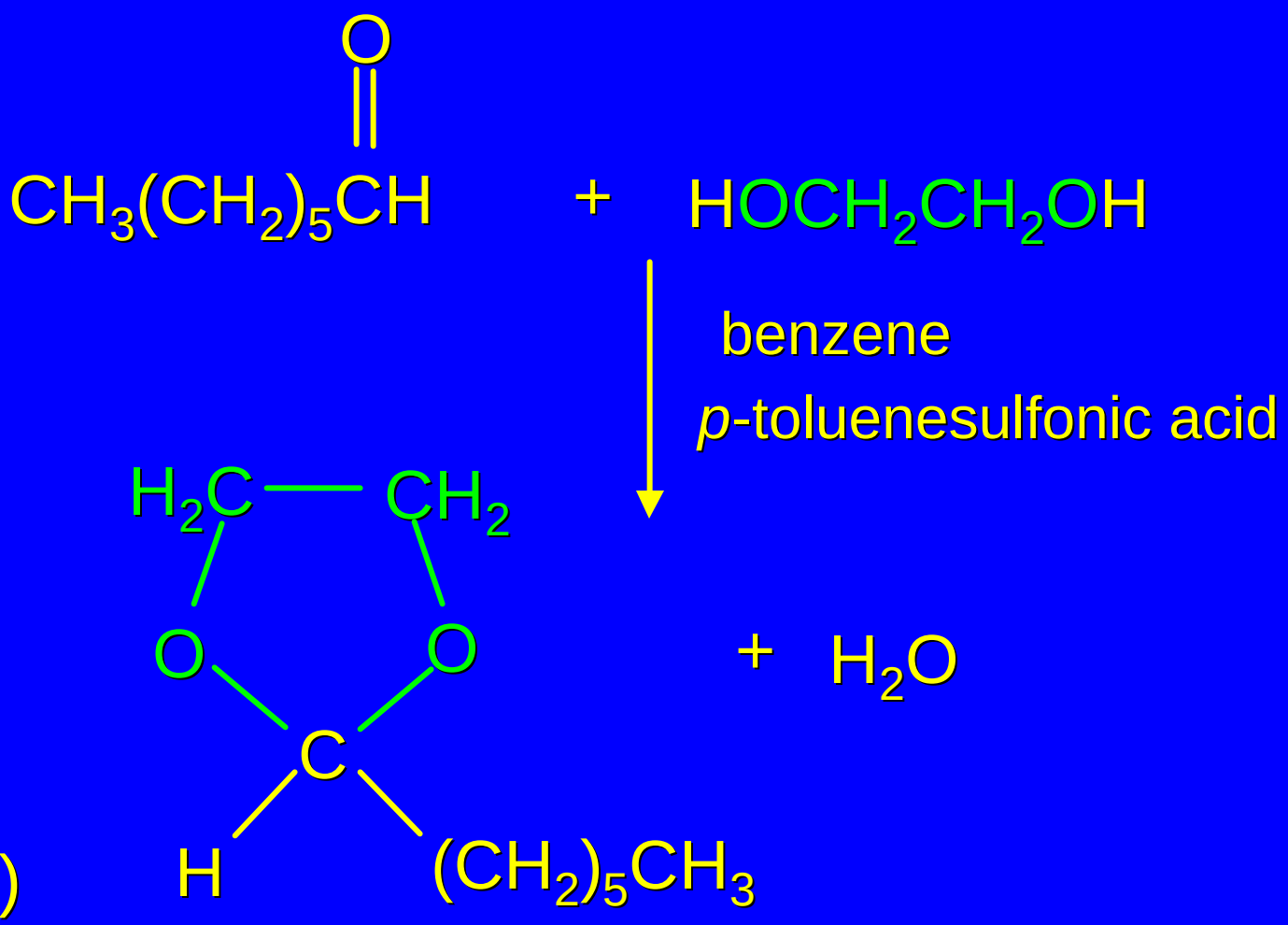
Product is called a *hemiacetal*.

Example



Benzaldehyde diethyl acetal (66%)

Diols Form Cyclic Acetals



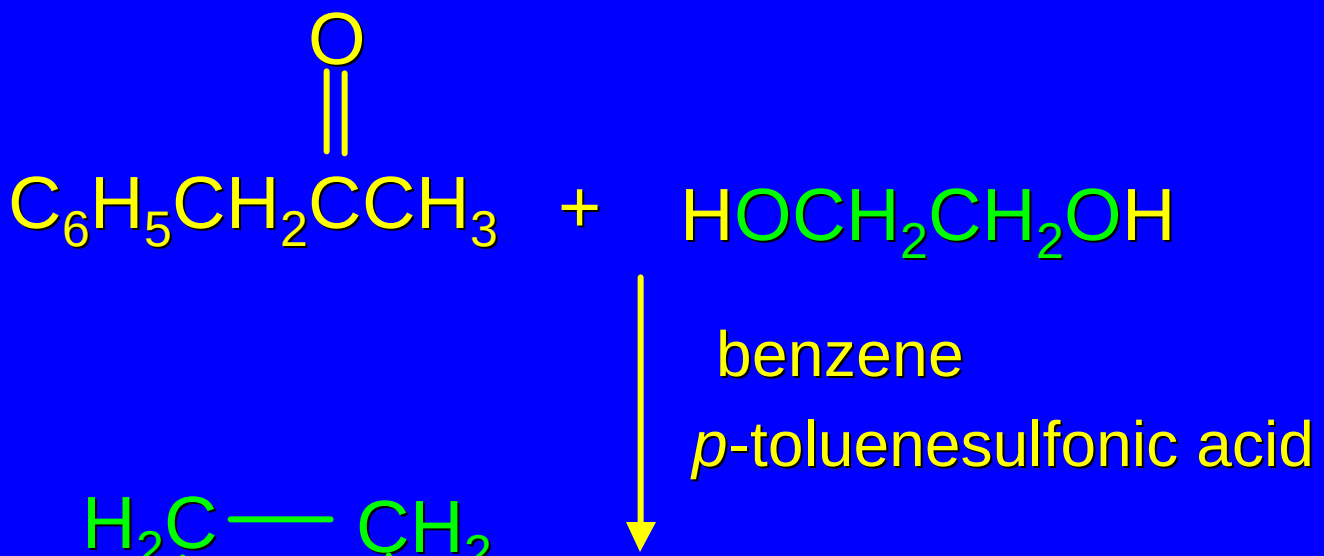
(81%)

