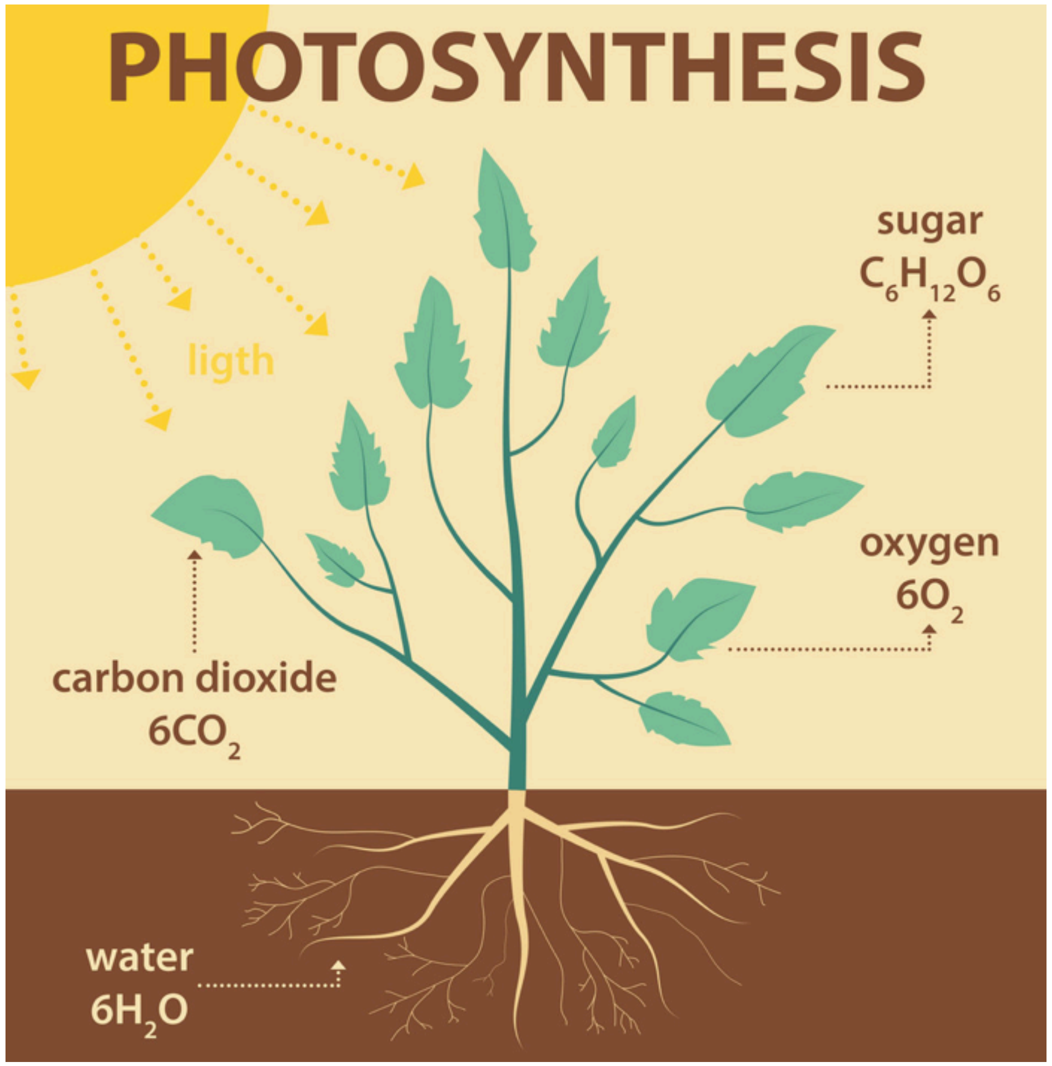
Artificial Photosynthesis: a synthetic organic perspective

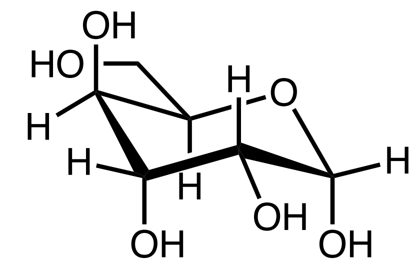
Wei Liu
MacMillan group meeting
Mar. 11th, 2020

image credit: Wiley-VCH

Photosynthesis: a brief overview



Net reaction

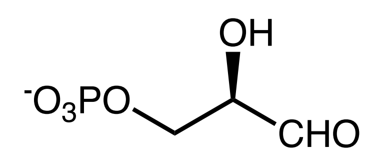
$6\ CO_2 + 6\ H_2O \xrightarrow{\text{sunlight}}$  $+ 6\ O_2$

Water-splitting reaction (Light-dependent)

$$2\ H_2O \xrightarrow{\text{sunlight}} O_2 + 4\ H^+ + 4\ e^-$$

(stored in NADPH and ATP)

CO_2 fixation (Light-independent)

$3\ CO_2 \overset{\text{RuBisCO}}{\Longrightarrow}$ 

(G3P)

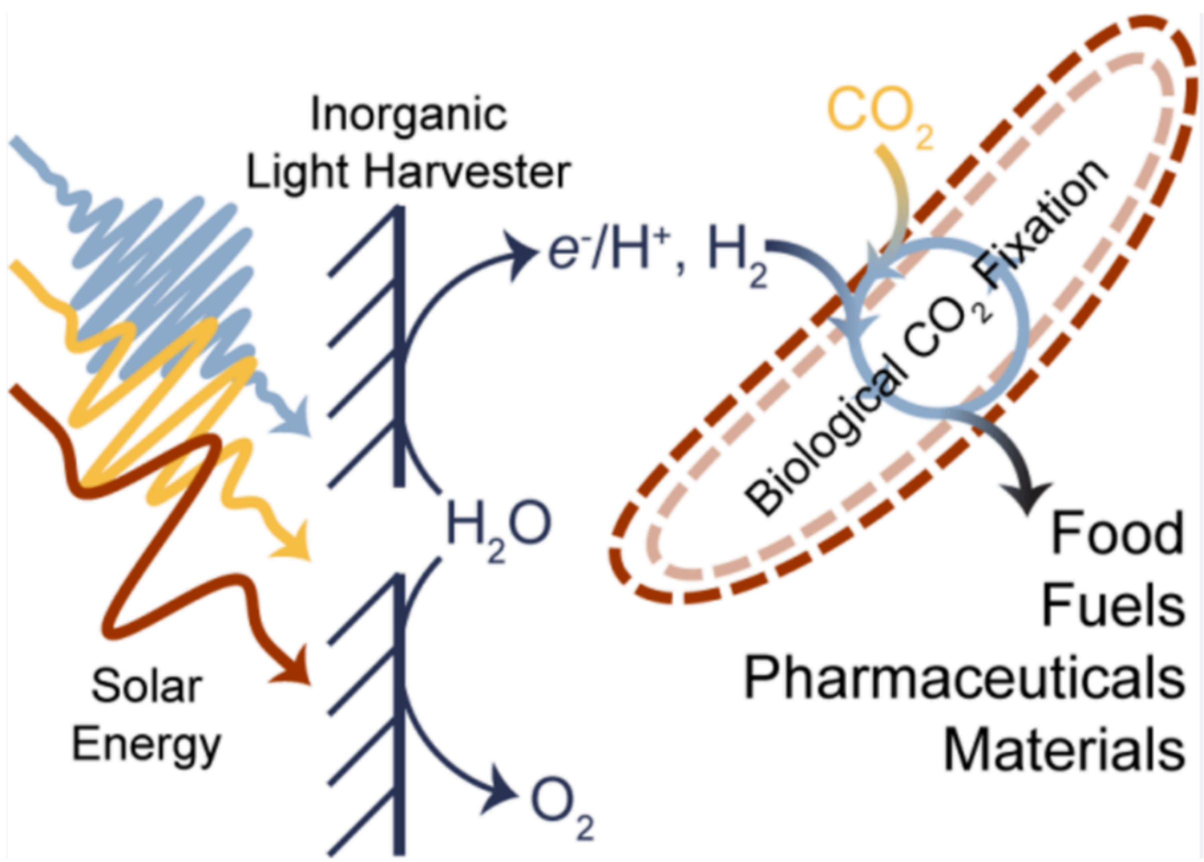
Jack Twilton, **MacMillan group meeting**, “*Photosynthesis – An Organic Chemists Guide*”

Artificial photosynthesis: a brief overview

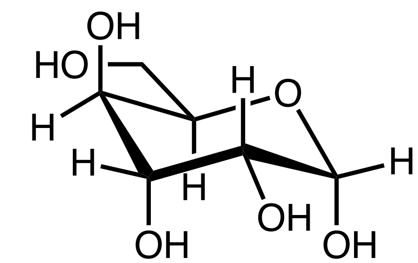
Artificial photosynthesis

$$2\,H_2O \xrightarrow{\text{sunlight}} O_2 + 2\,H_2$$

$$CO_2 + H_2 \xRightarrow[\text{biological}]{\text{chemical}} CO \quad CH_4 \quad CH_3OH \quad C_4H_9OH \quad \text{and more…}$$



Outlook



- Complex organic molecules
- Socioeconomic considerations
- Progress in synthetic biology

Representative review: *Chem. Rev.* **2013**, *113*, 6621; *Acc. Chem. Res.* **2017**, *50*, 476

CO_2 Conversion Challenge

NASA
CO_2 Conversion
Challenge

Challenge Targeted Compounds	Weighting Factor
D-Glucose	100
Other 6-carbon sugars (D-hexoses)	80
5-carbon sugars (D-pentoses)	50
4-carbon sugars (D-tetroses)	10
3-carbon sugars (D-trioses)	5
D-Glycerol	5

Started by NASA in 2019 (now in Phase II)

Space exploration to Mars

CO_2 recycling (life support system)

CO_2 fixation (availabe SM on Mars)

Why NASA wants glucose?

Energy sources for microbial fermentation

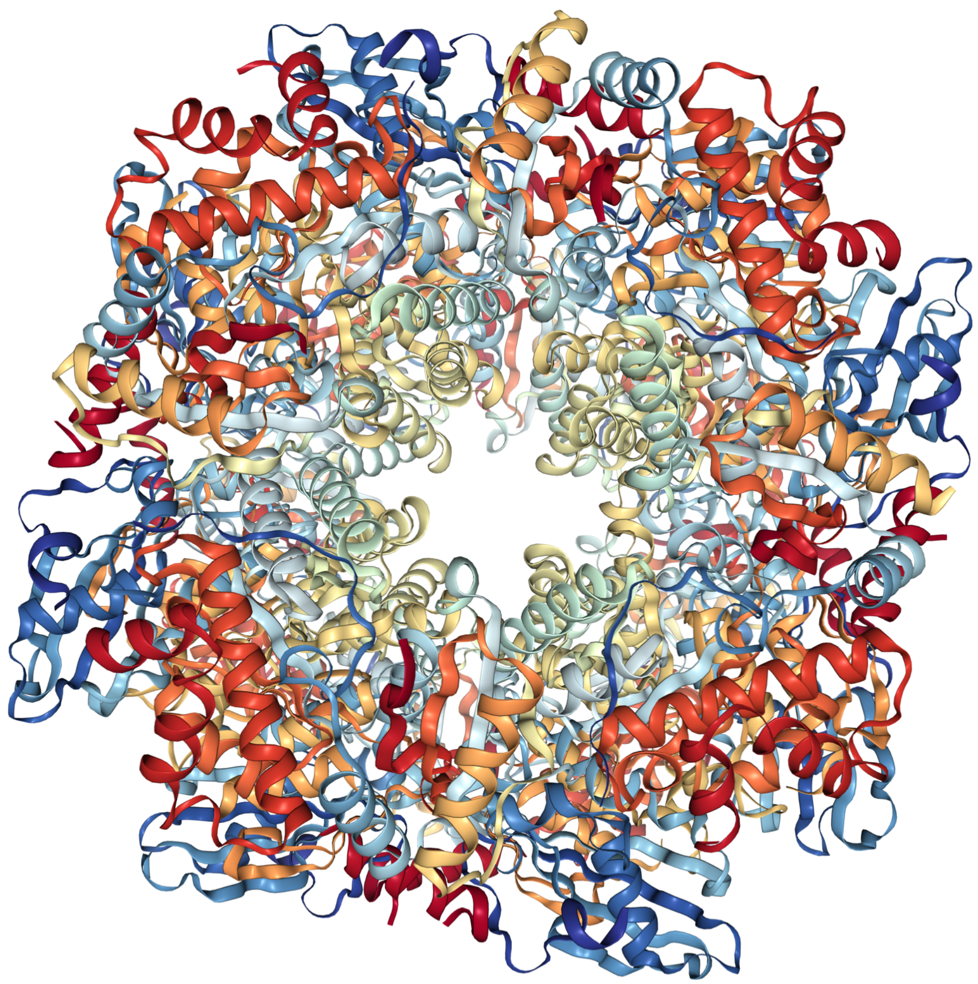
C6 sugar is preferred in microbial system

Total synthesis of glucose on Mars?

