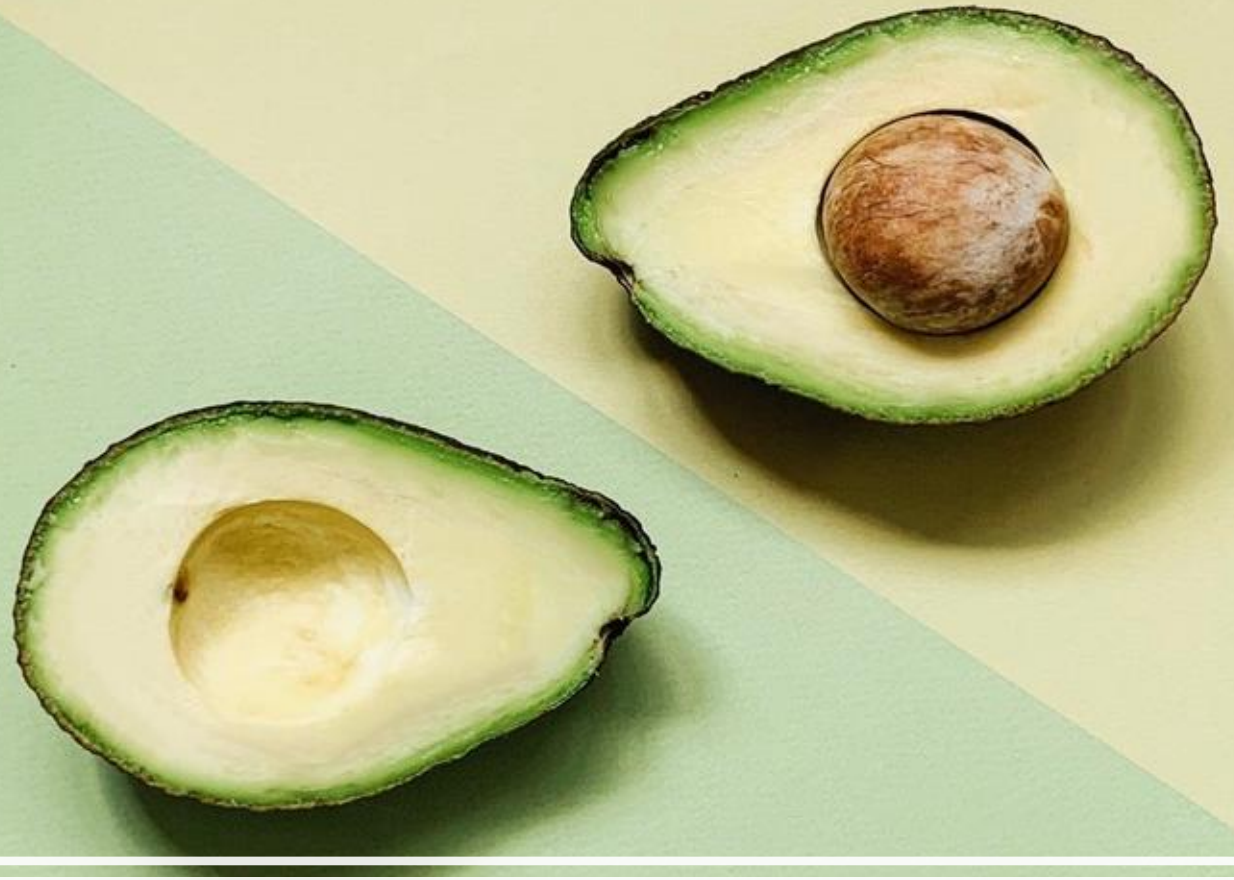
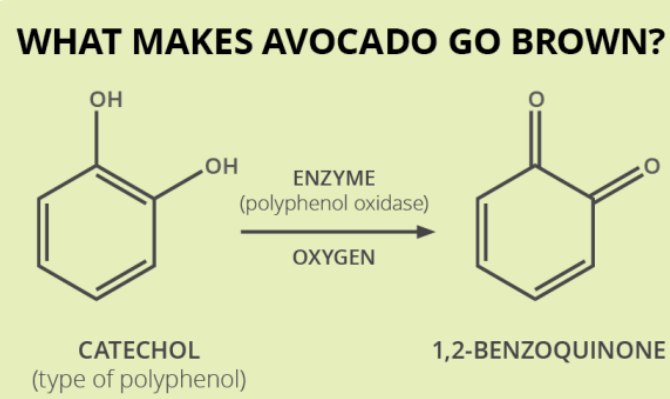
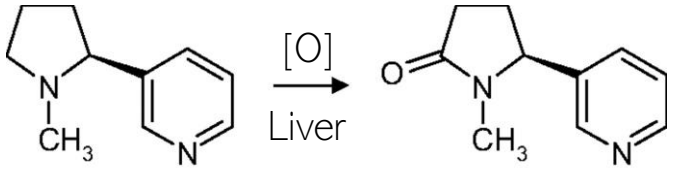


