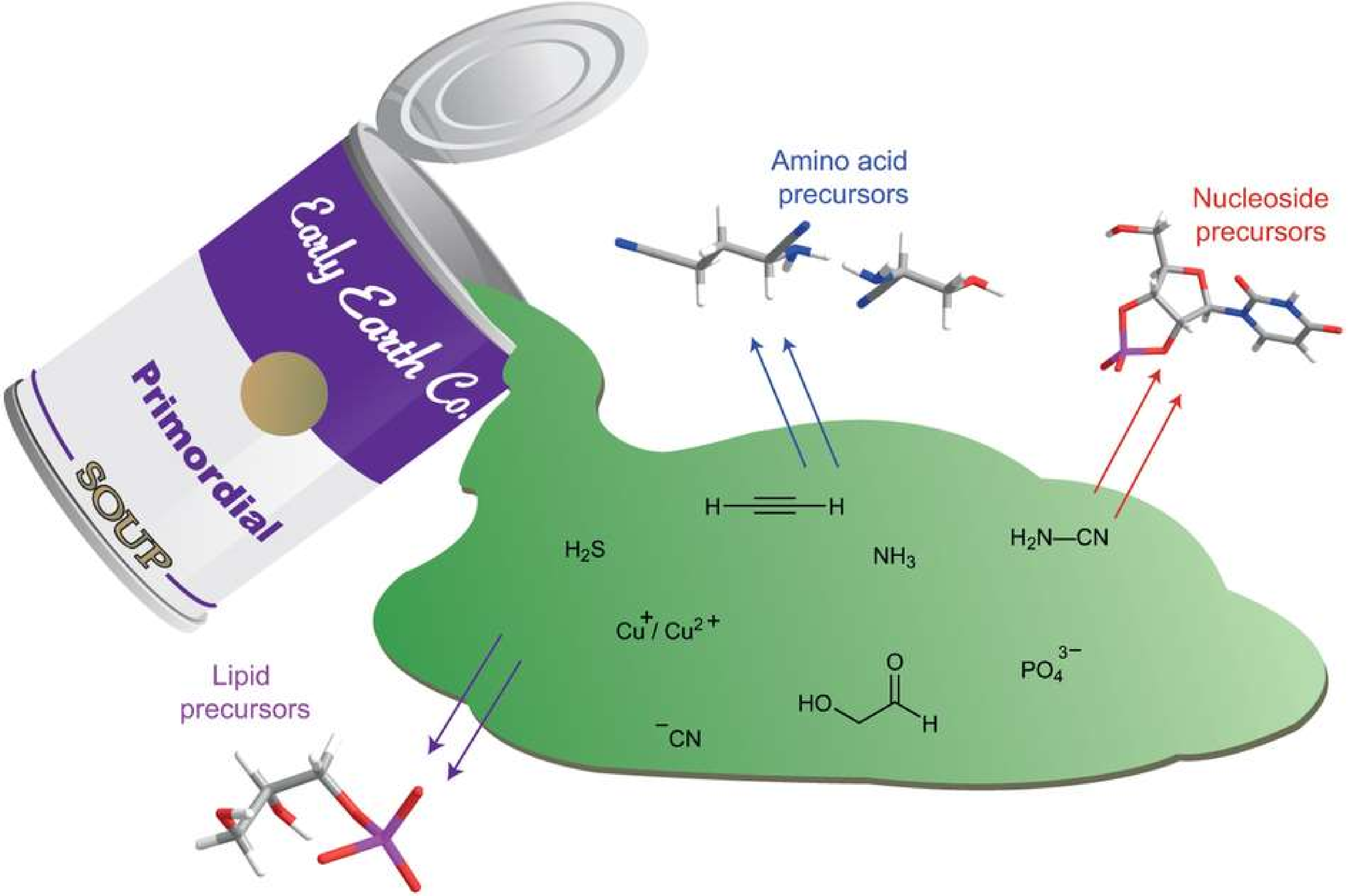
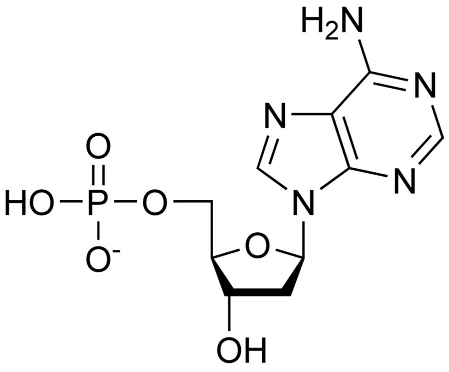
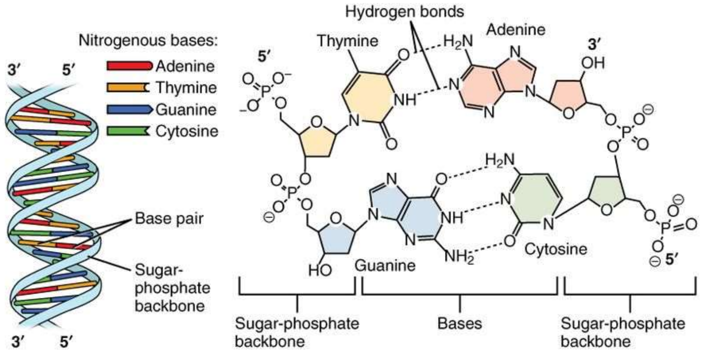
# *Basic classes of biomolecules*

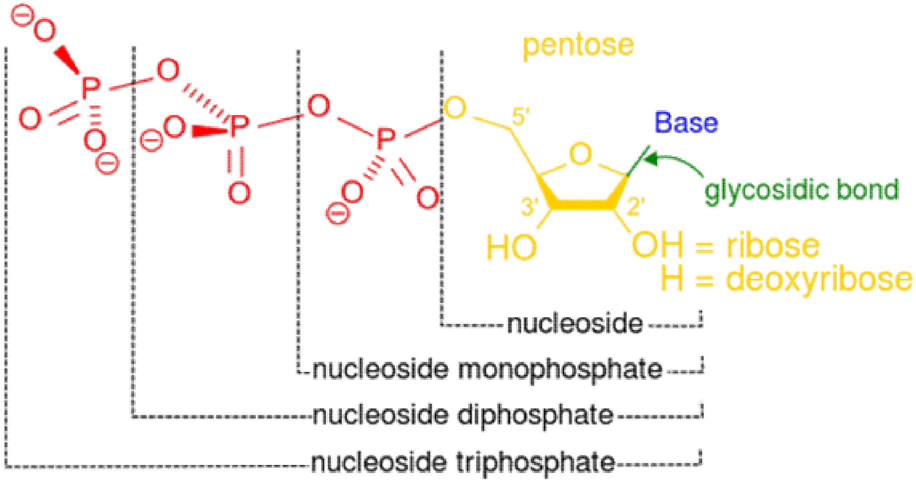


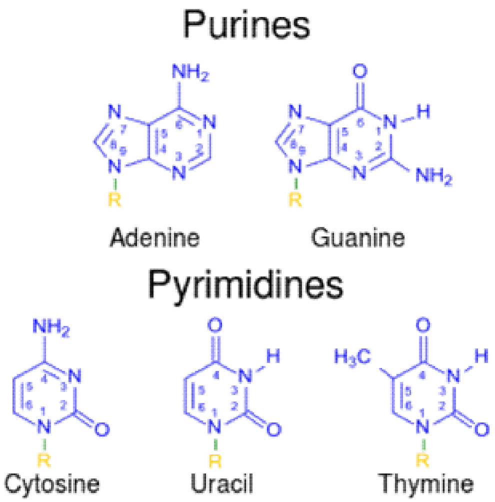
- Aminoacids
- Lipids
- **Carbohydrates (sugars)**
- **Nucleobases**
- **Nucleosides (sugar+nucleobase)**