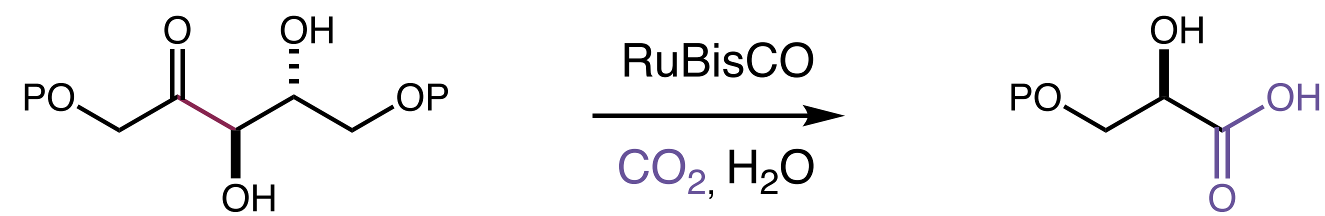
What about earthly synthesis of glucose?

https://www.co2conversionchallenge.org

Nature's approach: Calvin-Benson cycle



RuBisCO (ribulose-1,5-bisphosphate carboxylase/oxygenase)



responsible for more than 90% carbon fixation

one of the most abdundant enzyme on earth

low turnover frequency (1 to 10 s^{-1})

3 to 10 molecules of CO_2 fixed per second per enzyme

low specificity (CO_2 vs O_2)

targets for synthetic biology

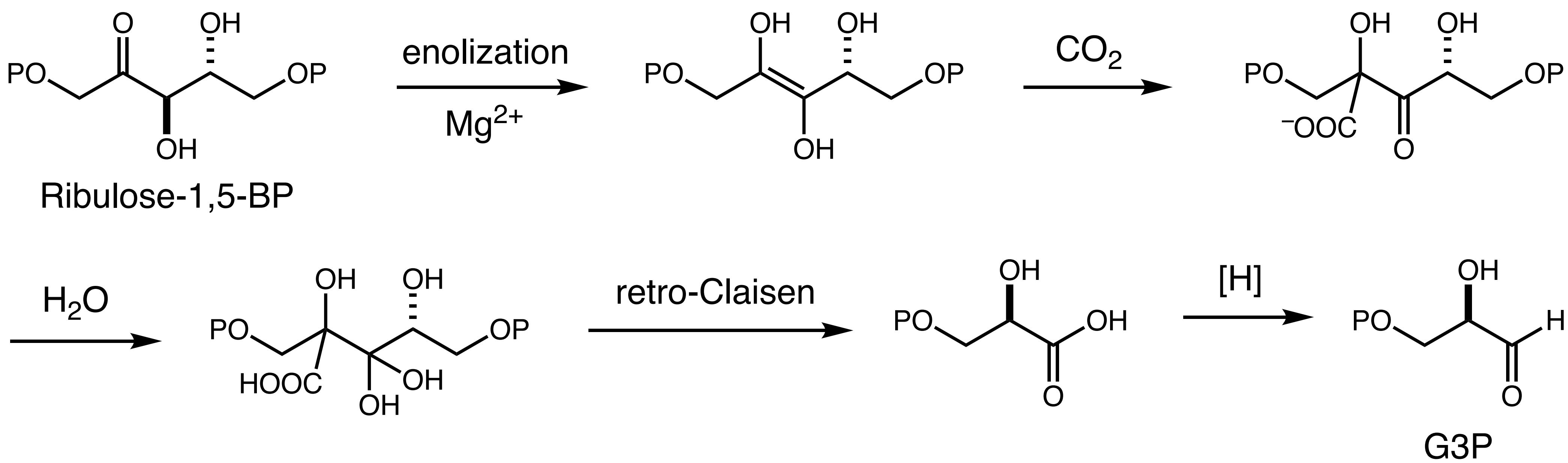
Erb, T. J.; Zarzycki, J. *Curr. Opin. Biotech.* **2018**, *49*, 100

Bar-Even, A.; Noor, E.; Lewis, N. E.; Milo, R. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 8889

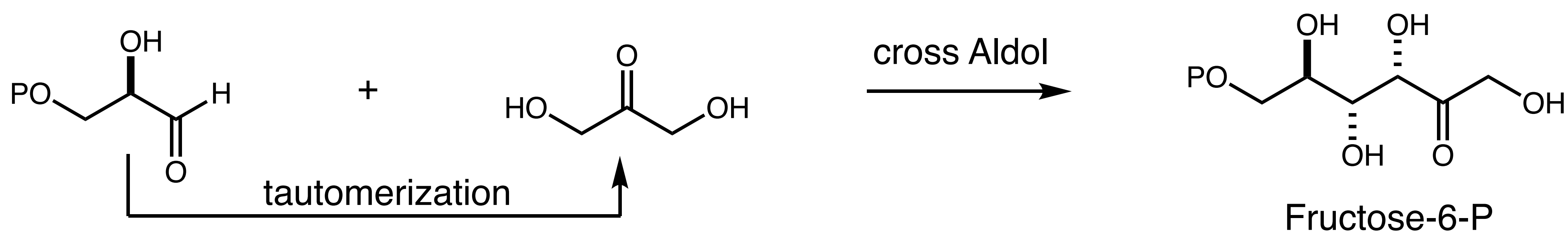
Schwander T.; Schada, v. B. L.; Burgener, S.; Cortina, N. S.; Erb, T. J. *Science*, **2016**, *354*, 900

Nature's approach: Calvin-Benson cycle

Mechanism of RuBisCO



CO_2 to C6 sugar



Economics of RuBisCO

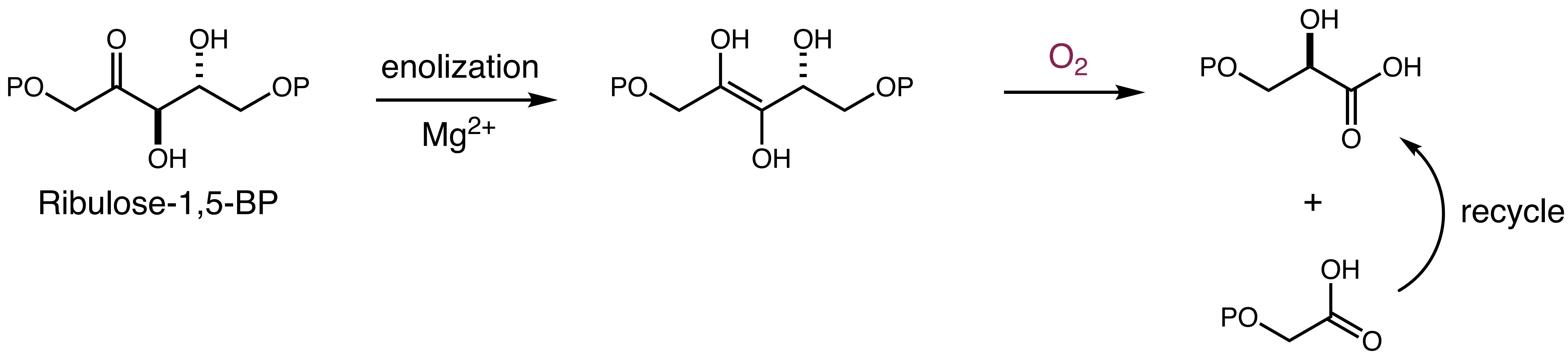
3 Ribulose-1,5-BP + 3 CO_2 ⟶ 5 G3P 1 G3P

3 x C5 3 x C1 5 x C3 **1 x C3**

Erb, T. J.; Zarzycki, J. *Curr. Opin. Biotech.* **2018**, *49*, 100

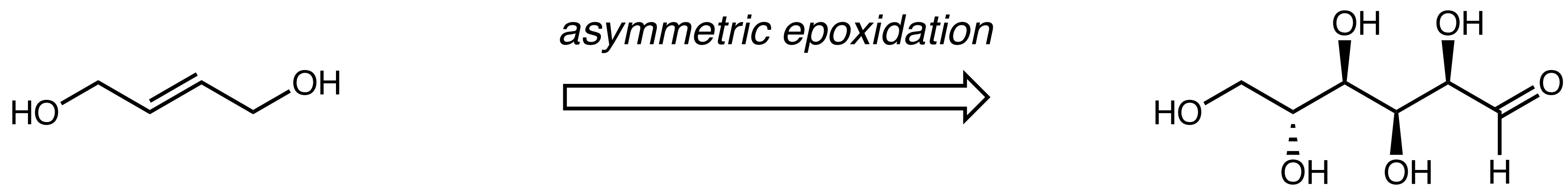
Nature's approach: Calvin-Benson cycle

Mechanism of RuBisCO

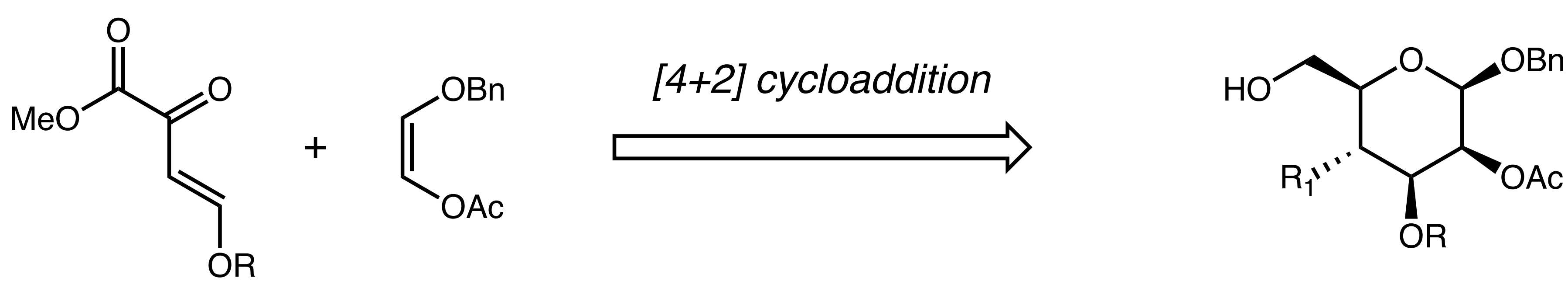


Erb, T. J.; Zarzycki, J. *Curr. Opin. Biotech.* **2018**, *49*, 100

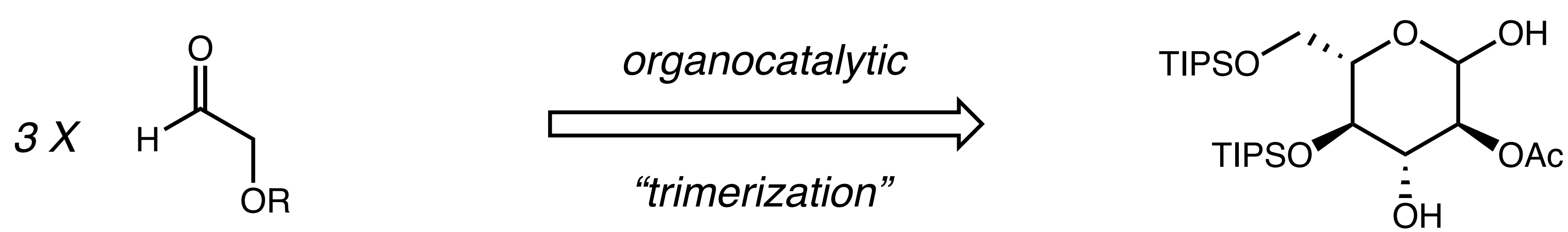
De novo synthesis of Hexose



Masamune & Sharpless, *Science* **1983**, *220*, 949

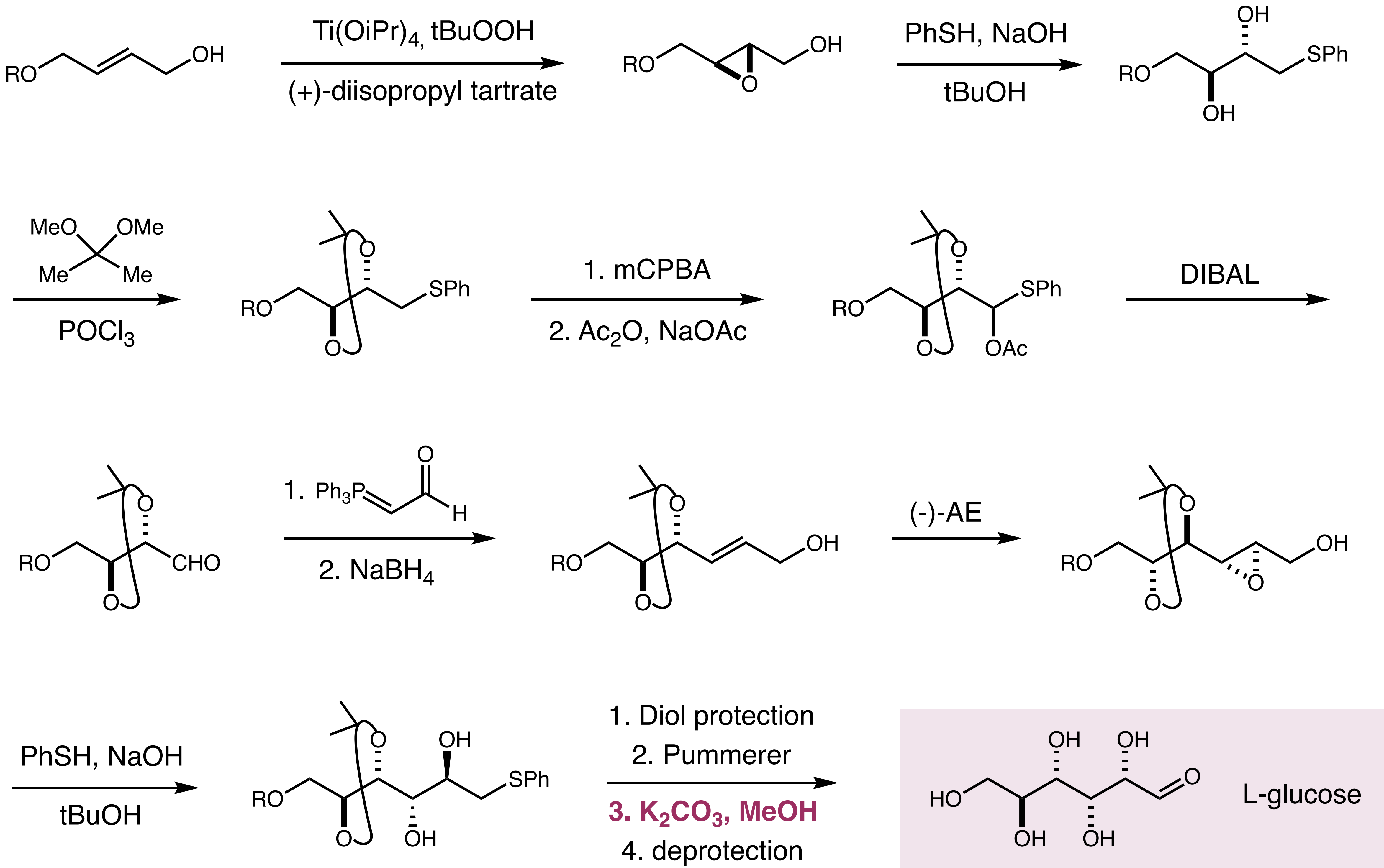


Boger, *J. Org. Chem.* **1988**, *53*, 5793



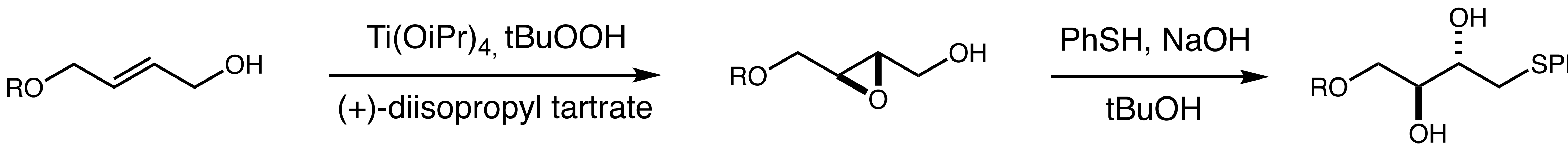
MacMillan, *Science* **2004**, *305*, 1752

