

Synthesis of Lidocaine

Week 1: Part A (p. 751) and Part B (p. 753) (p 733/735 4th ed)

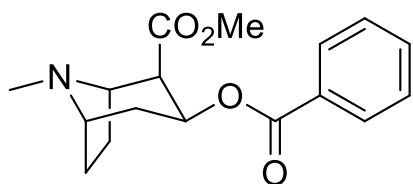
Week 2: Part C (p. 755) (p 736 4th ed)

Important Concepts

- Multi-Step synthesis
 - Pharmaceutical/Medicinal Chemistry
- Metal mediated reduction of Nitro groups
 - S_N2 reaction
 - Anesthetics

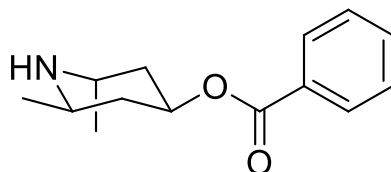
Anesthetic Compounds

Cocaine



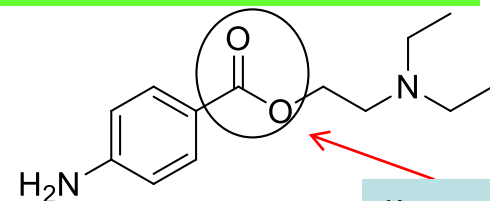
- Highly Addictive
- Damages Central Nervous Systems

Eucaïne



- Not Addictive
- Highly Toxic

Procaine

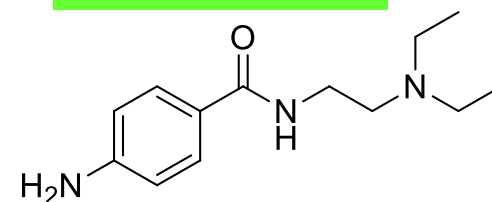


Novocain

- Not Addictive
- Less Toxic
- Short half-life in vivo

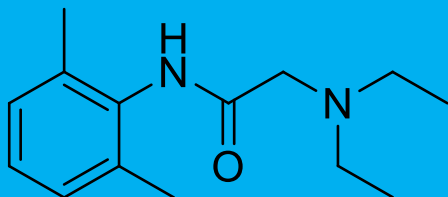


Procainamide



- longer half-life
- antiarrhythmic agent

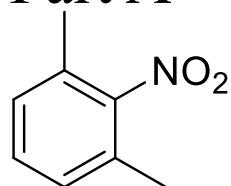
Lidocaine



Small structural changes can have a large effect on the medicinal properties.

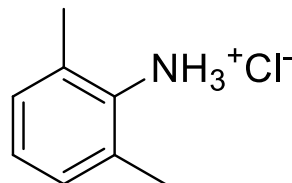
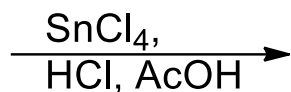
Synthesis - Week 1

Part A



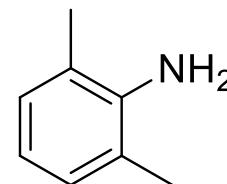
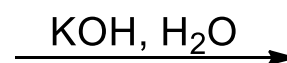
1

2,6-Dimethyl-nitrobenzene



2

2,6-Dimethylanilinium hydrochloride

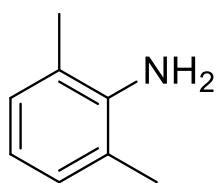


3

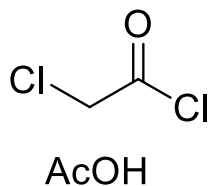
2,6-Dimethylaniline

- make sure rotovap runs for an extra 10-15 minutes after solvent appears to have evaporated.
- save enough of product to run a TLC and get an IR.

