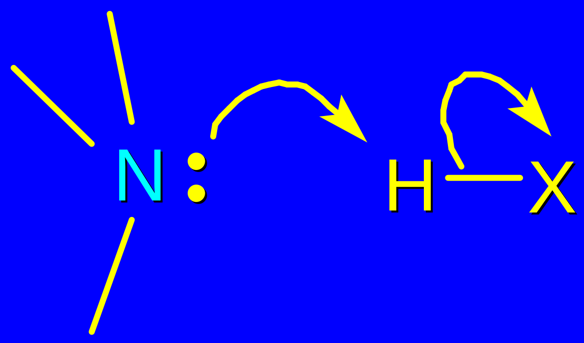
22.12

Reactions of Amines:
A Review and a Preview

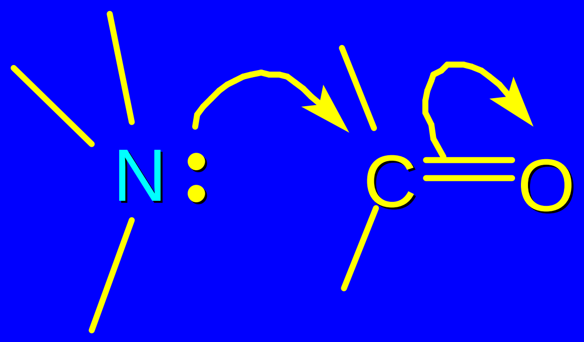
Reactions of Amines

Reactions of amines almost always involve the nitrogen lone pair.

as a base:



as a nucleophile:



Reactions of Amines

Reactions already discussed

basicity (Section 22.5)

reaction with aldehydes and ketones (Sections 17.10, 17.11)

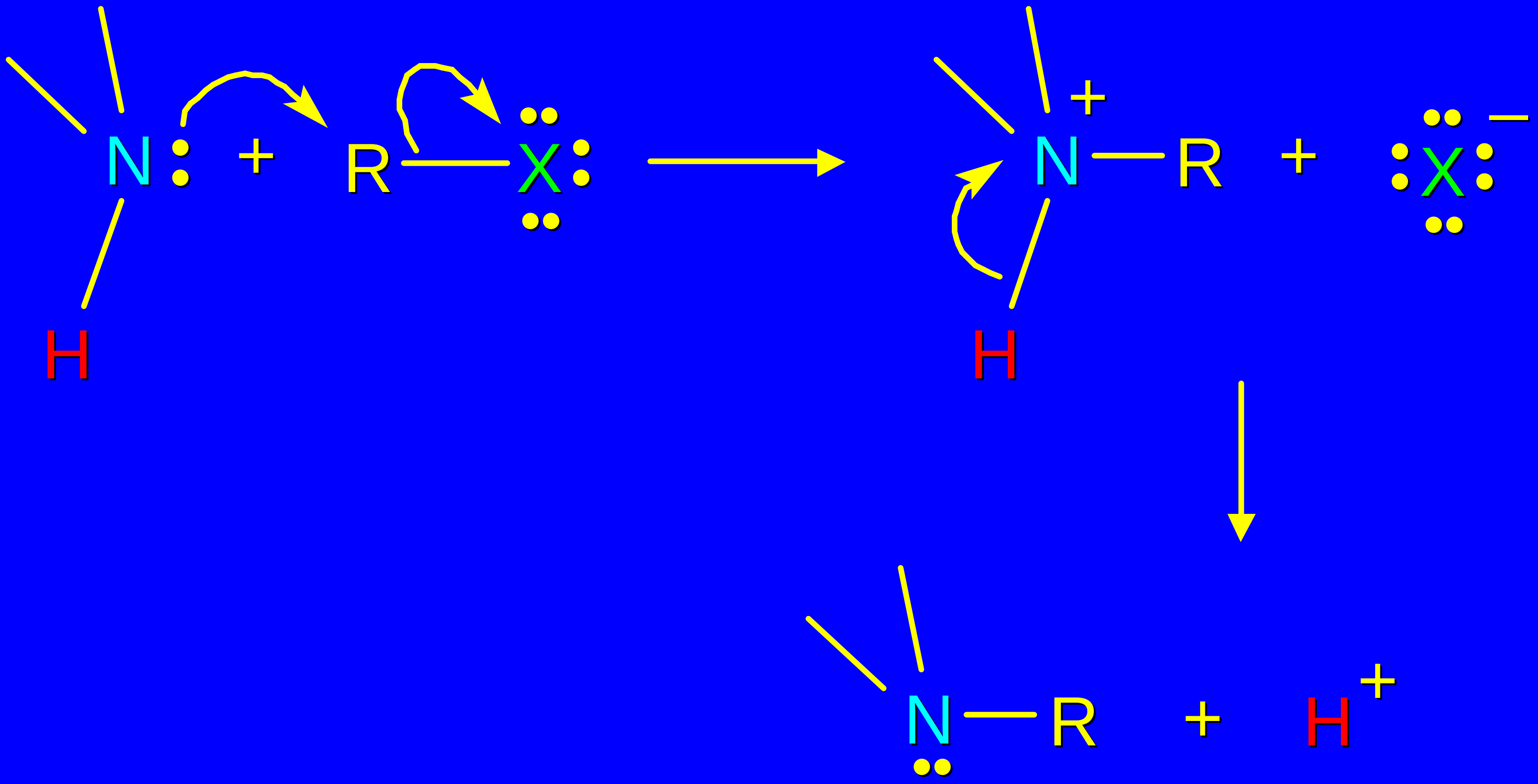
reaction with acyl chlorides (Section 20.3), anhydrides (Section 20.5), and esters (Section 20.11)

