Lab Expectations

Completed Experiments 1-4

due
- 4 Extraction — Lab notes, Questions, Report Section
- 3 Crystallization — Lab notes, Questions, Report Section
- 2 Solubility — Same

5 Part Chromatography
6 Distillation
7 Boiling pt & FTIR Unknowns
} nothing Due

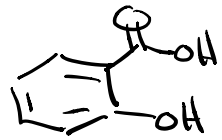
8 Synthesis Acetysalicylic Acid

3-days

Synthesis
Characterization of product

⇒ Formal reports

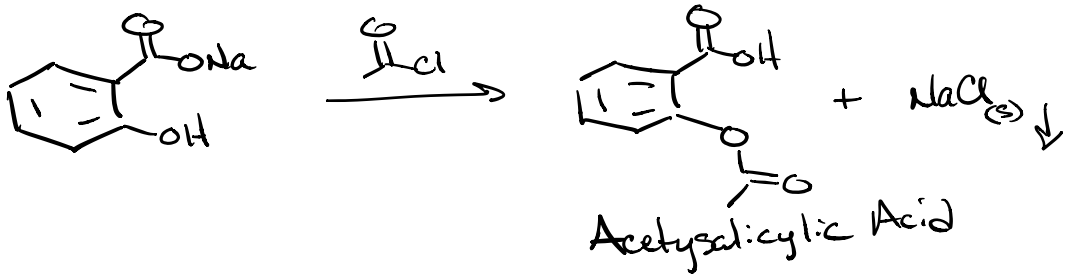
Synthesis of Acetysalicylic Acid



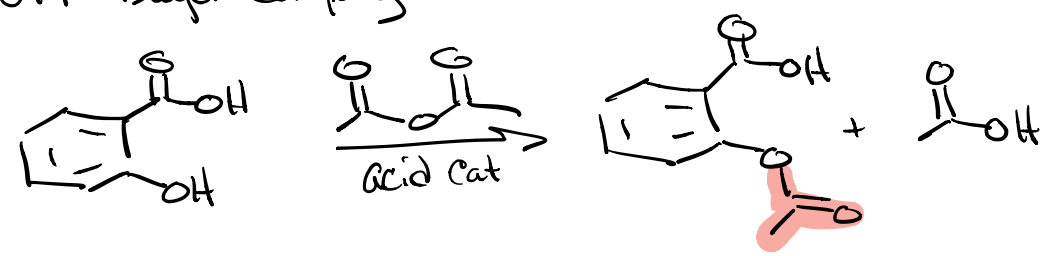
β-hydroxy acid
Salicylic acid
(Salix - latin for willow tree)
natural product

1853 Charles Frédéric Gerhardt

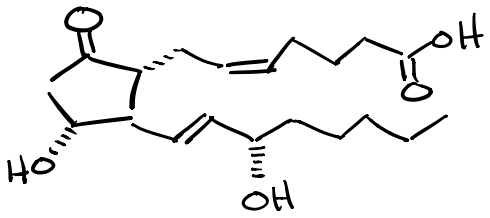
Extracts from willow bark were too acidic
they could be taken in tea (bitter),
couldn't be taken in concentrated ⟹ formed ulcers