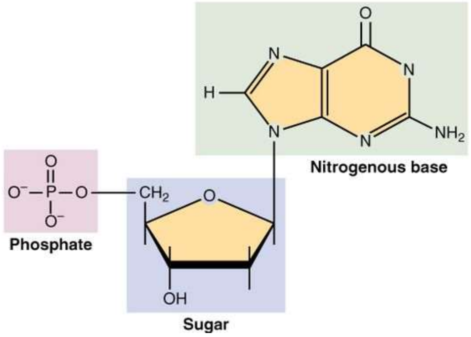
# *Nucleotides - components*



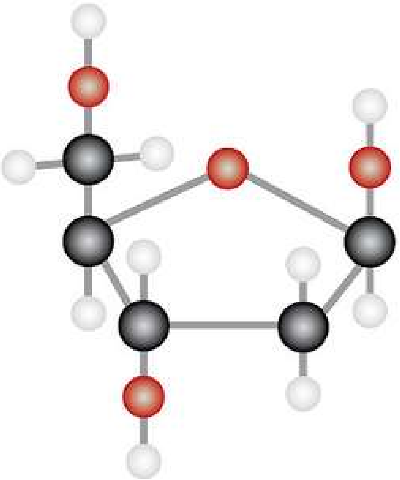




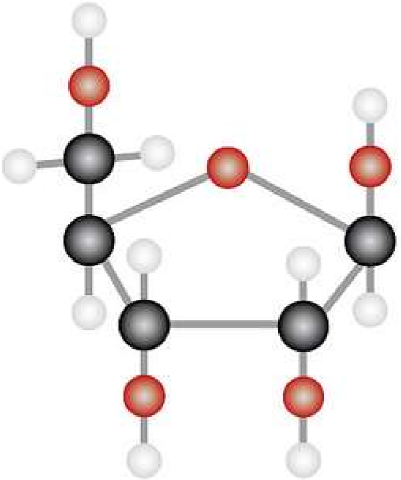




# *Nucleosides - nucleobases + sugars*

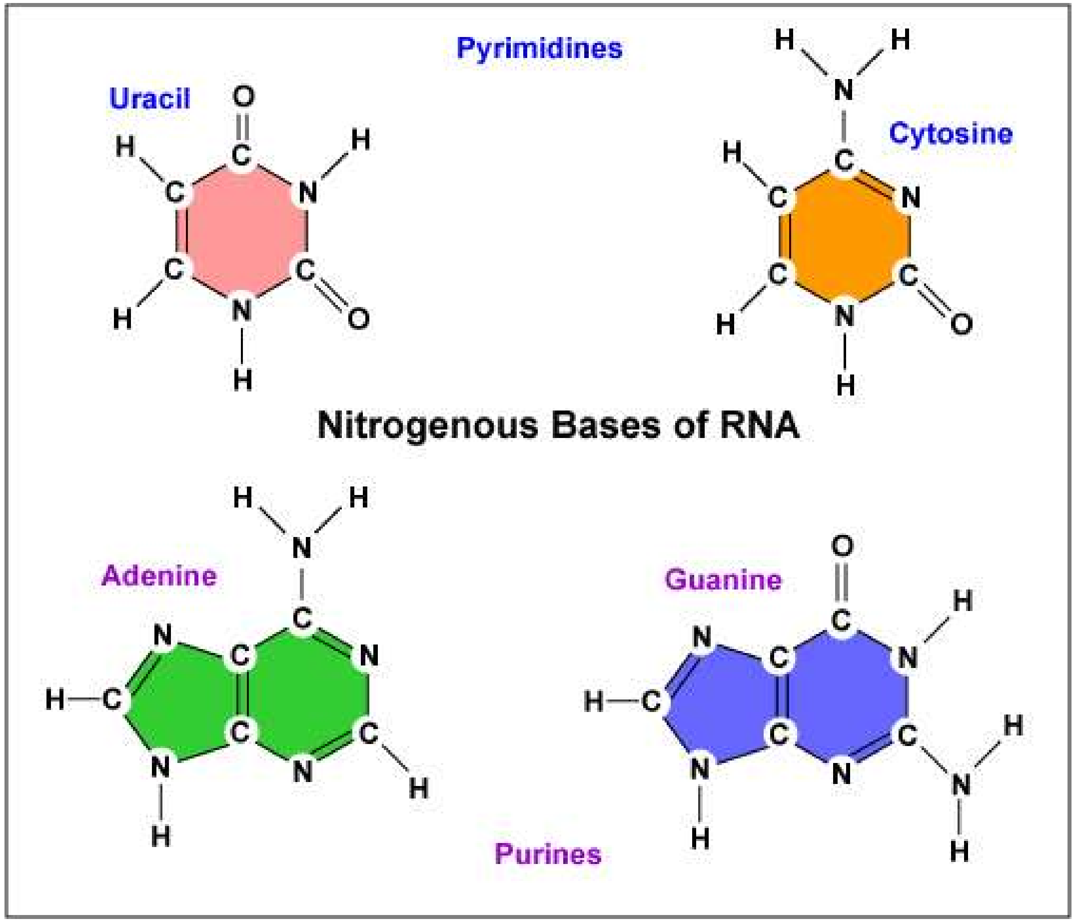


**Deoxyribose**
used in DNA backbone

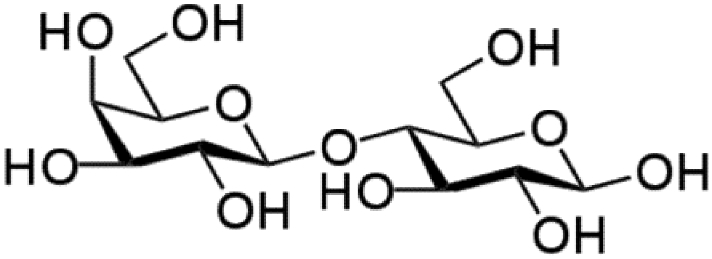


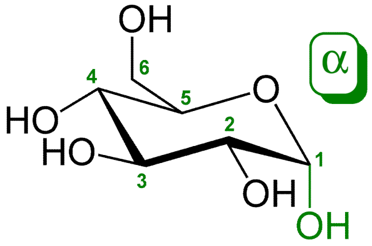
**Ribose**
used in RNA backbone

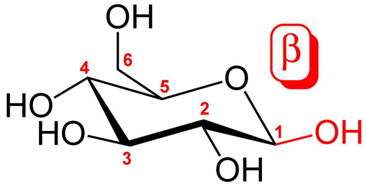
Key
○ Hydrogen
🔴 Oxygen
⚫ Carbon



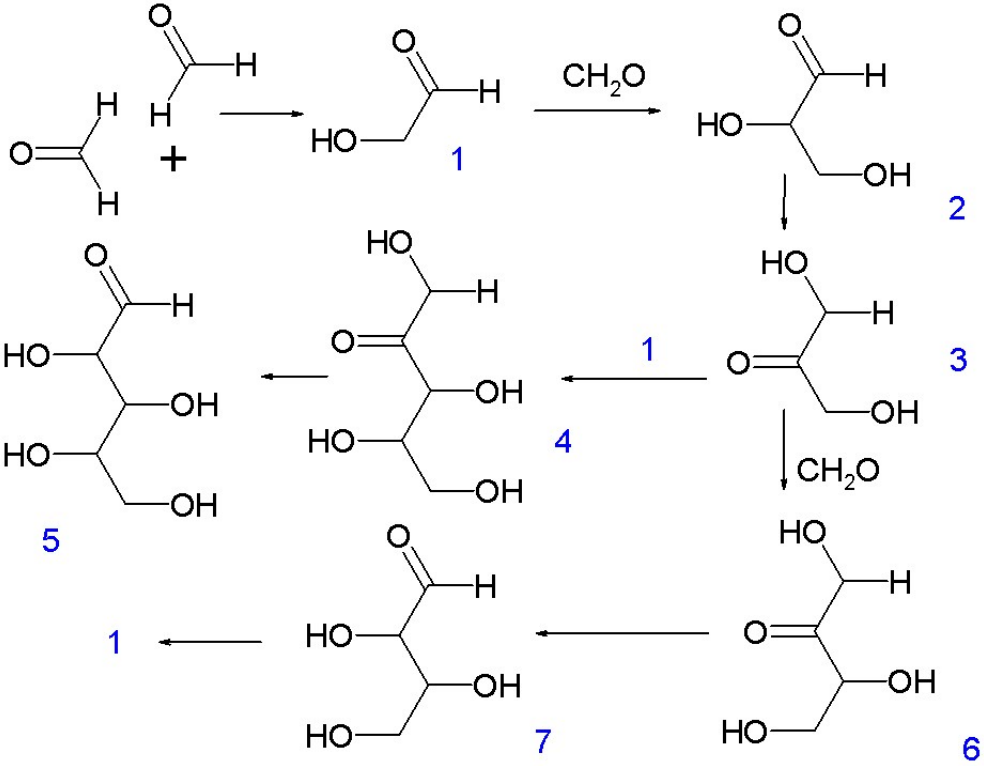
# *Carbohydrates*







# *Formose reaction*

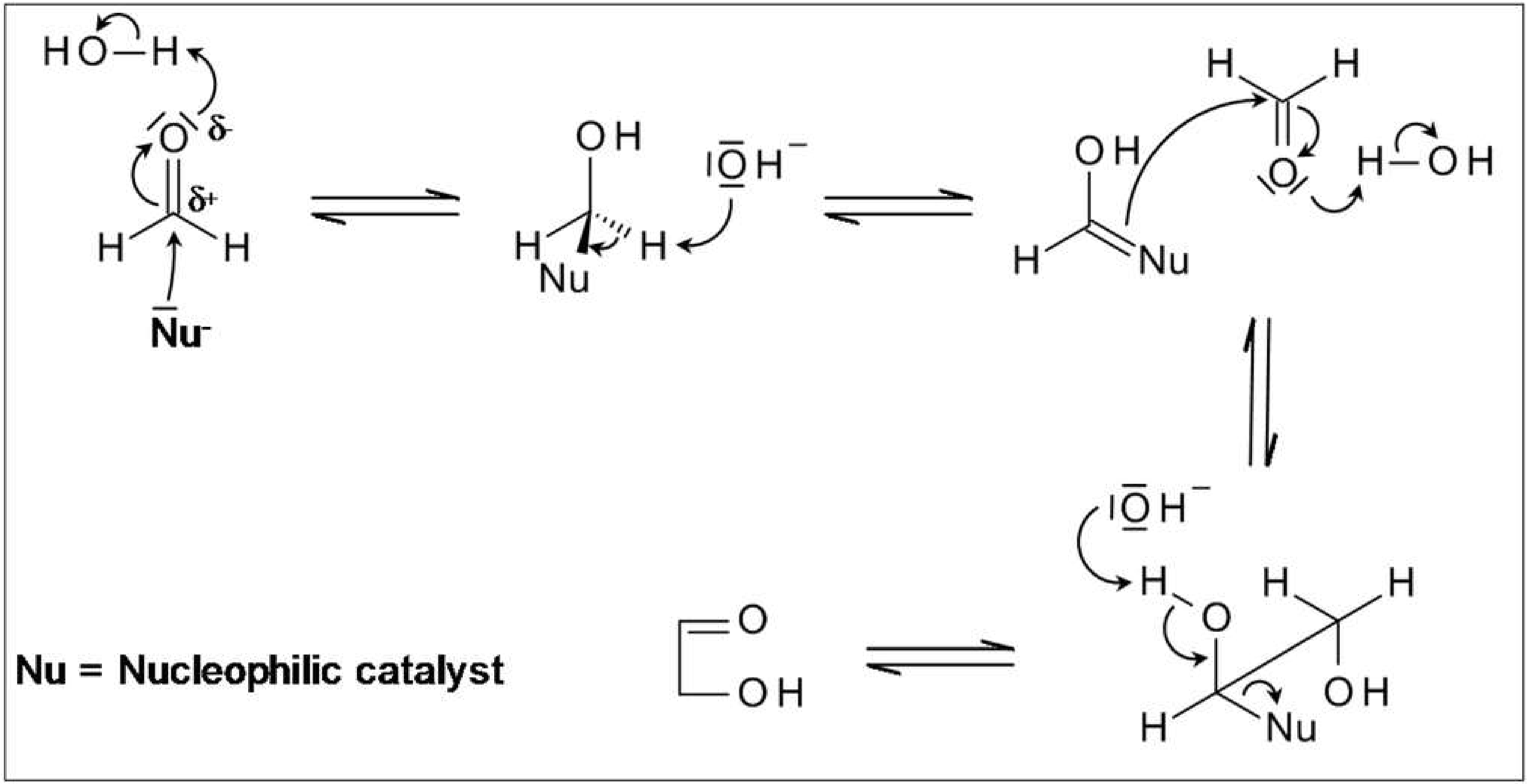


The reaction begins with two formaldehyde molecules condensing to make glycolaldehyde **1** which further reacts in an aldol reaction with another equivalent of formaldehyde to make glyceraldehyde **2**. An aldose-ketose isomerization of **2** forms dihydroxyacetone **3** which can react with **1** to form ribulose **4**, and through another isomerization ribose **5**. Molecule **3** also can react with formaldehyde to produce tetrulose **6** and then aldoltetrose **7**. Molecule **7** can split into **2** in a retro-aldol reaction.