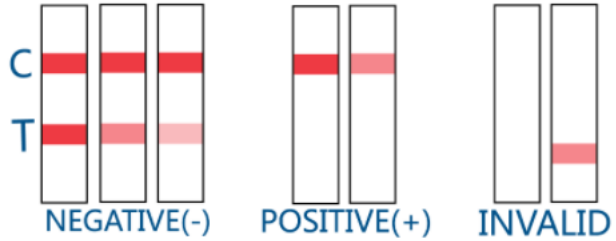
Lab 8

Green Alcohol Oxidation with Copper Catalyst

1. Oxidation


WHAT MAKES AVOCADO GO BROWN?
OH
OH
ENZYME
(polyphenol oxidase)
OXYGEN
O
O
CATECHOL
(type of polyphenol)
1,2-BENZOQUINONE
0 HOURS
3 HOURS
6 HOURS
9 HOURS
12 HOURS


N
CH3
N
[O]
Liver
O
N
CH3
N
Nicotine
Cotinine


C
T
NEGATIVE(-)
POSITIVE(+)
INVALID

2. Green Chemistry

The 12 Principles of GREEN CHEMISTRY

Green chemistry is an approach to chemistry that aims to maximize efficiency and minimize hazardous effects on human health and the environment. While no reaction can be perfectly 'green', the overall negative impact of chemistry research and the chemical industry can be reduced by implementing the 12 Principles of Green Chemistry wherever possible.

1. WASTE PREVENTION
Prioritize the prevention of waste, rather than cleaning up and treating waste after it has been created. Plan ahead to minimize waste at every step.

2. ATOM ECONOMY
Reduce waste at the molecular level by maximizing the number of atoms from all reagents that are incorporated into the final product. Use atom economy to evaluate reaction efficiency.

3. LESS HAZARDOUS CHEMICAL SYNTHESIS
Design chemical reactions and synthetic routes to be as safe as possible. Consider the hazards of all substances handled during the reaction, including waste.

4. DESIGNING SAFER CHEMICALS
Minimize toxicity directly by molecular design. Predict and evaluate aspects such as physical properties, toxicity, and environmental fate throughout the design process.

5. SAFER SOLVENTS & AUXILIARIES
Choose the safest solvent available for any given step. Minimize the total amount of solvents and auxiliary substances used, as these make up a large percentage of the total waste created.

6. DESIGN FOR ENERGY EFFICIENCY
Choose the least energy-intensive chemical route. Avoid heating and cooling, as well as pressurized and vacuum conditions (i.e. ambient temperature & pressure are optimal).

7. USE OF RENEWABLE FEEDSTOCKS
Use chemicals which are made from renewable (i.e. plant-based) sources, rather than other, equivalent chemicals originating from petrochemical sources.

8. REDUCE DERIVATIVES
Minimize the use of temporary derivatives such as protecting groups. Avoid derivatives to reduce reaction steps, resources required, and waste created.

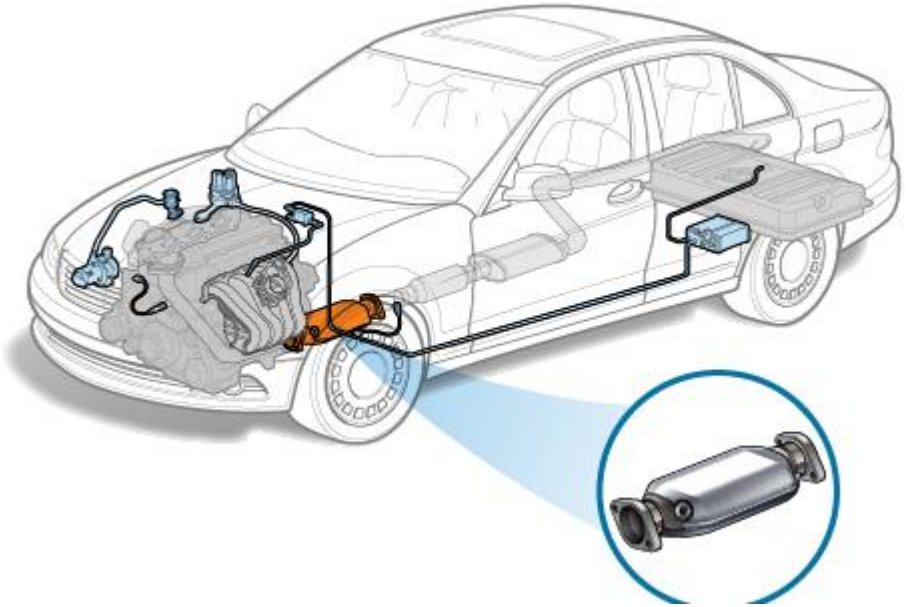
9. CATALYSIS
Use catalytic instead of stoichiometric reagents in reactions. Choose catalysts to help increase selectivity, minimize waste, and reduce reaction times and energy demands.

