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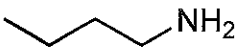
Chapter 22 (Klein) Amines

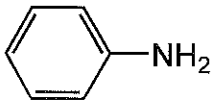
IUPAC: Identify the parent carbon chain. Drop the alkane "e" and add "amine" to give "**alkanamine**." List other alkyl groups as *N*- substituents. Those with simple alkyl groups are commonly called "**alkylamines**." If a higher priority functional group is present, the NH_2 is referred to as an "amino" substituent.

SkillBuilder 22.1

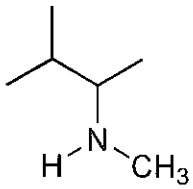


butanamine
(butylamine)

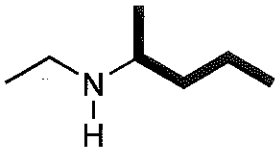
NH_3
ammonia



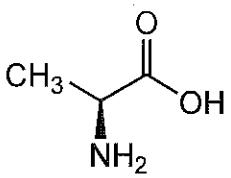
aniline



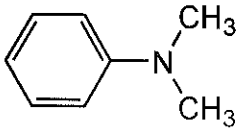
IUPAC:_____

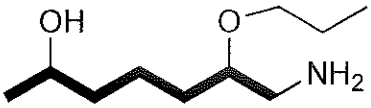


N-ethyl-2-pentanamine

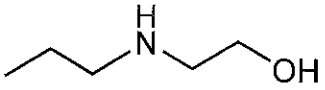


S-2-aminopropanoic acid
(alanine)

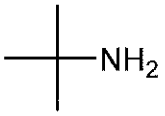




7-amino-6-propoxy-2-heptanol



IUPAC:_____



IUPAC:_____

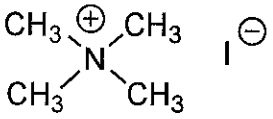
IUPAC:_____

Common:_____

Draw diisopropylamine.

What is its IUPAC name?

Classification of amines (each can be alkyl or aryl):

Primary (1°, RNH_2)	**Secondary** (2°, R_2NH)	**Tertiary** (3°, R_3N)	**Quaternary Salt** (R_4N^+)
CH_3-NH_2	$CH_3-NH-CH_3$	$(CH_3CH_2)_3N$	
methylamine (methanamine)	dimethylamine (*N*-methylmethanamine)	triethylamine (*N,N*-diethylethanamine)	tetramethylammonium iodide

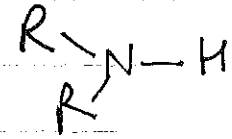
Chapter 22 Outline

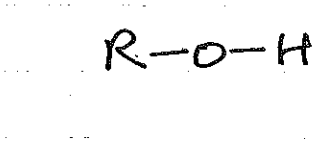
I. Nomenclature and Classification (22.2)
II. Properties of Amines (22.3)
III. Reactions of Amines
  A. Hofmann Elimination (22.9)
  B. Nucleophilic rxns (22.8)
  C. Nitrosation (22.10, 22.11)
  D. Imines and Enamines (19.6)
IV. Preparation of Amines (22.4 - 22.7)
  A. via Amides
  B. via Nitriles
  C. Gabriel Synthesis
  D. via Nitro compounds
  E. via Azides
V. Biological Amines (22.1)

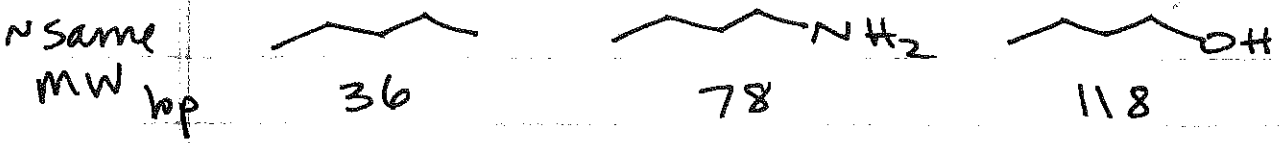
II Properties + Reactivity (compare to alcohols)
(22.3)