In general:

Position of equilibrium is usually unfavorable for acetal formation from ketones.

Important exception:
Cyclic acetals can be prepared from ketones.

Example


O
C6H5CH2CCH3
+
HOCH2CH2OH
benzene
p-toluenesulfonic acid
H2C
CH2
O
O
C
C6H5CH2
CH3
+ H2O

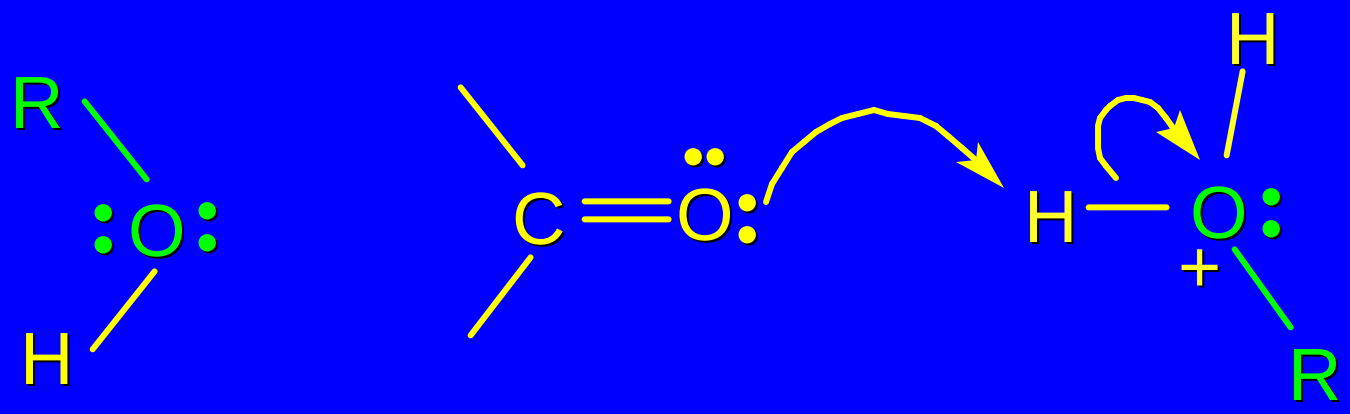
(78%)

Mechanism of Acetal Formation

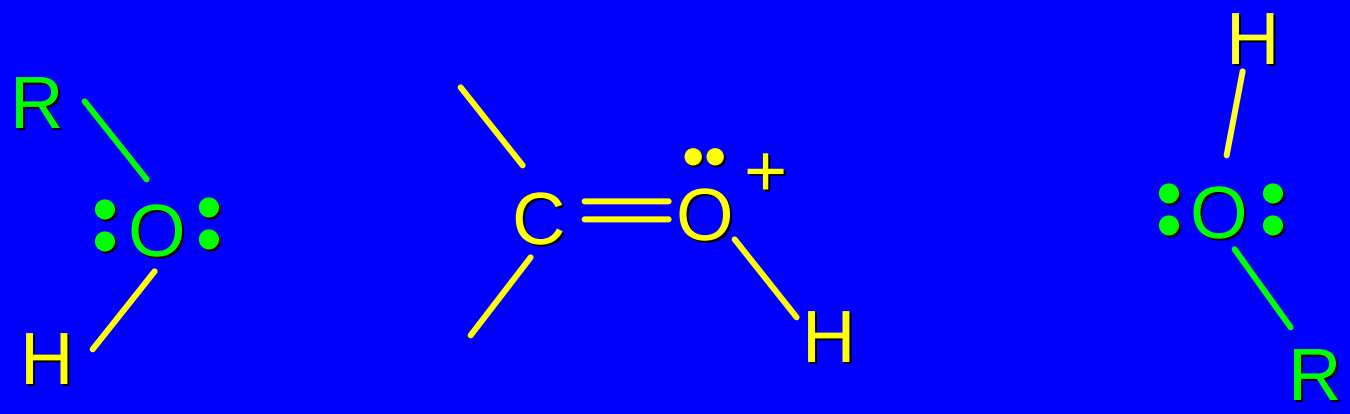
First stage is analogous to hydration and leads to hemiacetal

