OC2

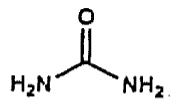
Synthesis
–
Putting Things Together & Introduction to Alcohols

Dr. Michael J. Bojdys

michael.bojdys@kcl.ac.uk
http://bojdyslab.org
@mjbojdys

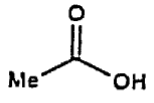
History of Organic Synthesis

22 Nobel Prize winners in Organic Synthesis in the 20th century



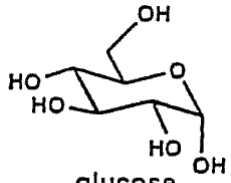
urea

(Wöhler, 1828)



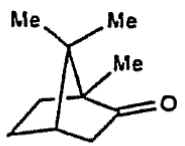
acetic acid

(Kolbe, 1845)



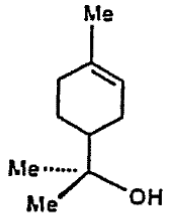
glucose

(Fischer, 1890)



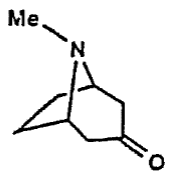
camphor

(Komppa, 1903; Perkin, 1904)



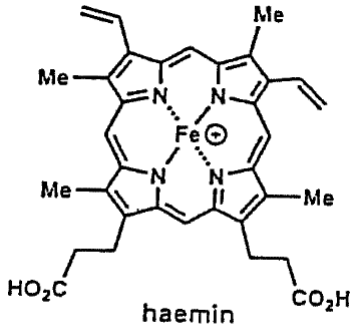
α-terpineol

(Perkin, 1904)



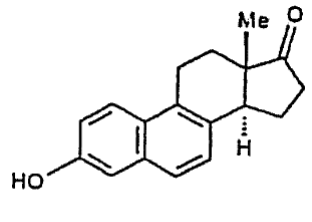
tropinone

(Robinson, 1917)



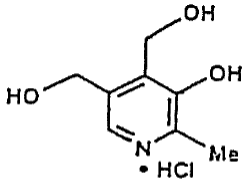
haemin

(Fischer, 1929)



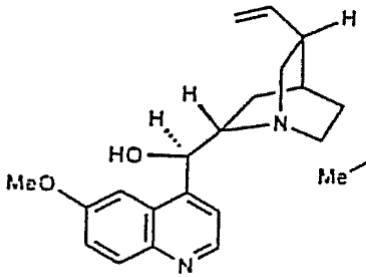
equilenin

(Bachmann, 1939)



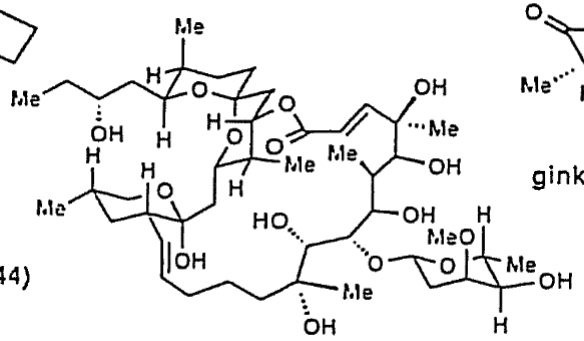
pyridoxine hydrochloride

(Folkers, 1939)

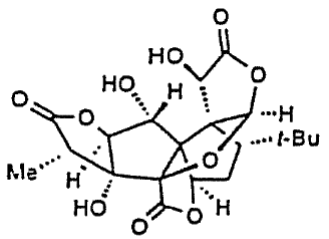


quinine

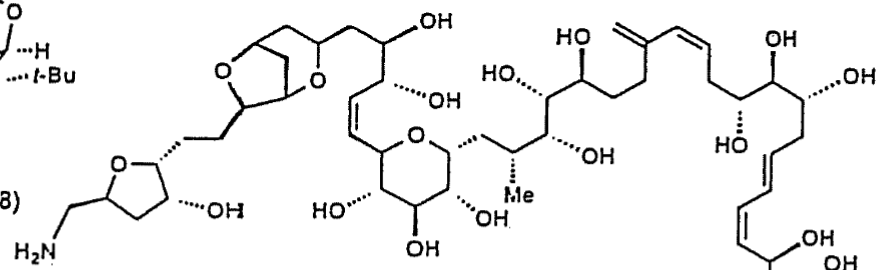
(Woodward & Doering, 1944)