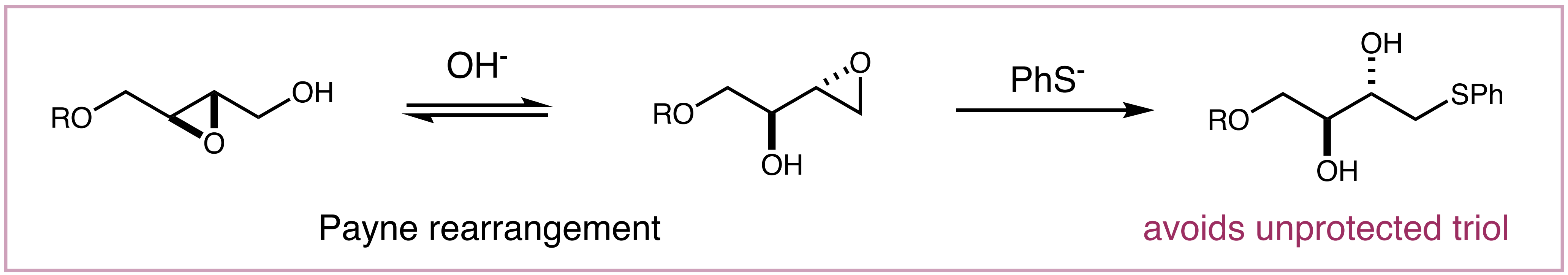
De novo synthesis of Hexose



Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed, L. A.; Sharpless, K. B. *Science* **1983**, *220*, 949

De novo synthesis of Hexose





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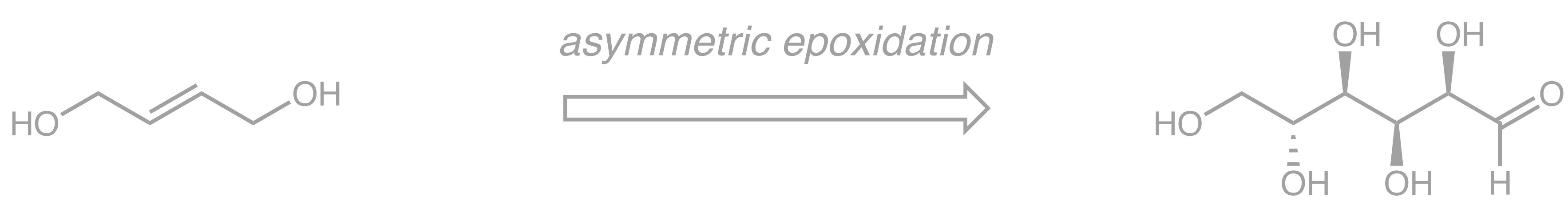
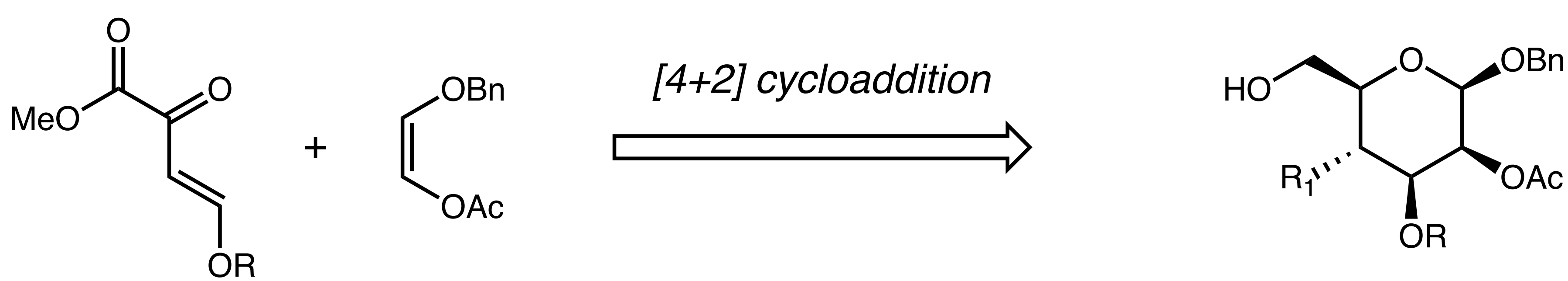
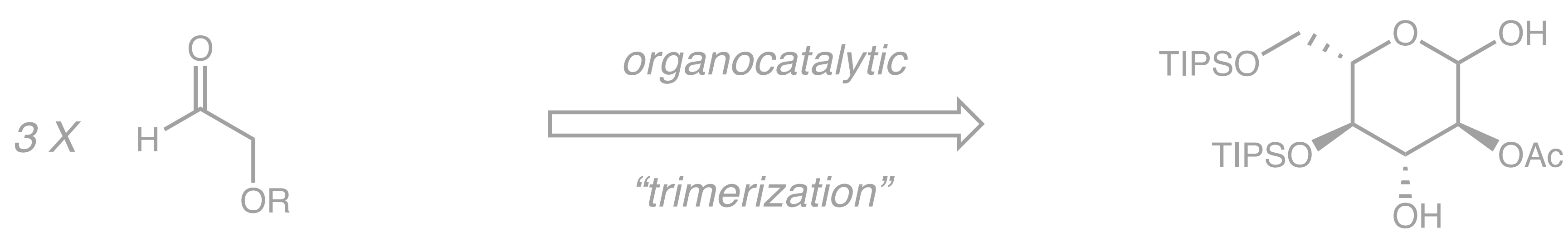
De novo synthesis of Hexose



Masamune & Sharpless, *Science* **1983**, *220*, 949



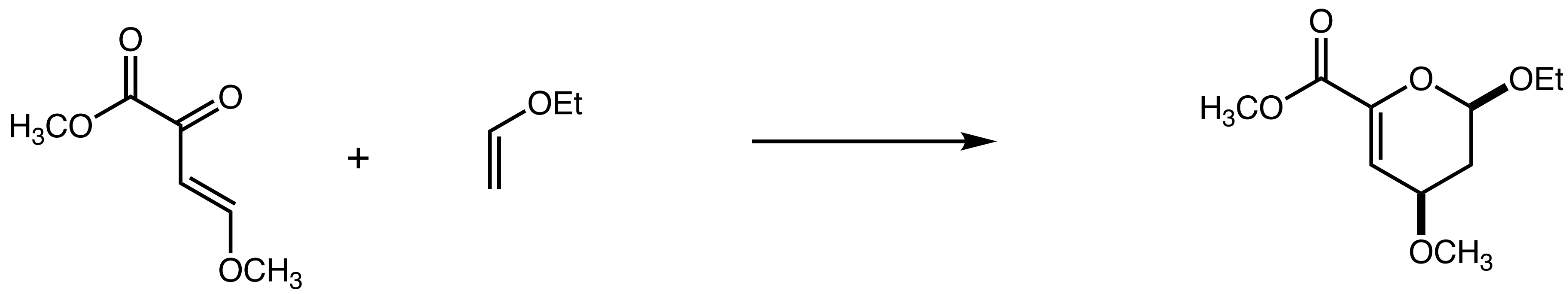
Boger, *J. Org. Chem.* **1988**, *53*, 5793



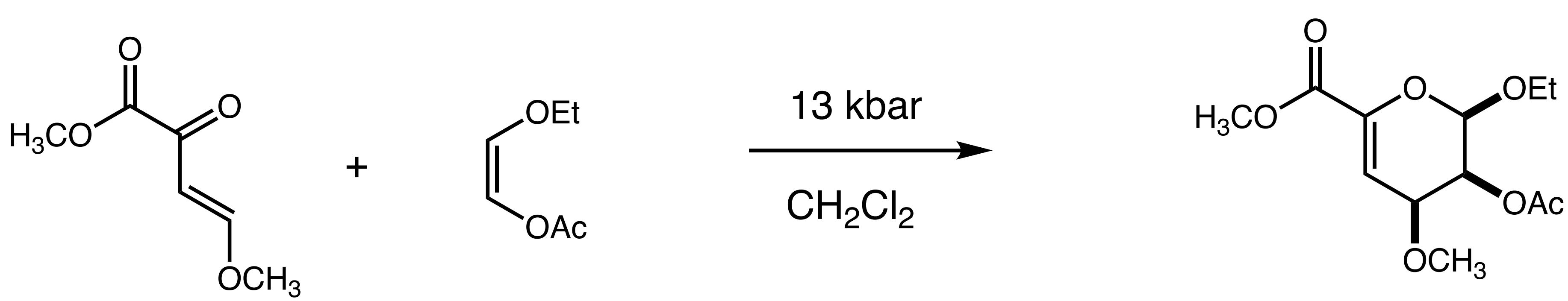
MacMillan, *Science* **2004**, *305*, 1752

De novo synthesis of Hexose

Inverse electron demand [4+2] cycloaddition



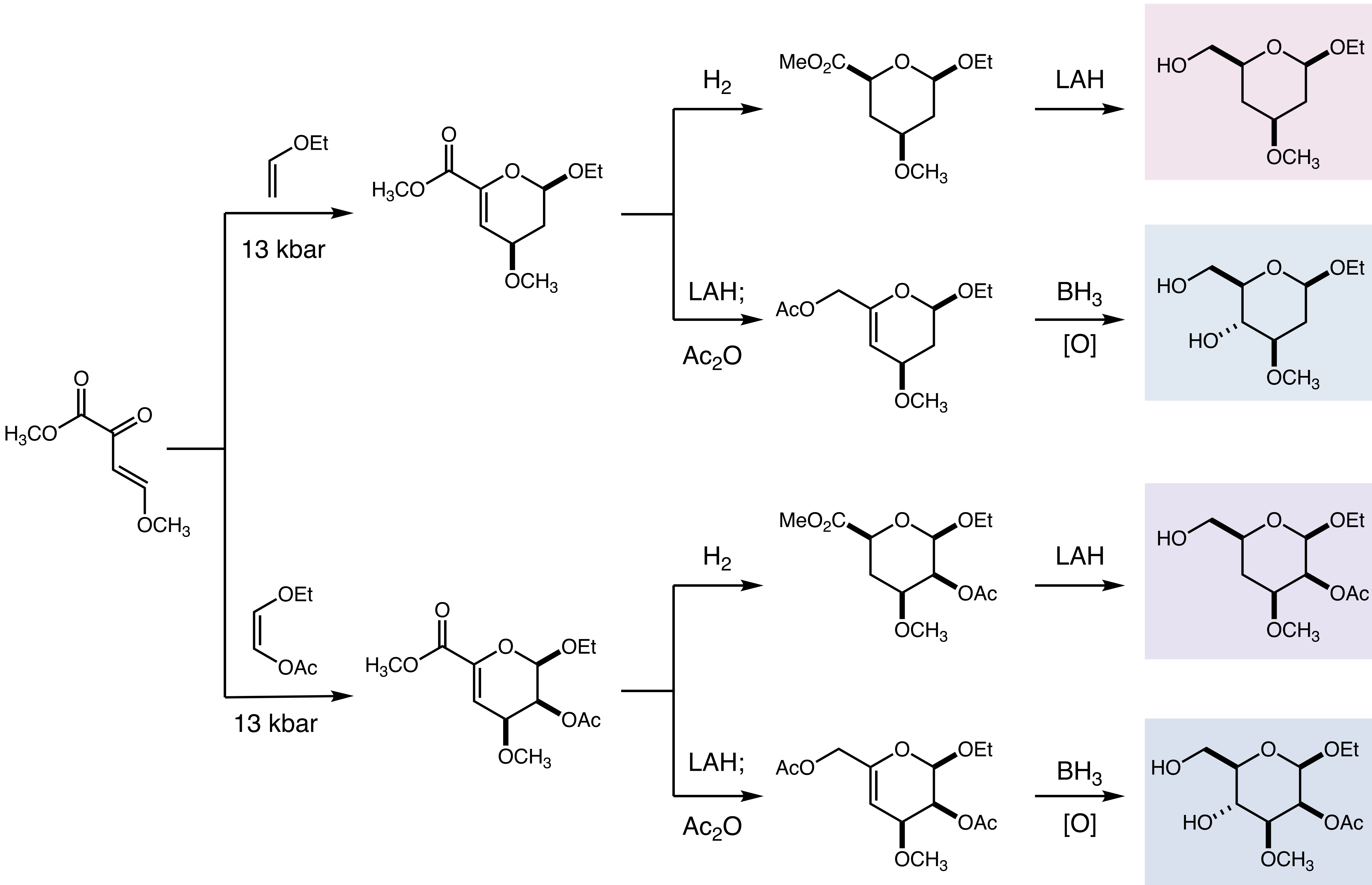
Condition	Result
$EtAlCl_2$ or $TiCl_4$	complex mixture
Toluene, 110^{o}C	48% yield (2:1 endo:exo)
neat, 13 kbar	82% yield (6:1 endo:exo)
CH_2Cl_2, 6 kbar	75% yield (6:1 endo:exo)



49% yield (>45:1 endo:exo)