acid-catalyzed nucleophilic addition of alcohol to C=O

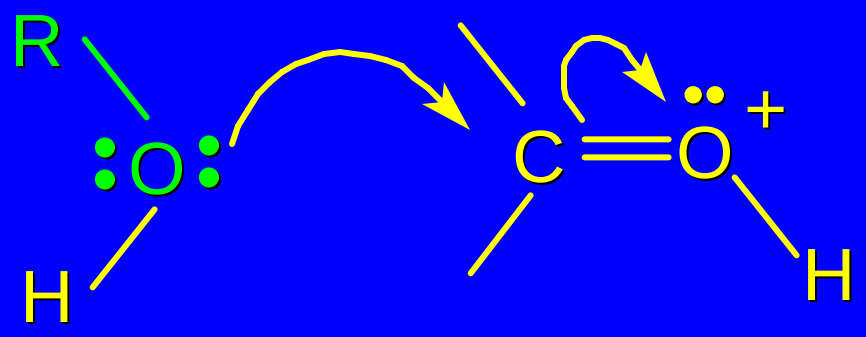
Mechanism



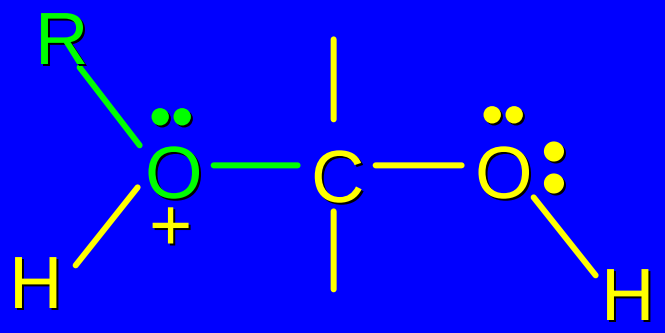
Mechanism



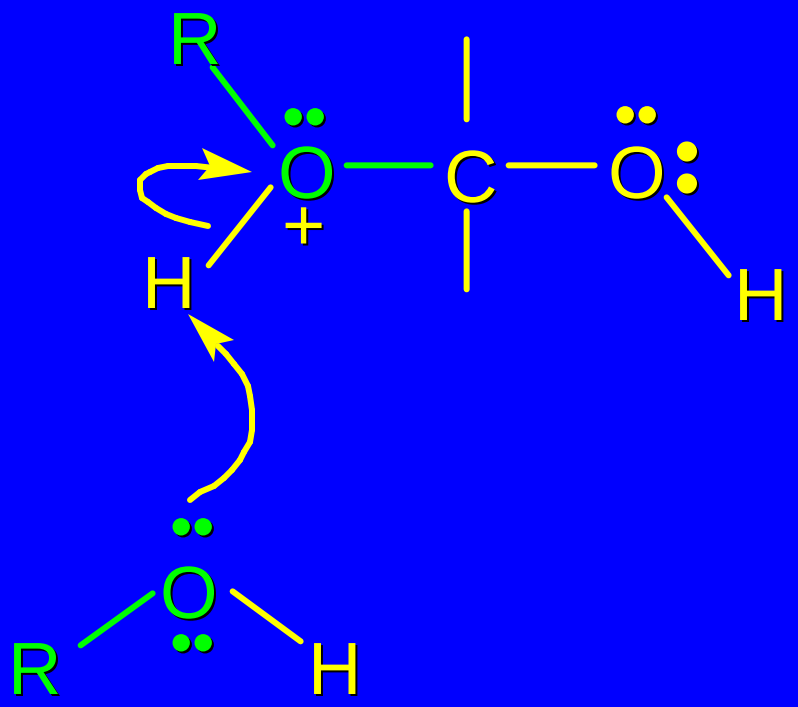
Mechanism



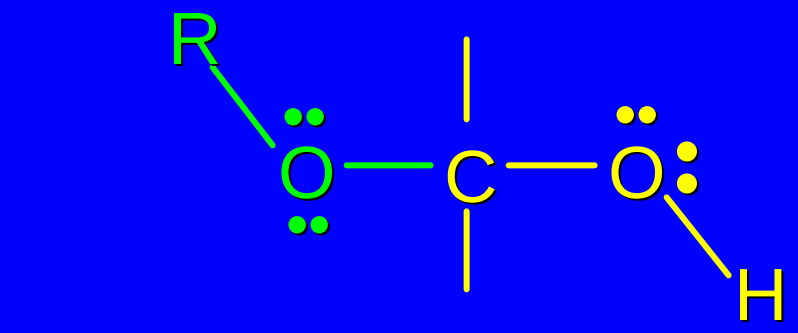