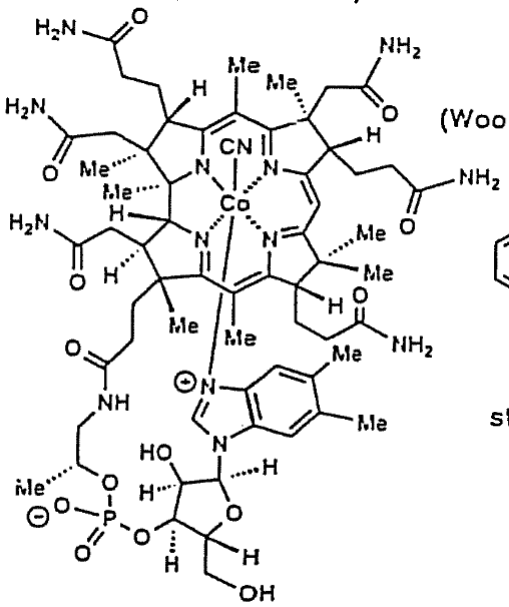


cytovaricin (1990)

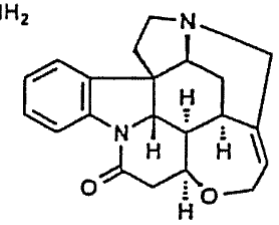


ginkgolide B (1988)

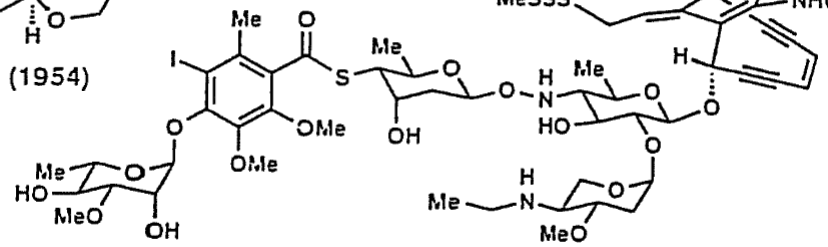




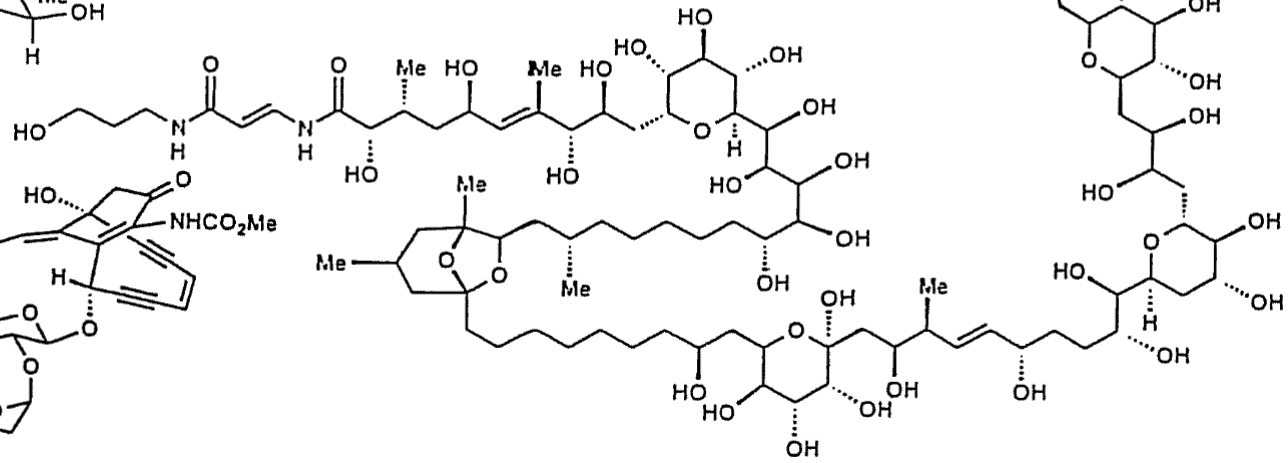
vitamin B_{12} (1973)



strychnine (1954)