22.13

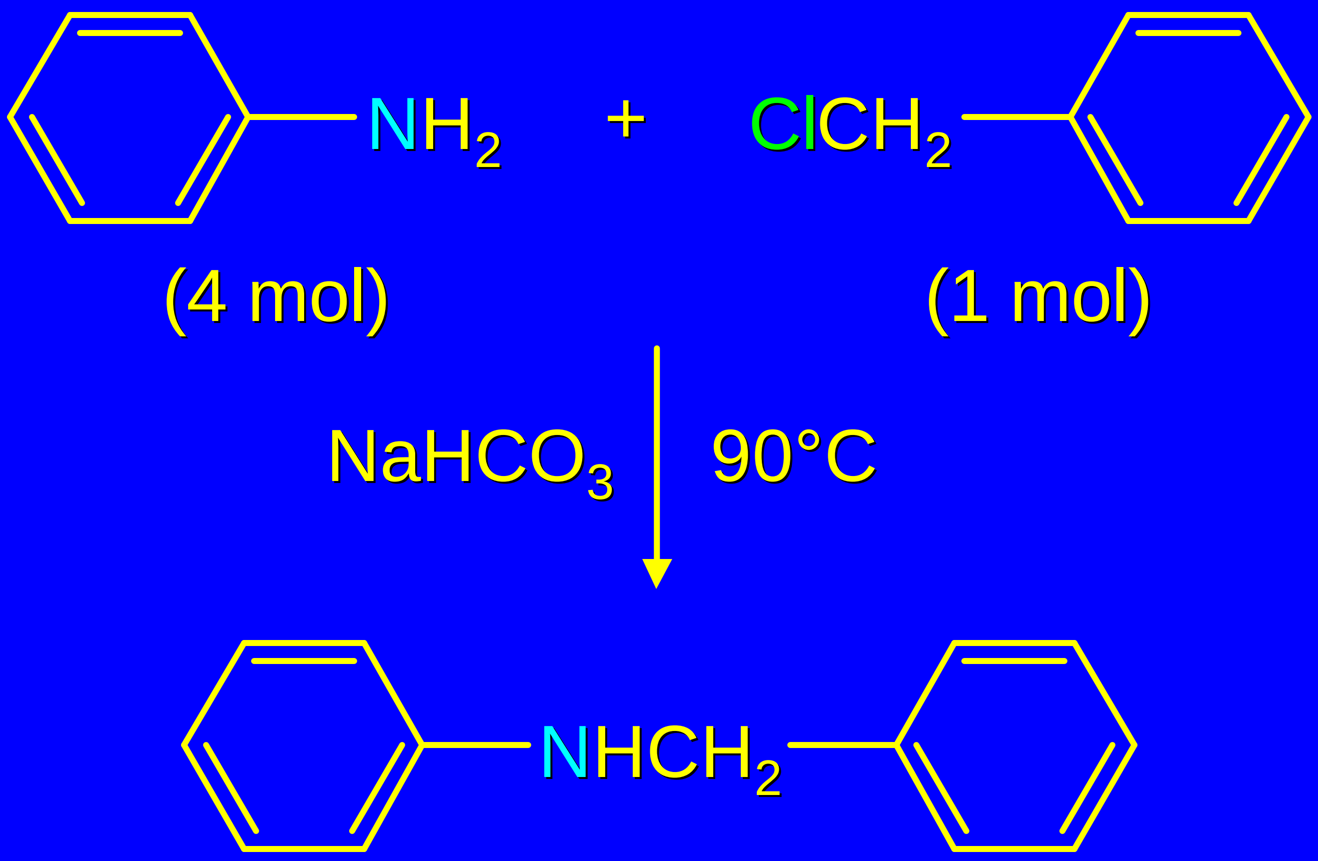
Reactions of Amines with Alkyl Halides

Reaction with Alkyl Halides

Amines act as nucleophiles toward alkyl halides.

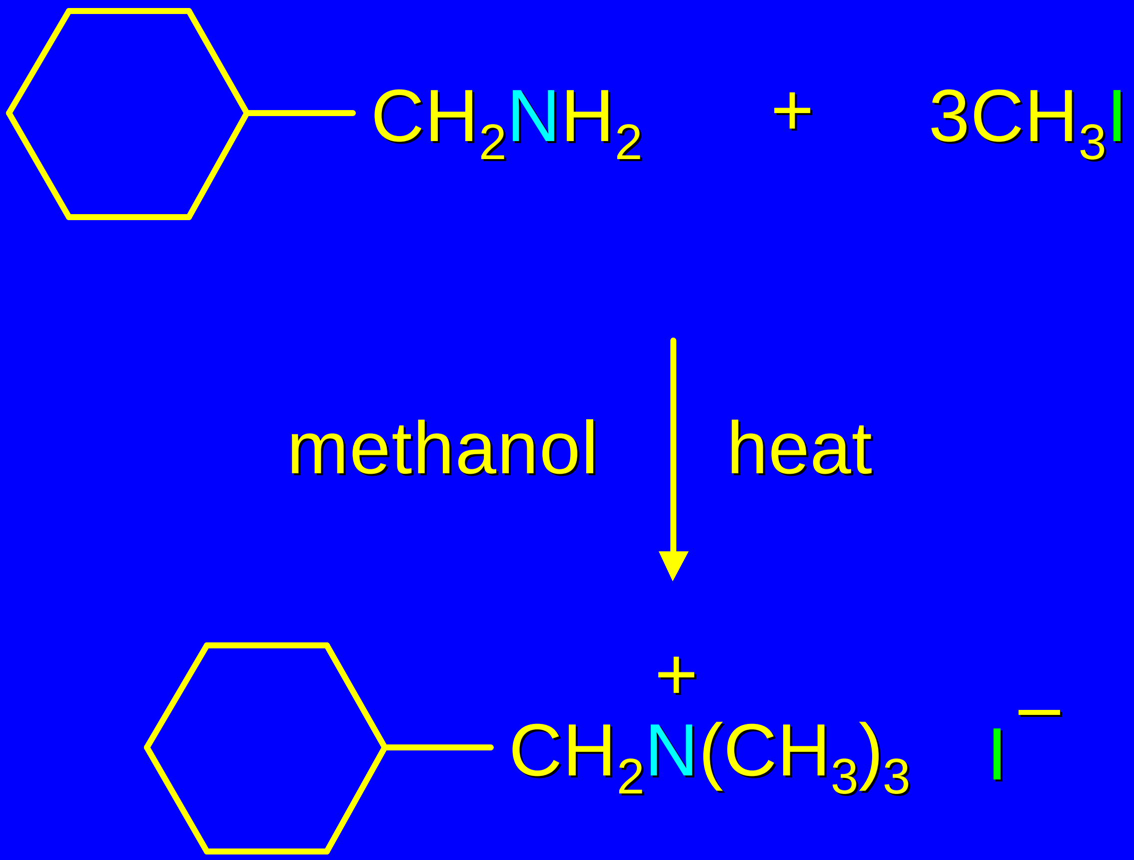


Example: excess amine



(85-87%)

Example: excess alkyl halide



$C_6H_{11}CH_2NH_2 + 3CH_3I \xrightarrow[\text{heat}]{\text{methanol}} C_6H_{11}CH_2\overset{+}{N}(CH_3)_3\ I^-$

(99%)