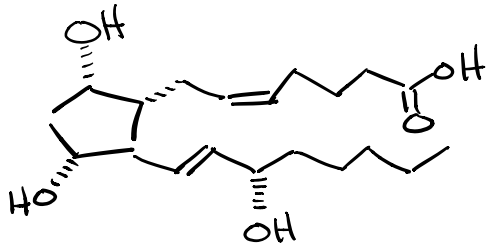
1897 Bayer Company



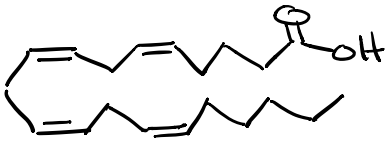
Mode of Action



Prostaglandin E_2

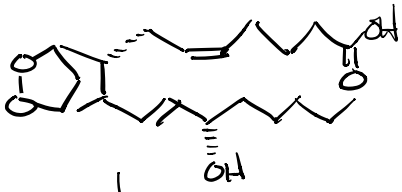


Protaglandin $F_{2\alpha}$

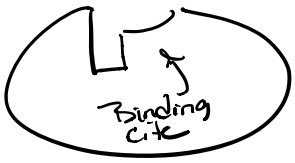


Arachidonic Acid

$+ O_2$ Cyclo-oxygenase →

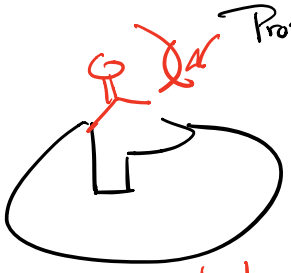


Prostaglandin

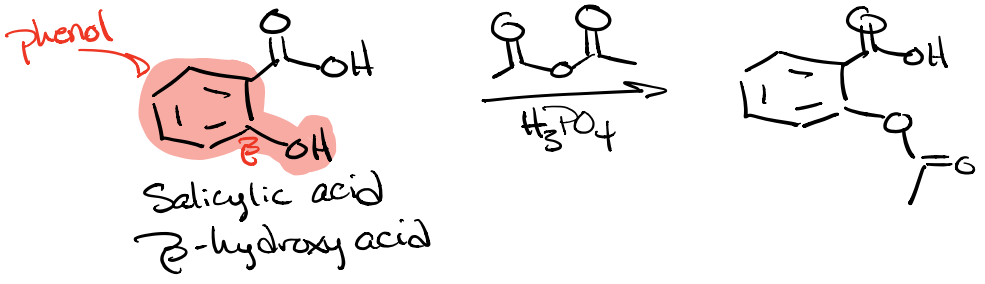


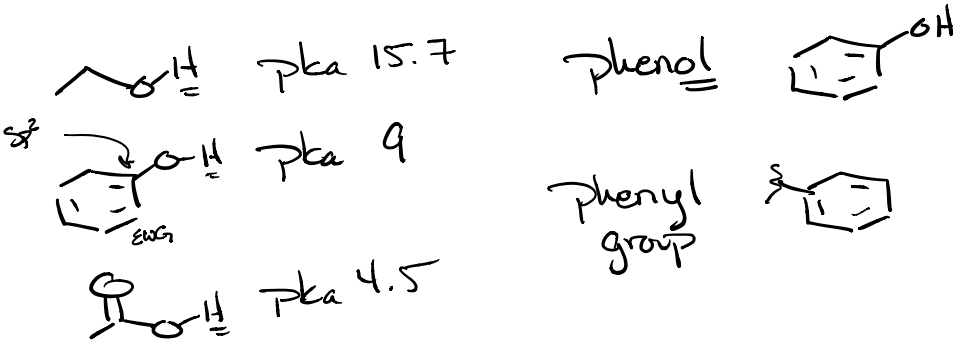
Enzyme
Cyclo-oxygenase

Prostaglandin + acetysalicylic acid →

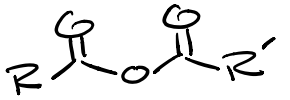


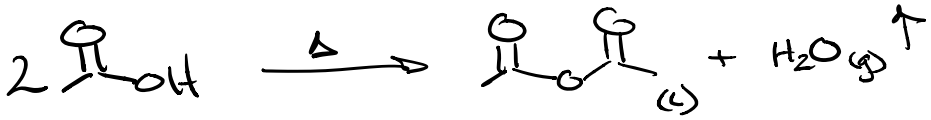