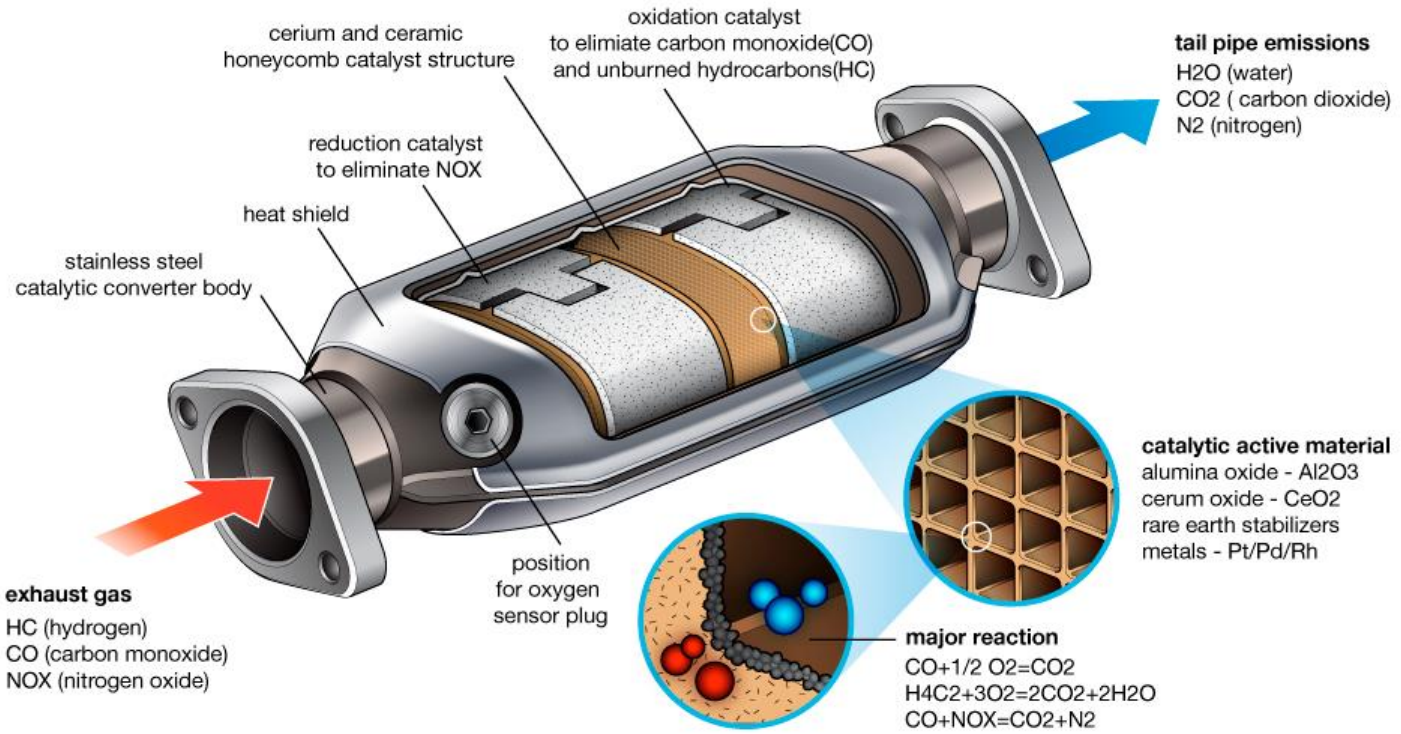
10. DESIGN FOR DEGRADATION
Design chemicals that degrade and can be discarded easily. Ensure that both chemicals and their degradation products are not toxic, bioaccumulative, or environmentally persistent.

11. REAL-TIME POLLUTION PREVENTION
Monitor chemical reactions in real-time as they occur to prevent the formation and release of any potentially hazardous and polluting substances.

12. SAFER CHEMISTRY FOR ACCIDENT PREVENTION
Choose and develop chemical procedures that are safer and inherently minimize the risk of accidents. Know the possible risks and assess them beforehand.

3. Catalytic Reactions

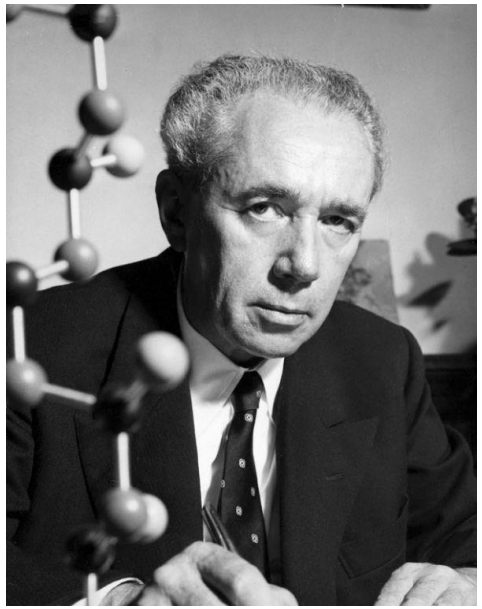




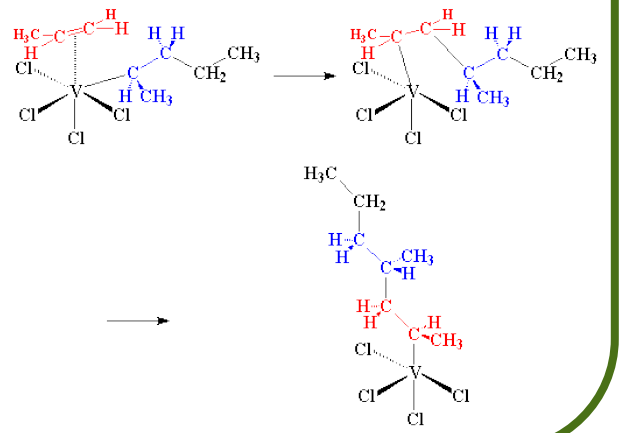
$$CO + \tfrac{1}{2}\, O_2 \rightarrow CO_2$$