Alexander Butlerov (1828-1886)
*St. Petersburg, Kazan, Russia*

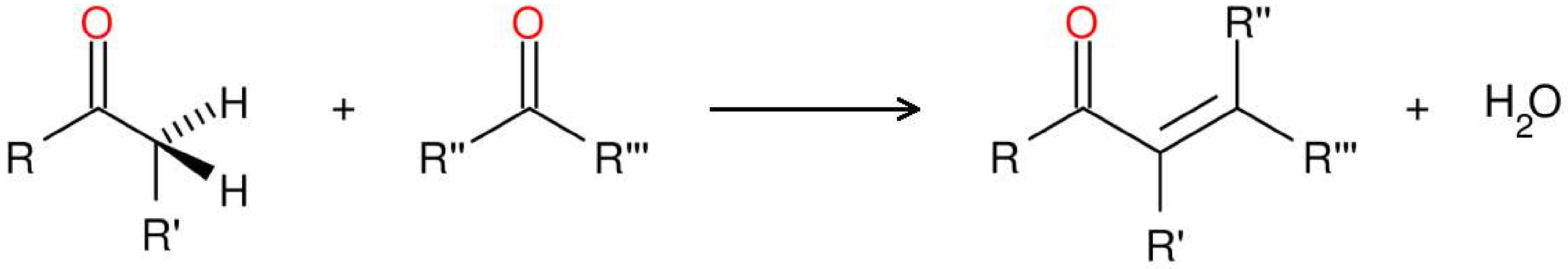
Ronald Breslow (1931-)
*Columbia University, USA*

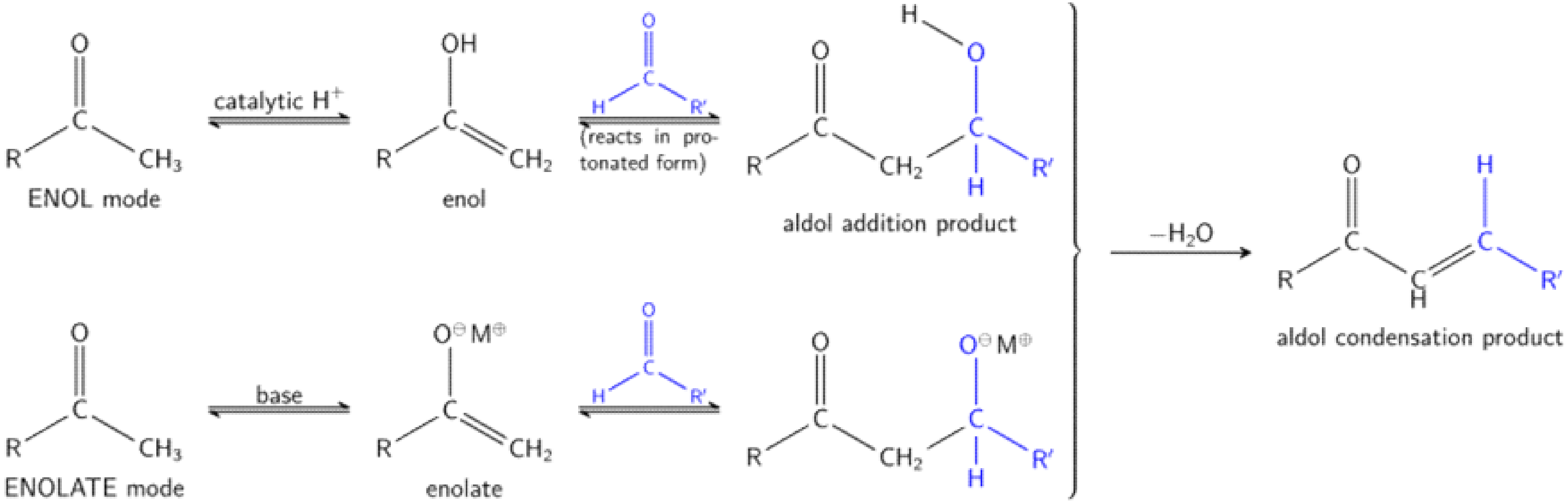
# *Formaldehyde condensation*



Nu = Nucleophilic catalyst

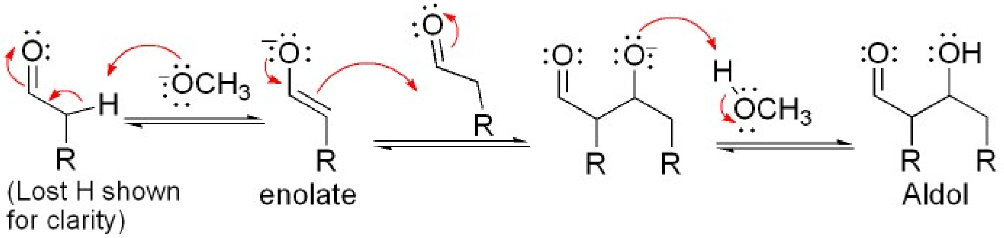
# *Aldol reaction*



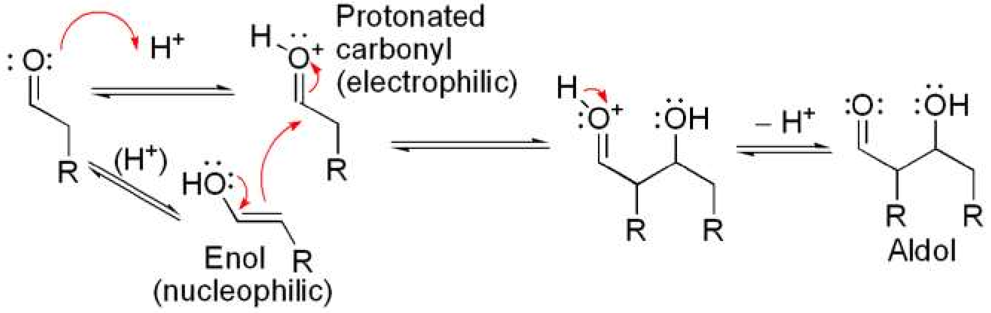


# *Aldol reaction*

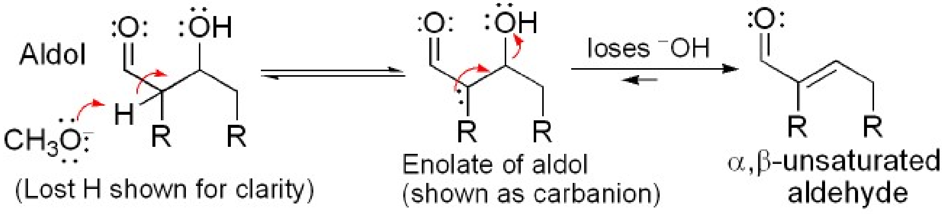
Base catalyzed aldol reaction (shown using $^{-}OCH_3$ as base)



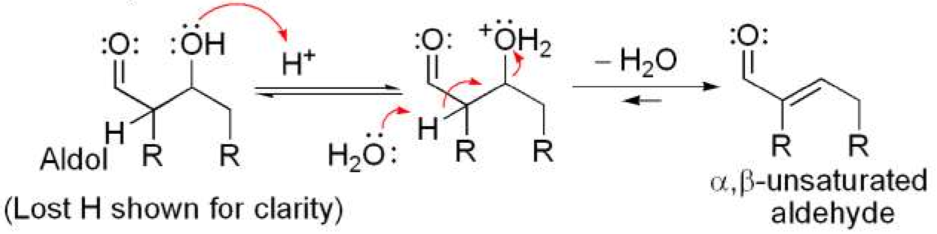
Acid catalyzed aldol reaction



Base catalyzed dehydration (sometimes written as a single step)

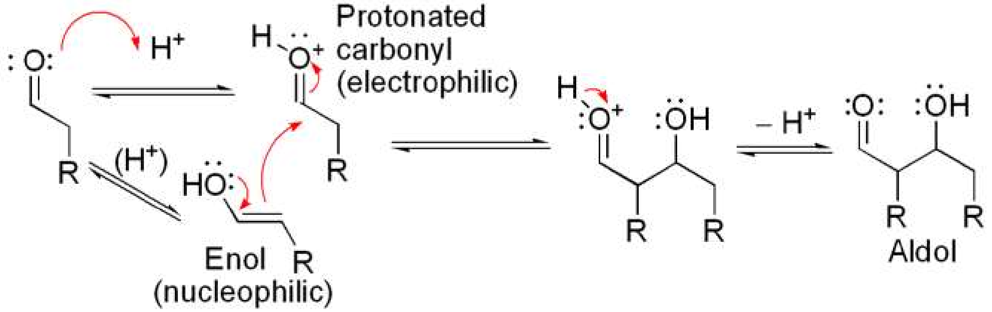


Acid catalyzed dehydration



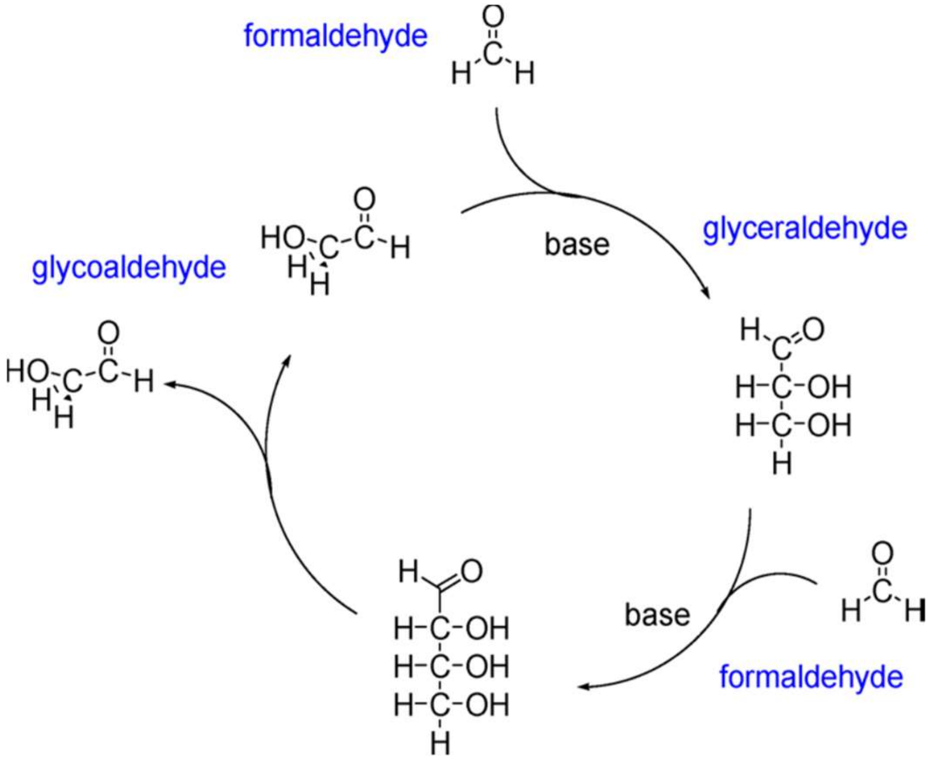
Reversible process
→ retro-aldol reaction