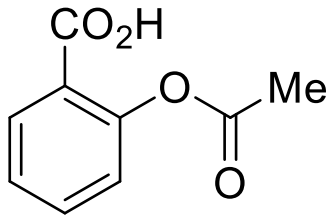
calicheamicin γ_1^I (1992)



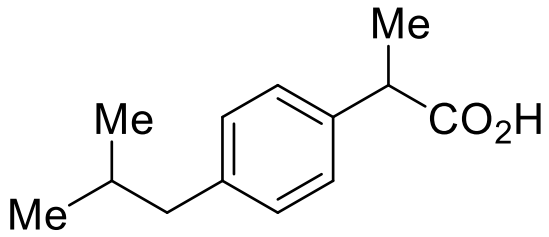
palytoxin (1994)

Alcohols and Amines in Some Common Organic Compounds

- **Pain killers (Analgesics)**

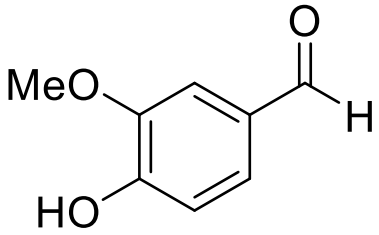


Aspirin

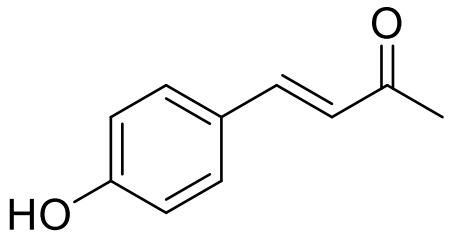


Ibuprofen

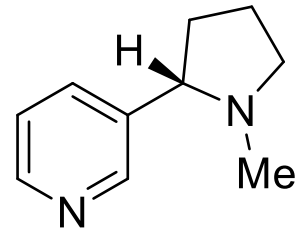
- **Flavour compounds ("aromatics")**



Vanillin
"vanilla" ice creams

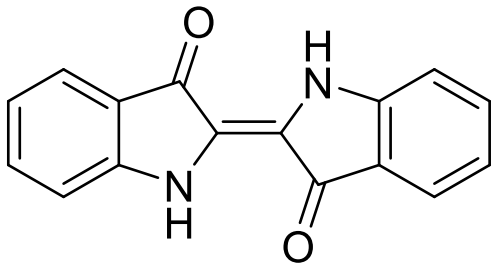


"Raspberry Ketone"
"raspberry" yoghourt

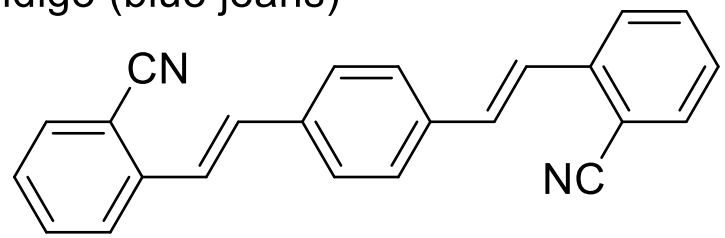


Nicotine

- **Dyestuffs**

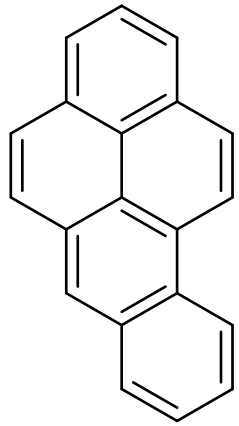


Indigo (blue jeans)