$$C_2H_4 + 3\, O_2 \rightarrow 2CO_2 + H_2O$$

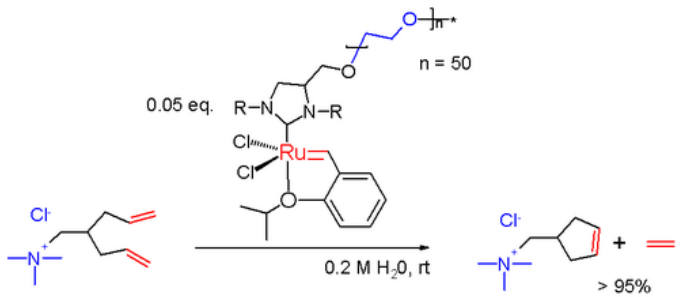
$$CO + NO_x \rightarrow CO_2 + N_2$$



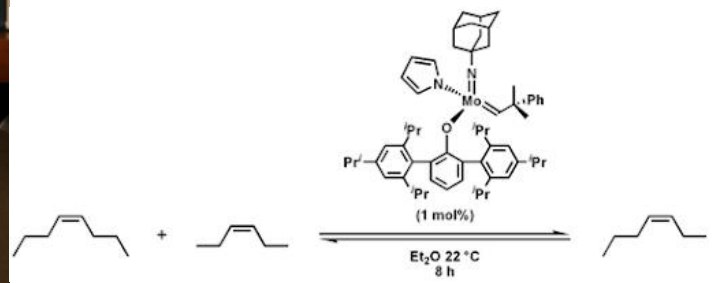
Natta - 1963



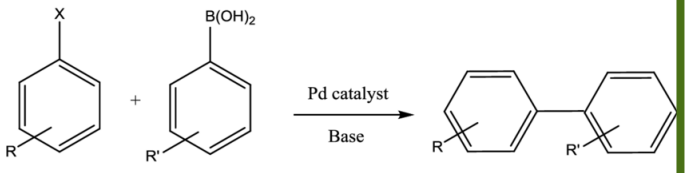
Grubbs - 2005

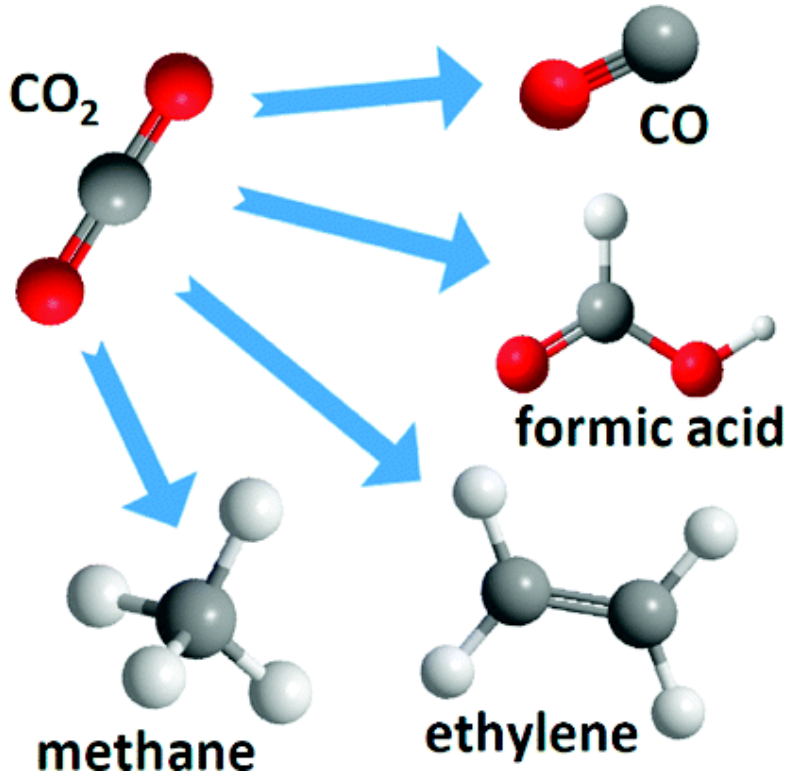


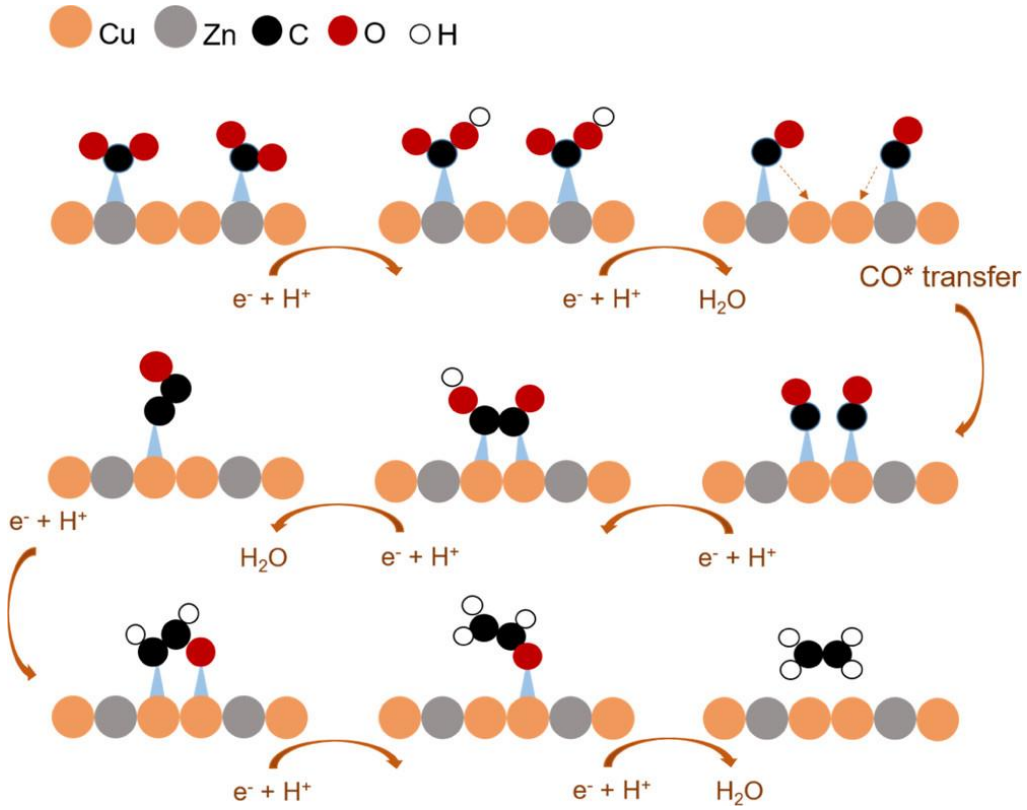
Schrock - 2005

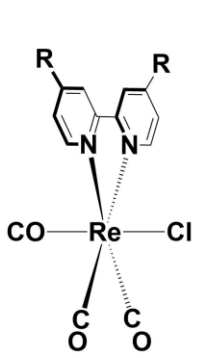


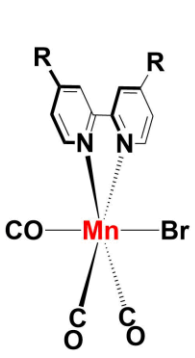
Suzuki - 1981

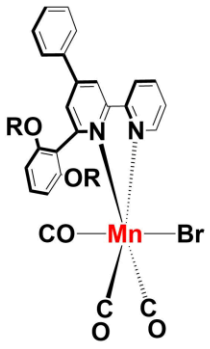


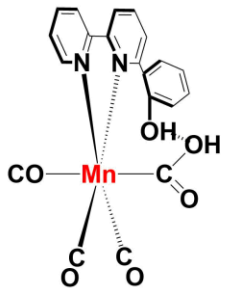