Acid catalyzed aldol reaction



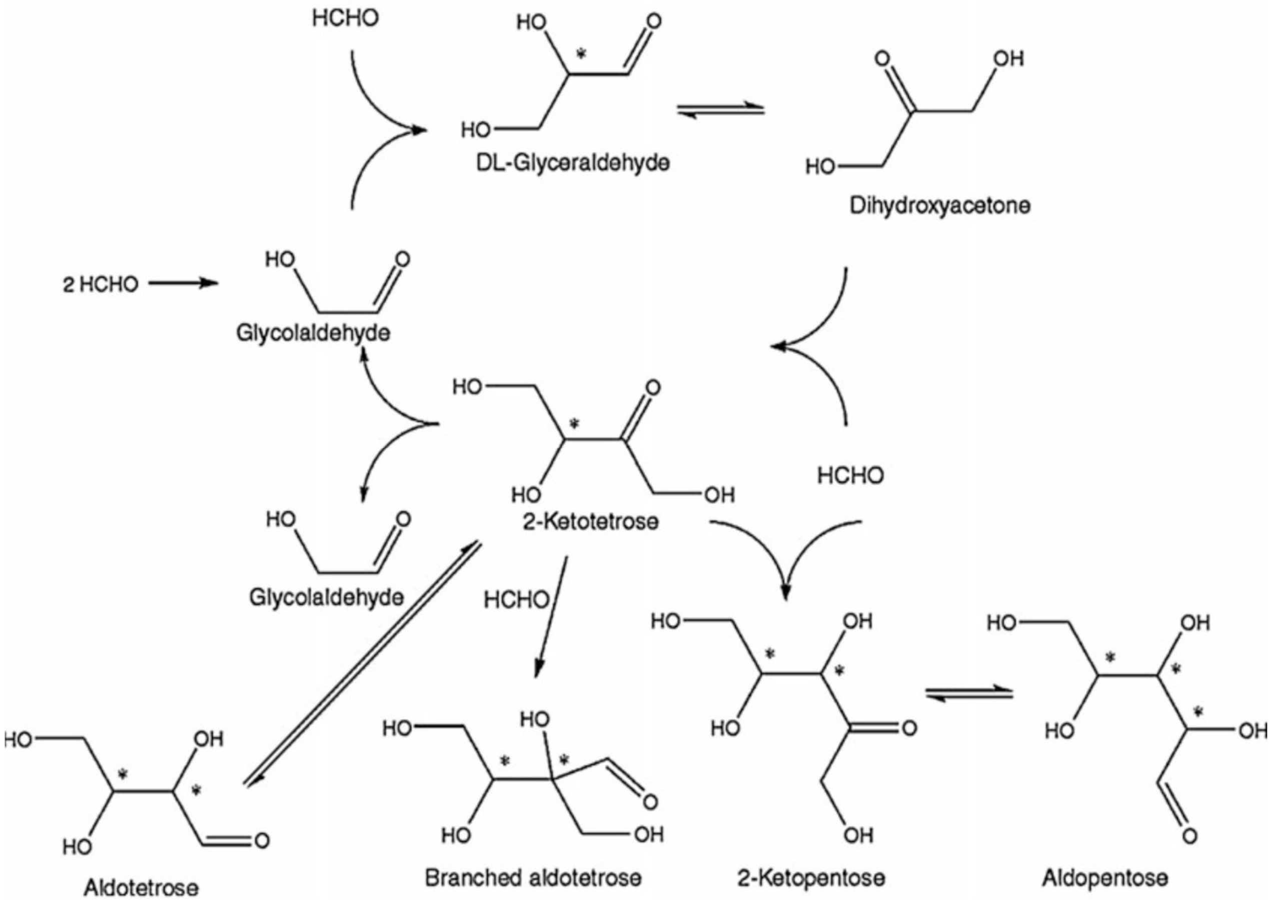
# *Formose reaction as an autocatalytic process*

Formose reaction starts in concentrated alkaline aqueous solutions of formaldehyde
alkali are typically calcium, magnesium or lead



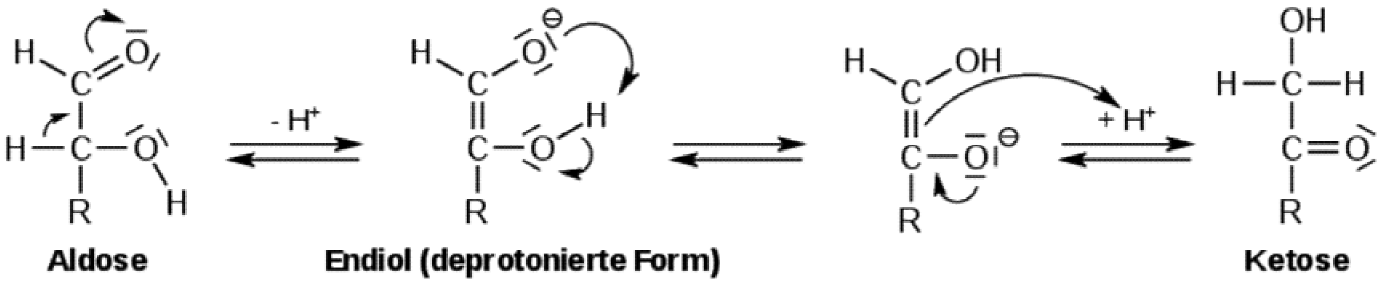
# *Detailed conditions for the formose reaction*

Formose reaction starts in concentrated alkaline aqueous solutions of formaldehyde
alkali are typically calcium, magnesium or lead

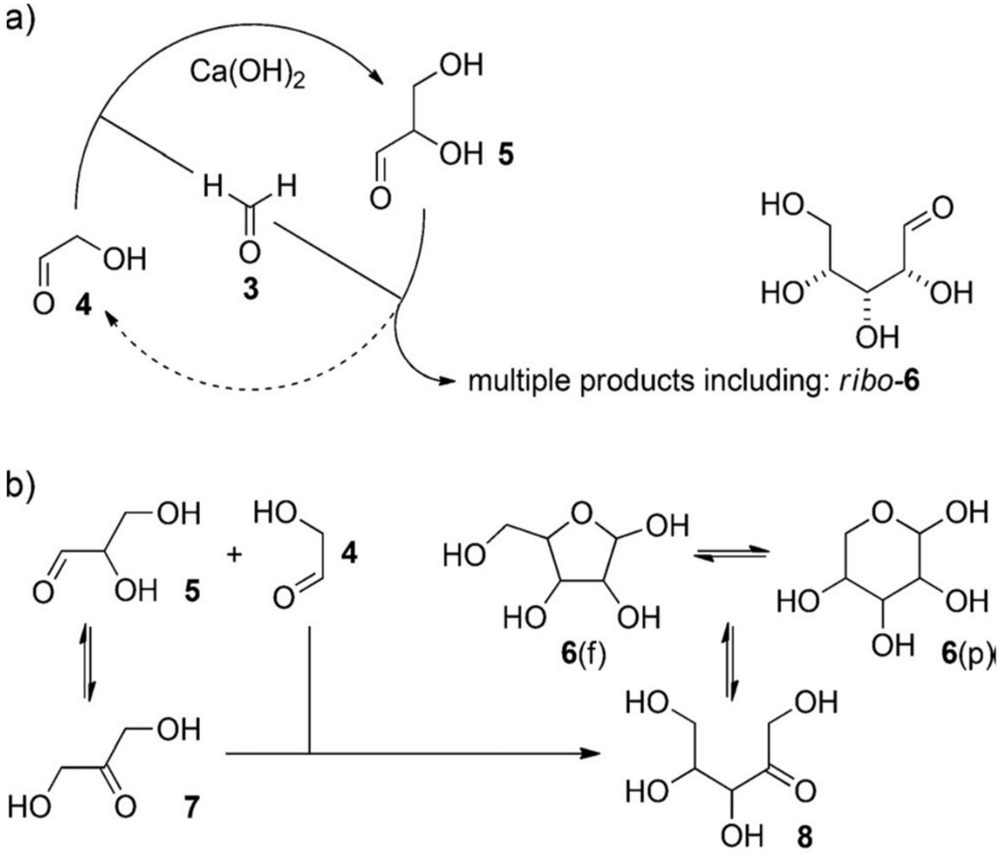


# ***Aldose-ketose isomerization***

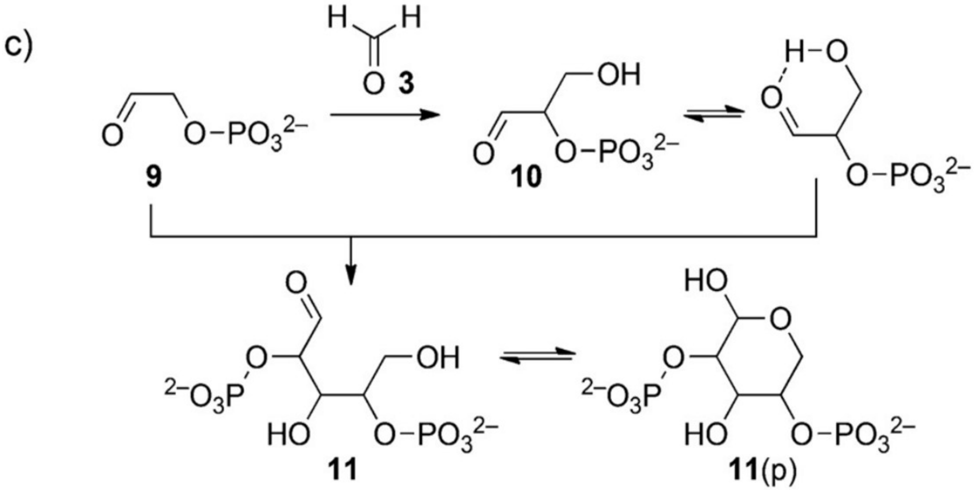
## *Lobry de Bruyn(–Alberda)-van Ekenstein transformation*