22.14

The Hofmann Elimination

The Hofmann Elimination

a quaternary ammonium hydroxide is the reactant and an alkene is the product

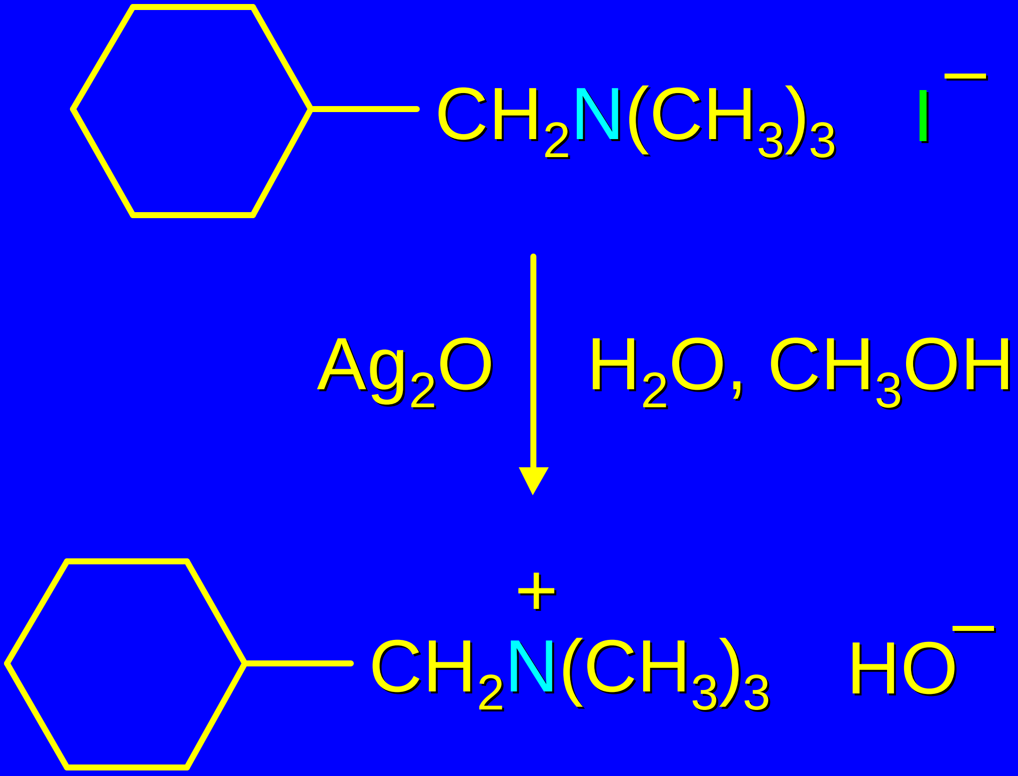
is an anti elimination

the leaving group is a trialkylamine

the regioselectivity is opposite to the Zaitsev rule.