Deactivated by Salicylic acid

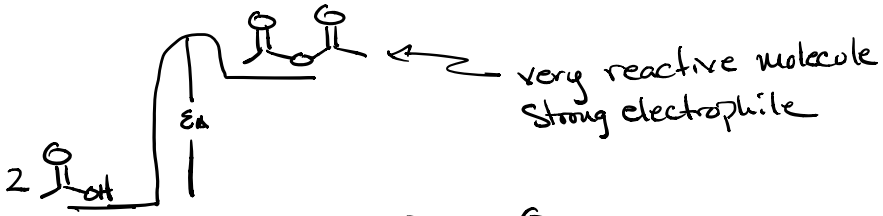

phenol
OH
OH
H_3PO_4
O
Salicylic acid
β-hydroxy acid

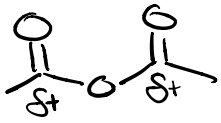

pka 15.7
sp²
pka 9
EWG
pka 4.5
phenol
OH
phenyl group

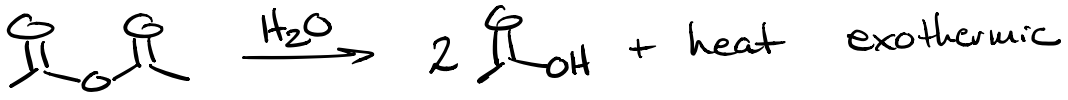

acetic anhydride

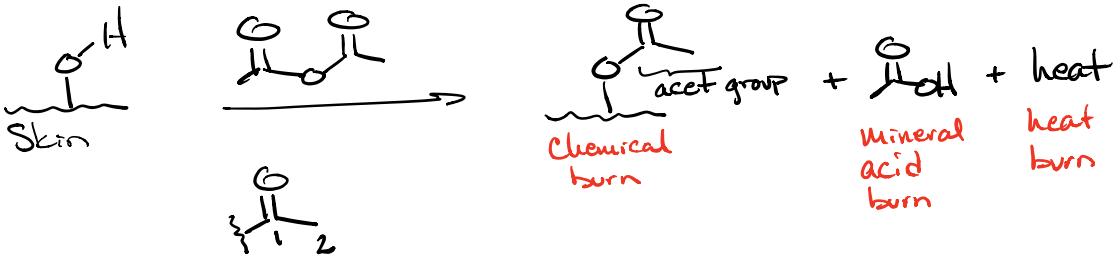

R
R'
where R = R' or R ≠ R'


2
OH
Δ
(l)
+ $H_2O_{(g)}$


very reactive molecule
strong electrophile
Ea
2
OH

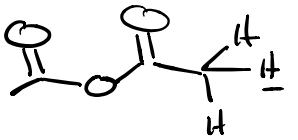

O
O


H_2O
2
OH
+ heat
exothermic

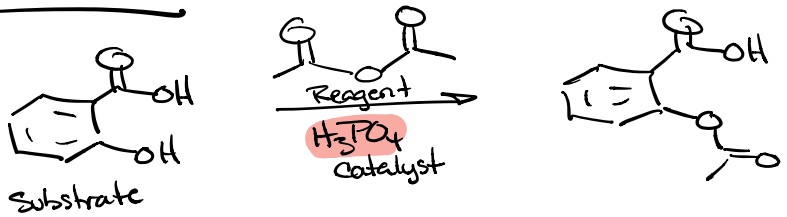


HCl con.

H_2SO_4 Con.