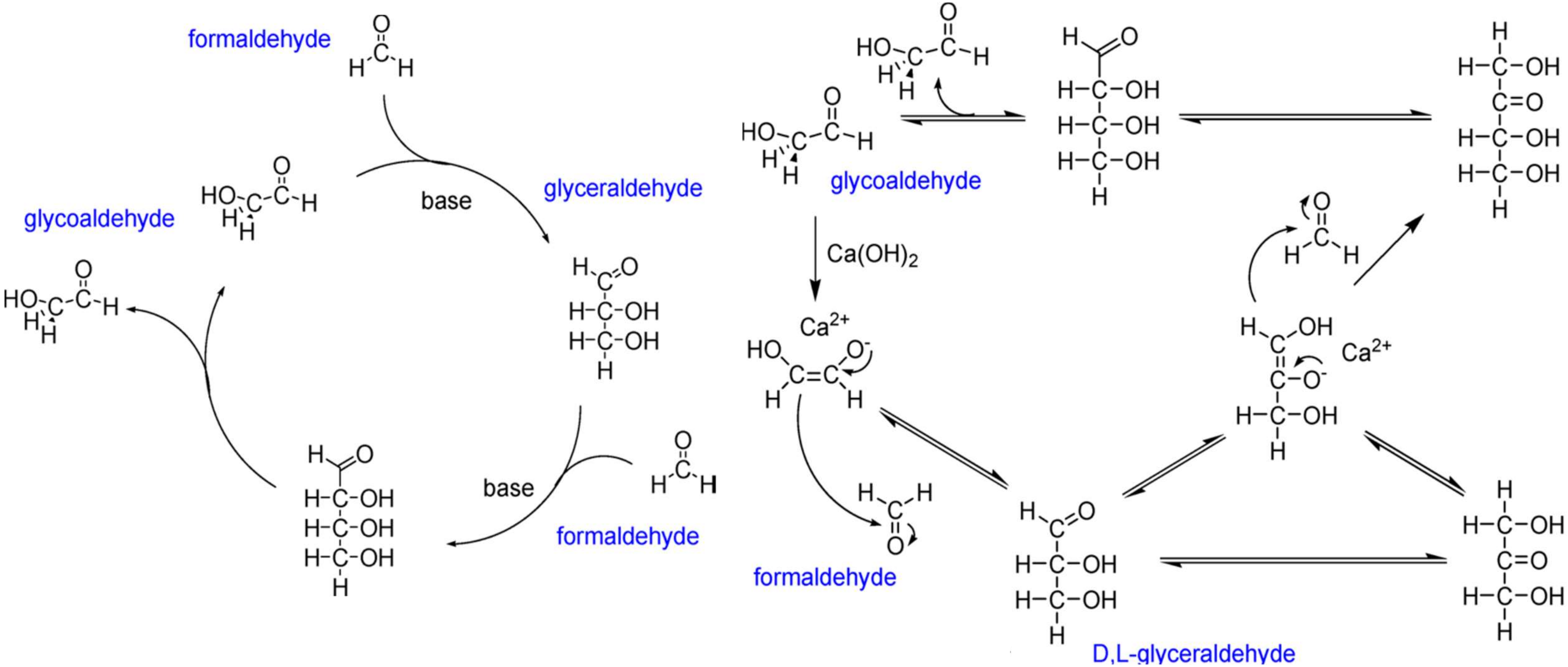
# *Formose reaction – substrate modifications*