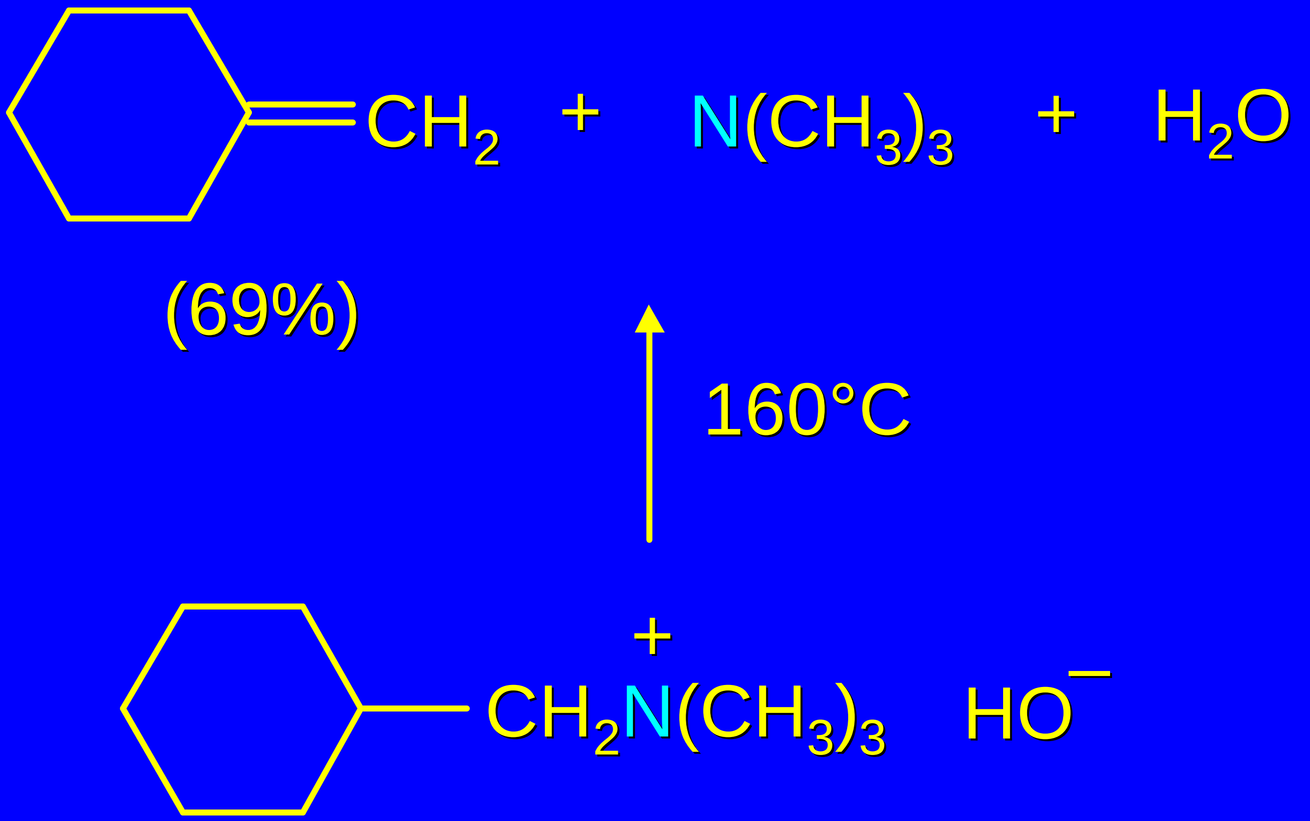
Quaternary Ammonium Hydroxides

are prepared by treating quaternary ammmonium halides with moist silver oxide



The Hofmann Elimination

on being heated, quaternary ammonium hydroxides undergo elimination



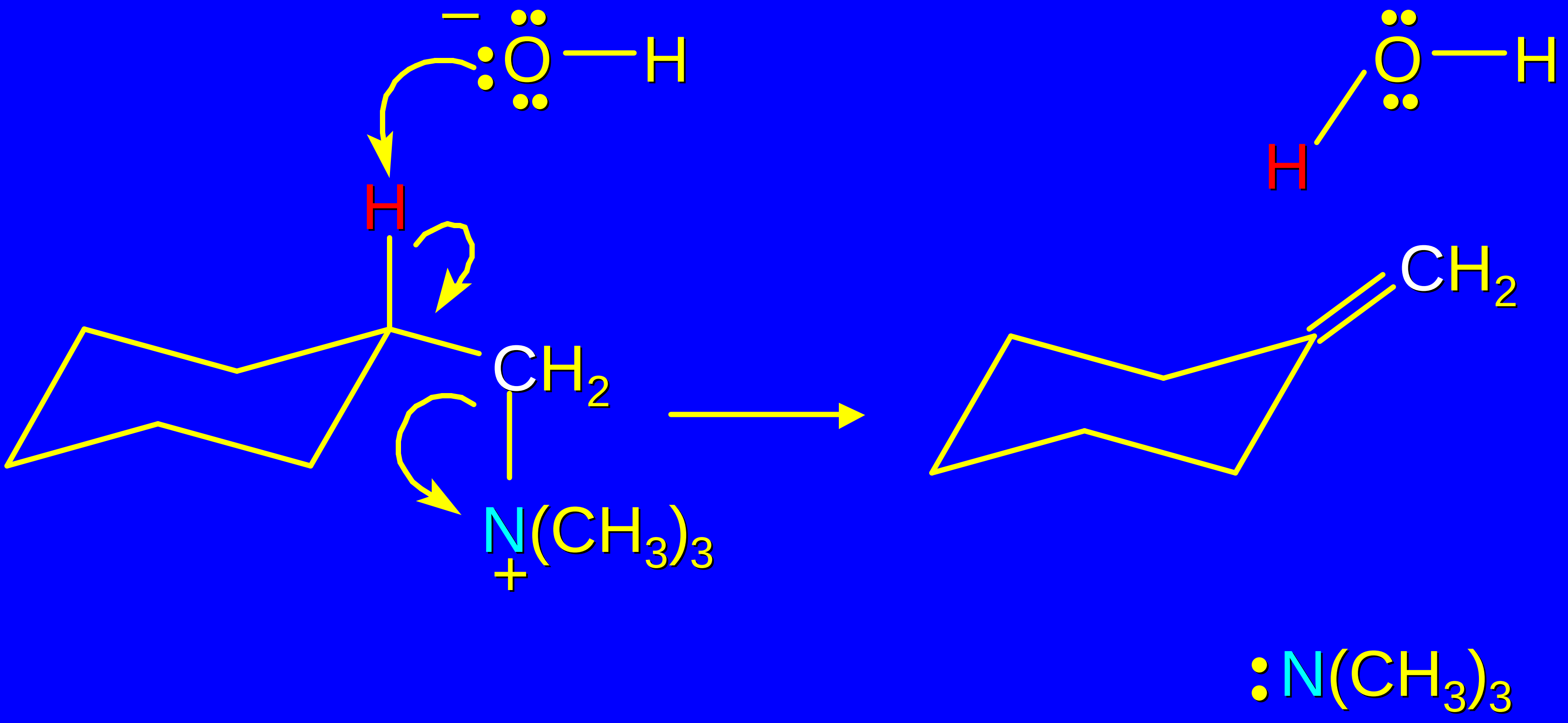
CH_2 + $N(CH_3)_3$ + H_2O

(69%)

160°C

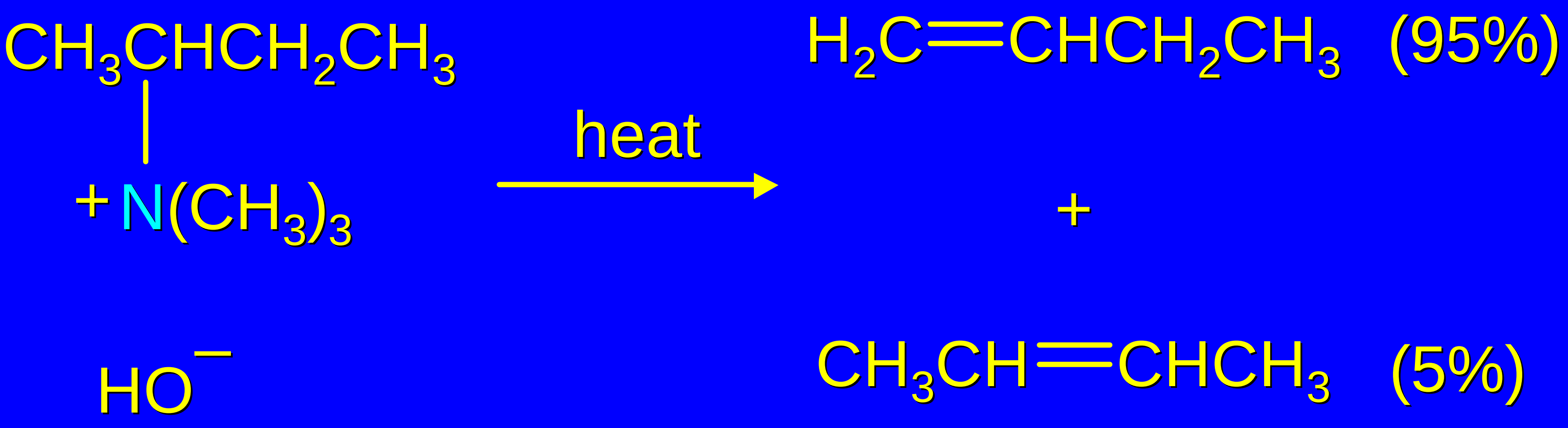
$CH_2\overset{+}{N}(CH_3)_3$ HO^-

Mechanism



Regioselectivity

Elimination occurs in the direction that gives the less-substituted double bond. This is called the Hofmann rule.