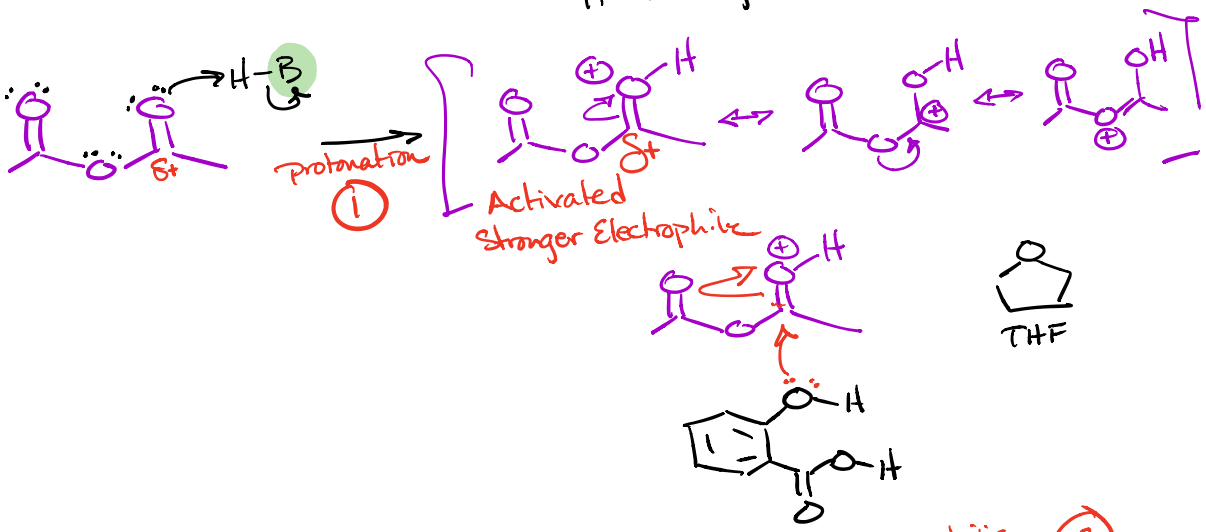


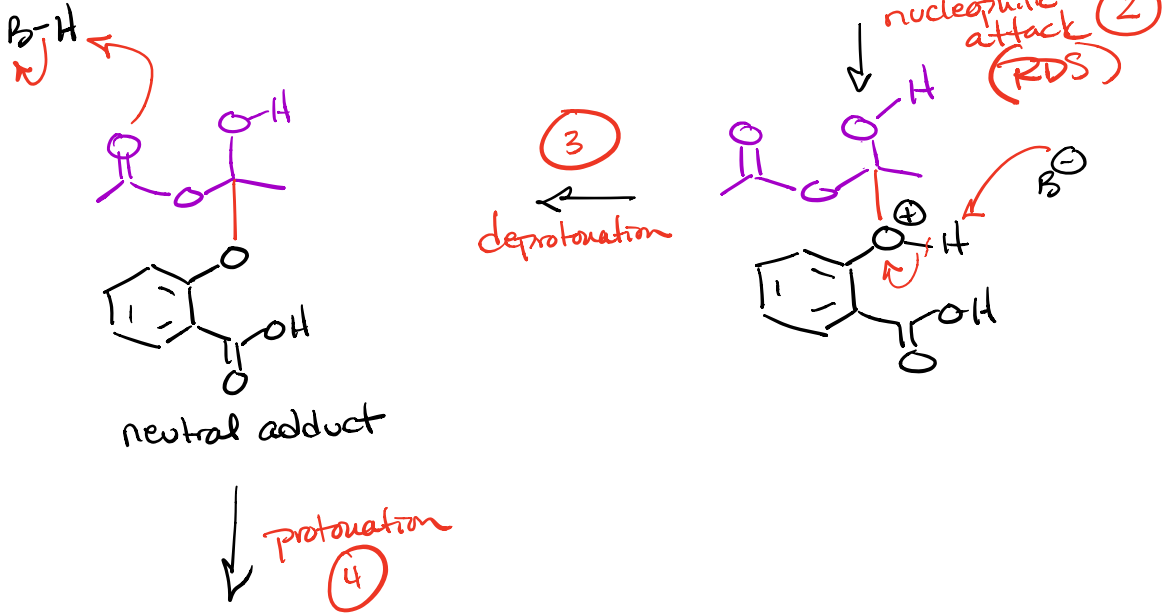
Ron Mechanism

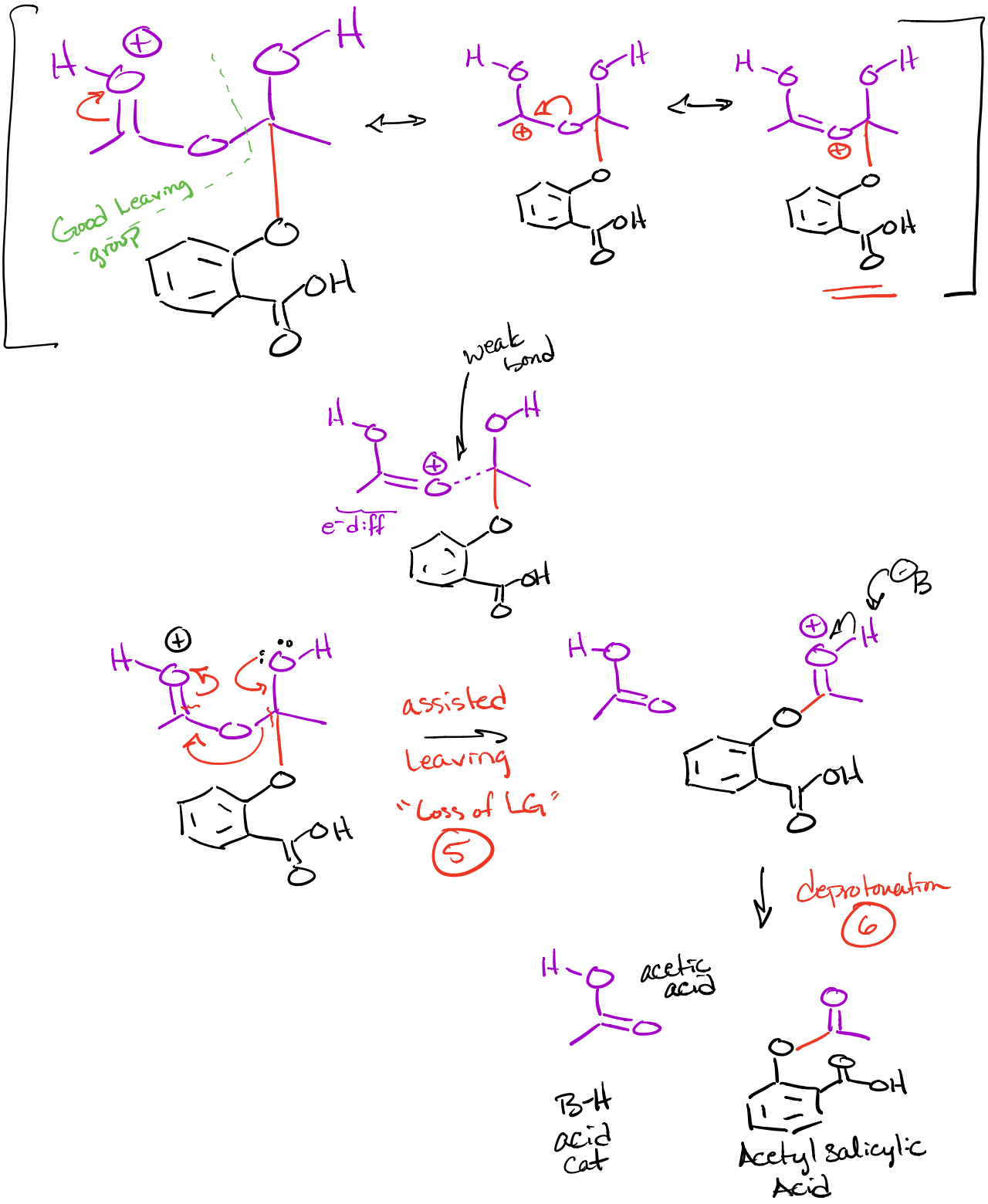


Acid catalysed ⟹ protonation
base catalysed ⟹ deprotonation
} general rule

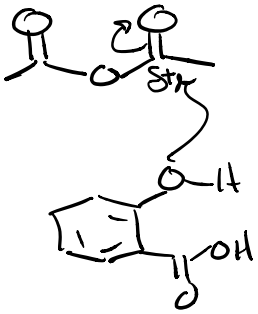
$\ominus B$ = general Base
$H-B$ = general Acid
} Conjugates

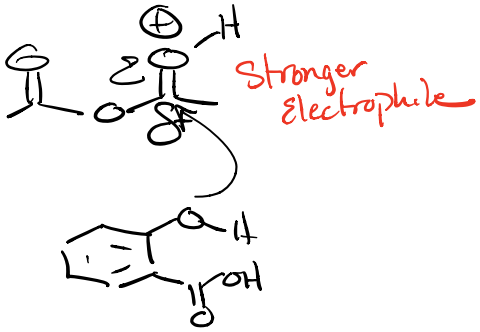


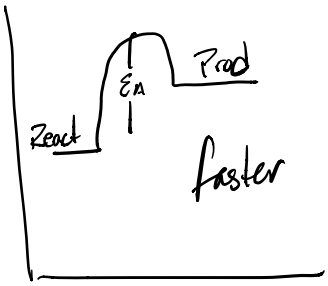



Good Leaving group
weak bond
e⁻ diff
assisted