# *Formose reaction – substrate modifications*

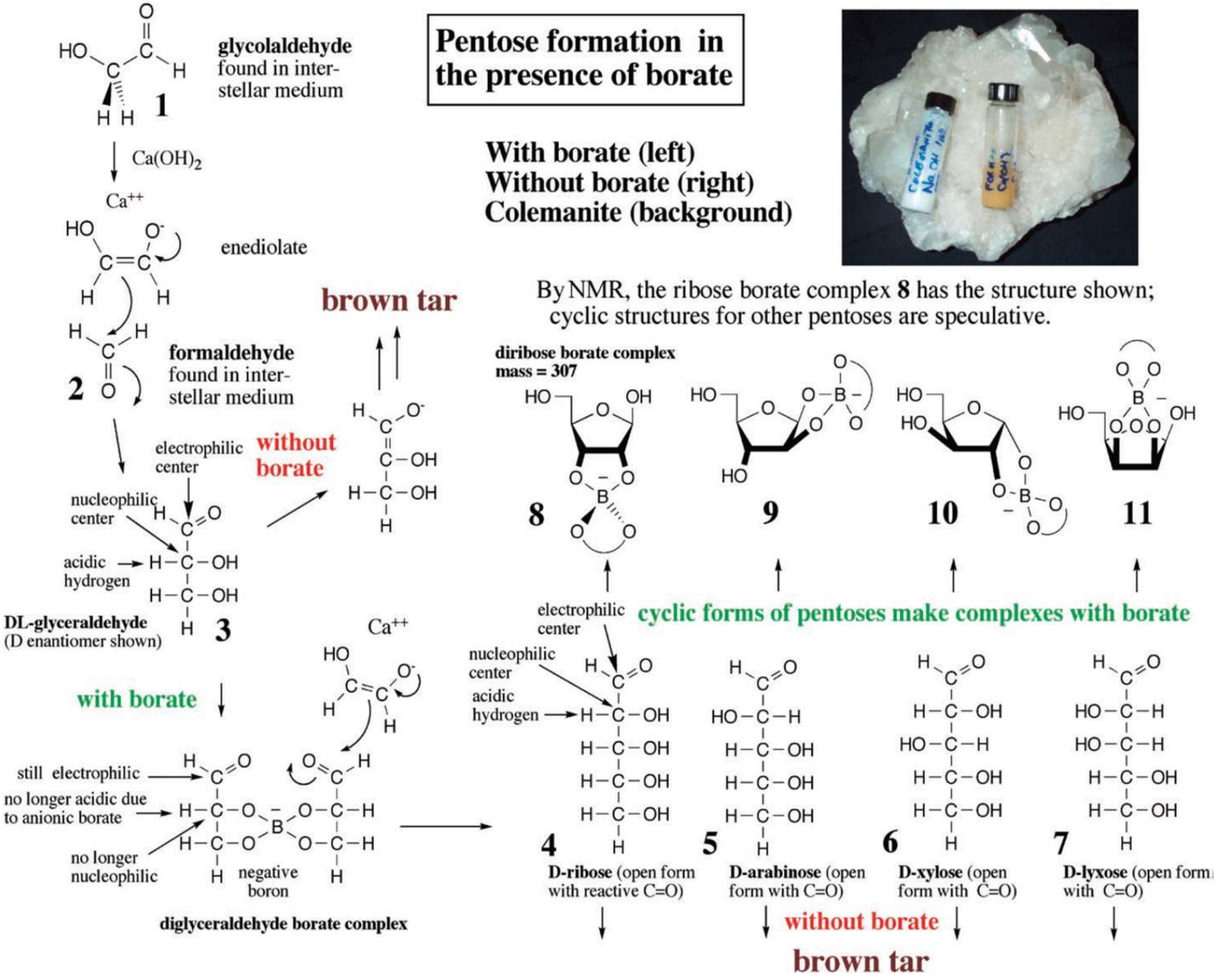


# *Formose reaction under standard basic catalysis*



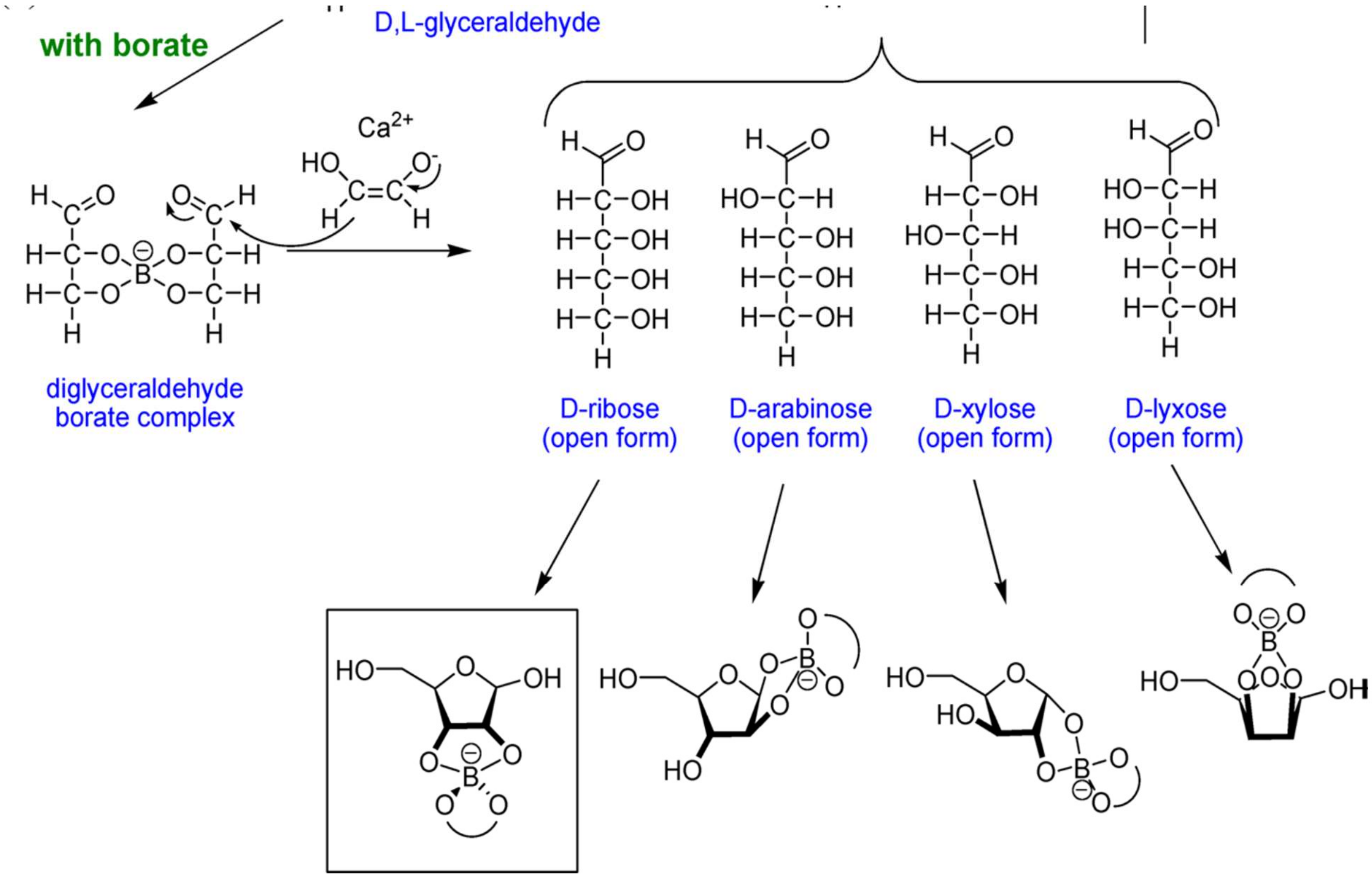
*Escosura*

# *Formose reaction in presence of borates*



A. Ricardo, M. A. Carrigan, A. N. Olcott, S. A. Benner *Science* **2004**, *303*, 196

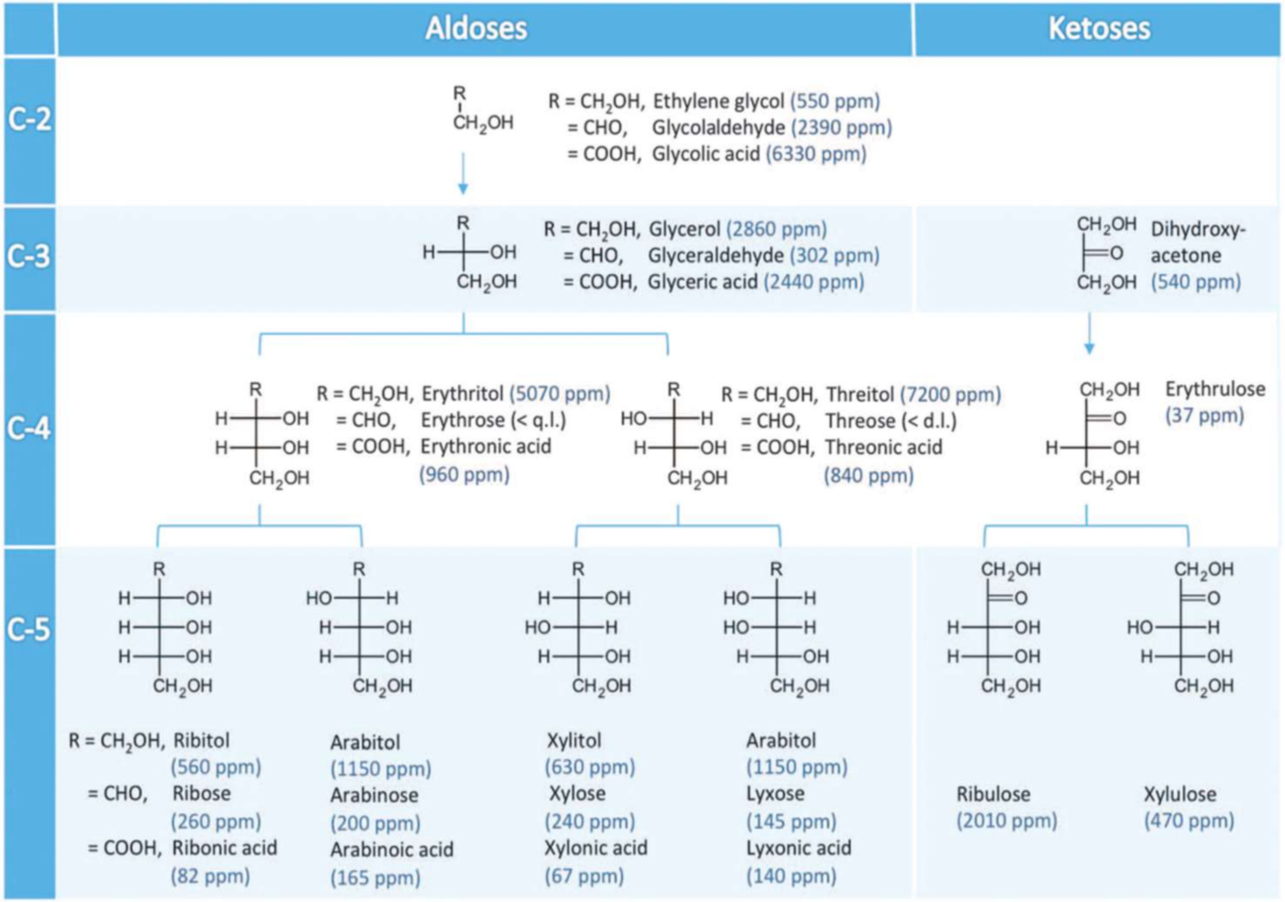
# *Formose reaction in presence of borates*



*Escosura*

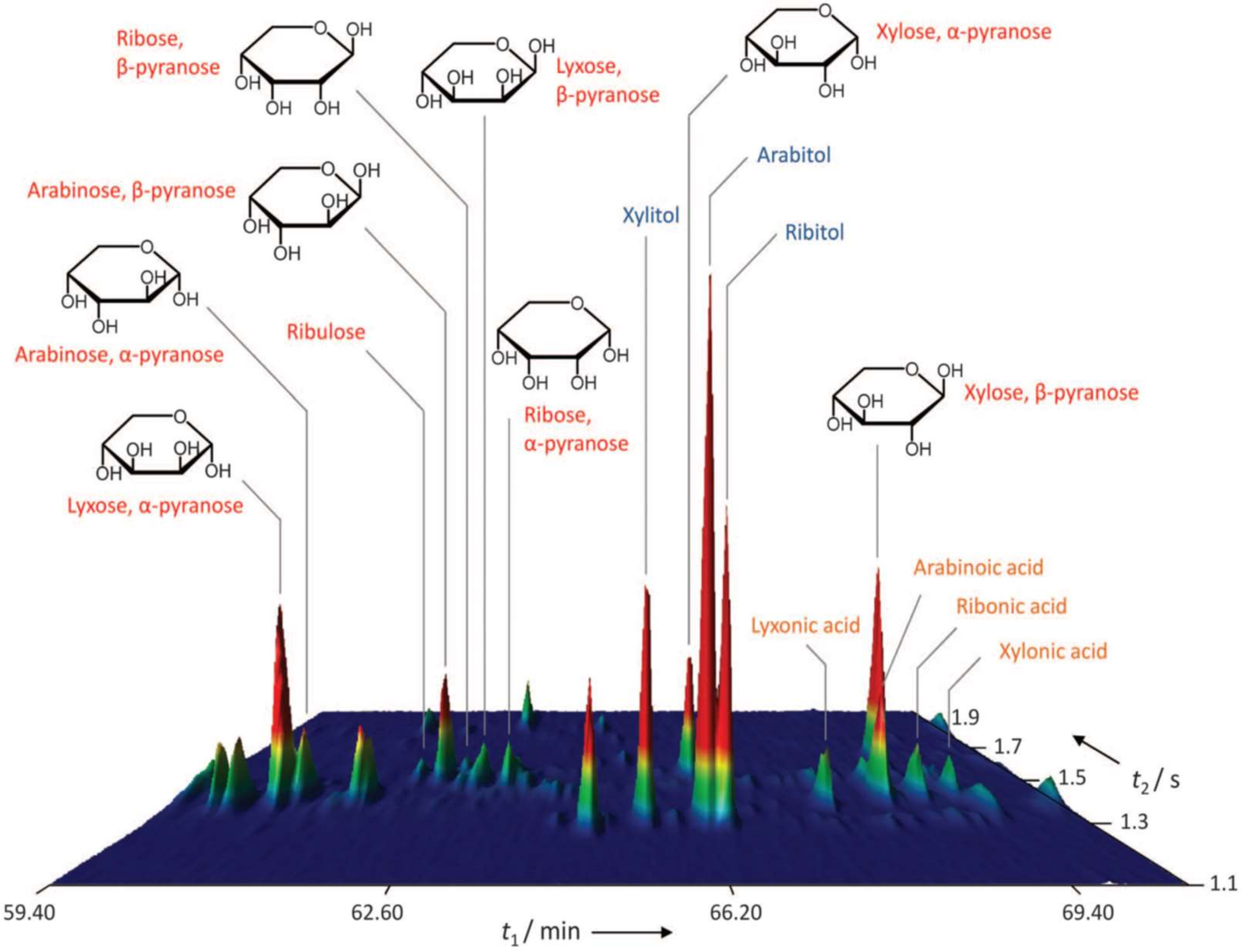
# *Interstellar origin of carbohydrates*

Simulations of photo- and thermochemistry of interstellar ice (silicate/carbon grains surrounded by ice $H_2O$, $CH_3OH$ and $NH_3$) exposed on UV light, low pressure ($10^{-7}$ bar) and temperature (78K) delivers a mixture of sugars