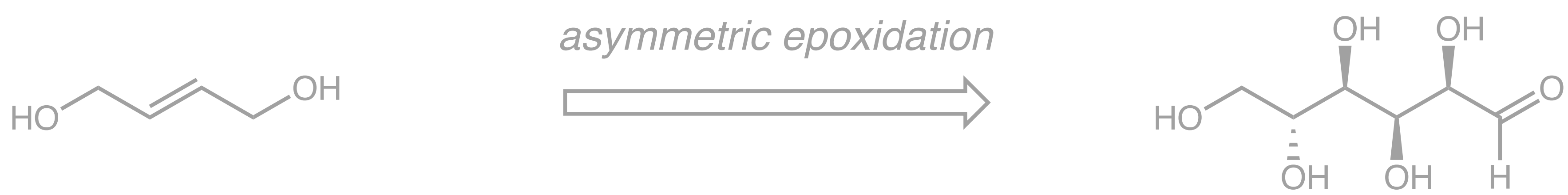
Boger, D. L.; Robarge, K. D. *J. Org. Chem.* **1988**, *53*, 5793

De novo synthesis of Hexose



Boger, D. L.; Robarge, K. D. *J. Org. Chem.* **1988**, *53*, 5793

De novo synthesis of Hexose



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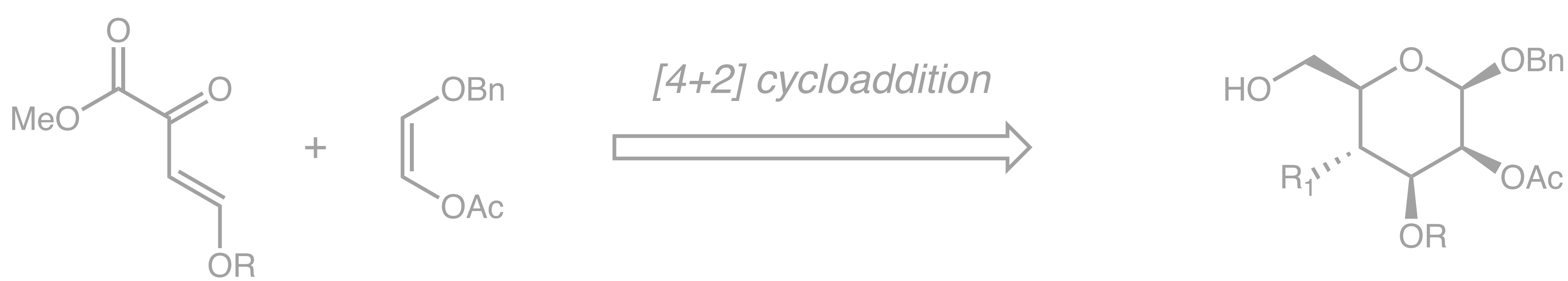
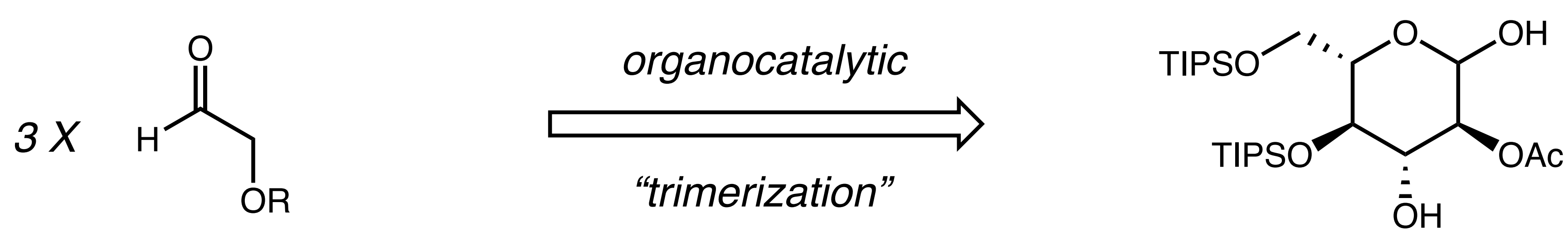


Boger, *J. Org. Chem.* **1988**, *53*, 5793



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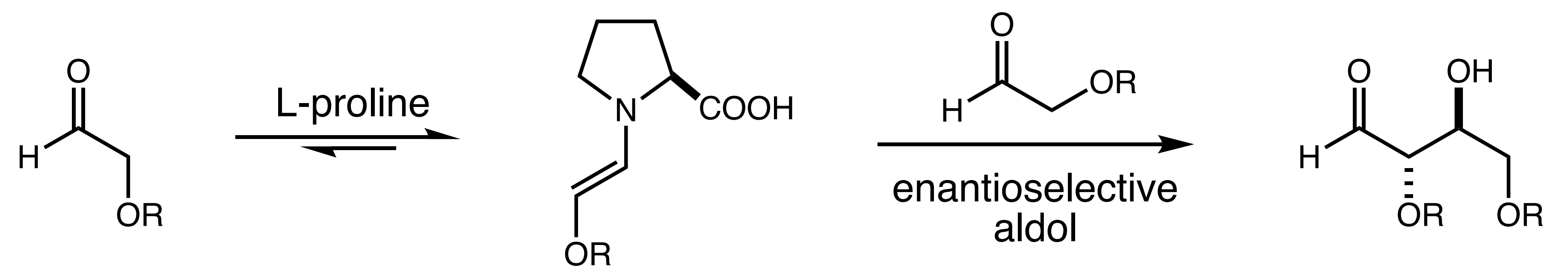
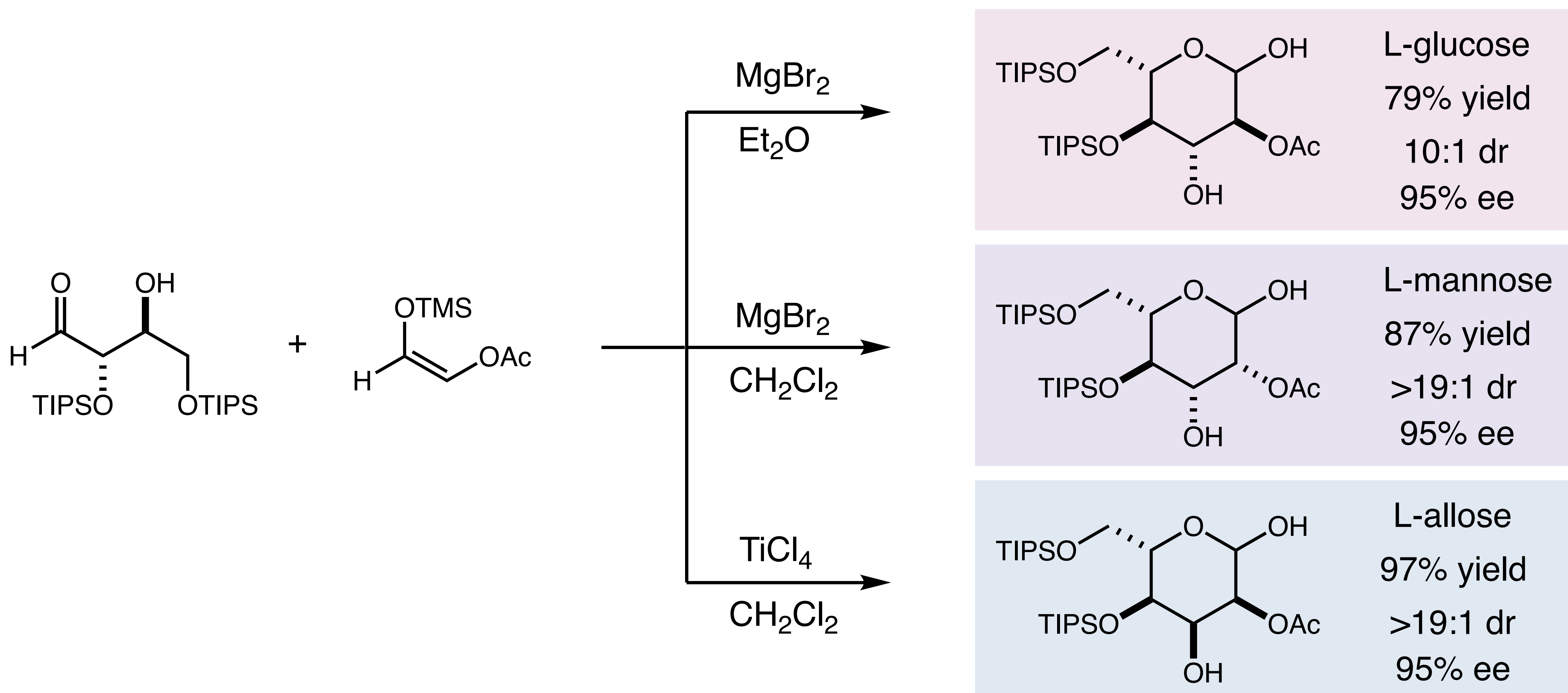
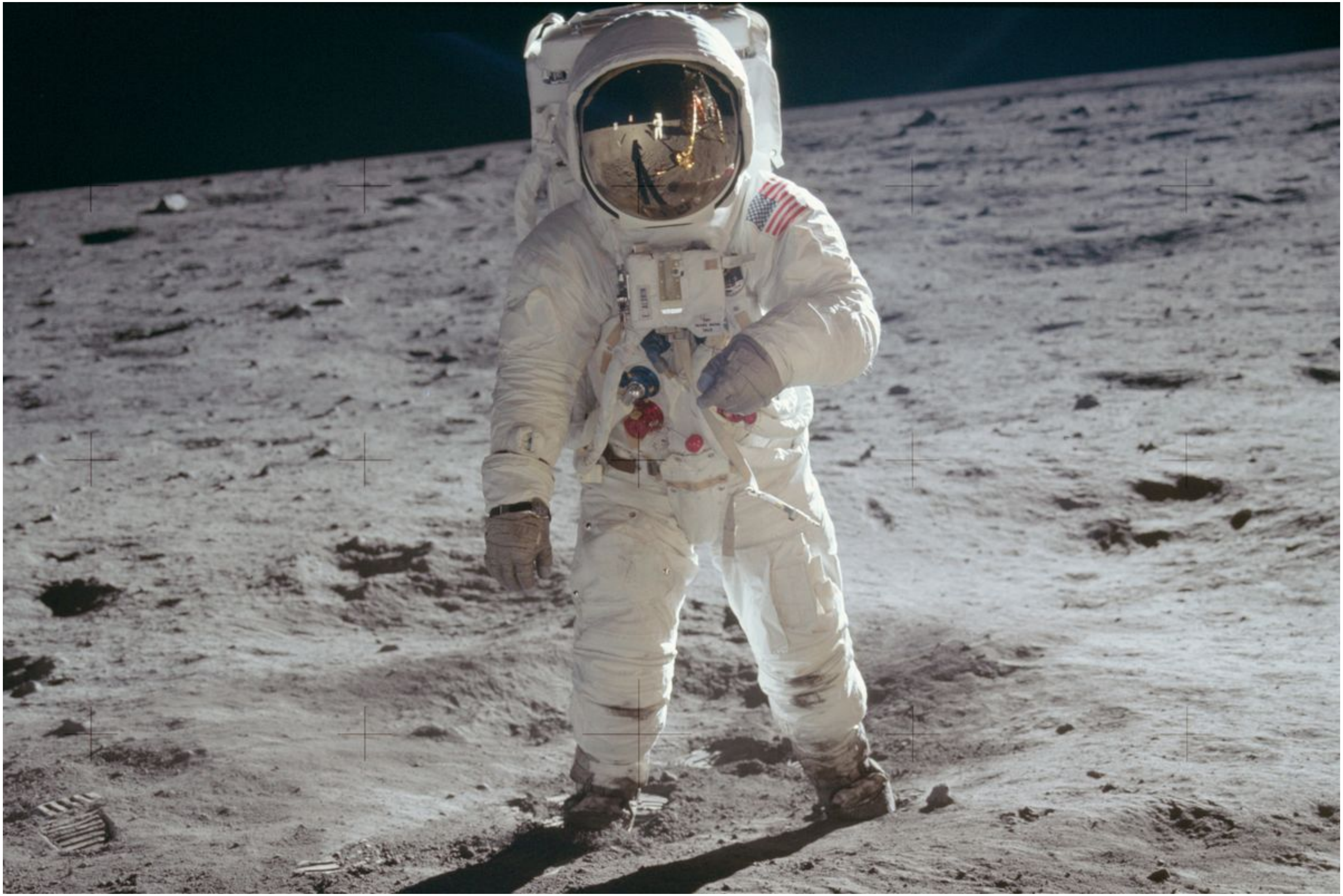
De novo synthesis of Hexose



92% yield, 4:1 anti:syn, 95% ee (R = TIPS)
78% yield, 4:1 anti:syn, 98% ee (R = Bn)



Northrup, A. B.; MacMillan, D. W. C. *Science* **2004**, *305*, 1752
Northrup, A. B.; Mangion, I. K.; Hettche, F.; MacMillan, D. W. C. *Angew. Chem. Int. Ed.* **2004**, *43*, 2152



NASA's approach

NASA CELSS Program
FINAL REPORT
Grant No. NCC 2-231

FEASIBILITY OF PRODUCING A RANGE OF FOOD PRODUCTS FROM A LIMITED RANGE OF UNDIFFERENTIATED MAJOR FOOD COMPONENTS

Principal Investigator:

Dr. Marcus Karel
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Research Associate:

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NASA Technical Officer:

Dr. Robert D. MacElroy
Advanced Life Support Office, 239-E
NASA-Ames Research Center
Moffett Field, California 94035

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ACCESS DEPT.