Leaving
"Loss of LG"
5
deprotonation
6
acetic acid
B-H
acid
Cat
Acetyl salicylic Acid

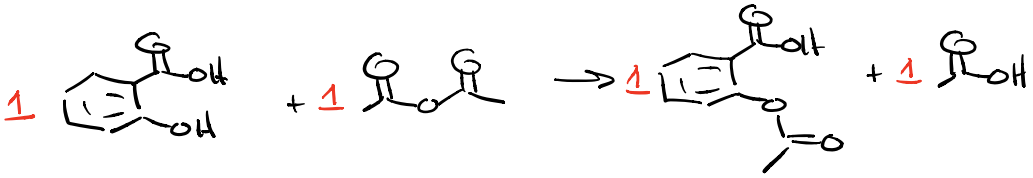
What if no H_3PO_4 used ?

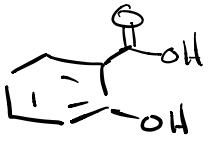




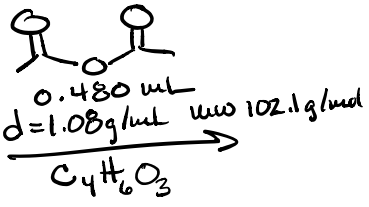


Stoichiometry





0.210g
mw 138.1 g/mol
$C_7H_6O_3$

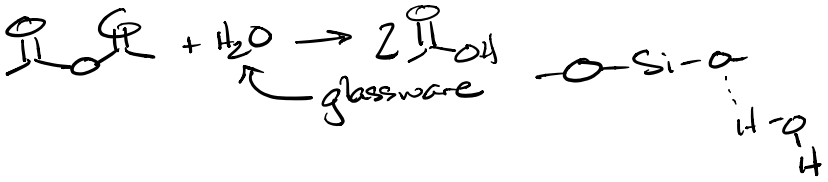


$$0.210\,g\ C_7H_6O_3 \times \frac{1\ mole}{138.1\ g} \times \frac{1000\ mmol}{1\ mole} = 1.52\ mmole\ C_7H_6O_3$$