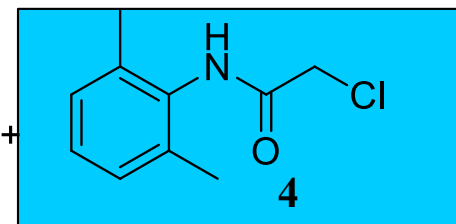
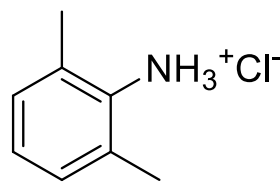
Part B



2,6-Dimethylaniline

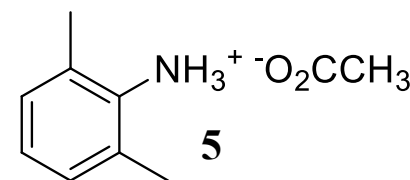


AcOH



α -chloro-2,6-dimethylacetanilide

Reaction conditions: NaOAc



5

water soluble

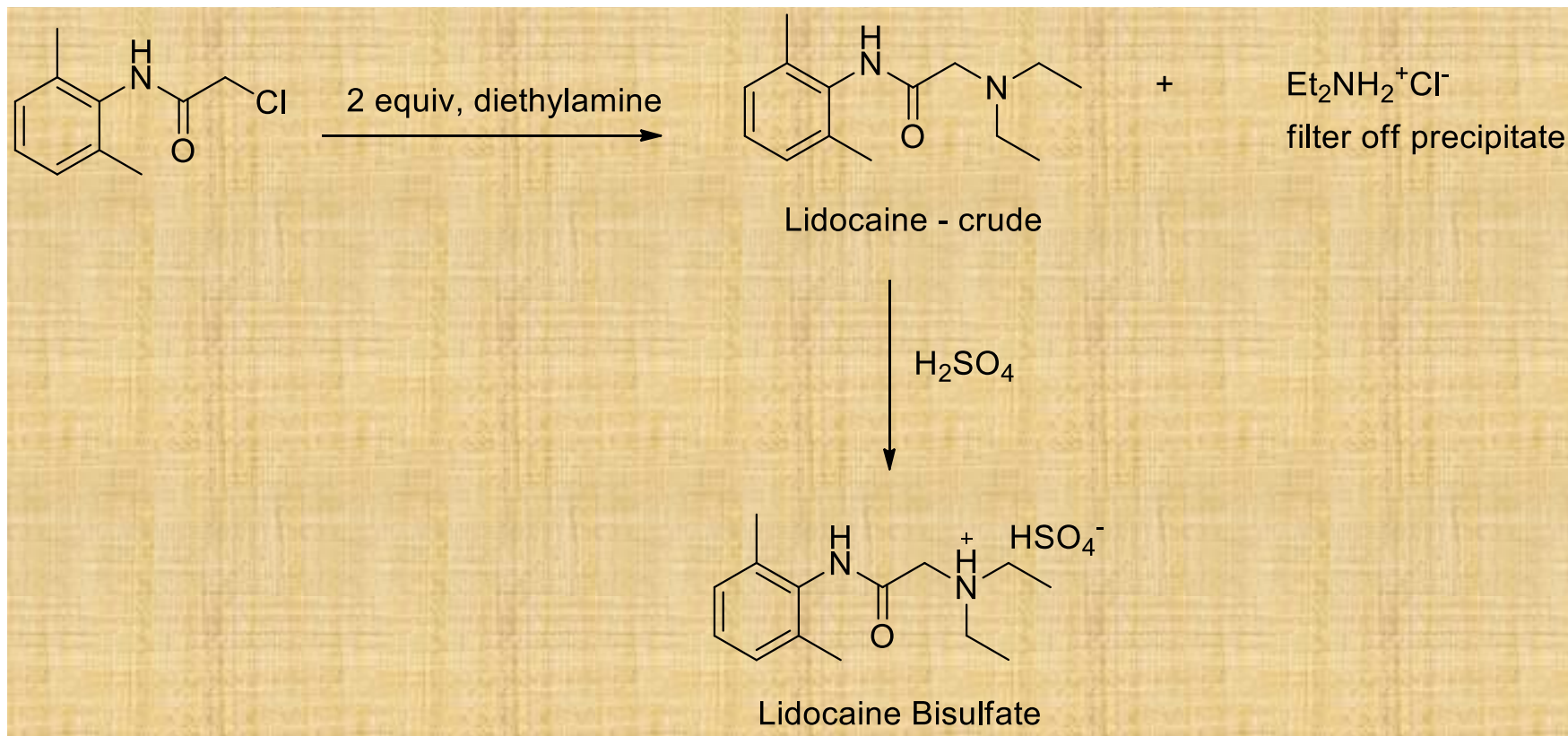
- allow product to dry until next week.