https://ntrs.nasa.gov/archive/nasa/casi.ntrs.nasa.gov/19850008164.pdf

NASA's approach

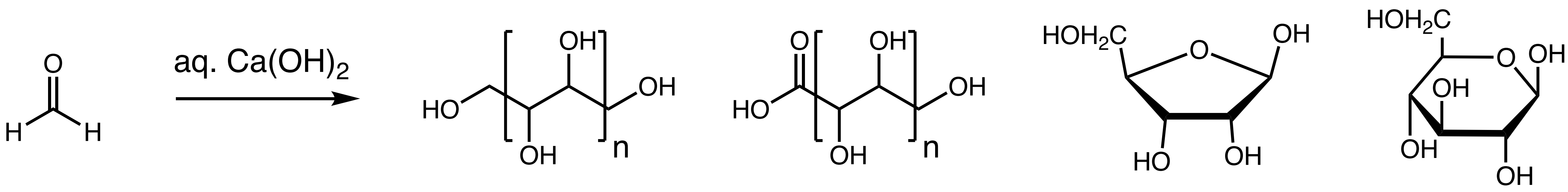
One approach which has been investigated by NASA as well as other investigators is the conversion of formaldehyde to "formose" sugars. Hydrogenolysis of "formose" produces glycerol, 1,3-propanediol, and 1,4-butanediol which are believed to be at least partially utilizable as energy sources and which can be produced also by other synthetic routes (Shapira, 1968; Shapira, 1970B; Weiss and Shapira, 1971). The formaldehyde is assumed to be attainable with suitable energy input by catalytic conversion, from CO_2 and H_2O as follows:

$$4H_2O \rightarrow 4H_2 + 2O_2$$
$$CO_2 + 4H_2 \rightarrow CH_4 + 2H_2O$$
$$O_2 + CH_4 \rightarrow HCHO + H_2O$$

Recently, researchers at MIT have accomplished the total synthesis of all 8 L-hexoses, using a reiterative two-carbon extension cycle consisting of four steps (Ko et al., 1983). Should such procedures produce D-hexoses and prove amenable to utilization under CELSS conditions, they may offer a new approach to synthesis of nutrients.

https://ntrs.nasa.gov/archive/nasa/casi.ntrs.nasa.gov/19850008164.pdf

Formose reaction



a mixture of sugars: “formose sugar”

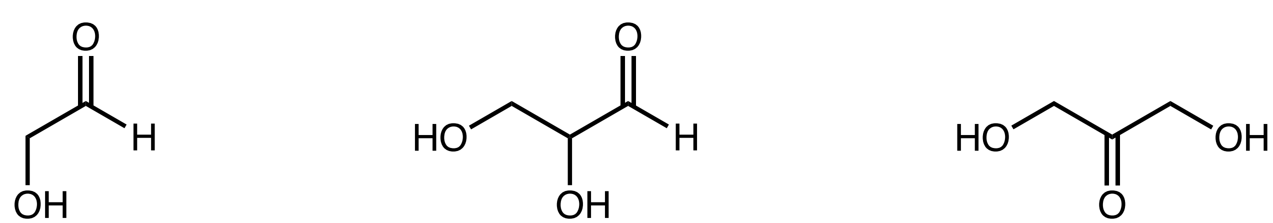
Discovered by Aleksandr Butlerow in 1861

Considered by NASA as a way to synthesize glycerol

Now accepted mechanism proposed by Breslow in 1959

Autocatalytic: long induction period, followed by fast reaction

Addition of intermediates removes induction, but doesn’t increase rate

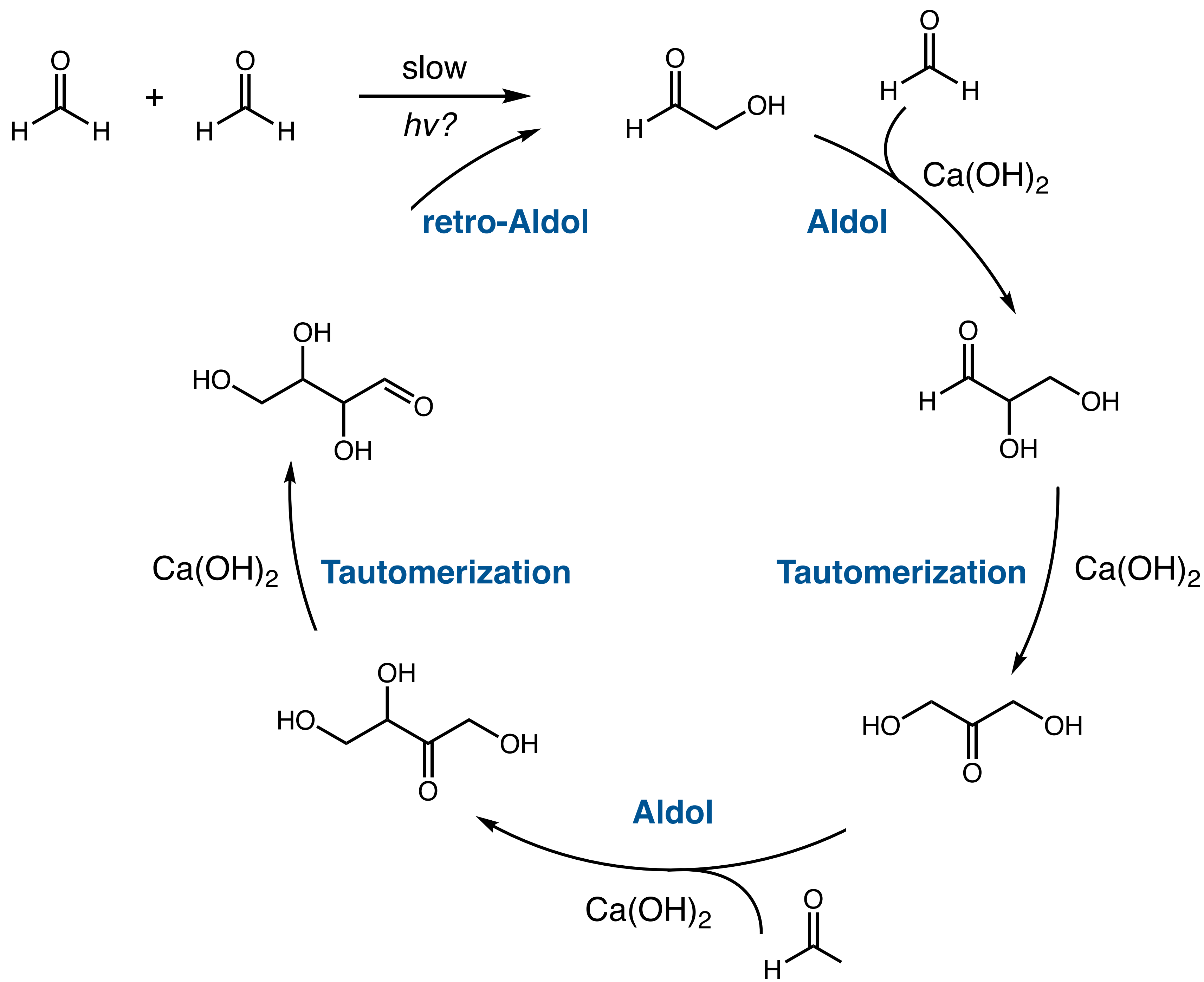


Butlerow, A. *Justus Liebigs Annalen der Chemie,* **1861**, *120*, 295

Breslow, R. *Tetrahedron Lett.* **1959**, *21*, 22

Formose reaction

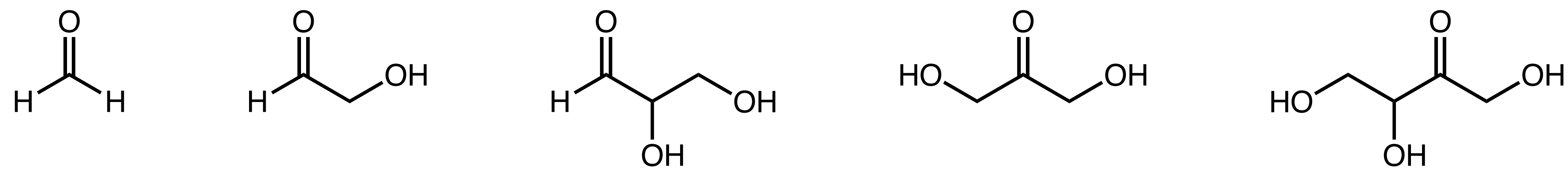
Autocatalytic cycle



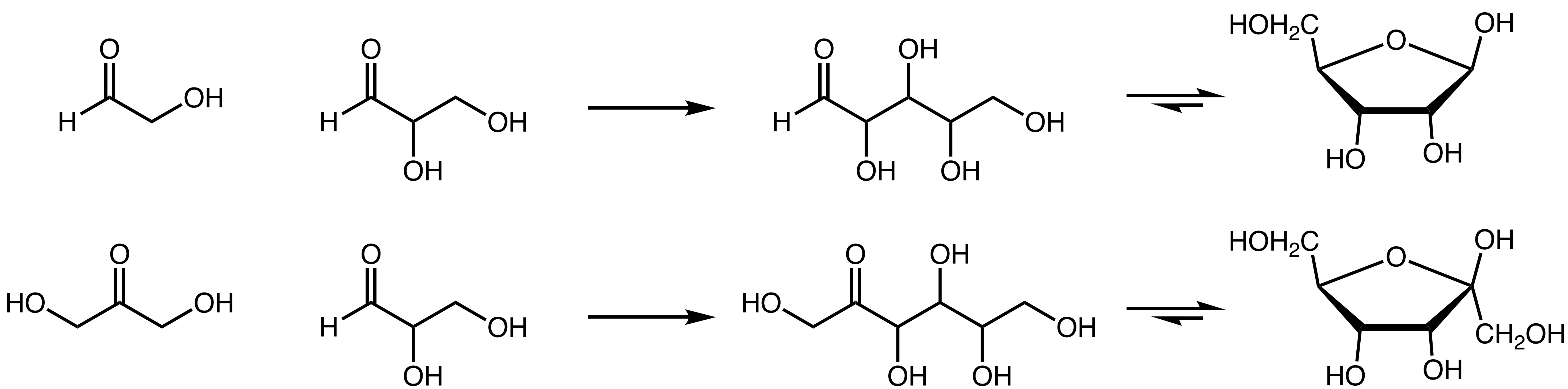
Breslow, R. *Tetrahedron Lett.* **1959**, *21*, 22