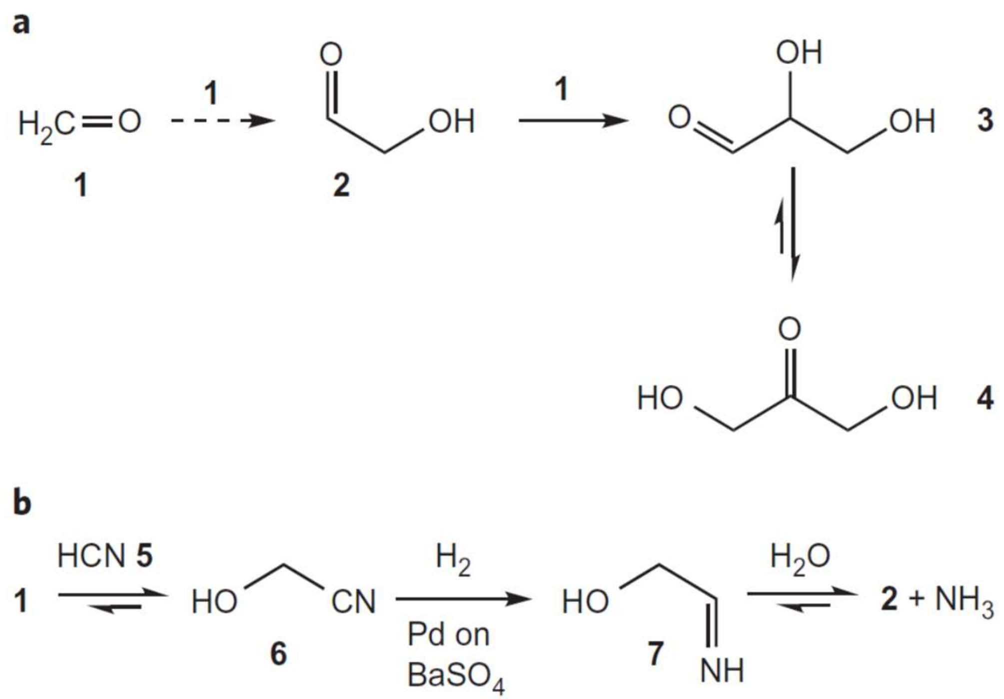
U. Meierhenrich, *et al. Science* **2016**, *352(6282)*, 208-212

## *Interstellar origin of carbohydrates*



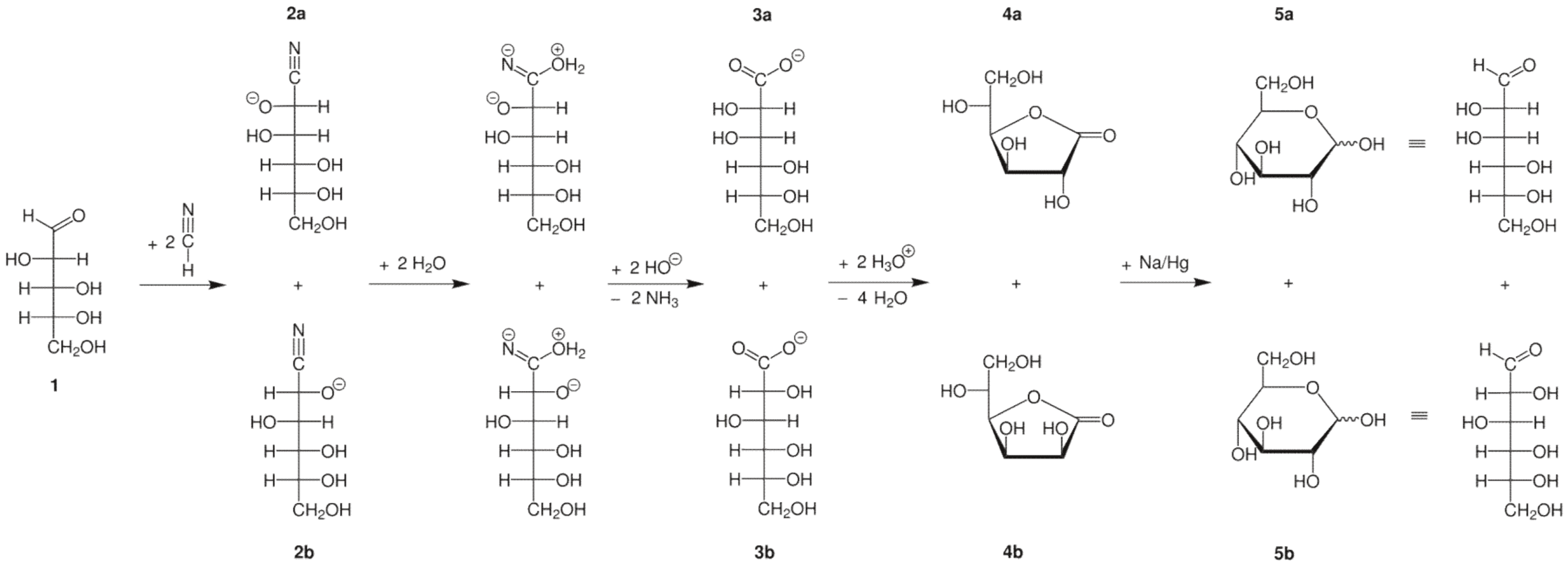
U. Meierhenrich, *et al. Science* **2016**, *352(6282)*, 208-212

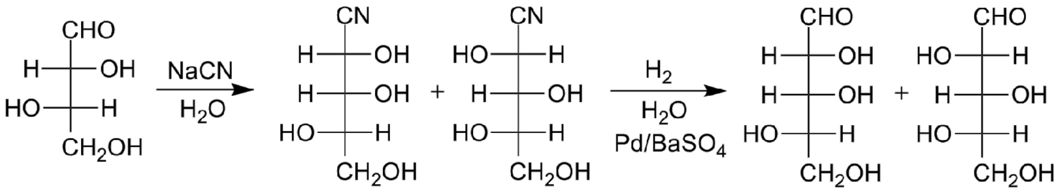
# *Prebiotically plausible alternatives to formose process*



Homologation routes to simple sugars from formaldehyde **1**.
a, Direct homologation of formaldehyde **1** is problematic, because the first dimerization step (dashed) requires umpolung, and because the trimer is more stable as the ketose **4** than the aldose **3** under conditions where **3** can be formed from **1** and **2**. b, Kiliani–Fischer homologation of **1** in conventional synthetic chemistry involves favourable formation of the cyanohydrin **6** by reaction of **1** with hydrogen cyanide **5**, followed by the selective reduction of **6** using very specific conditions.