RNH_2 vs ROH * N is ____ electronegative than O

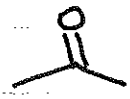
① RNH_2 has a lower boiling point



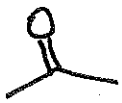




② RNH_2 is a great nucleophile

ex ROH  →

weak Nu:

ex RNH_2  →

good Nu:

* N holds lone pair more loosely → better Nu *

Ex. $\ddot{N}H_3$ CH_3-I $\xrightarrow{SN2}$

ammonia ⊖

good Nu:

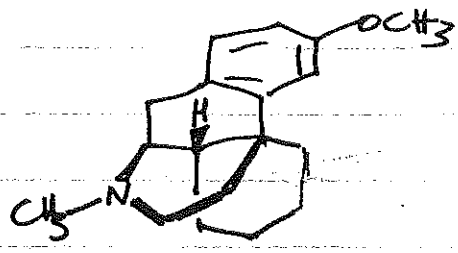
* overalkylation is possible (see amine synthesis strategies)

③ RNH_2 is a good base (22.3)

CH_3NH_2 + H–Cl ⇌

base acid

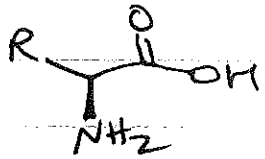
Ex. Amine drugs are prepared as salts (more stable)
Dextromethorphan HBr
(cough suppressant



Ex. Electrophilic Ar.
Substitution – nitration

$\xrightarrow[H_2SO_4]{HNO_3}$ (Ch 18)

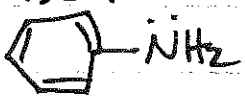
Ex. Amino Acids are zwitterions



⇌

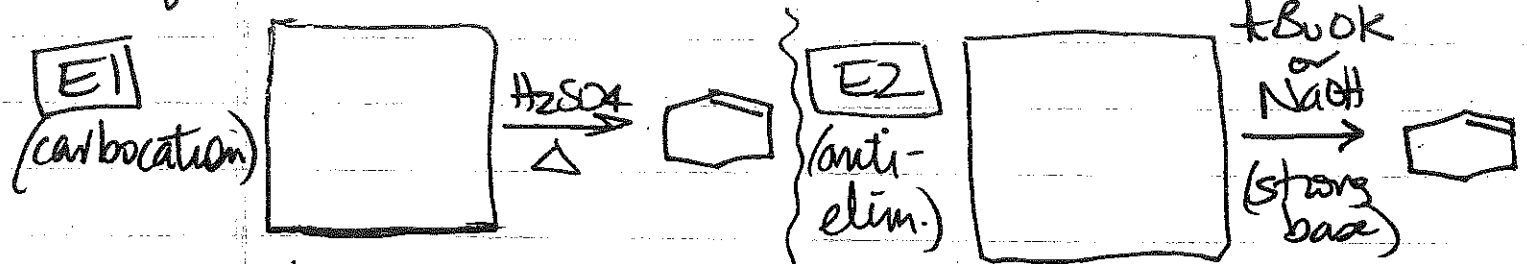
Ex. alkyl vs. aryl amines
Which is better base?

$CH_3CH_2NH_2$

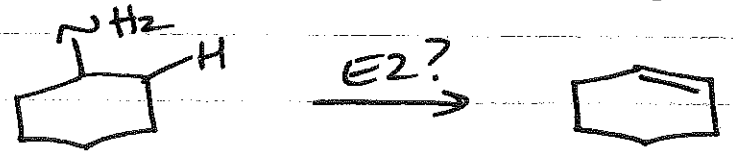


III Reactions of Amines

* Hofmann Elimination (22.9) * SkillBuilder 22.5 *

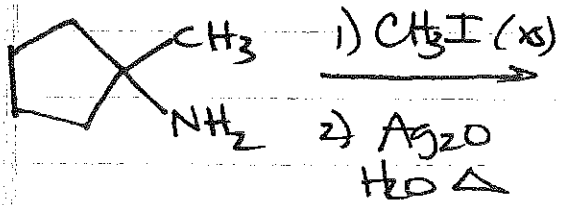


How can an amine undergo elimination?