Mechanism

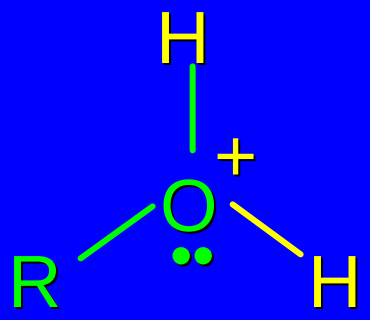


Mechanism



Mechanism



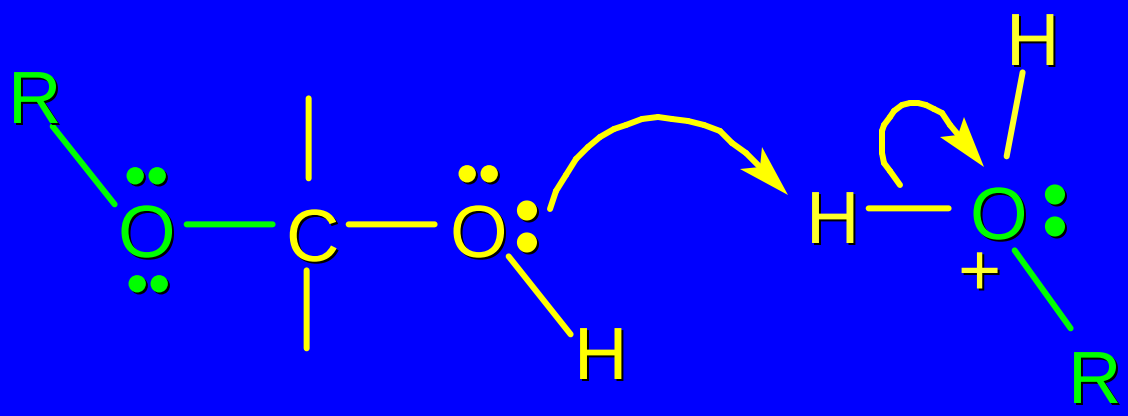


Mechanism of Acetal Formation

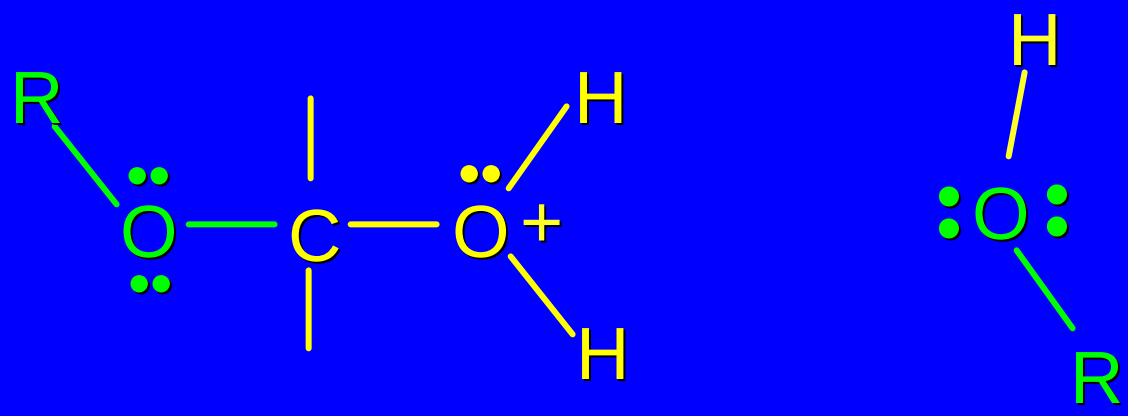
Second stage is hemiacetal-to-acetal conversion