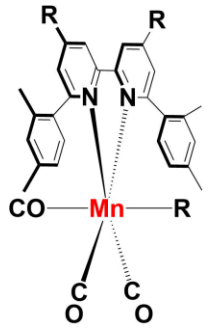


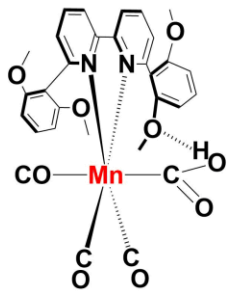

Lehn - 1984

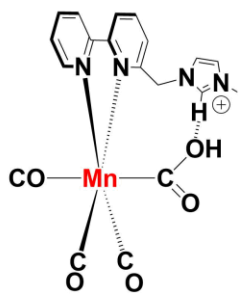

Bourrez - 2011

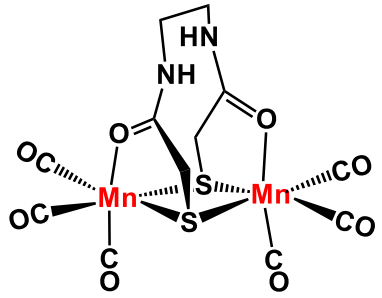

Franco - 2014


Bocarsly - 2015


Kobiak - 2016


Ngo - 2017

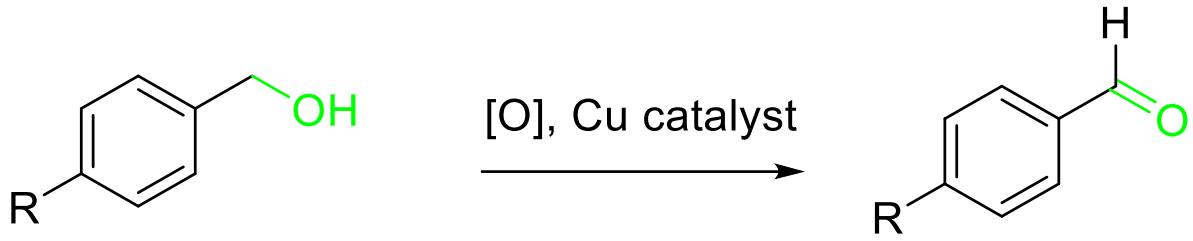

Nippe - 2019

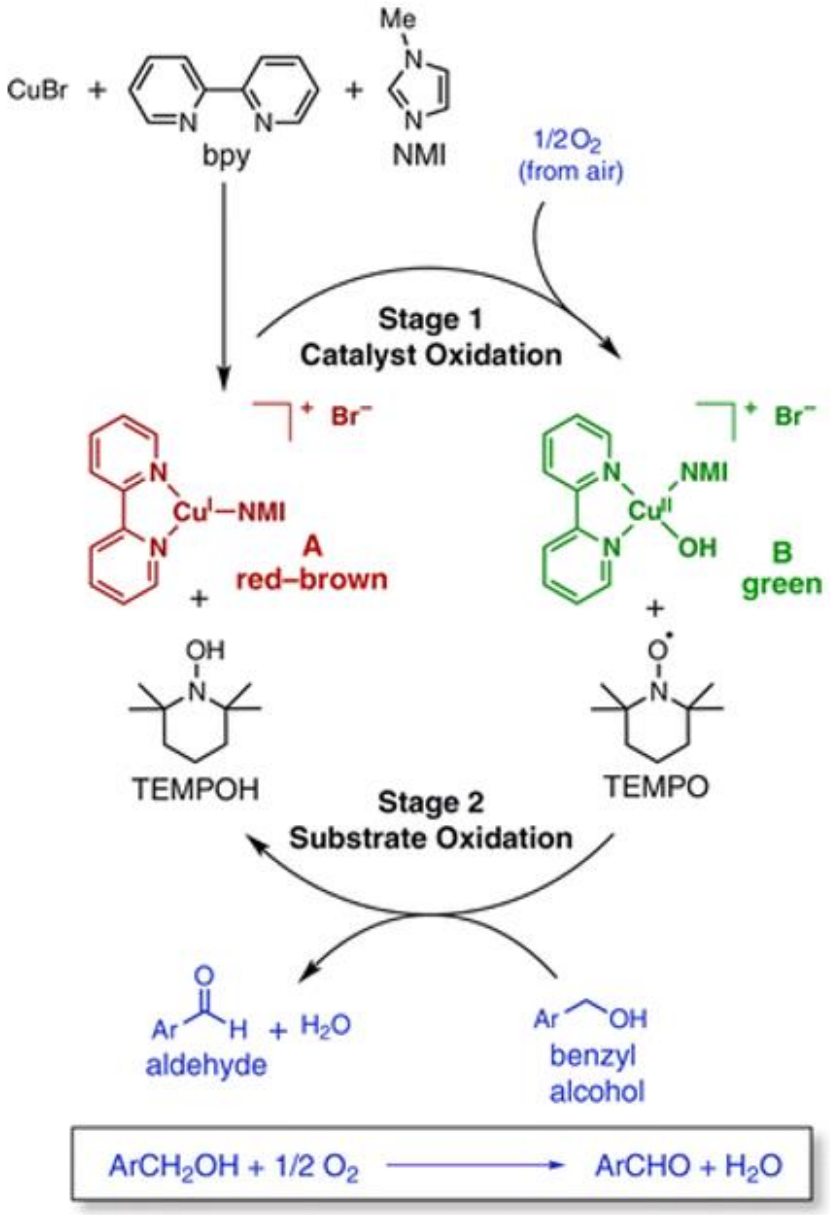

Le & Nguyen - 2019

Purpose

- oxidize an unknown alcohol to the corresponding aldehyde using green chemistry
- purify the product
- identify the unknown aldehyde using GC-MS, NMR, and MP (if solid)

R	Name
H	benzyl alcohol
Cl	4-chlorobenzyl alcohol
$CH(CH_3)_2$	4-isopropylbenzylalcohol
OCH_3	4-methoxybenzyl alcohol
CH_3	4-methylbenzyl alcohol
NO_2	4-nitrobenzyl alcohol





Why Cu?

Copper is used catalytically, not stoichiometrically
Copper is less toxic

Catalytic reactions

-catalytic amount of copper (sub-stoichiometric)
-bipyridine and NMI are used as ligands which bind to copper
-TEMPO is used as a co-catalyst to oxidize the alcohol (a stable, commercially available radical)