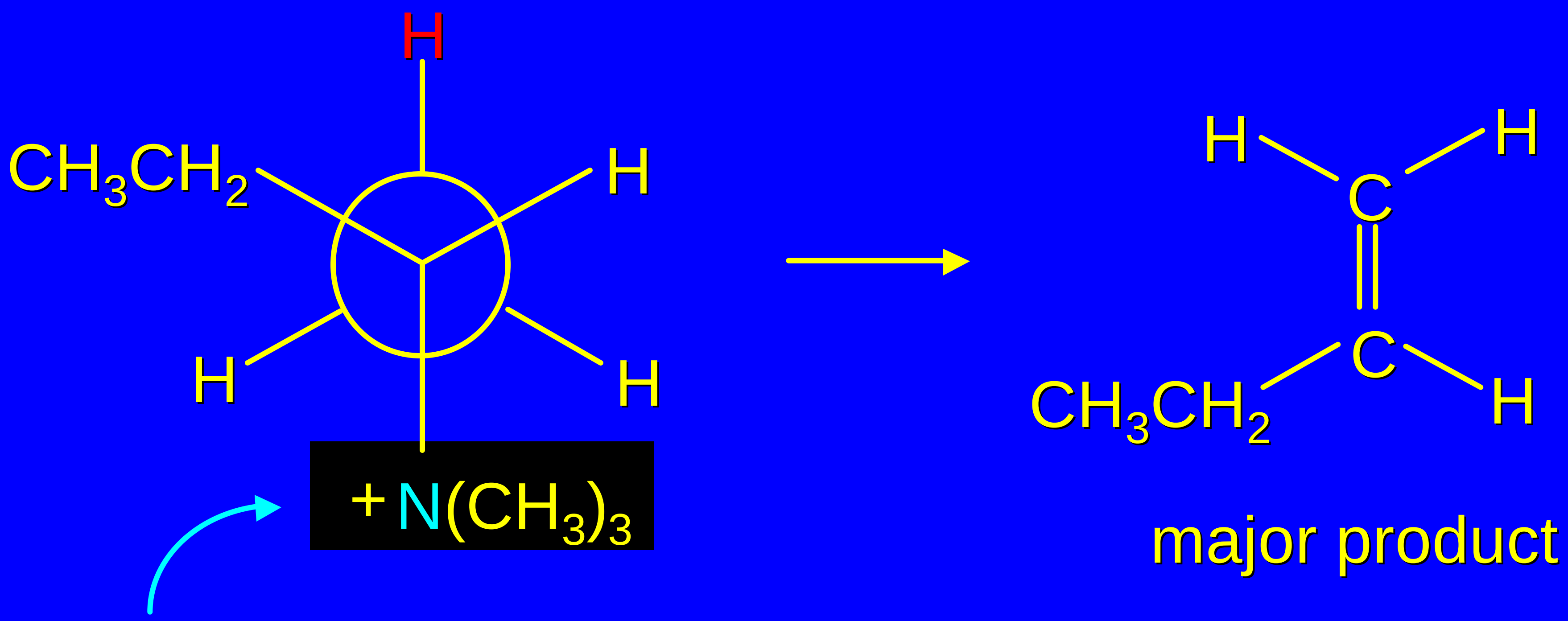


$$\underset{\overset{|}{^{+}N(CH_3)_3}}{CH_3CHCH_2CH_3} \quad HO^{-} \xrightarrow{\text{heat}} H_2C{=}CHCH_2CH_3 \ (95\%) \ + \ CH_3CH{=}CHCH_3 \ (5\%)$$

Regioselectivity

Steric factors seem to control the regioselectivity.
The transition state that leads to 1-butene is
less crowded than the one leading to cis
or trans-2-butene.