involves carbocation chemistry

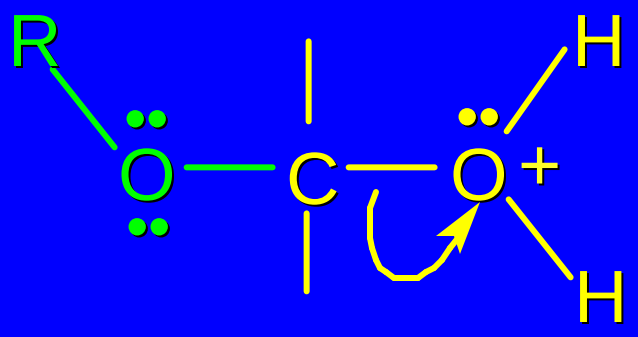
Hemiacetal-to-acetal Stage



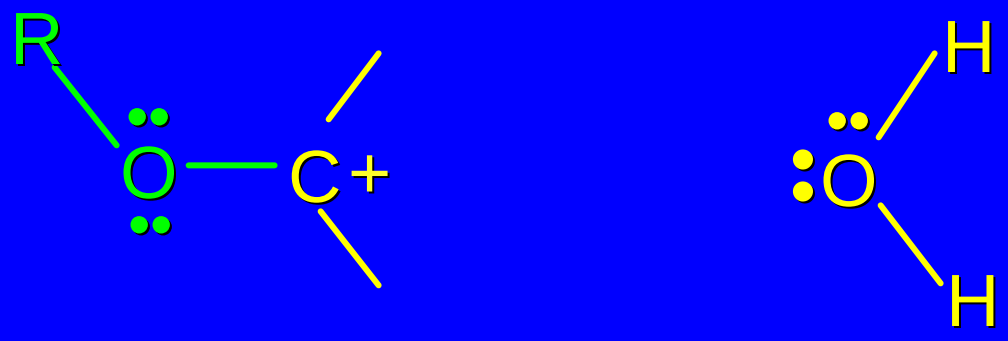
Hemiacetal-to-acetal Stage



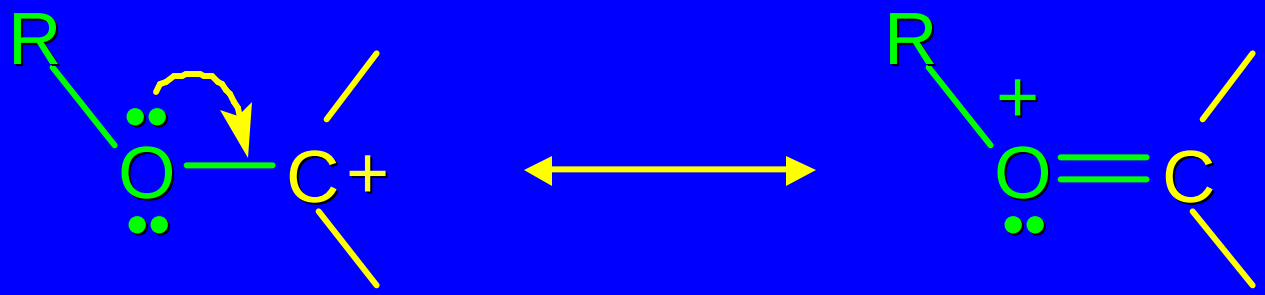
Hemiacetal-to-acetal Stage



Hemiacetal-to-acetal Stage

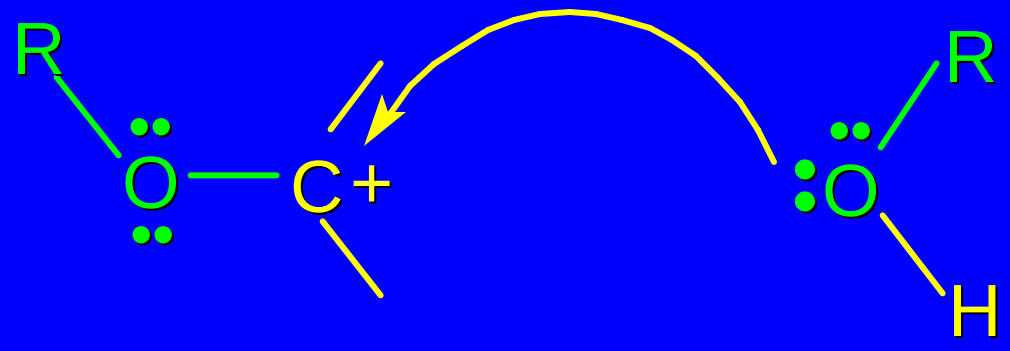


Hemiacetal-to-acetal Stage

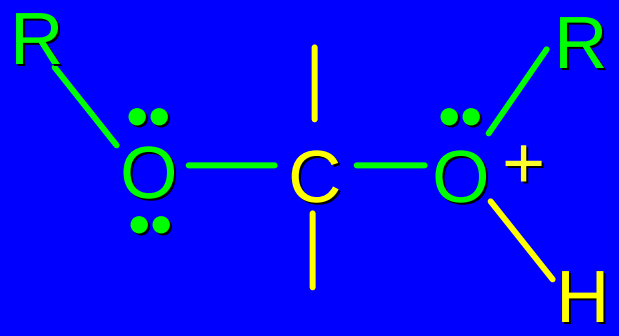


Carbocation is stabilized by delocalization of unshared electron pair of oxygen