Formose reaction

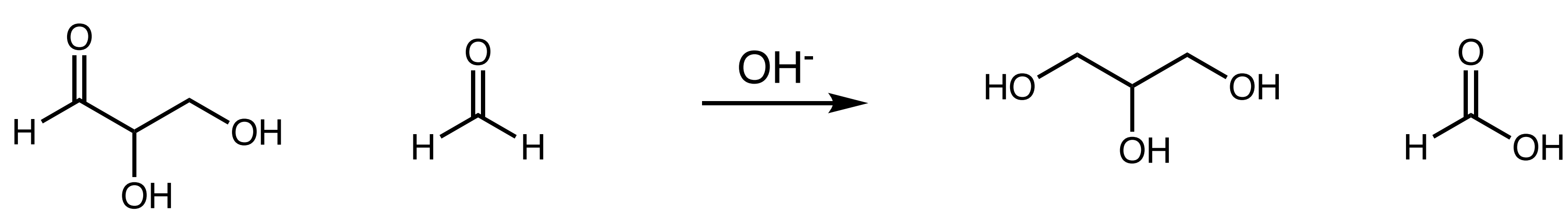
Product-forming pathway



Cross Aldol reaction



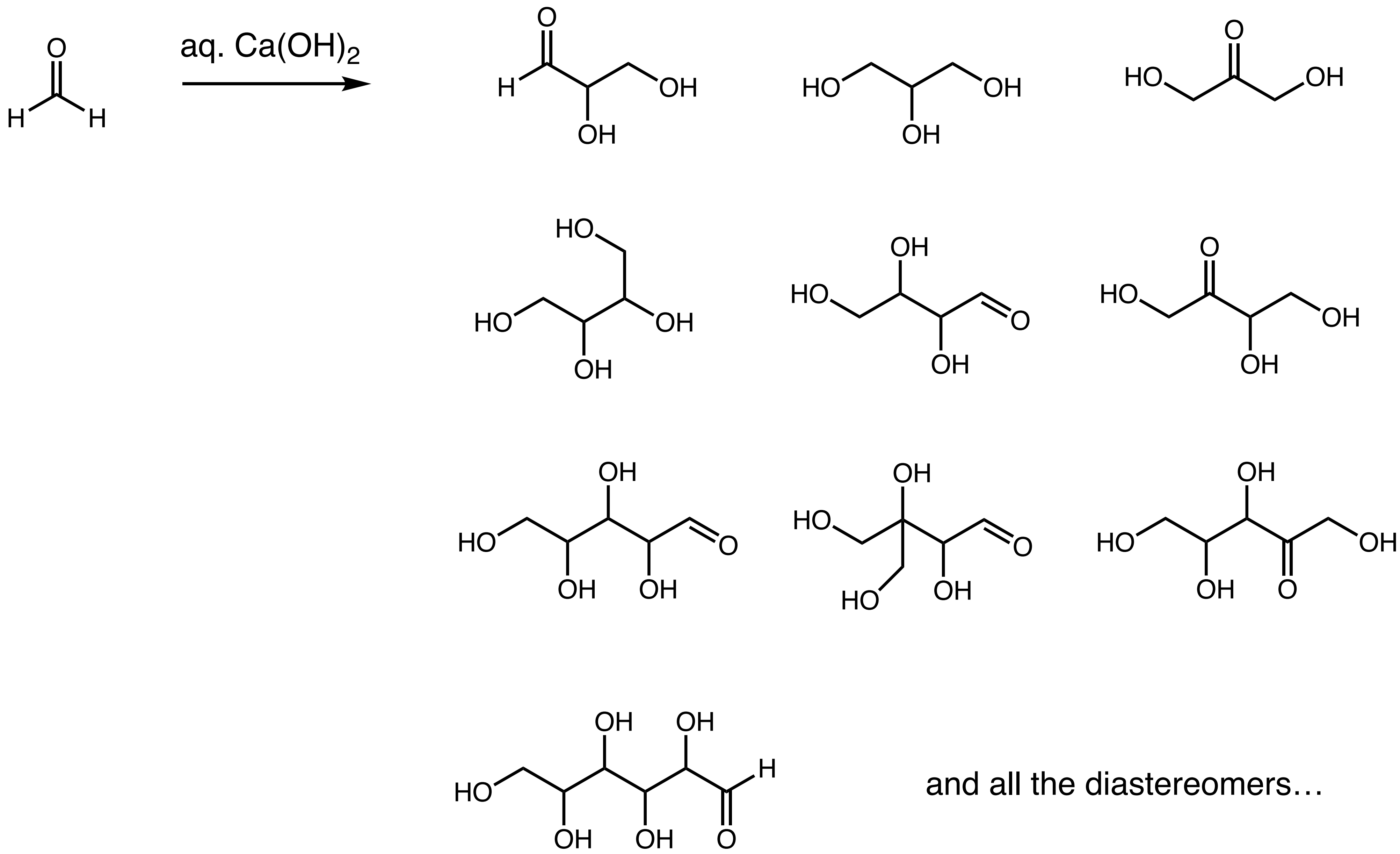
Cannizzaro reaction



Breslow, R. *Tetrahedron Lett.* **1959**, *21*, 22

Formose reaction

The reality



Decker, P.; Schweer, H.; Pohlmann, R. *J. Chromatogr. A* **1982**, *244*, 281

The reality

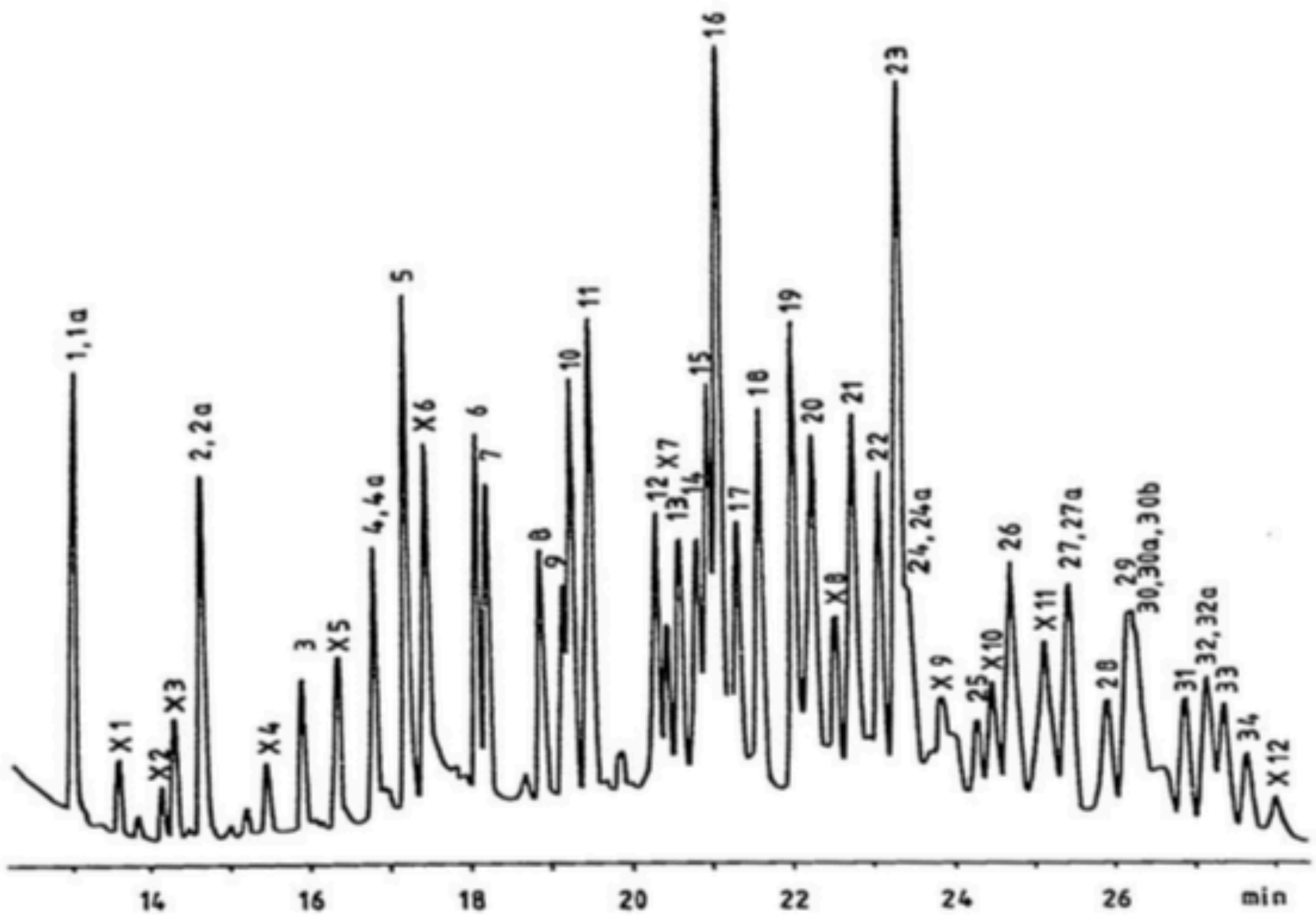
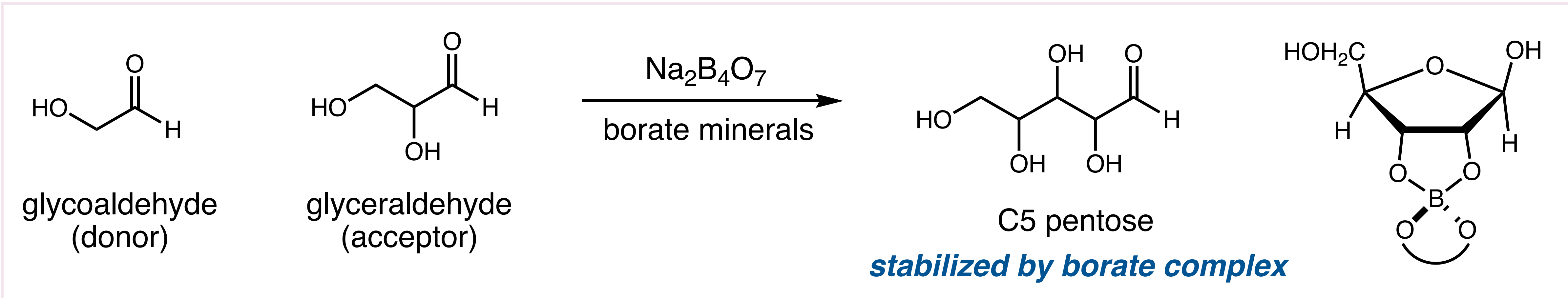


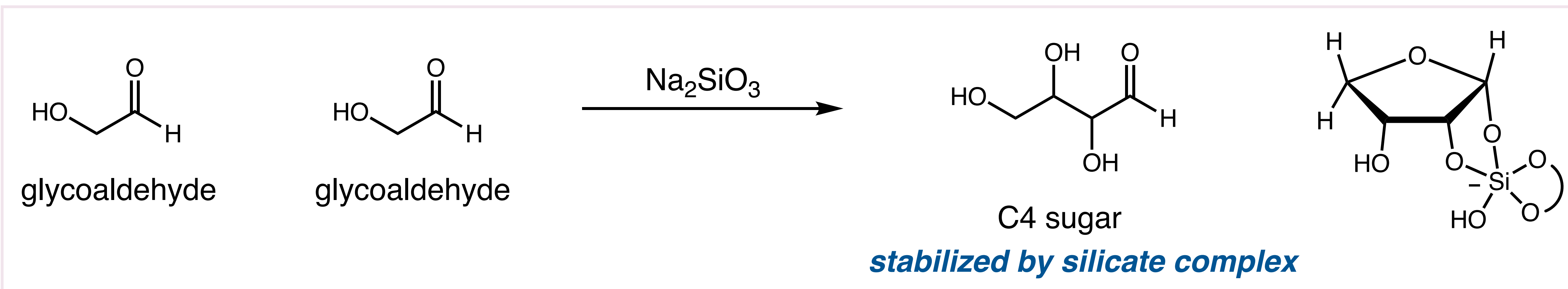
Fig. 1. Gas chromatogram of *n*-butoxime trifluoroacetyl derivatives of carbohydrates arising in the condensation of formaldehyde. Temperatures: column, 100°C for 2 min, then increased from 100 to 180°C at 5°C/min, final temperature 180°C; injection and detector, 250°C. Gas flow-rates: nitrogen carrier gas, 2 ml/min; hydrogen, 20 ml/min; air, 200 ml/min. Sample volume: 1 μl. Splitting ratio: 1:12. Peak identities: see Table I(A).

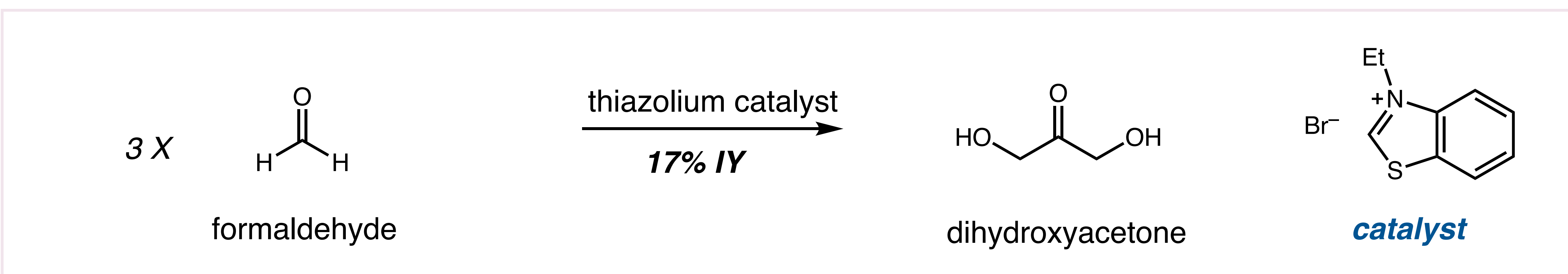
"***the formose product can be regarded as a carbohydrate analog of petroleum****, in that it contains so many carbohydrates of varying molecular weight and isomeric structure*" (Weiss et al., 1970)

Decker, P.; Schweer, H.; Pohlmann, R. *J. Chromatogr. A* **1982**, *244*, 281

Selective Formose reaction

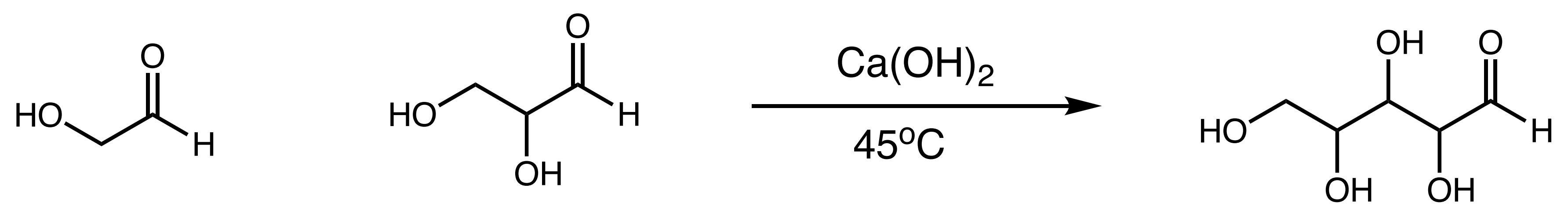






Ricardo, A.; Carrigan, M. A.; Olcott, A. N. Benner, S. A. *Science* **2004**, *303*, 196
Lambert, J. B.; Gurusamy-Thangavelu, S. A.; Ma, K. *Science* **2010**, *327*, 984
Matsumoto, T.; Yamamoto, H.; Inoue, S. *J. Am. Chem. Soc.* **1984**, *106*, 4829

Selective Formose reaction



Original Formose condition

pentose detected after 20 mins

pentose disappeared after 1 hour

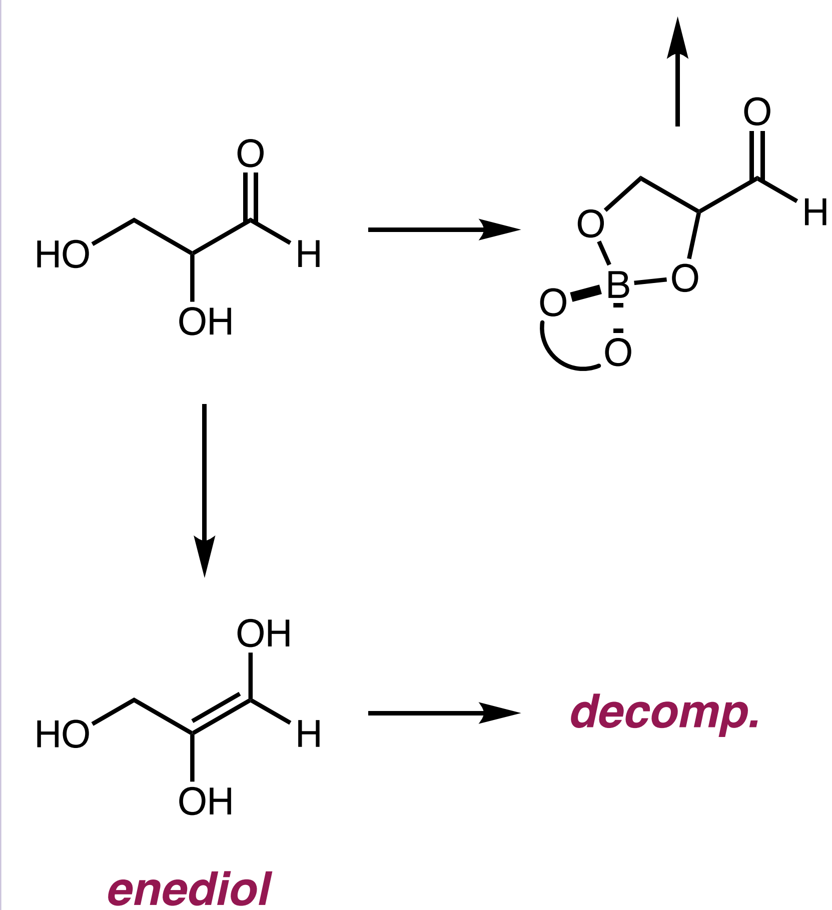
reaction turned brown

Borate mineral condition

pentose is the majority of total carbon

ribose remains stable for days

suggest prebiotic ribose synthesis



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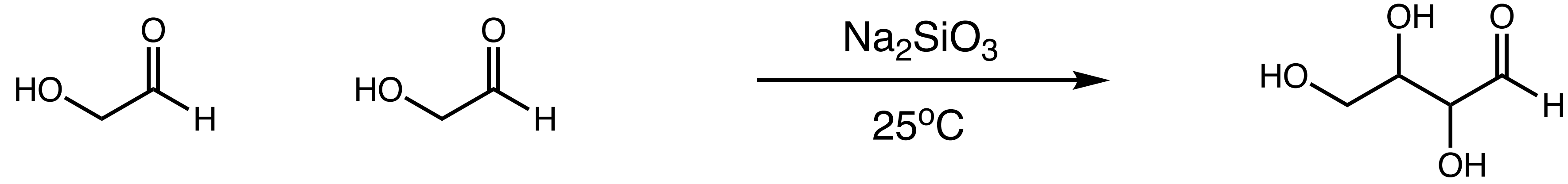
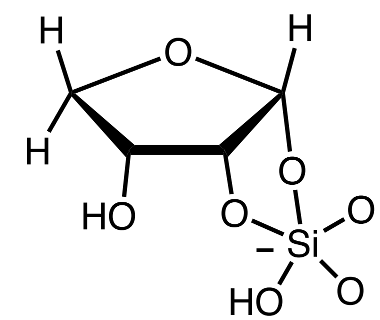
Selective Formose reaction