Synthesis - Week 2

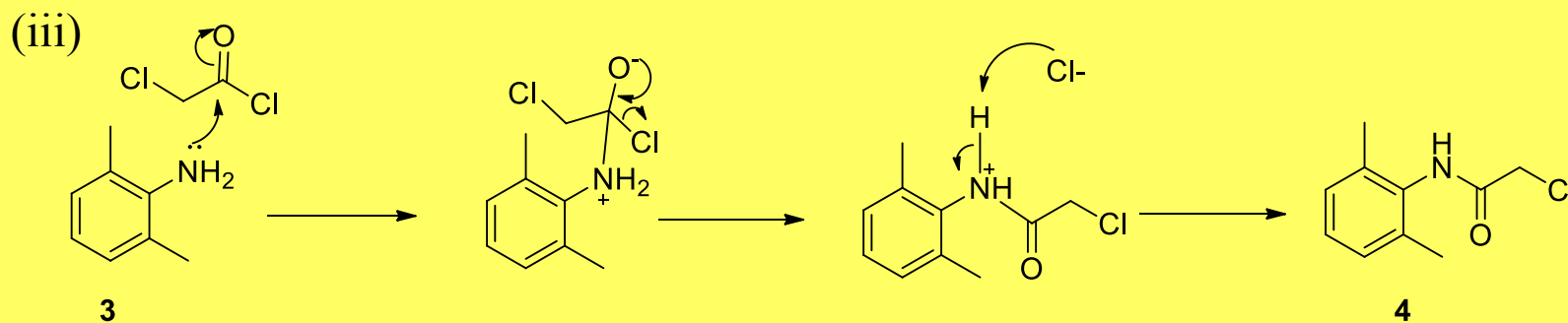
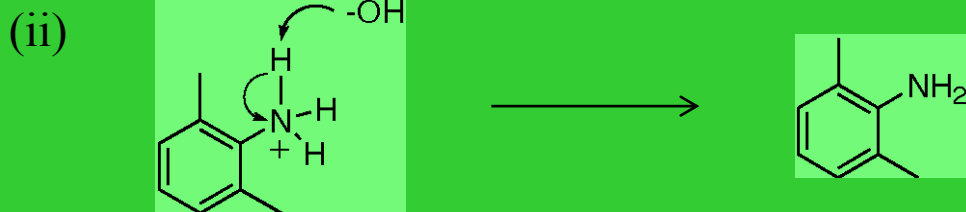
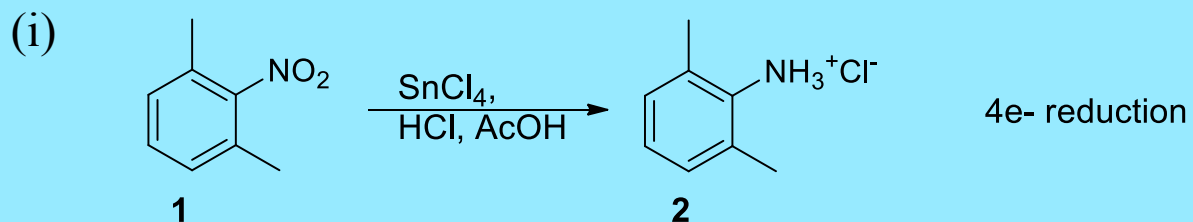
Part B - cont.

- recrystallize any remaining **4** from toluene during 90 minute reflux in Part C.
- Use a Hirsch funnel for filtering if you have a small amount.