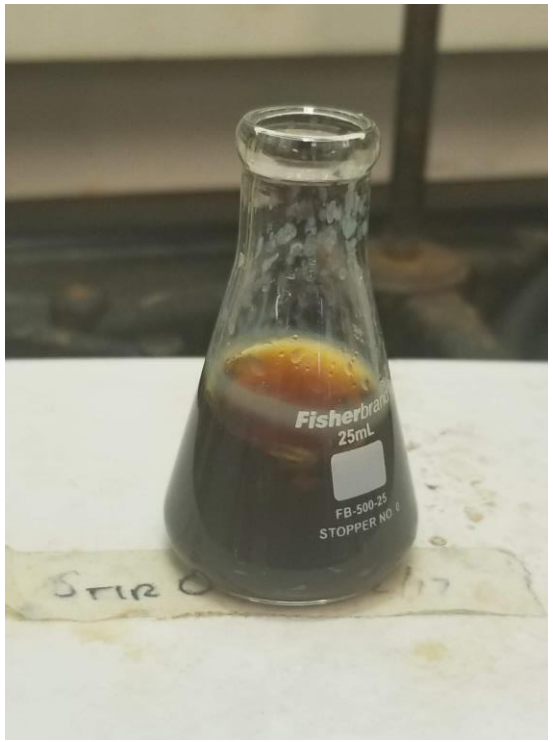
The limiting reagent is the alcohol, not the copper or oxygen.

% yield should take into account the purity of the aldehyde

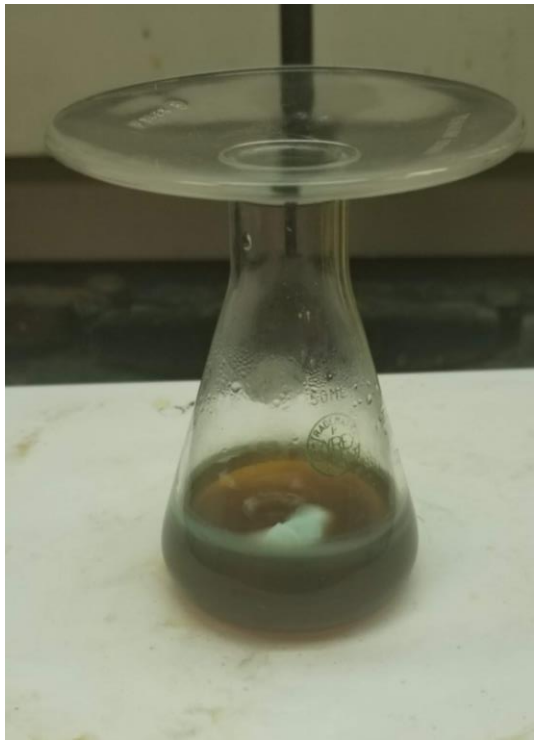
	Appearance	Amount (mg)	MW (g/mol)	mol	Equivalent	Note
Unknown						
…						
CuBr	White powder	35				
2,2'-bipyridine	White crystalline	40				
TEMPO	Orange crystalline	40				Skin corrosion, MP: 37°C
acetone		15 mL	Solvent			Flammable
Product						
…						

Color change can be used to monitor the reaction's progress:

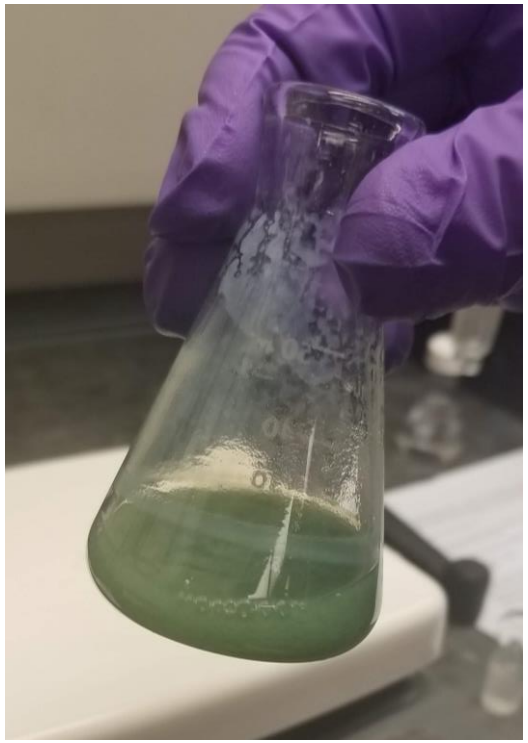
-bipyridine and NMI bind to copper to form a red-brown Cu(I) complex
-TEMPO is added which oxidizes the copper to a green Cu(II) complex
-a lighter, murky green color indicates the reaction is complete
-the aqueous phase of the extraction will be a cyan color due to Cu(II) salts