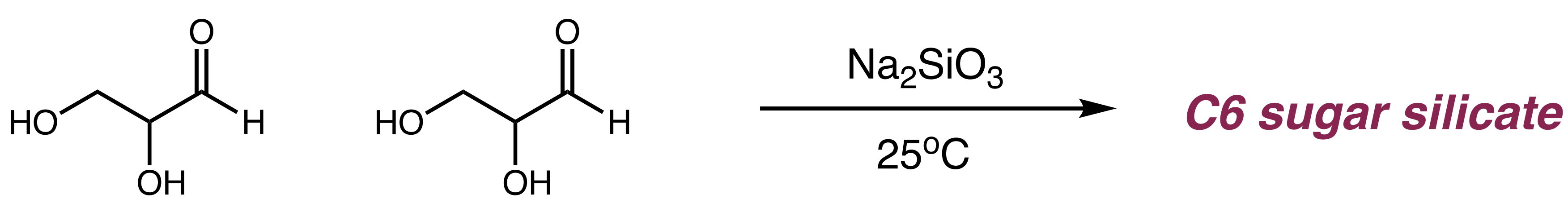


major C4 with some C6 product after 20 mins

C6 becomes major product after 12 hours

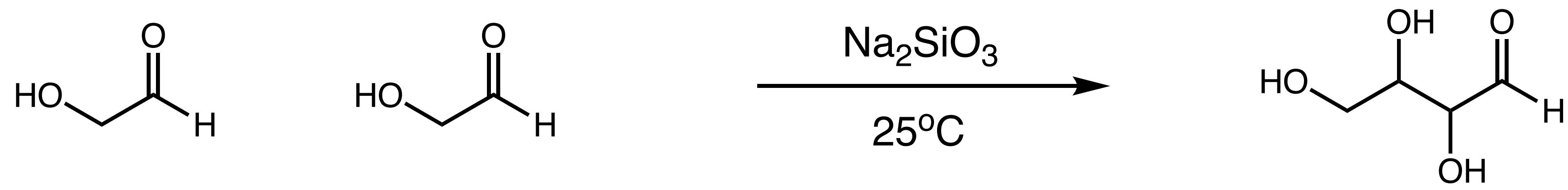
product decomposes or oligomerizes if it can't form silicate

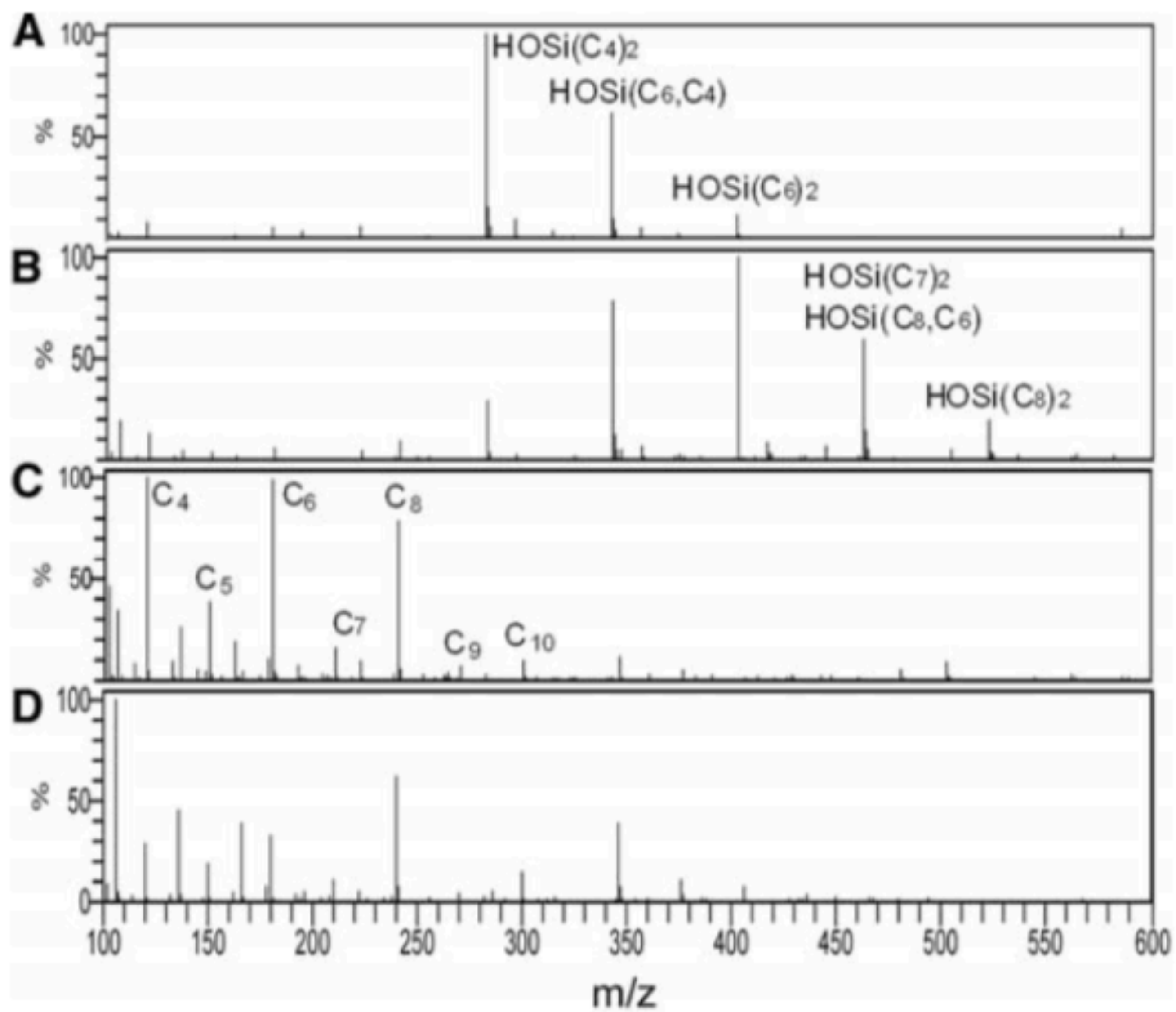




Lambert, J. B.; Gurusamy-Thangavelu, S. A.; Ma, K. *Science* **2010**, *327*, 984

Selective Formose reaction





silicate, 30 mins

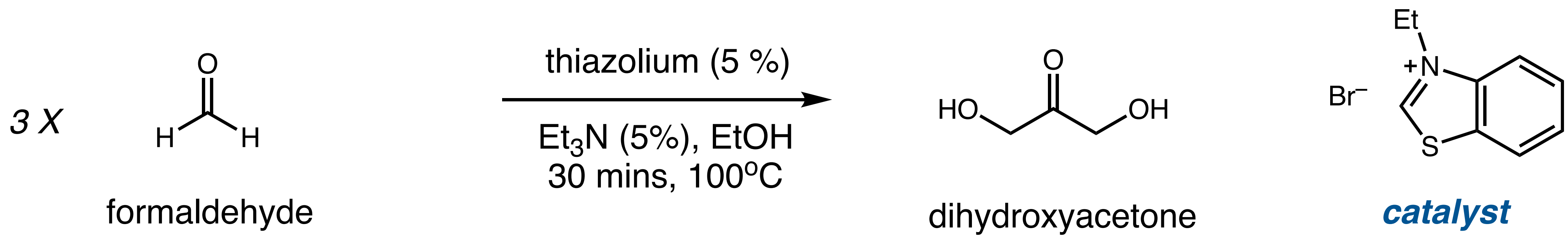
silicate, 12 hours

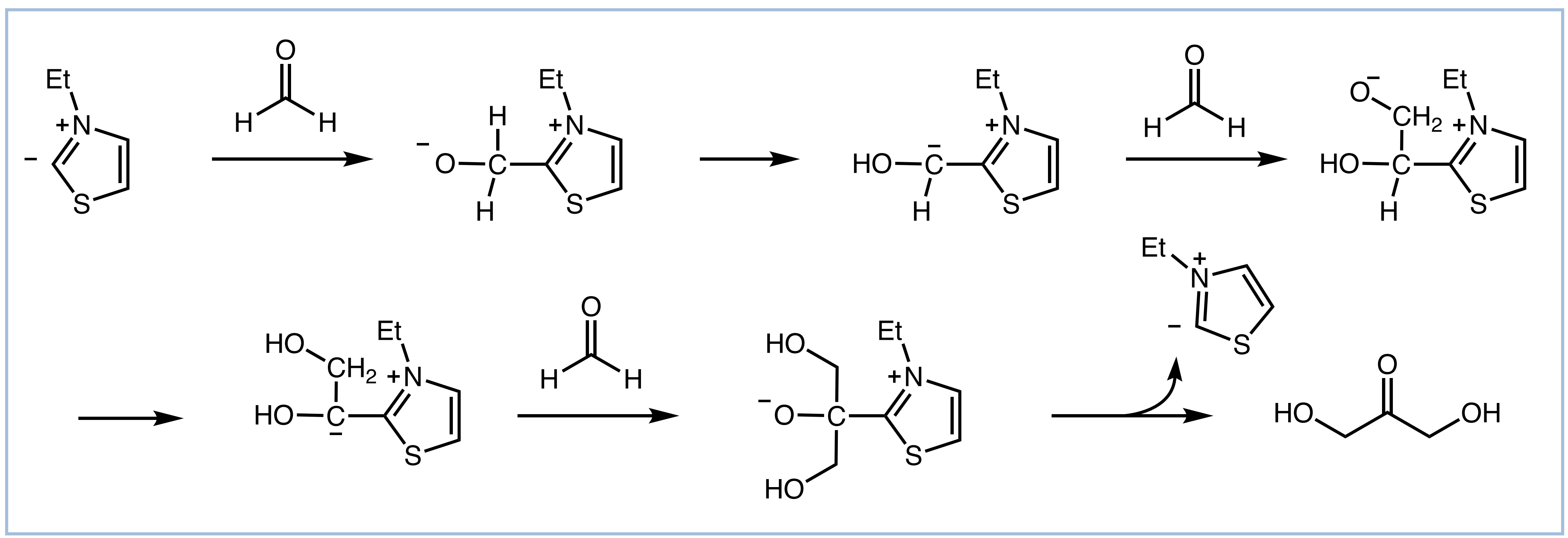
NaOH, 30 mins

NaOH, 12 hours

Lambert, J. B.; Gurusamy-Thangavelu, S. A.; Ma, K. *Science* **2010**, *327*, 984