Part C

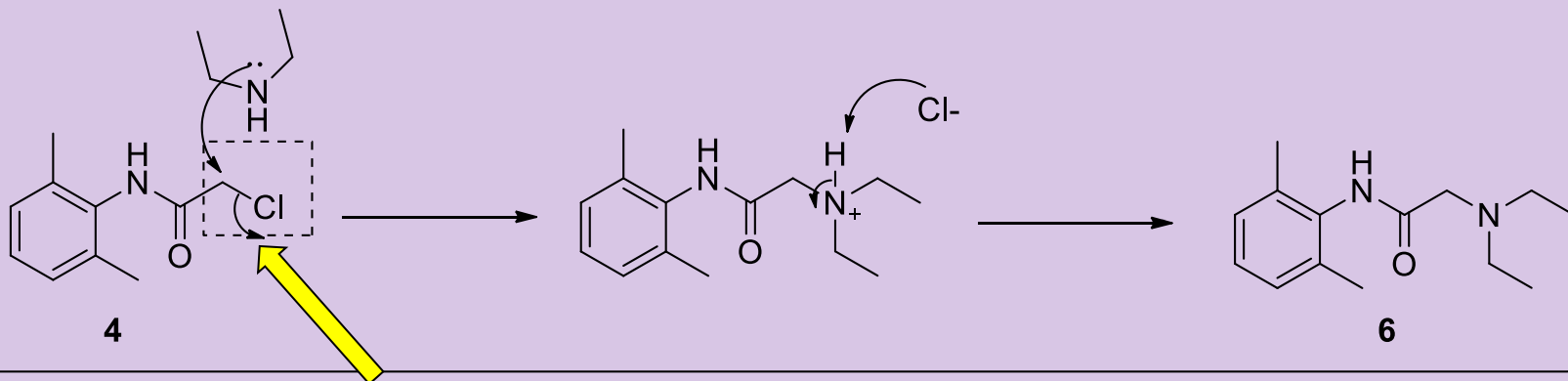


Reaction Mechanisms



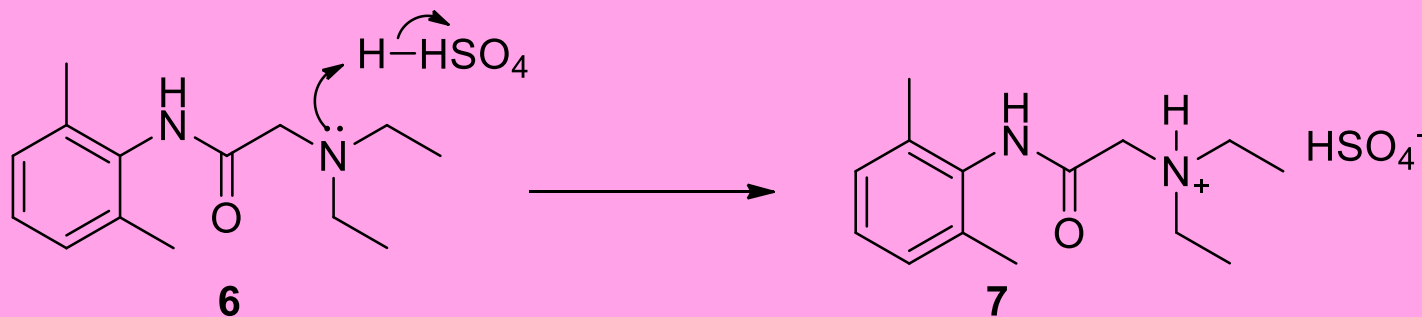
Reaction Mechanisms – cont'd

iv



SN2

(v)



Required Data

Part A

- Yield, % yield
- TLC of product and starting material (use 80/20 - Hex/EtOAc)
- IR of product and starting material
- ^1H NMR of product and starting material

Part B

- yield, %yield
- TLC of product and starting material (use 40/60- Hex/EtOAc)
- IR of product and starting material
- ^1H NMR of product and starting material
- m. p. of recrystallized product

Part C

- yield, %yield
- TLC of product and starting material
- IR of product and starting material
- ^1H NMR of product and starting material
- m. p. of recrystallized product