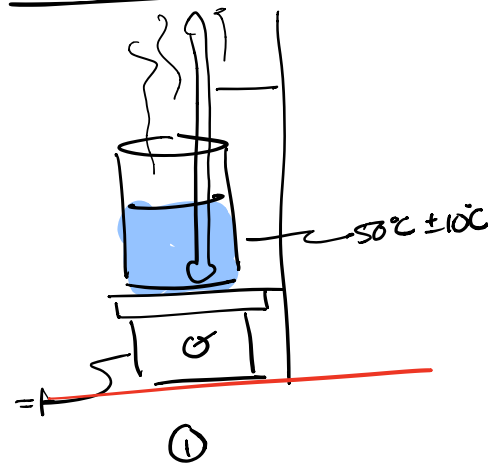
$$0.480\,mL\ C_4H_6O_3 \times \frac{1.08\ g}{1\ mL} \times \frac{1\ mol}{102.1\ g} \times \frac{1000\ mmol}{1\ mol} = 5.08\ mmol\ C_4H_6O_3$$

$$\frac{5.08\ mmol\ acetic\ anhydride}{1.52\ mmol\ Salicylic\ acid} = 3.34\times\ excess\ of\ acetic\ anhydride?$$

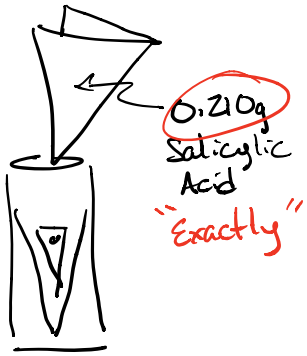
Acetic Anhydride

1. Solvent
2. Le Chatleirs Principle $\Rightarrow$ products
3. 

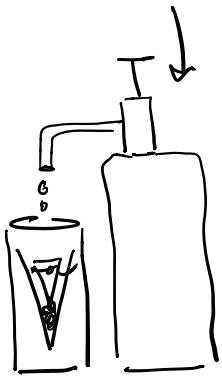
Pavia Instructions



①



②



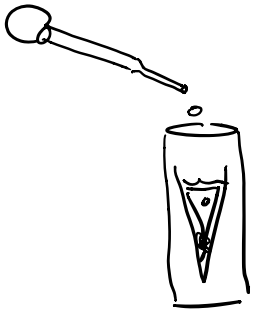
Add 0.480 mL acetic anhydride

"Exactly"

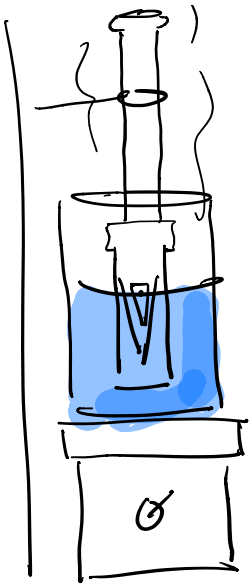
0.480 mL

− 0.5 mL

③



④ Add drop H_3PO_4 conc.



? H_2O bath?

Heat @ 50°C
8-10 min

⑤

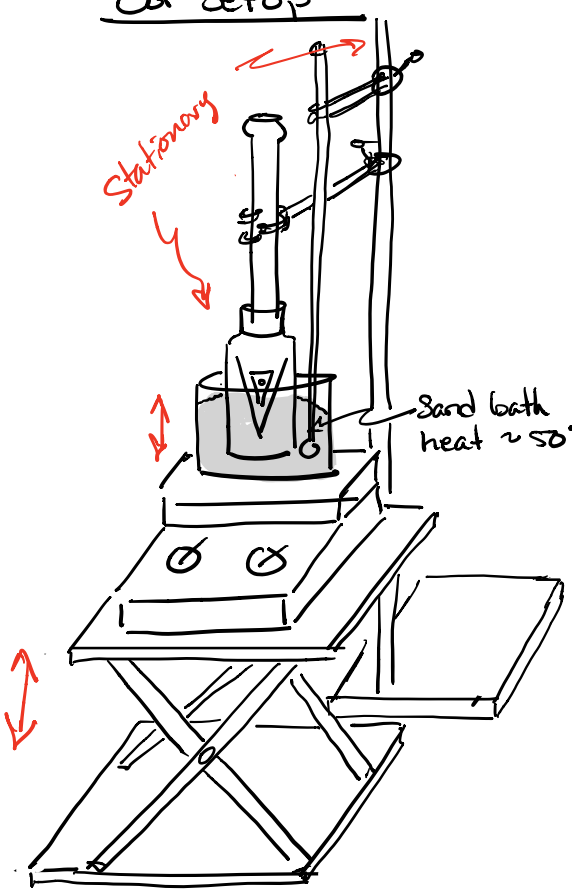
⑥ Cool RT
⑦ Add 3.0 mL DI H_2O
⑧ Filter on hirsch
⑨ Rinse w/ 1 mL 0°C DI H_2O
⑩ Air dry 5-10 min
⑪ Tare petri dish
⑫ Weigh Crystals
⑬ Label & Store in locker