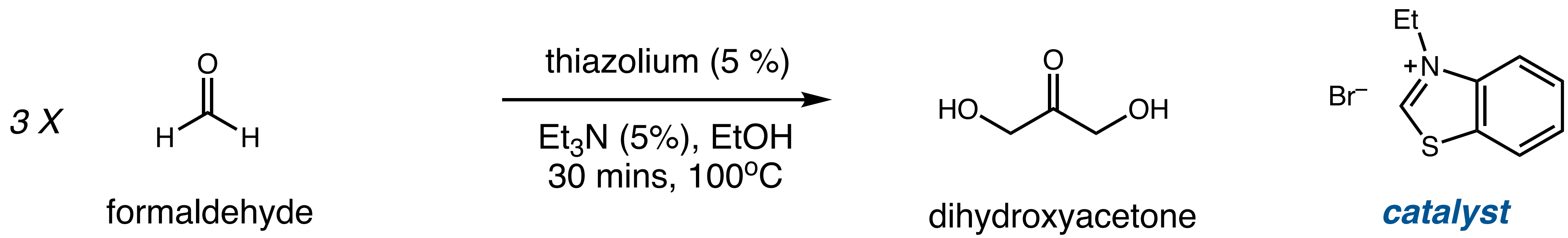
Selective Formose reaction

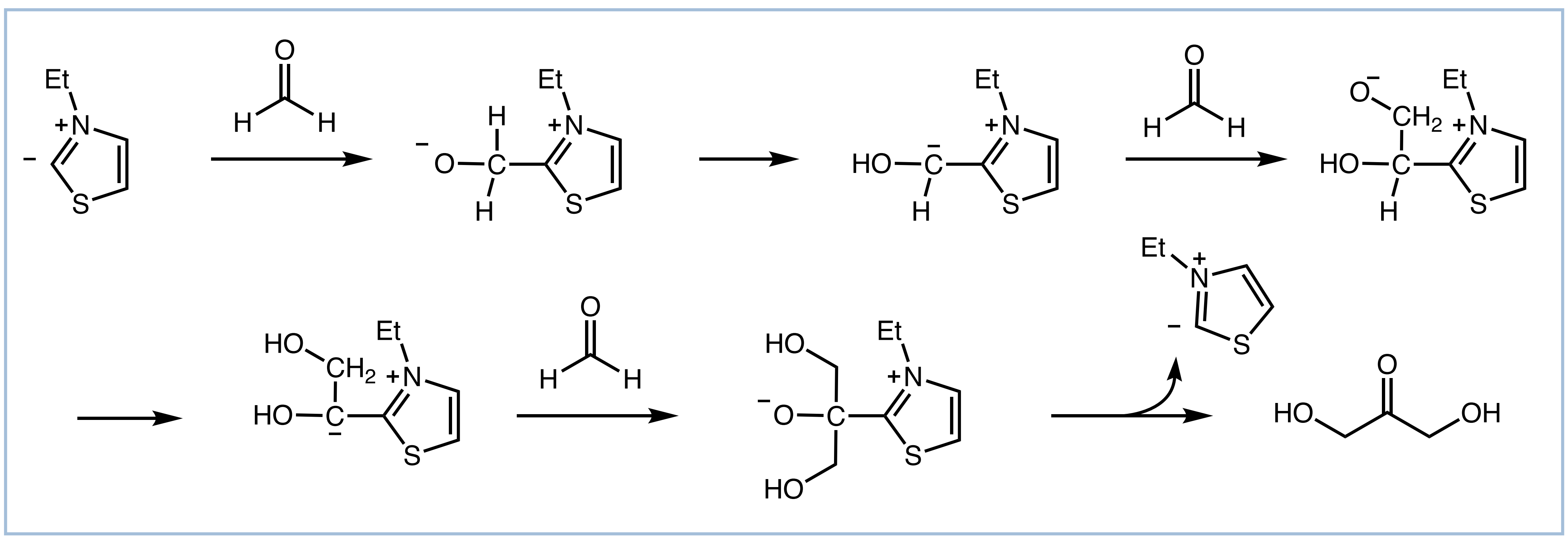




Matsumoto, T.; Yamamoto, H.; Inoue, S. *J. Am. Chem. Soc.* **1984**, *106*, 4829

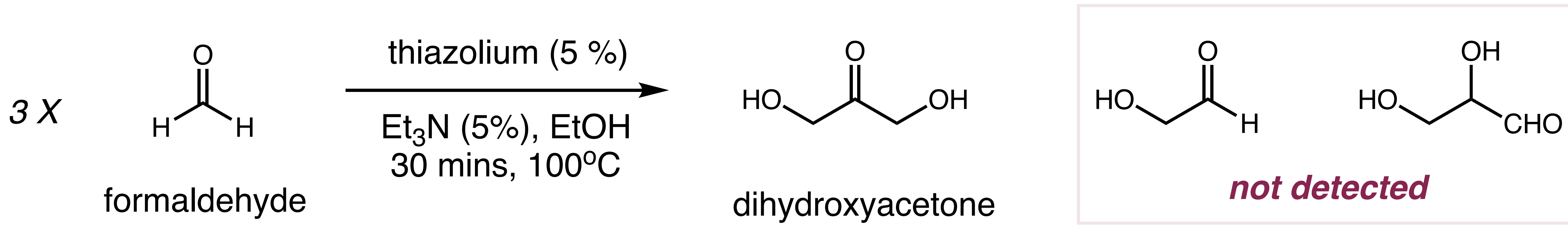
Selective Formose reaction



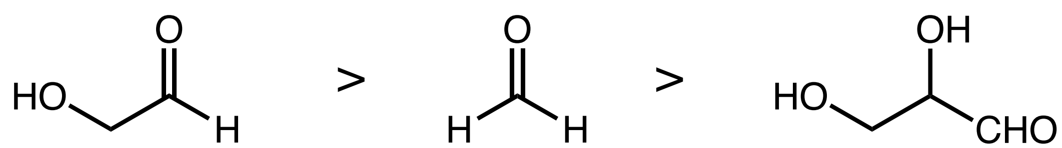


Matsumoto, T.; Yamamoto, H.; Inoue, S. *J. Am. Chem. Soc.* **1984**, *106*, 4829

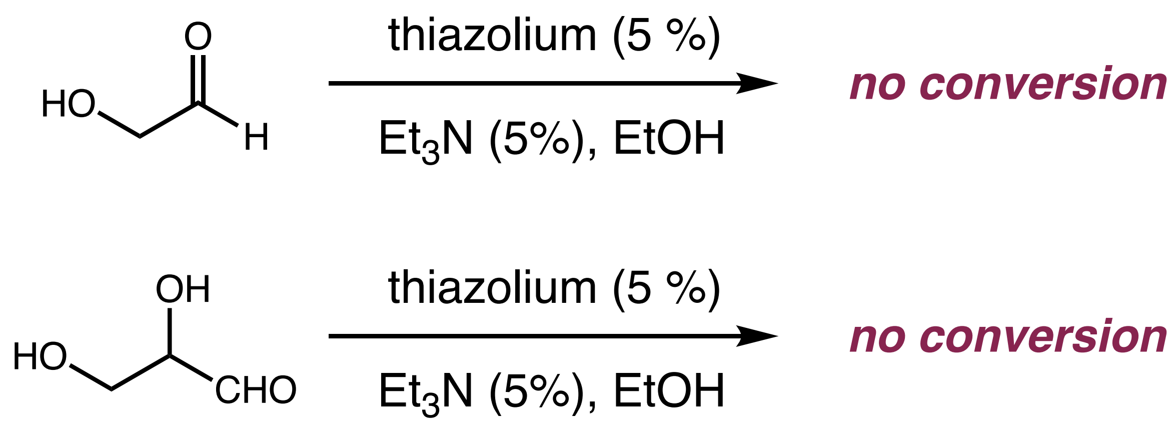
Selective Formose reaction



Reactivity with thiazolium:

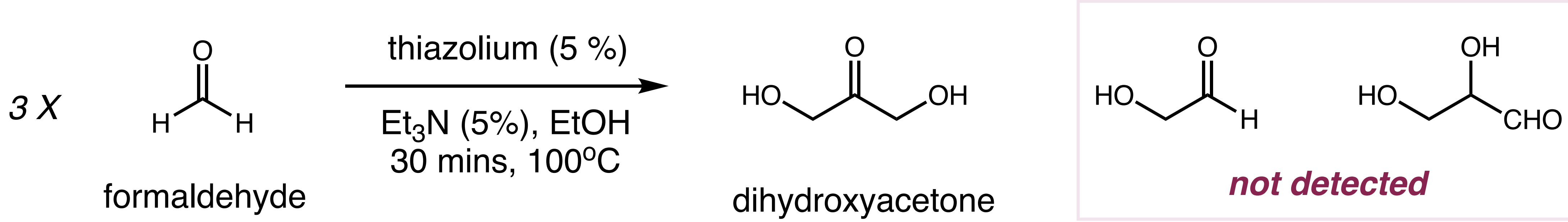


Control experiments:

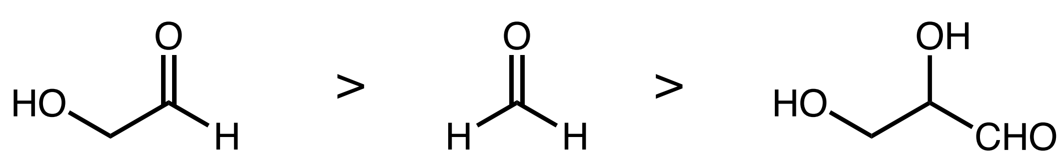


Matsumoto, T.; Yamamoto, H.; Inoue, S. *J. Am. Chem. Soc.* **1984**, *106*, 4829

Selective Formose reaction



Reactivity with thiazolium:



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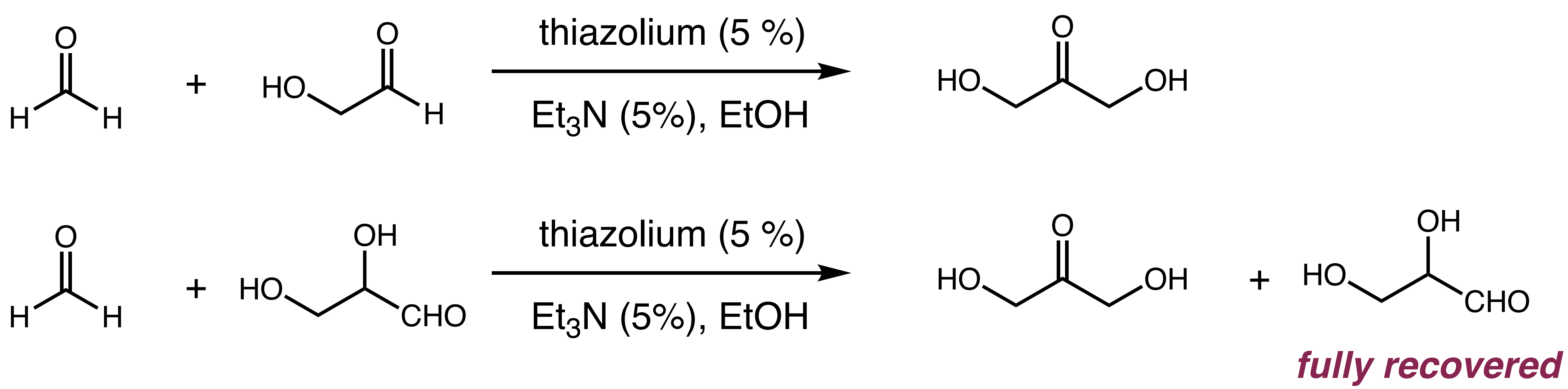
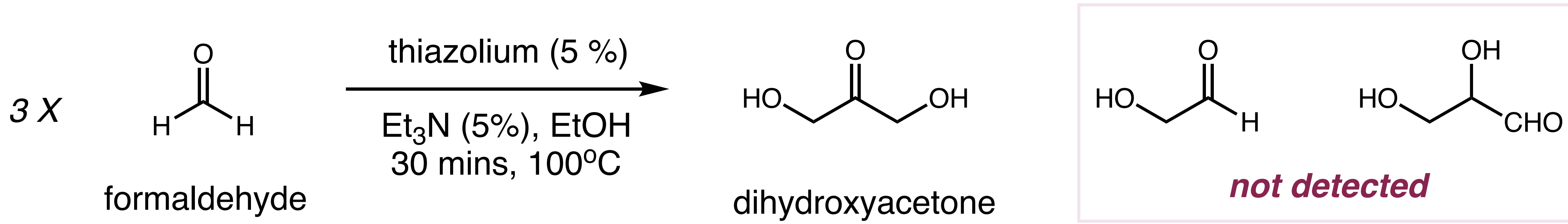
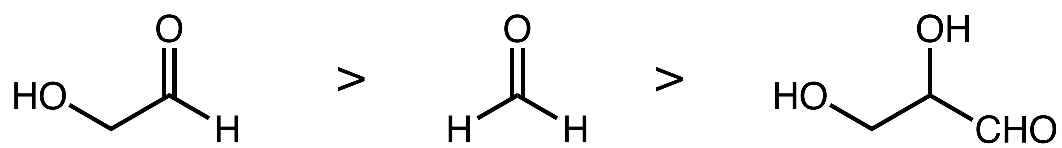


Matsumoto, T.; Yamamoto, H.; Inoue, S. *J. Am. Chem. Soc.* **1984**, *106*, 4829

Selective Formose reaction



Reactivity with thiazolium:



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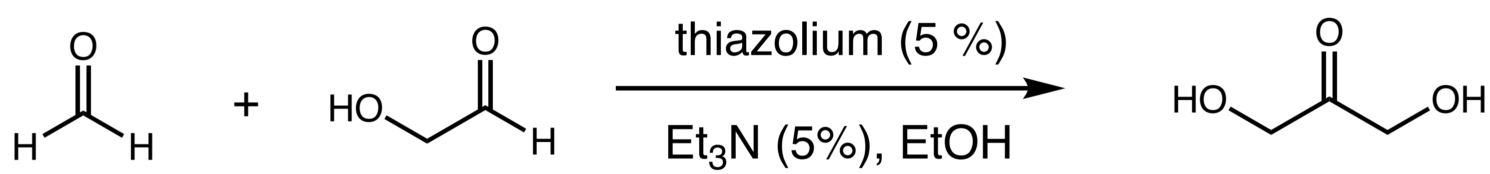
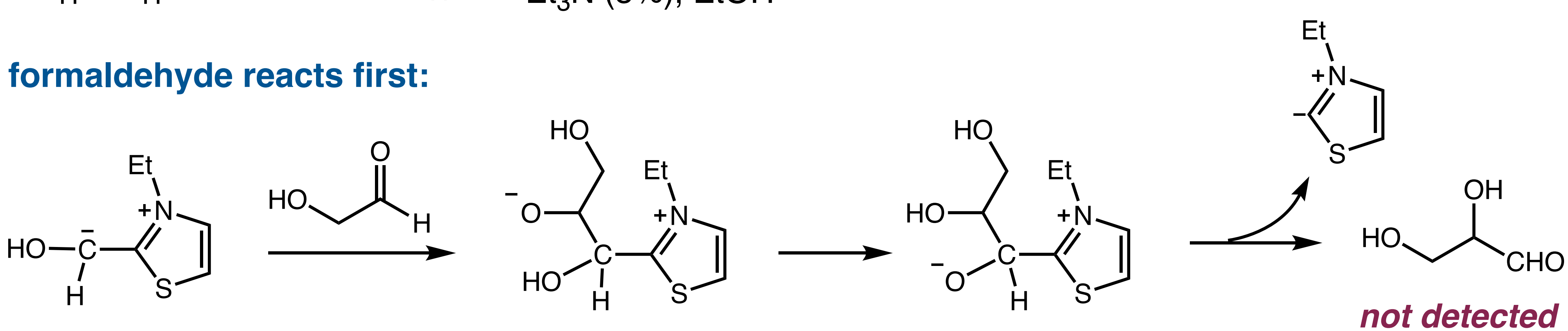


If formaldehyde reacts first:



Matsumoto, T.; Yamamoto, H.; Inoue, S. *J. Am. Chem. Soc.* **1984**, *106*, 4829