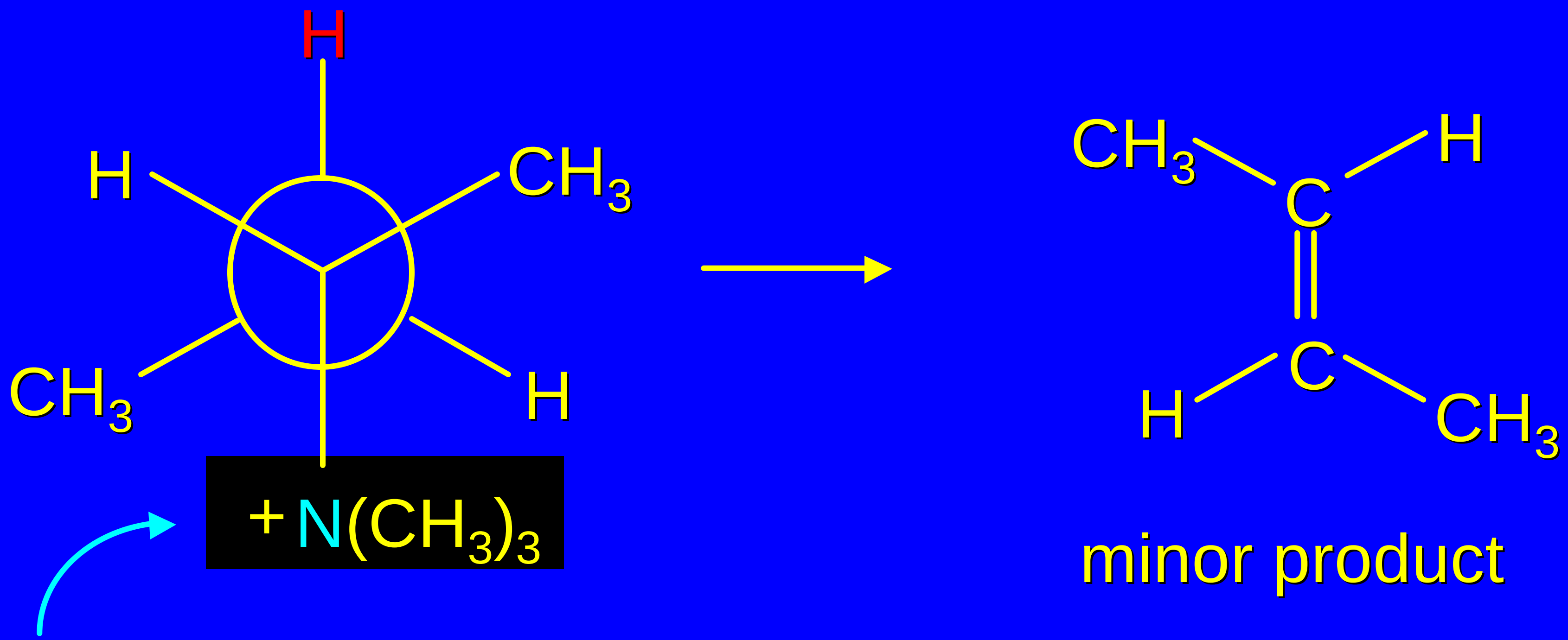
Regioselectivity



major product

largest group is between two H atoms

Regioselectivity



minor product

largest group is between an H atom and a methyl group

22.15

Electrophilic Aromatic Substitution in Arylamines

Nitration of Anililne

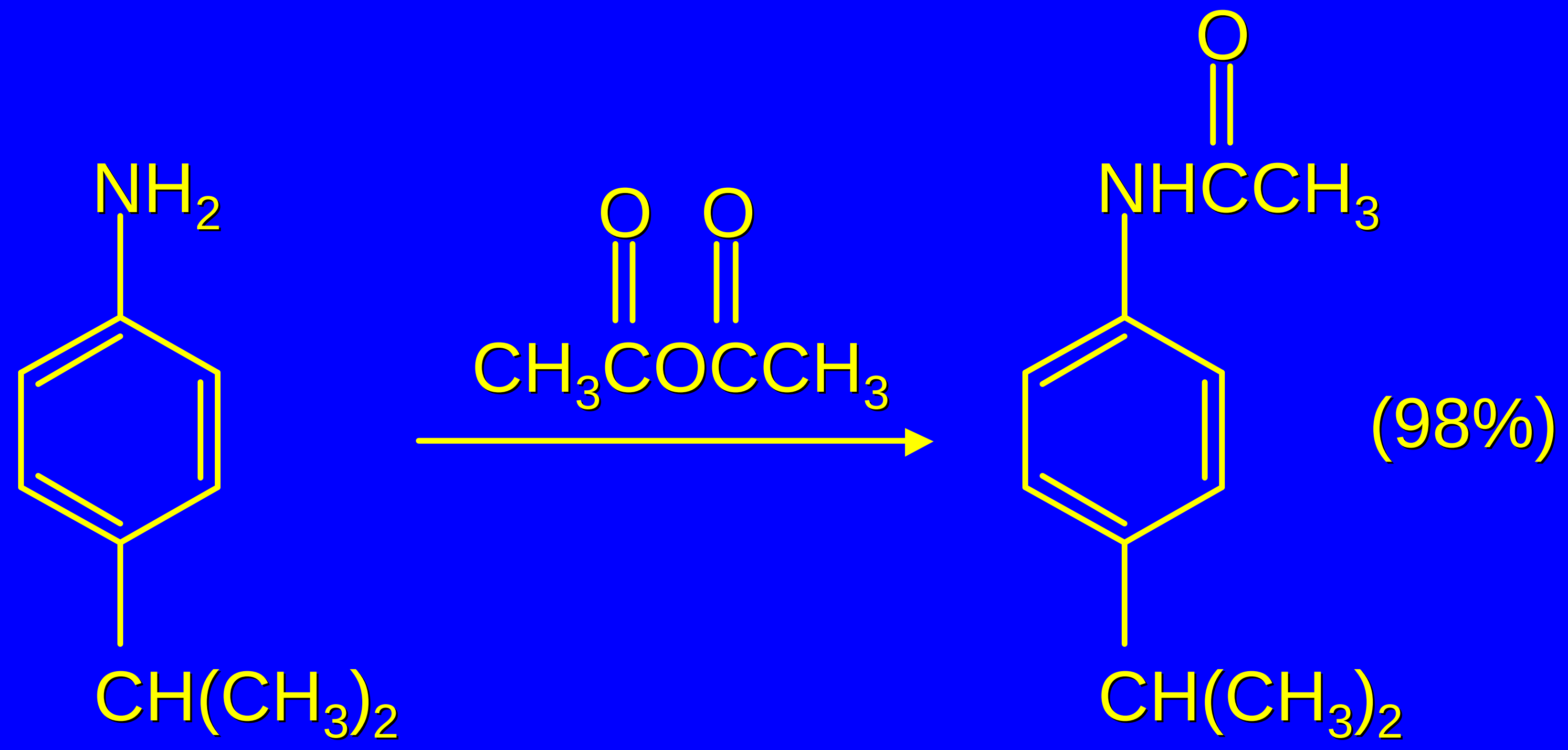
NH_2 is a very strongly activating group

NH_2 not only activates the ring toward electrophilic aromatic substitution, it also makes it more easily oxidized

attemped nitration of aniline fails because nitric acid oxidizes aniline to a black tar

Nitration of Anililne

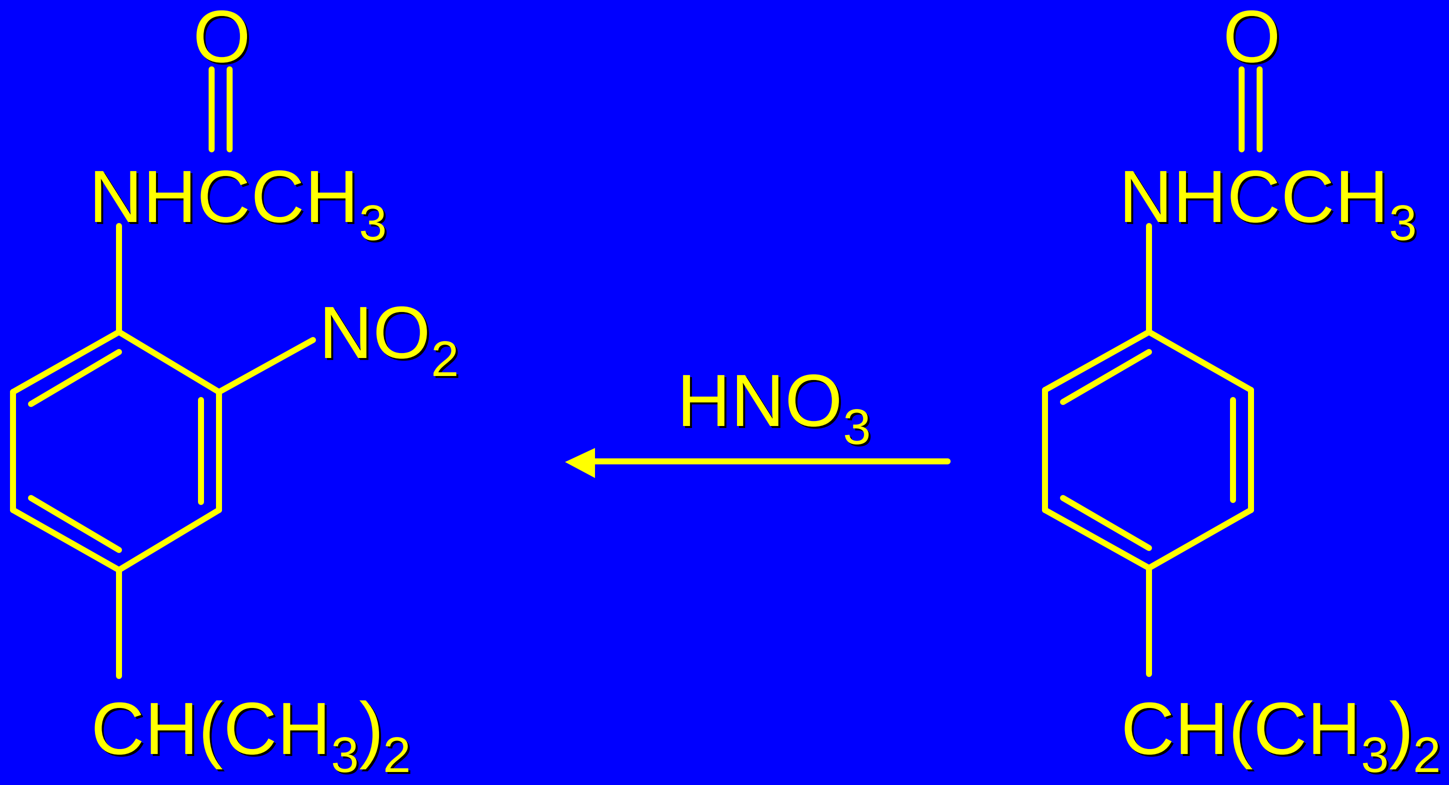
Strategy: decrease the reactivity of aniline by converting the NH_2 group to an amide