2-day

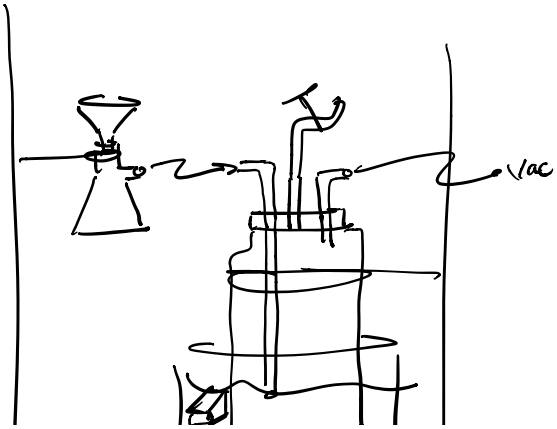
Reweig Crystal → dry mass
Calc % yield

Characterization of product
- $FeCl_3$ test
- MP
- FTIR

Our Setup



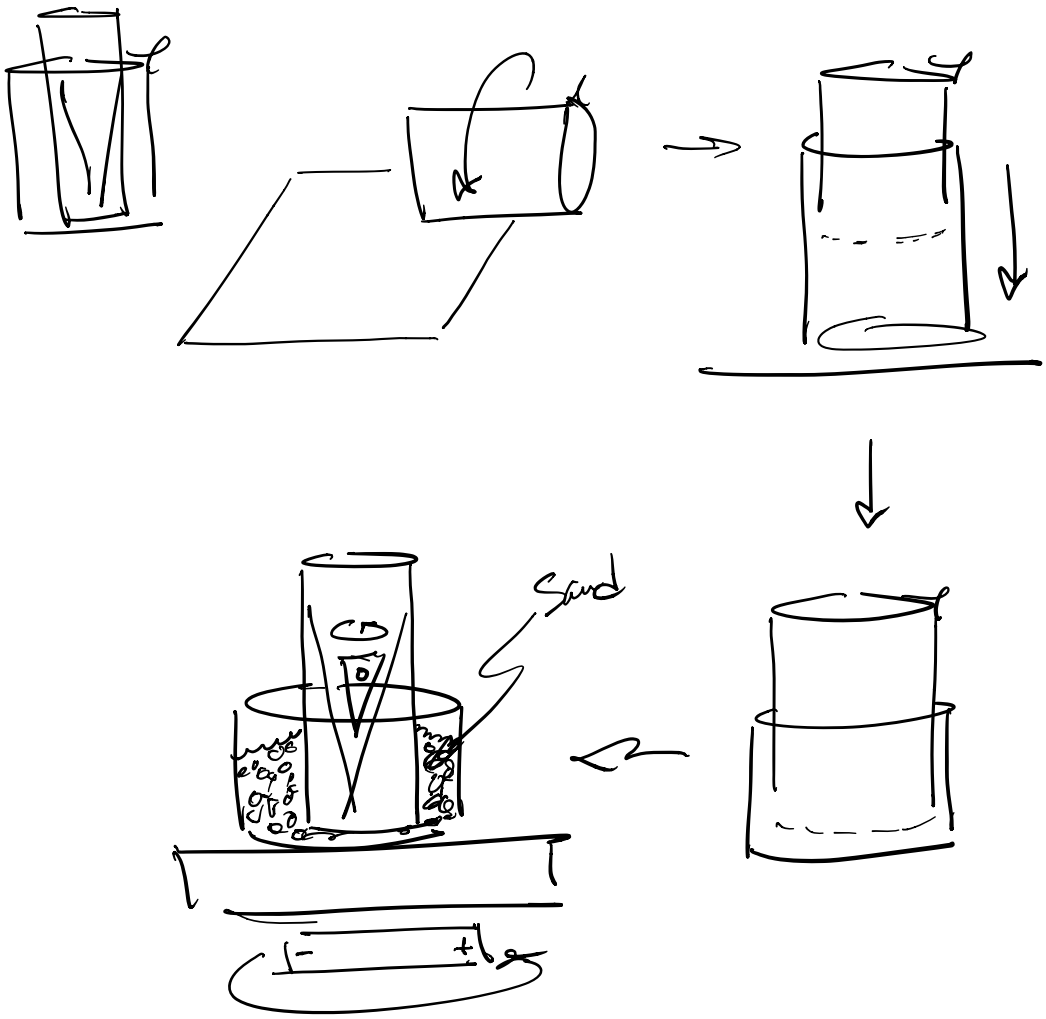
Jackstand
in elevated position
to allow for lowering