# Kiliani-Fischer homologation

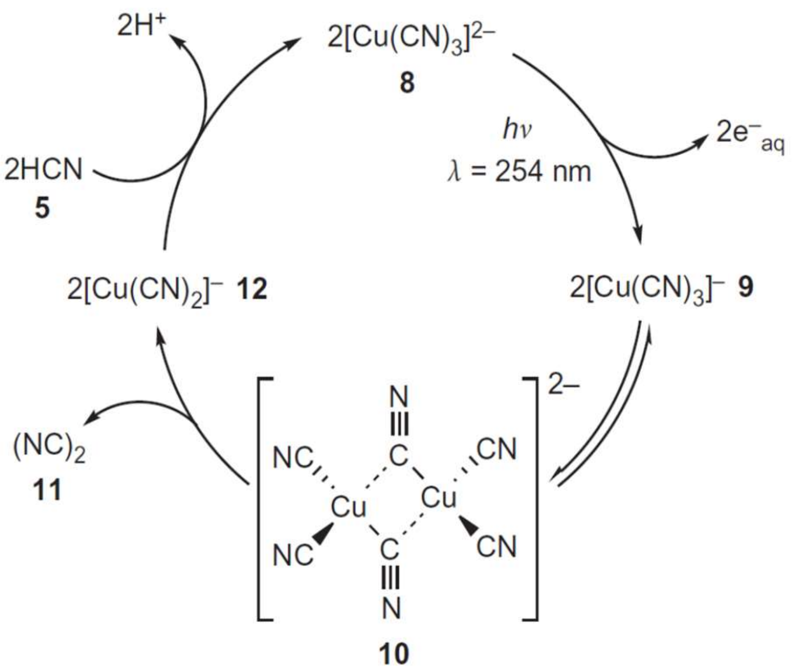


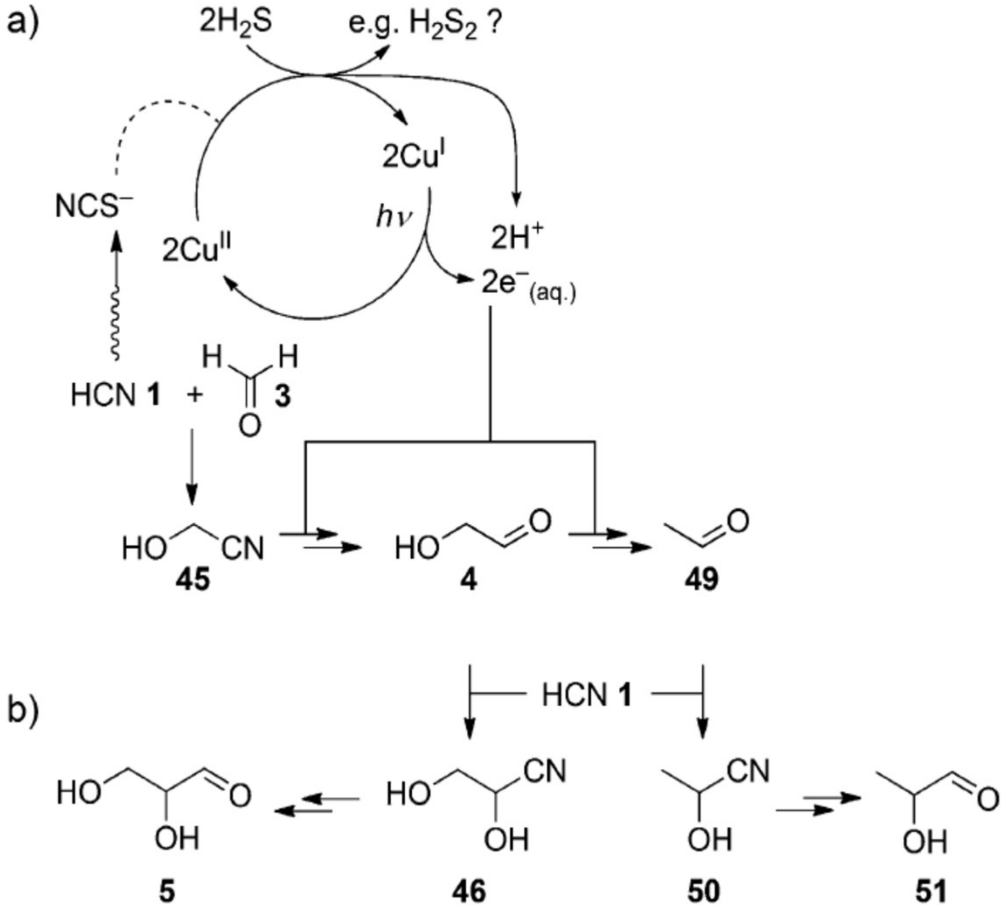


# *Cyanosulfidic chemistry for the Kiliani-Fischer homologation*

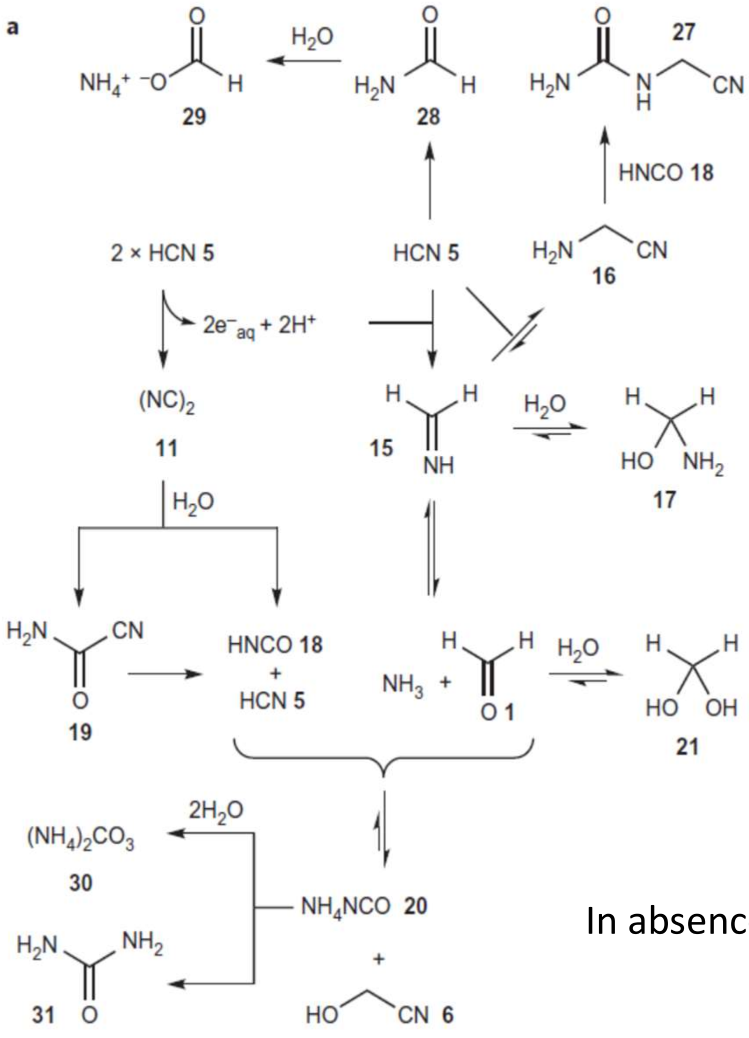
$Cu_2S + H_2O + 6CN^- \rightarrow 2[Cu(CN)_3]^{2-} + HS^- + OH^-$

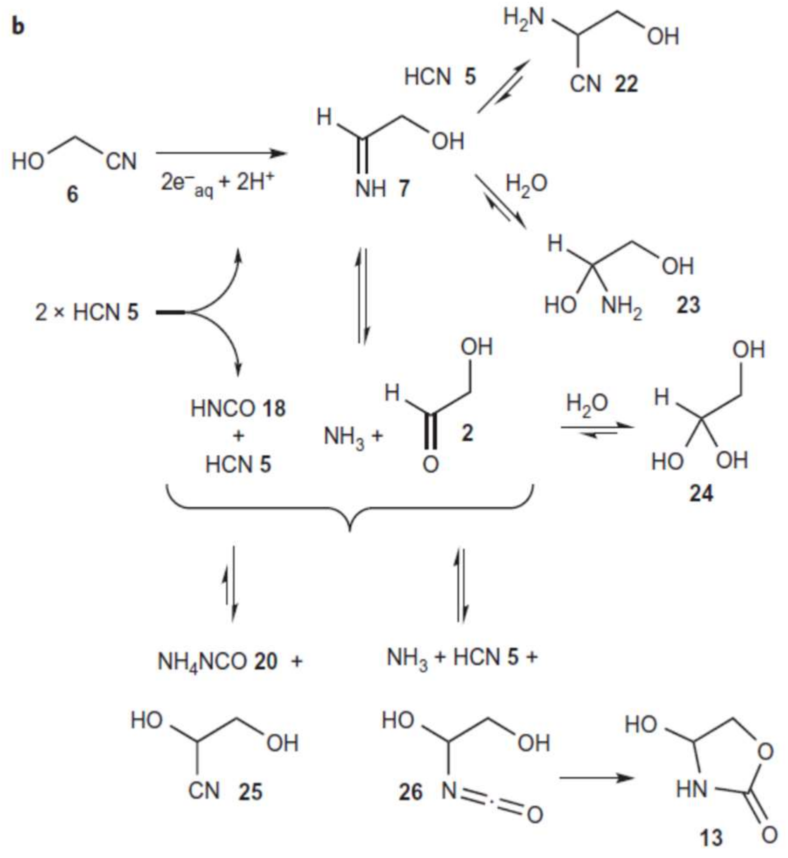
Photoredox cycle based on cyanocuprates may convert HCN into cyanogen





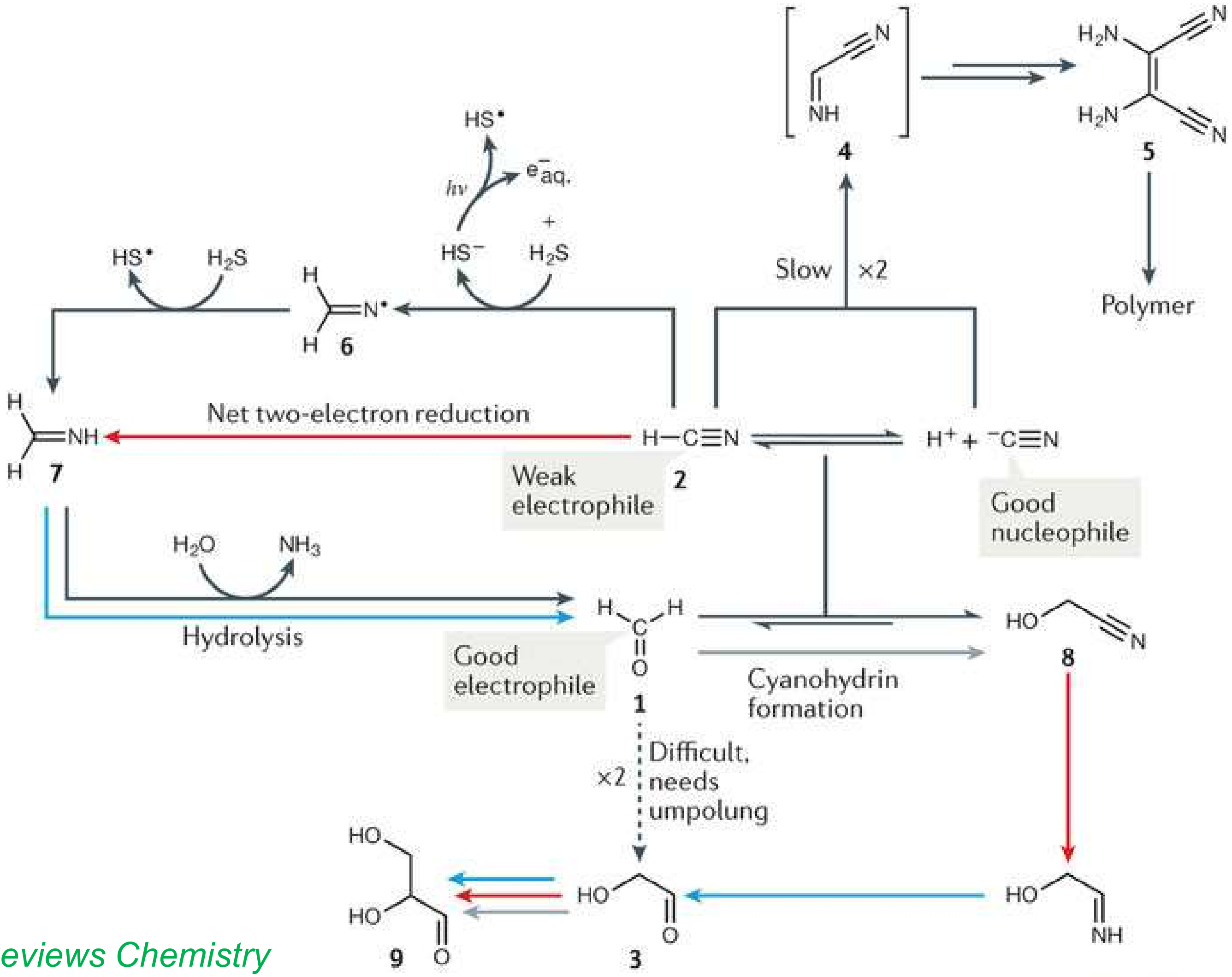
# *Cyanosulfidic chemistry for the Kiliani-Fischer homologation*





In absence of $HS^-$ glycolaldehyde **2** ends up mainly as a cyclic derivative **13**

# *Cyanosulfidic chemistry for the Kiliani-Fischer homologation*



Nature Reviews | Chemistry

J. Sutherland, *Nature Reviews Chemistry*
**2017**, *1*, Article 0012, doi:10.1038/s41570-016-0012

# *Carbohydrates - summary*

Formose reaction gives access to numerous $C_2$-$C_5$ and higher carbohydrates, but is difficult to direct towards particular outcome, and ultimately turns into polymeric tar if overcooked

In presence of borates, the formose reaction tends to deliver protected pentoses in high yields and stable form

Although formaldehyde is the simplest starting material, the reaction is autocatalytic in glycolaldehyde and without it long incubation period is required

Carbohydrate synthesis can also occur under simulated extraterrestrial conditions – by UV-light irradiation of cometary ice

Alternative prebiotic synthesis of simple carbohydrates involves Kiliani-Fischer homologation process based on HCN in presence of copper ions and hydrosulfides – all accessible by the meteorite-derived cyanide-metal chemistry

The same type of chemistry can also deliver a set of reactive intermediates like cyanogen, acetylene, ammonia, and activated forms of phosphate – the latest can derivatize sugars and, after redox processes, deliver numerous building blocks present in currently known metabolic cycles