(acetyl chloride may be used instead of acetic anhydride)

Nitration of Anililne

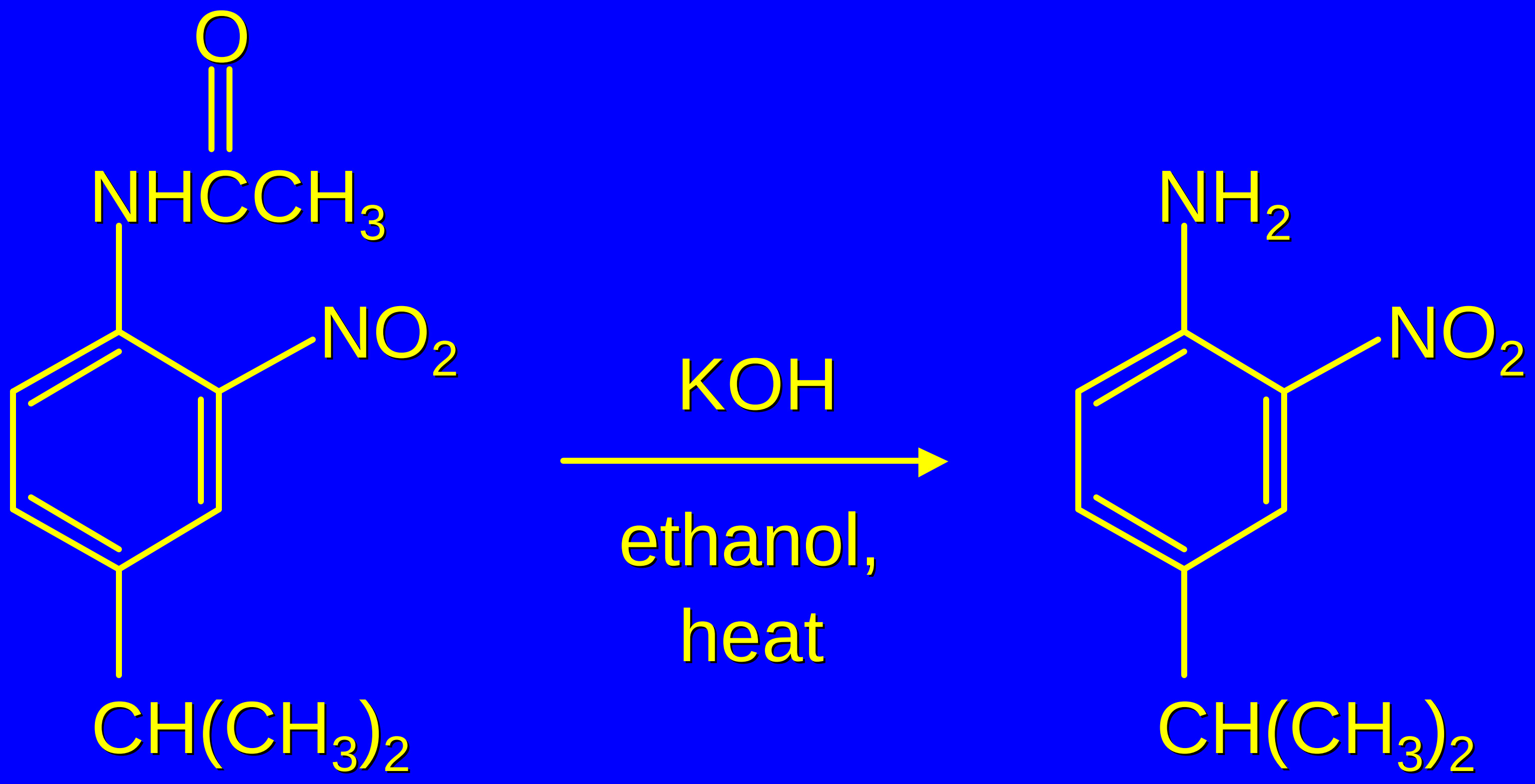
Strategy: nitrate the amide formed in the first step



(94%)