1. Set up hot plate, jackstand, ring stand, clamps, & sand bath.
2. heat sand bath ~ 50°C ±10°C
3. Obtain ~ 0.210 g Salicylic acid
4. Weigh flask & Salicylic acid
5. Add ~ 0.5 mL acetic anhydride
   ⇒ neutralize pipet
6. Reweigh flask to get mass of acetic anhydride
   ~ 0.5 g ??? d = 1.08 g/mL
7. Add 1 drop conc. H_3PO_4
8. Heat ~ 8-10 min (60°C 40°C)
   ← start timer when salicylic acid dissolves
9. Cool to rt
10. Add ~ 3.0 mL H_2O & Stir w/ spatula
11. Filter on hirsch
12. Rinse w ~ 1 mL 0°C DI
13. Air dry 5-10 min
14. Tare petri dish

(15) Weigh Crystals

(16) Label & Store in Locker



Conc H_3PO_4

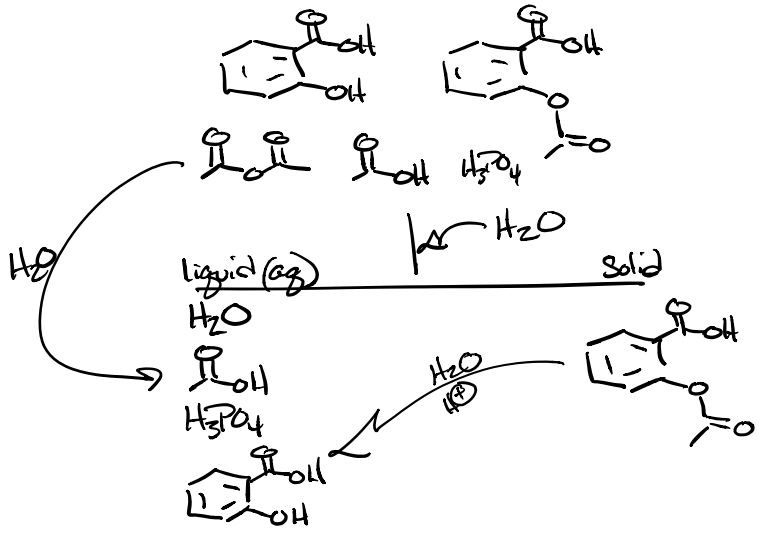
Need H_2O

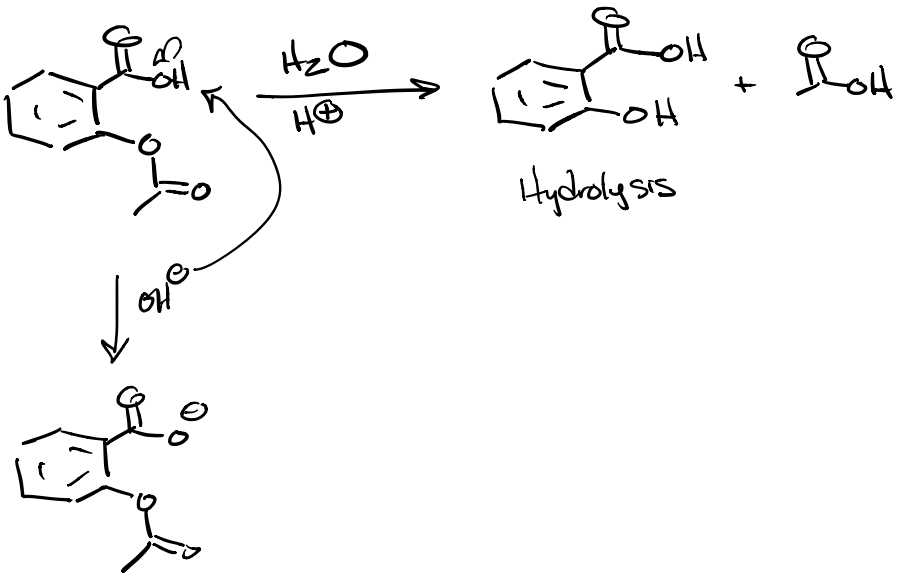
Seperation scheem

Reverse Reaction

	Conc	normality eq/L
Conc. HCl	12.1 M	12.1 N
Conc. H_2SO_4	18.0 M	36.0 N
Conc. H_3PO_4	14.8 M	44.4 N

$$HCl + H_2O \rightarrow Cl^- + H_3O^+$$





Retrosynthetic Analysis