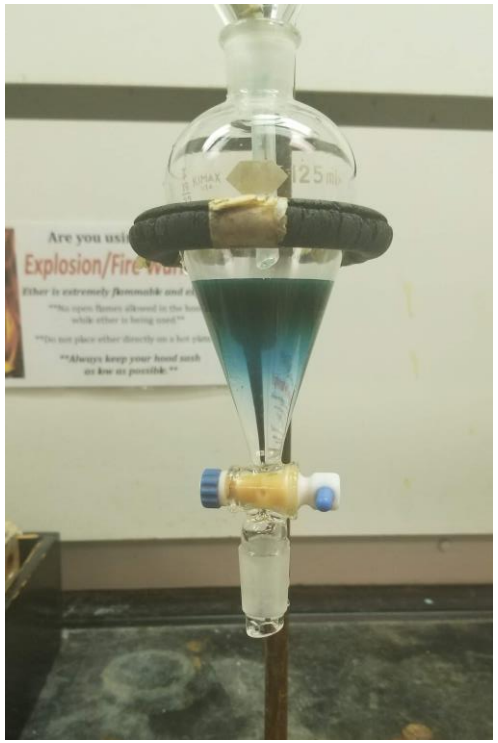
Mid-reaction



Nearing competition



Completed reaction



Post-reaction extraction

Purification

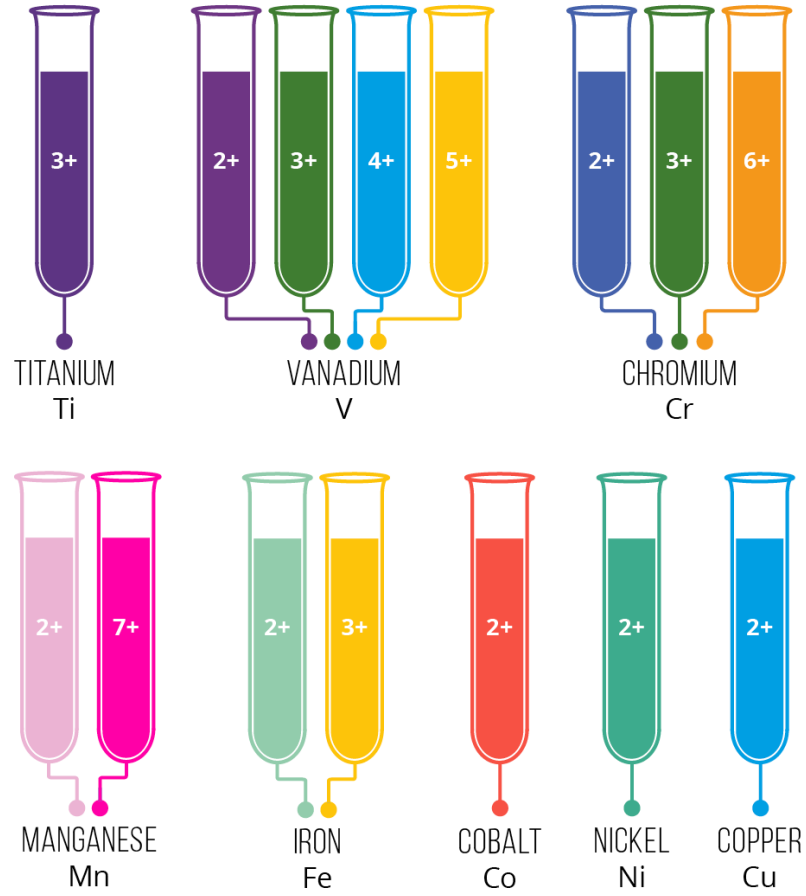
Extraction (remove copper salts):

-hexanes (organic layer): TEMPO/TEMPOH, alcohol starting material, aldehyde product

-water (aqueous layer): copper salts

which layer would be colored?

- A further purification technique would be needed to separate the ligands and TEMPO from the product. **What technique would do this? Why is it not a big deal in this case?**



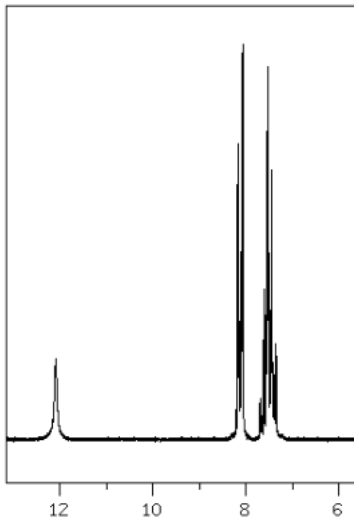
Copper sulfate solution (left)
After addition of ammonia (right)

Identifying the unknown

Melting point (if the aldehyde is a solid)

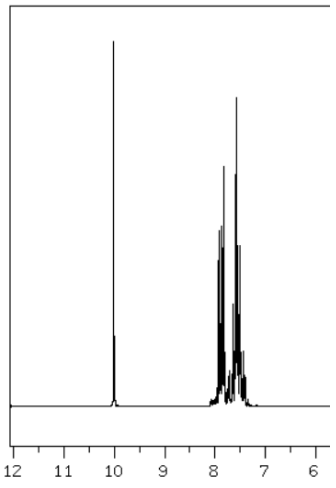
GC-MS
-GC separates the compounds, and MS "weighs" them
-GC tells us the relative amount of alcohol starting material versus aldehyde product
-MS tells us the identity of the alcohol

NMR
-aldehyde protons show up in the 9.5-10.5 ppm range and will show small (~1-3 Hz) coupling with adjacent protons
-in contrast, a carboxylic acid OH would show up 10-12 ppm as a broad singlet



Benzoic acid PhCOOH

vs.



Benzaldehyde PhCHO

NMR will also give us information on benzene's substituent:

-Cl and nitro group will not show up, but will change the integration and shifts of the aryl region
-methoxy (~3.5 ppm) and methyl (~2.2 ppm) will be singlets with different chemical shifts
-isopropyl group will show a 1H septet (~2.2 ppm) and 6H doublet (~1.2 ppm)
-H will show up as another aromatic proton