Nitration of Anililne

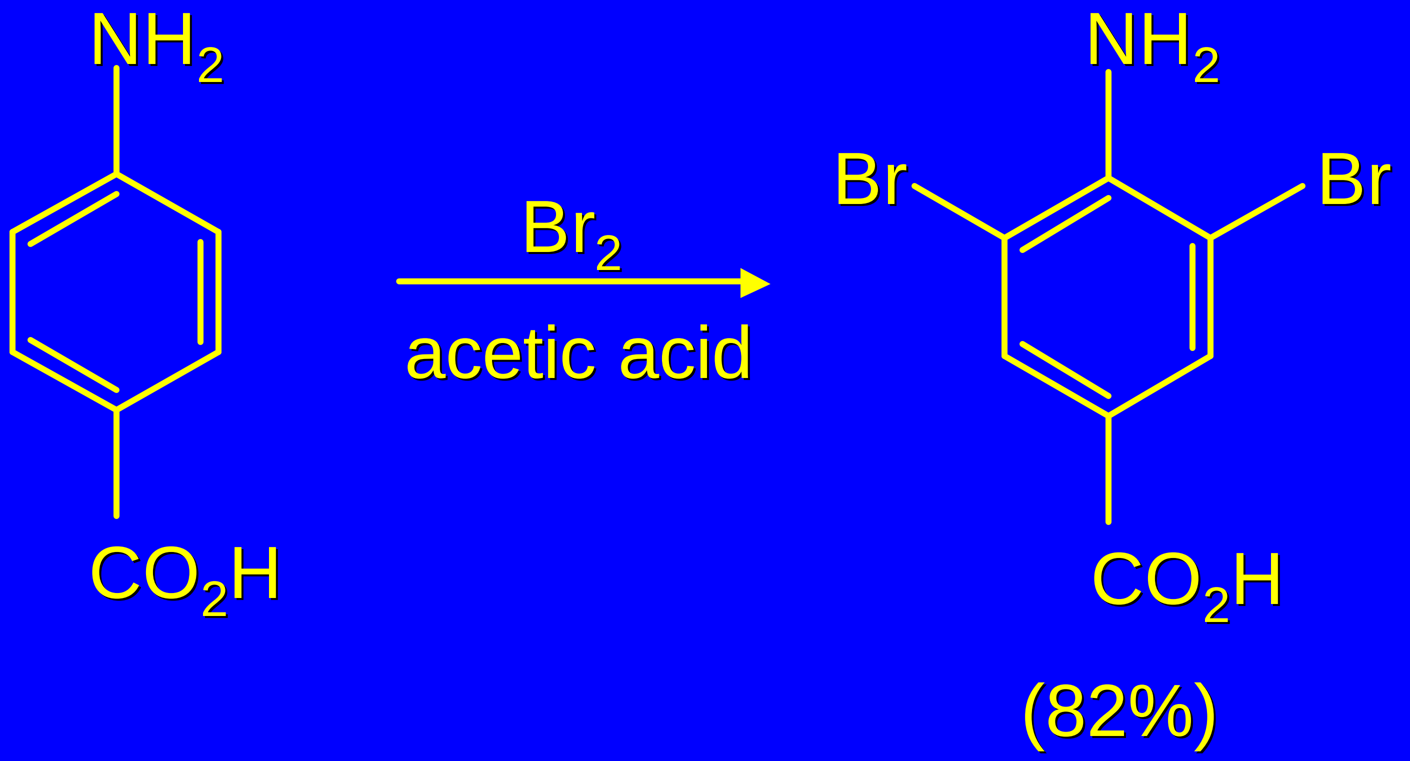
Strategy: remove the acyl group from the amide by hydrolysis



(100%)

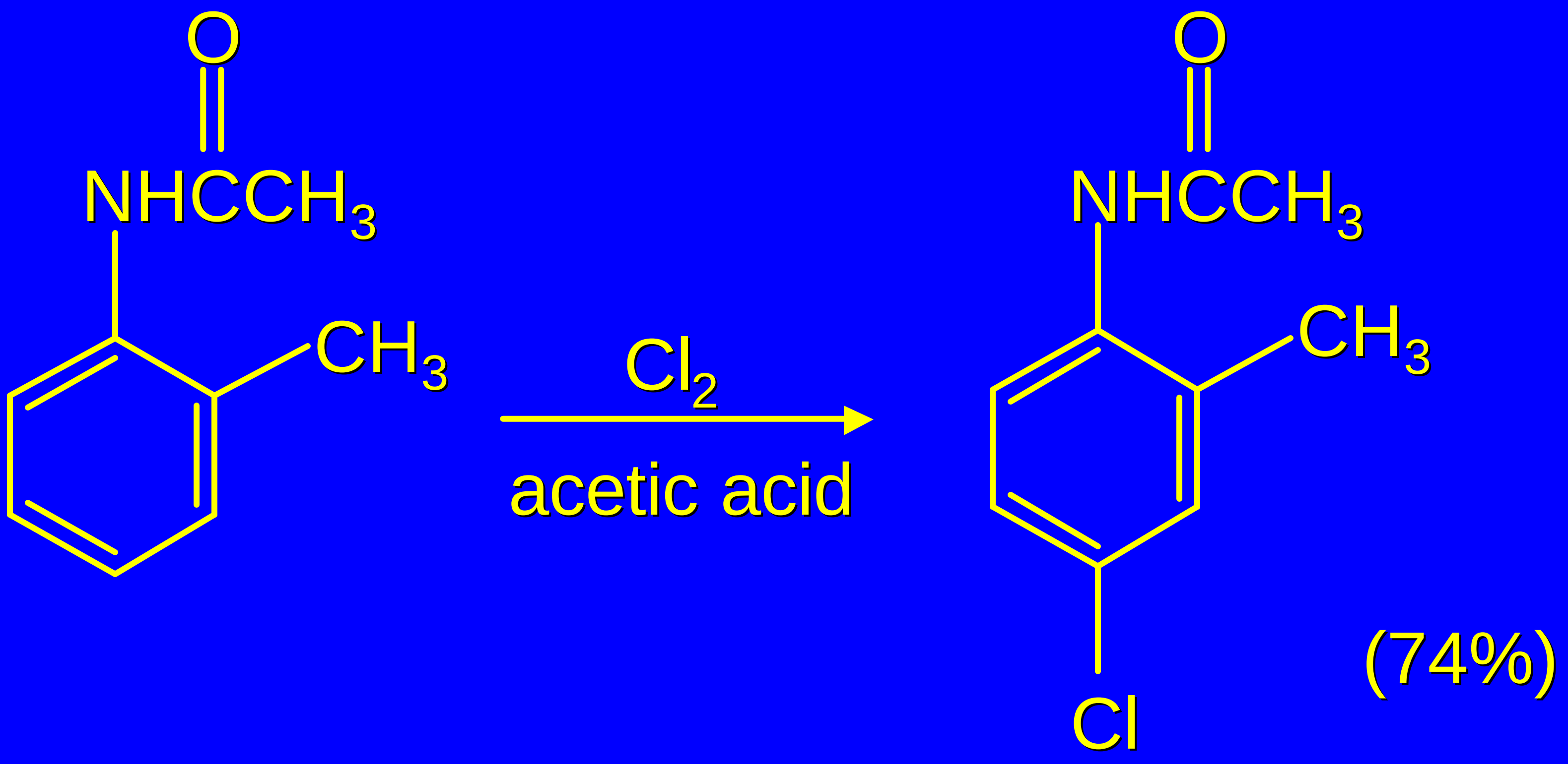
Halogenation of Arylamines

occurs readily without necessity of protecting amino group, but difficult to limit it to monohalogenation



Monohalogenation of Arylamines

Decreasing the reactivity of the arylamine by converting the NH_2 group to an amide allows halogenation to be limited to monosubstitution



Friedel-Crafts Reactions

The amino group of an arylamine must be protected as an amide when carrying out a Friedel-Crafts reaction.