Hofmann Rearrangement - 1° amides only

\[ R-\text{N}{}^1\text{H} \xrightarrow{\text{Br}_2, \text{NaOH}} R-\text{NH}_2 + (\text{CO}_2 + \text{H}_2\text{O}) \]

\[ \text{1° amine} \xrightarrow{\text{H}_2\text{O}} \text{HCO}_3^- \text{ etc.} \]

**Mechanism:**

- \( R-\text{N}{}^1\text{H} \) reacts with \( \text{Br}_2 \) and \( \text{NaOH} \) to form an intermediate.
- This intermediate undergoes hydration to form a carbamic acid (unstable).
- The carbamic acid can react with another amine (R-NH2) to form a new amine (R-NH2).

\[ R-\text{N}{}^1\text{H} \xrightarrow{\text{Br}_2, \text{NaOH}} \text{intermediate} \xrightarrow{\text{H}_2\text{O}} \text{carbamic acid} \xrightarrow{\text{eh.} + \text{R-NH}_2} \text{new amine} \]
Reactions of Amines - bases + nucleophiles

1. Rxn w/ aldehydes + ketones → imines + enamines
2. Rxn w/ acyl chlorides, esters, etc. → amides
3. Rxn w/ alkyl halides (S_N2) - most useful is exhaustive metalation (react w/ tBuLi)


\[
\text{X} + \text{CH}_3\text{I} \rightarrow \text{Ag}_2\text{O} \rightarrow \text{H} \rightarrow \text{O} + \text{H}\]

\[
\text{X} \rightarrow \text{Z} \rightarrow \Delta
\]
Hofmann elimination does not follow Zaitsev's rule - instead, we get the less substituted alkene. Why? Could be electronics (see book); it could be steric. Both give the same answer.
5. Oxidation of amines - use H$_2$O$_2$ or mCPBA

1°/2° amines $\rightarrow$ nothing useful

3° amine $\xrightarrow{H_2O_2}$ tertiary amine oxide

$\&$ Cope elimination
syn-elimination

6. Recall diazotization yields
Aromatic Heterocyclic Compounds

pyrrole  furan  thiophene  pyridine

pyrrolidine  piperidine

* these aromatics also go EAS.

pyrrole > furan > thiophene > benzene

> nitrobenzene > pyridine

very reactive

not very reactive
5-membered heterocycles

EAS is preferred @ #2
(sigma complex is more stable)

6-membered heterocycles

EAS is preferred @ #3

Sigma complexes for rxn @ #2 + #4
have N w/o complete octet and w/a

[SN2 nuclophilic aromatic substitution]