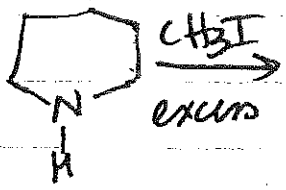


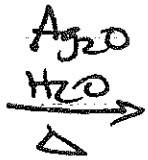
Zaitsef's Rule: most stable alkene product (thermo.)
Hofmann Elimination: Kinetic product (sterics/speed)

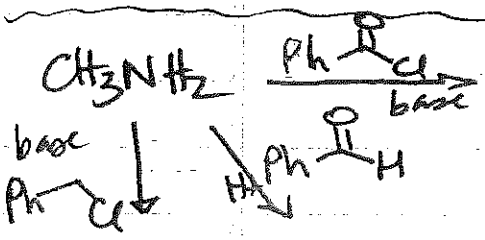
predict both products: (which is major?)

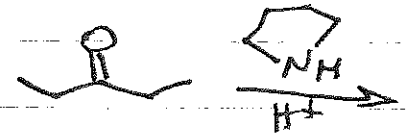


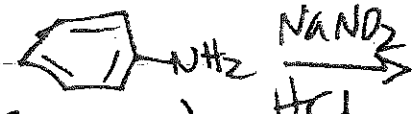
Sequential → structure ID







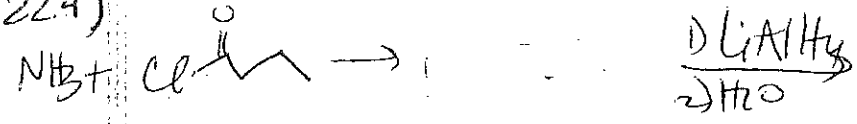


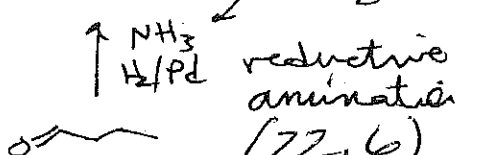


(22.10, 22.11)

IV Synthesis of Amines (22.4-22.7)

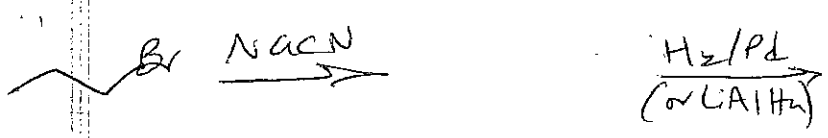
(A) via amides - NH_3 will only react once w/ acid chlorides (22.4)



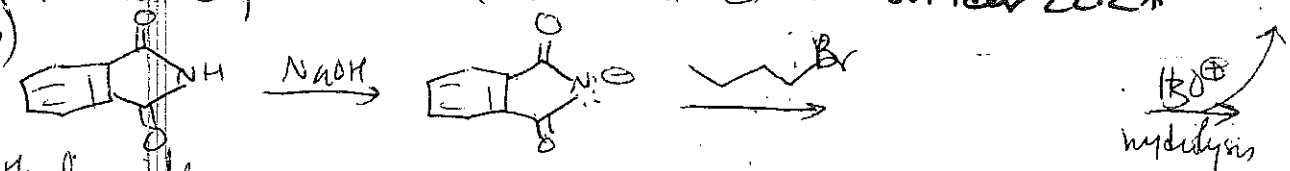


SkillBuilder 22.3

(B) via nitriles ($RX \rightarrow RCH_2NH_2$) (22.4)

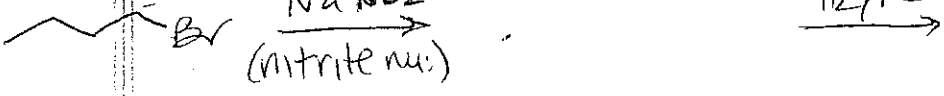


(C) Gabriel Synthesis ($RX \rightarrow RNH_2$) (22.5) *SkillBuilder 22.2*

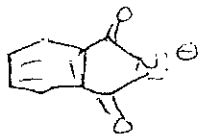


phthalimide

(D) via Nitro compounds ($RX \rightarrow RNH_2$)