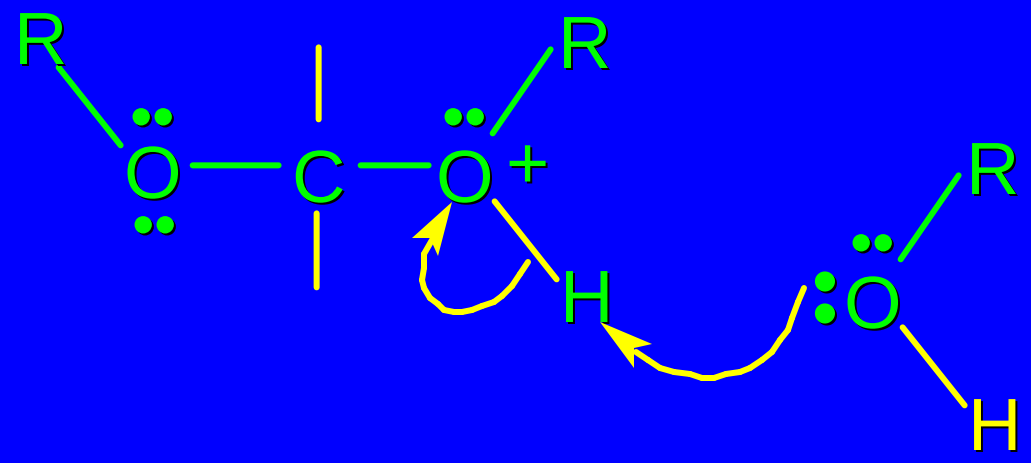
Hemiacetal-to-acetal Stage



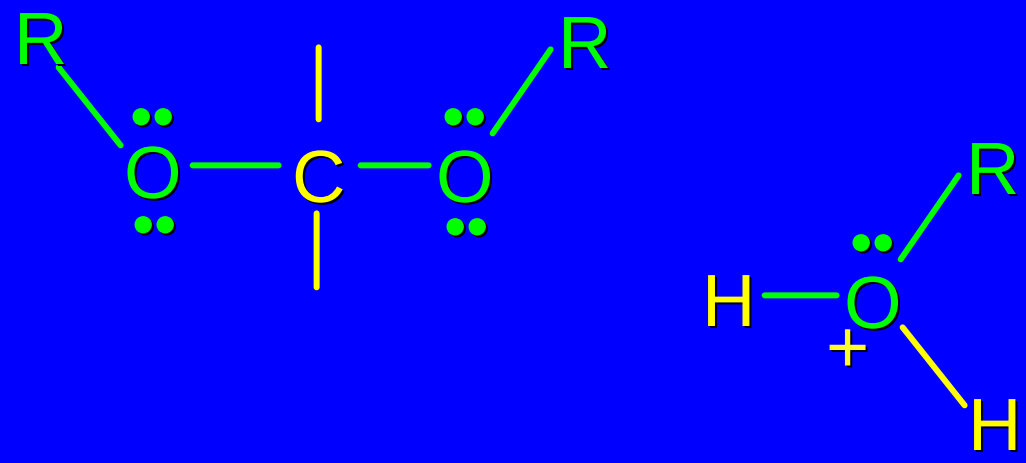
Hemiacetal-to-acetal Stage



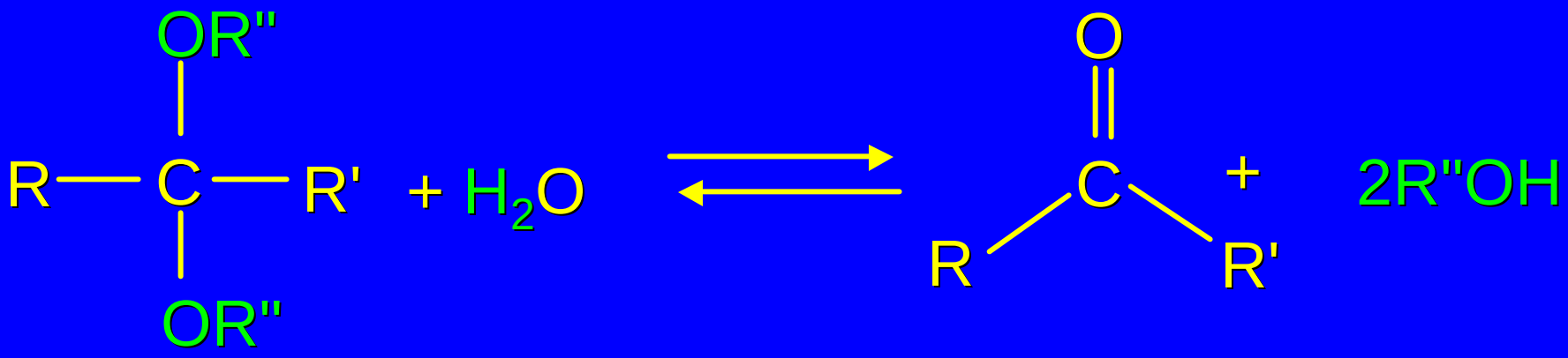
Hemiacetal-to-acetal Stage



Hemiacetal-to-acetal Stage



Hydrolysis of Acetals



mechanism:

reverse of acetal formation;
hemiacetal is intermediate

application:

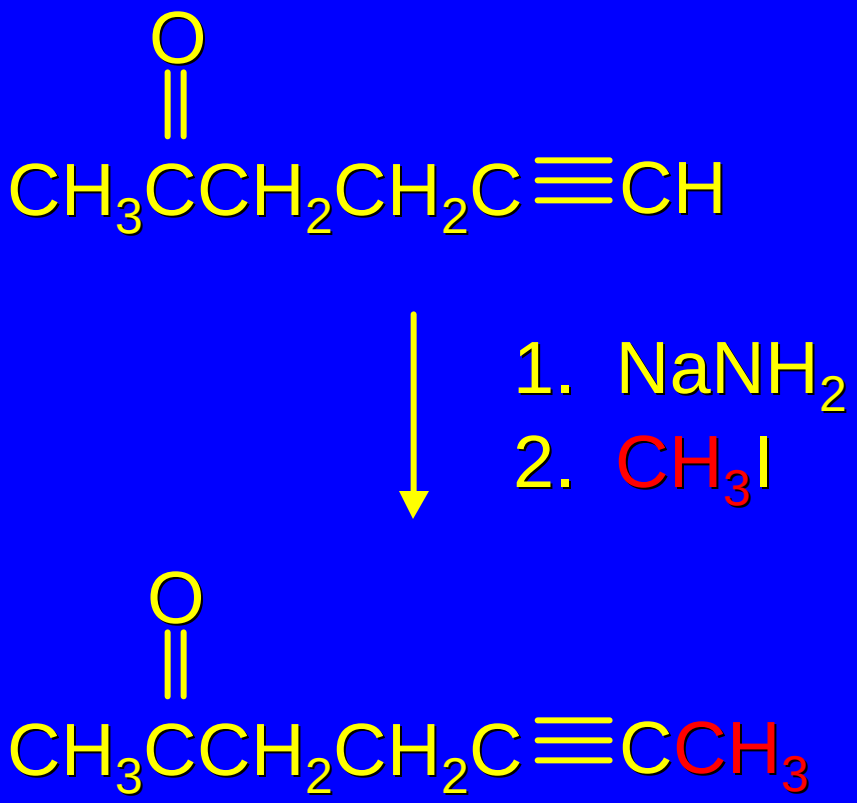
aldehydes and ketones can be "protected" as acetals.