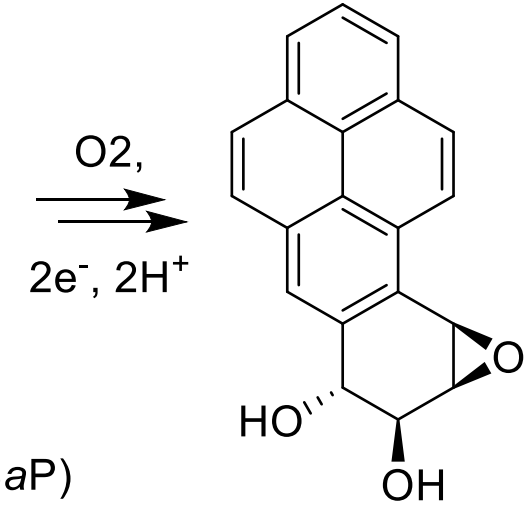


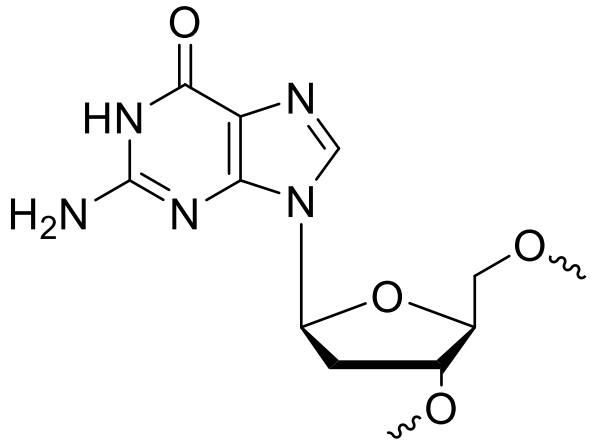
Palanil(R)
BASF's optical brightener for cotton and polyester

- **Biology**



Benzo[*a*]pyrene (B*a*P)

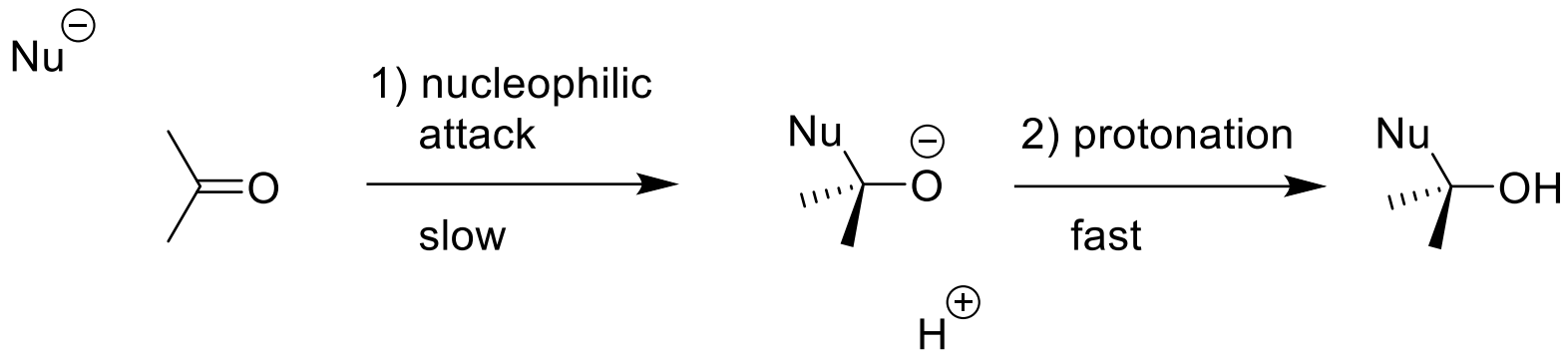




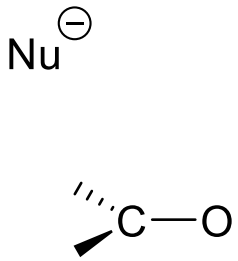
dG (Guanine)

Nucleophilic Addition to the Carbonyl Group

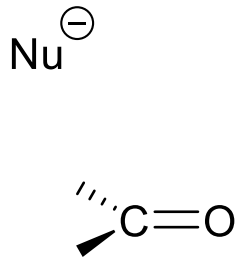
Mechanism of addition



Orbitals:

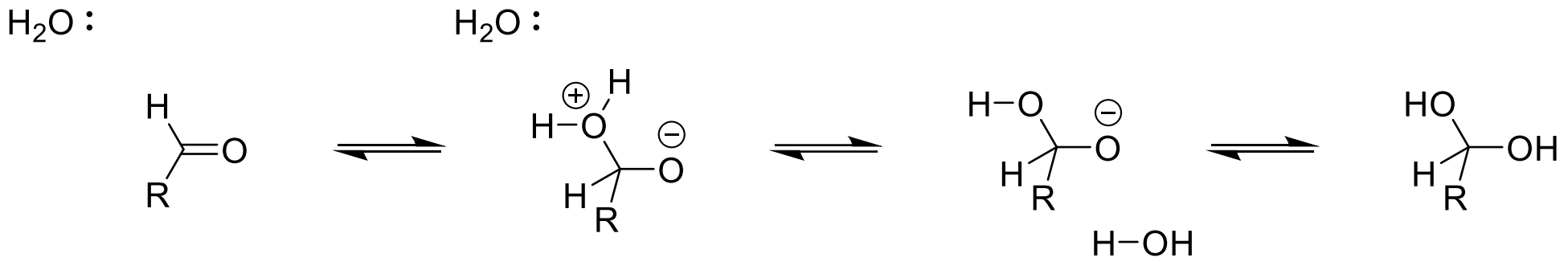


Trajectory:

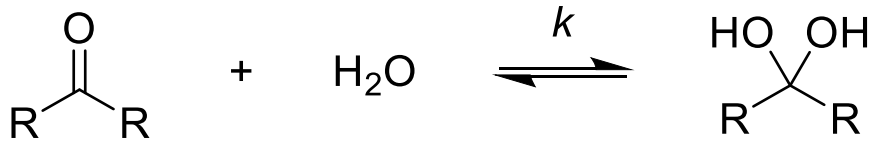


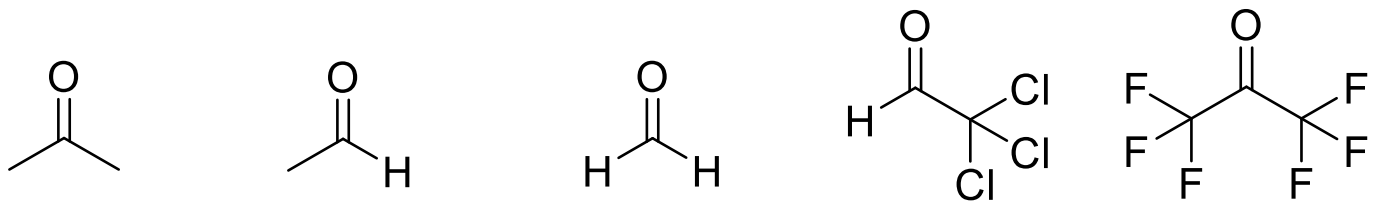
Hydration of Carbonyls

Carbonyl compounds, especially aldehydes, are prone to hydration:



Effects that influence the equilibrium:

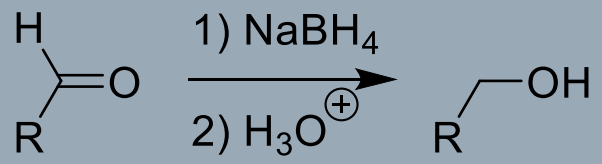




equilibrium const., *k*	0.001	1.06	2280	2000	~10^6

Borohydride Reduction

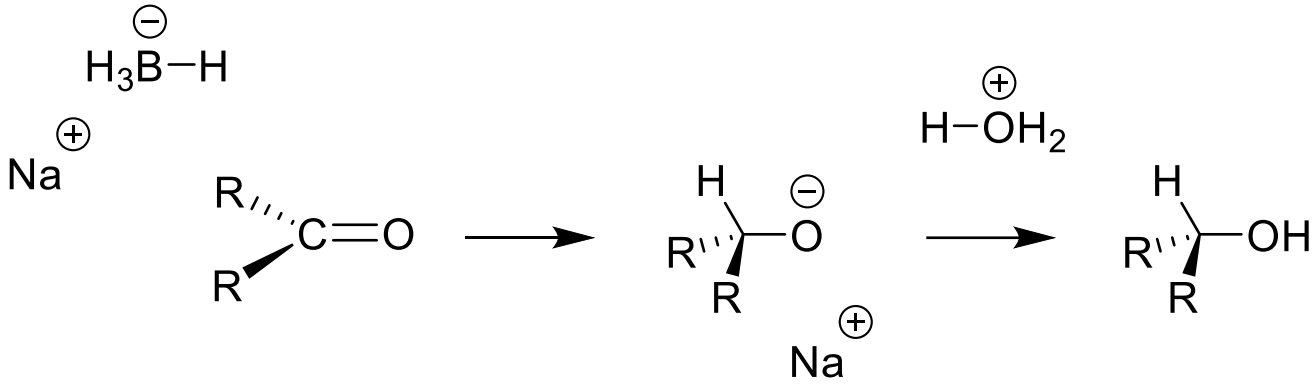
$NaBH_4$ is the standard reducing agent for aldehydes and ketones:



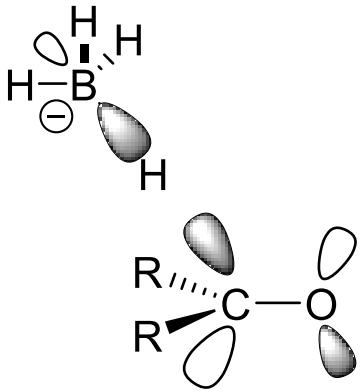
- solvent is usually H_2O/EtOH
- Effectively "$H^{(-)}$" attack, but never draw as this!
- Aldehydes react faster than ketones.

NOTE: $LiAlH_4$ is a much more reactive reducing agent, but will react violently with H_2O!

Mechanism of addition



Orbitals:



Organometallics as Carbon Nucleophiles

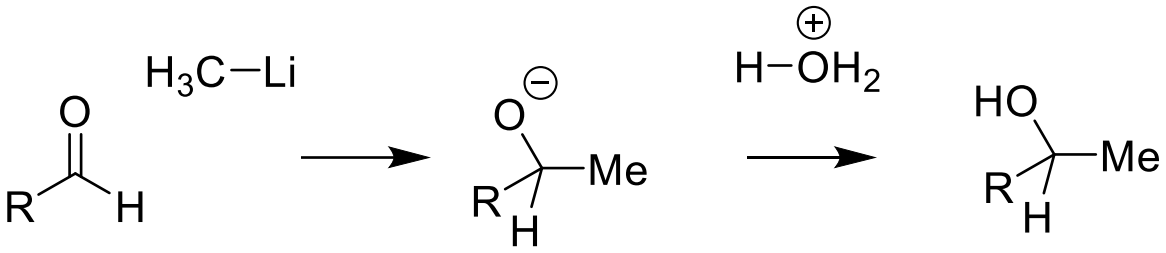
Organometallic reagents contain a C–Metal bond:

Consider the electronegativities of C, Li and Mg:

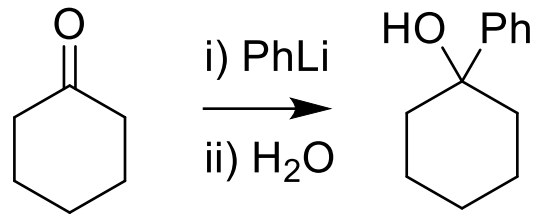
C	Li	Mg
2.5	1.0	1.2

Reaction of organolithium reagents:

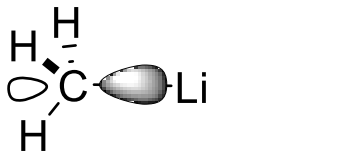
Example 1

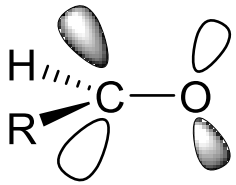


Example 2

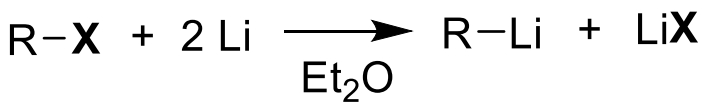


Orbitals:





Preparation:



X = Cl, Br, I

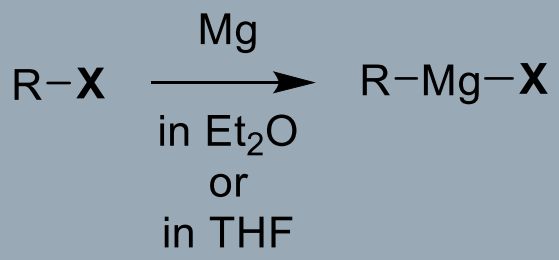
Organometallics as Carbon Nucleophiles

Grignard reagents

R−Mg−**X**

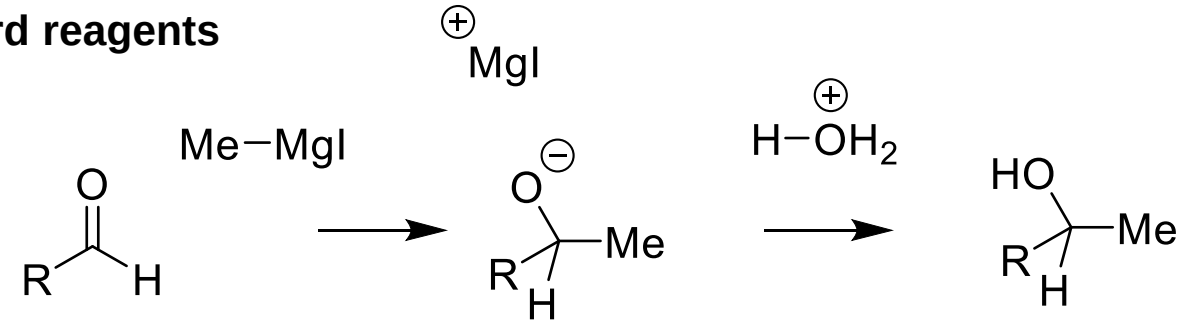
X = Cl, Br, I

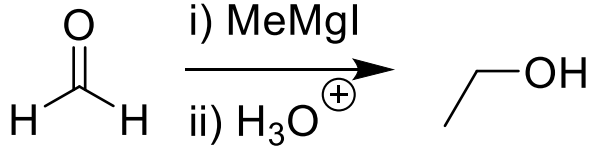
Preparation:



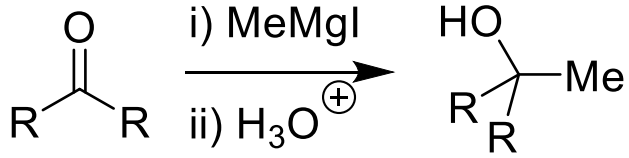
Reaction of Grignard reagents

With aldehydes:

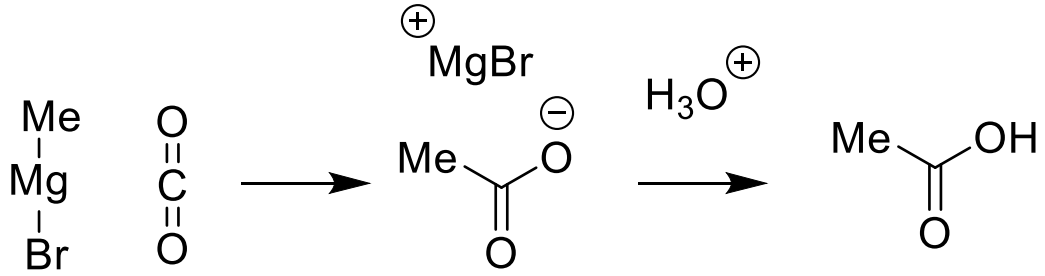




With ketones:



With carbon dioxide:



What’s next?

Reactivity of Alcohols