(E) via Azide compounds ($RX \rightarrow RNH_2$) (22.5)

Summary (22.7) since NH_3 is too strong a nu: ↑ can over-alkylate need an "NH_3" equivalent =  , NO_2, N_3

SkillBuilder 22.4

from benzene and any alcohol starting material

22-6

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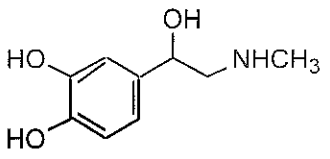
Chapter 22 Summary (Klein): Amines

I. Introduction & Nomenclature: alkanamine or alkyl amine, aniline (22.2) **SkillBuilder 22.1**
II. Properties of Amines (22.3)
- A) RNH_2 has lower b.p. than ROH
- B) RNH_2 is better Nu:/base than ROH
  - i) alkyl vs. aryl amine basicity; pK_a's of amine conjugate acids
  - ii) salts of amines (solubility, medicinal applications, crack cocaine)

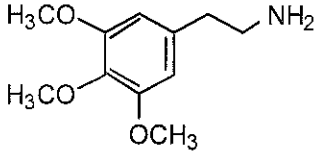
III. Reactions of Amines
- A) as Nu: (S_N2 with RX makes amine; reaction with RCOCl makes amide)
- B) Nitrosation (22.10, 22.11), reaction with HONO ($NaNO_2$ + HA)
  - i) gives diazonium salts (ArN_2^+), useful for synthesis of benzene derivatives
- C) Hofmann elimination (22.9) **SkillBuilder 22.5**
  - i) make amine good LG (excess CH_3I —› quaternary salt)
  - ii) E2 reaction (Ag_2O, H_2O, Δ)
  - iii) <u>least</u> substituted alkene formed as major product (opposite of Zaitsev)
- D) reaction with aldehydes/ketones to give imines and enamines (19.6)

IV. Preparation of Amines (synthesis) **SkillBuilder 22.4**
- A) RX —› RNH_2 (22.5) **SkillBuilder 22.2**
  - i) Gabriel synthesis (phthalimide anion Nu:, then hydrolysis)
  - ii) azide Nu:, then reduction (NaN_3, then H_2/cat or $LiAlH_4$)
  - iii) nitrite Nu:, then reduction ($NaNO_2$, then H_2/cat or Sn/HCl)
- B) RX —› RCH_2NH_2 (22.4)
  - i) cyanide Nu:, then reduction (NaCN, then H_2/cat or $LiAlH_4$)
- C) ketone/aldehyde —› amine (22.6) **SkillBuilder 22.3**
  - i) via reduction of imine (H_2/cat or $LiAlH_4$)
  - ii) *in situ* formation of imine: "reductive amination" of carbonyl
- D) acid chloride —› amine (22.4)
  - i) via reduction of amide ($LiAlH_4$)

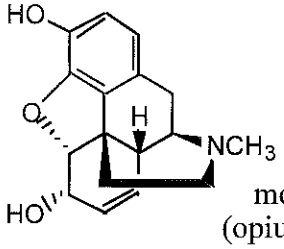
V. Biologically interesting amines (22.1):



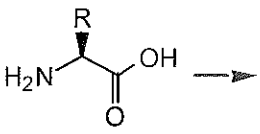
adrenaline
(hormone)



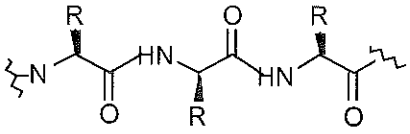
mescaline
(peyote alkaloid)



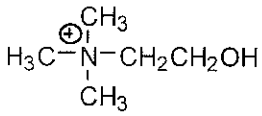
morphine
(opium alkaloid)



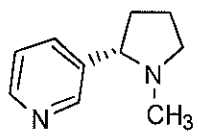
amino acids



protein



choline
(nerve impulse)



nicotine