17.9

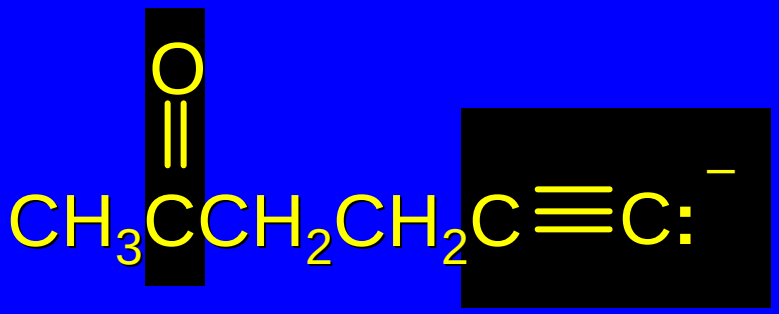
Acetals as Protecting Groups

Example

The conversion shown cannot be carried out directly...



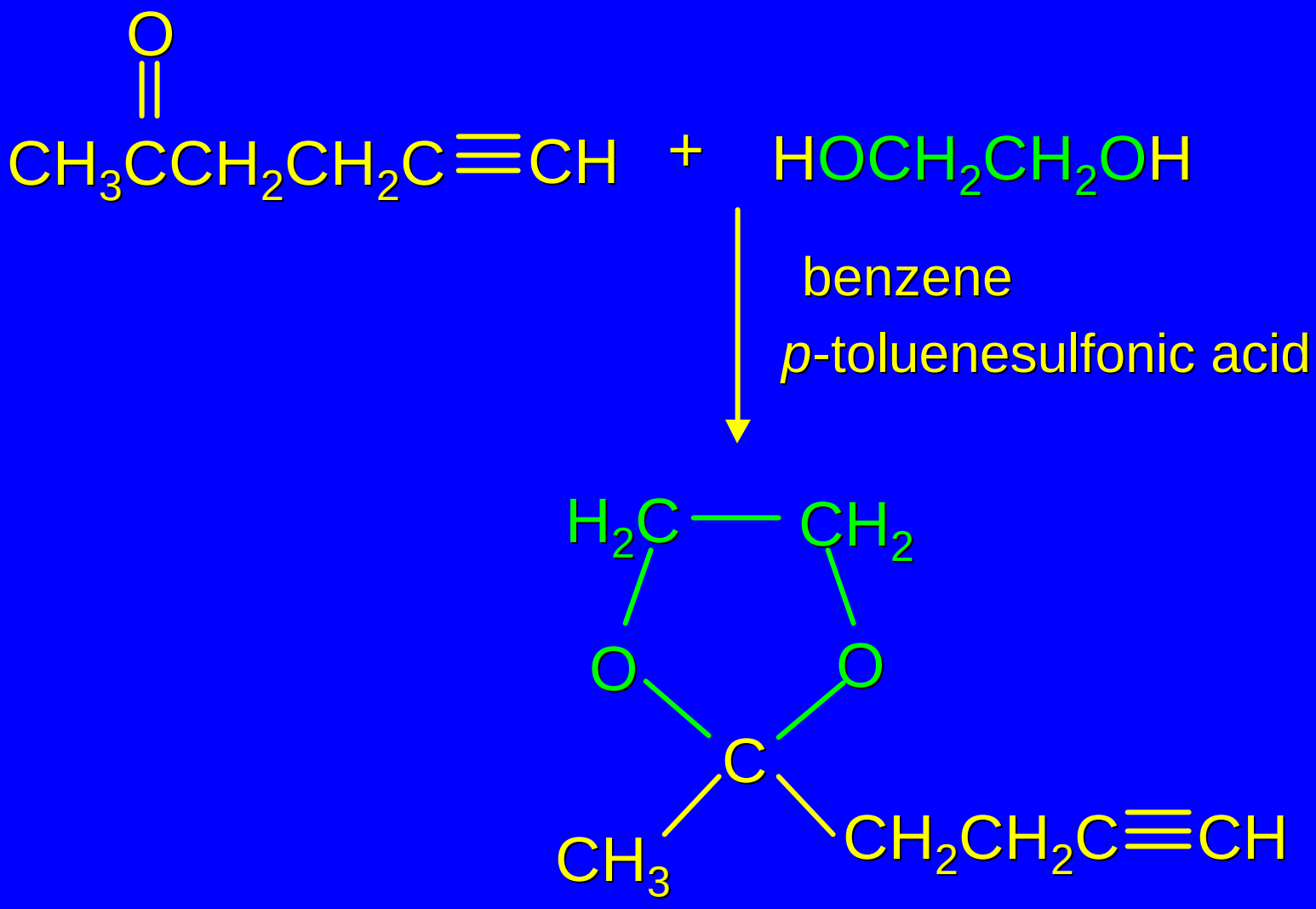
because the carbonyl group and the carbanion are incompatible functional groups.



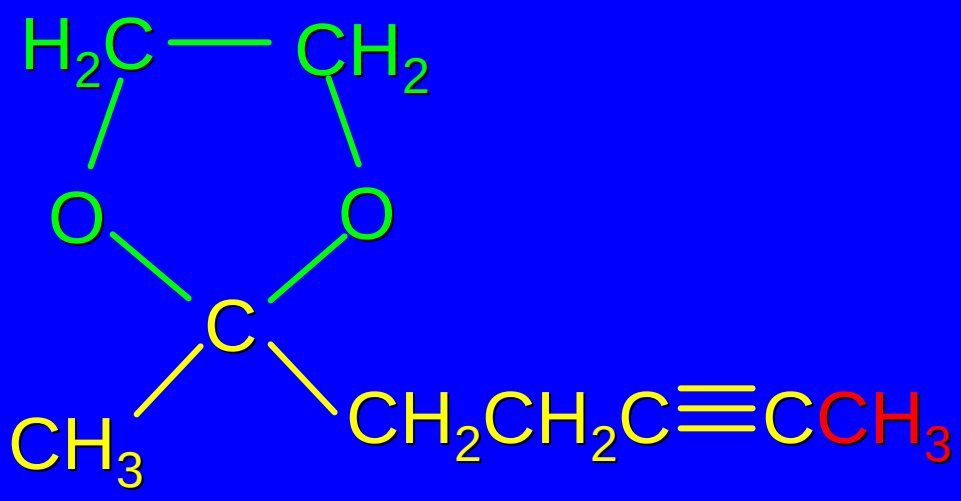
Strategy

1) protect C=O
2) alkylate
3) restore C=O

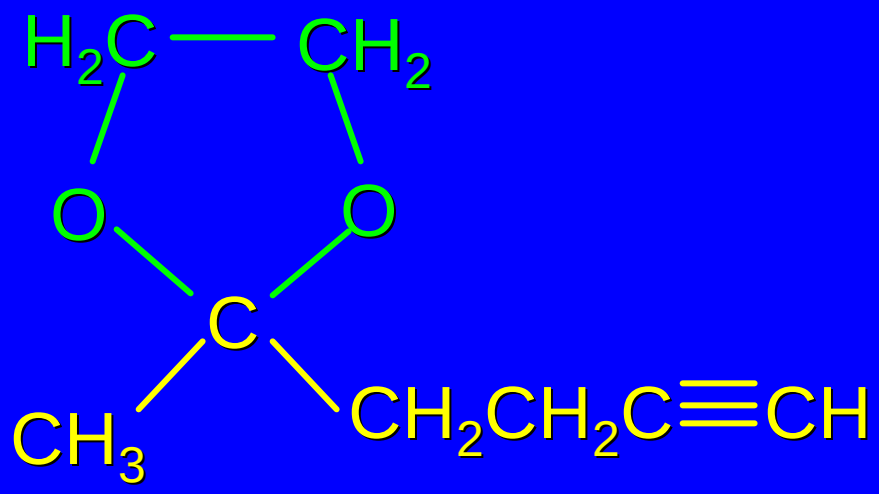
Example: Protect



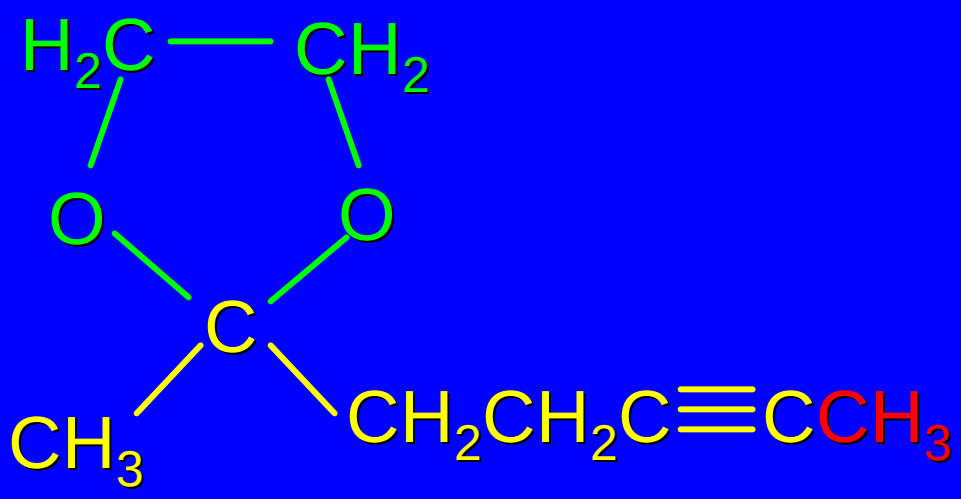
Example: Alkylate



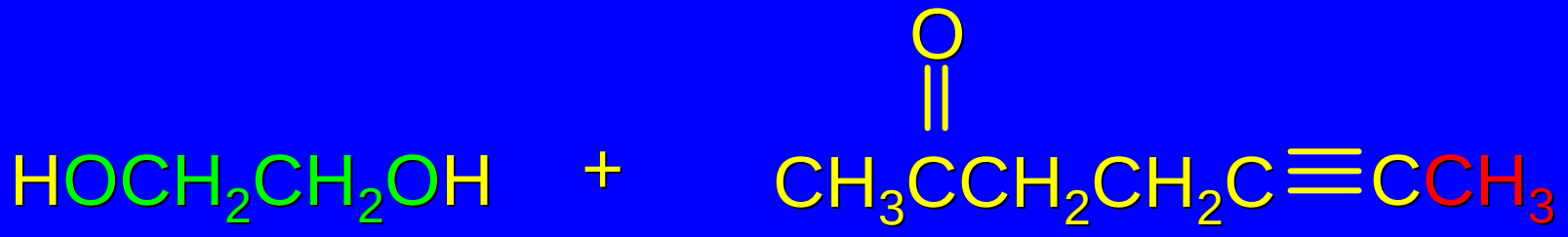
1. $NaNH_2$
2. CH_3I



Example: Deprotect



$\xrightarrow[HCl]{H_2O}$



(96%)