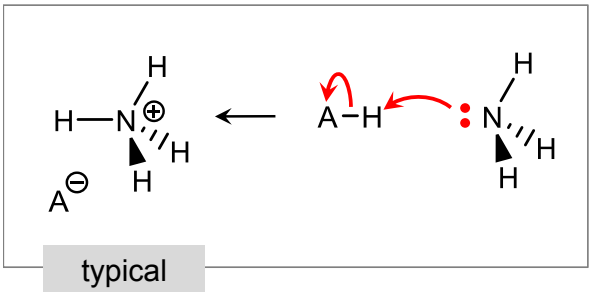
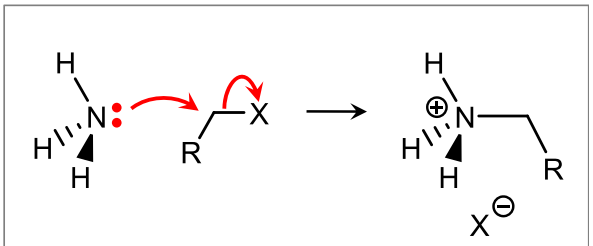
Amines Are Good Bases and Nucleophiles

as a base:

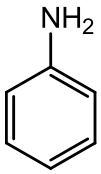


typical pK_a ≈ 10

as a nucleophile:



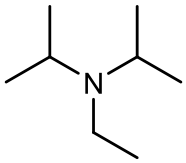
Conjugation decreases basicity and nucleophilicity.



conjugate acid pK_a = 5

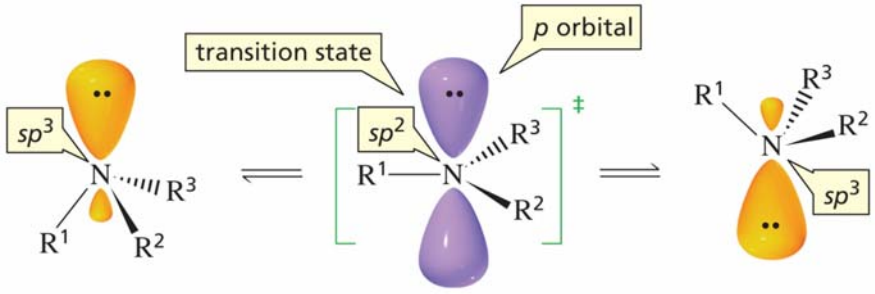
less basic than alkyl amines, but still more basic than H_2O.

Steric hindrance decreases nucleophilicity (but not basicity).



Example:
Hünig's base.
Reacts only by E2, not S_N2.

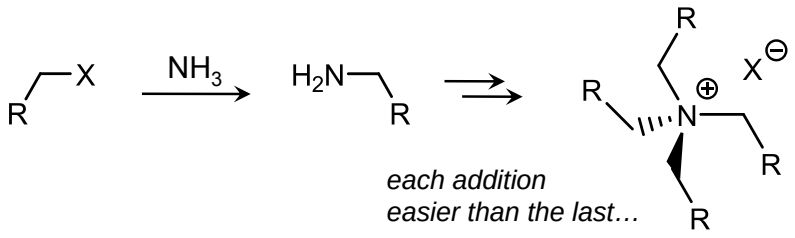
Rapid Amine Inversion



E_a = 6 kcal/mol.

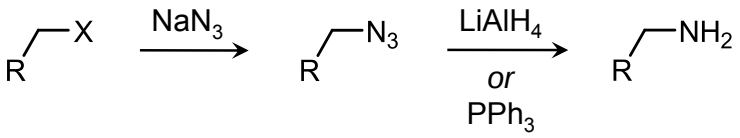
So, even though each conformation is chiral, the chiral conformers can't be isolated.

Synthesis of Primary Amines



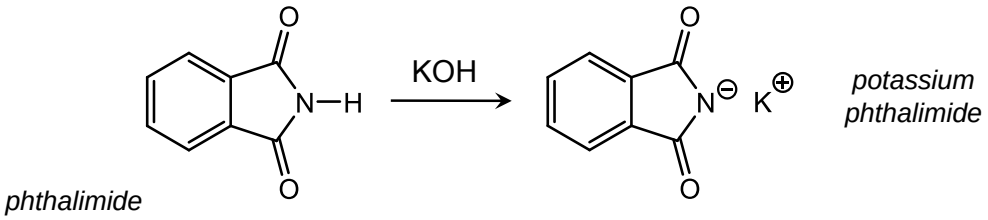
Simple nucleophilic substitution with NH_3 leads to multiple alkylation of nitrogen.
(Can address this somewhat by using excess NH_3.)

Alternative: Reduction of alkyl azides.

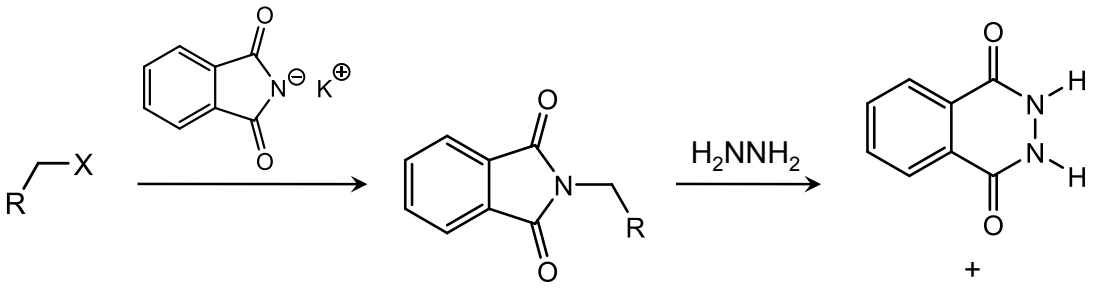


Amine is not in contact with alkylating agent, so no multiple alkylation.

The Gabriel Synthesis

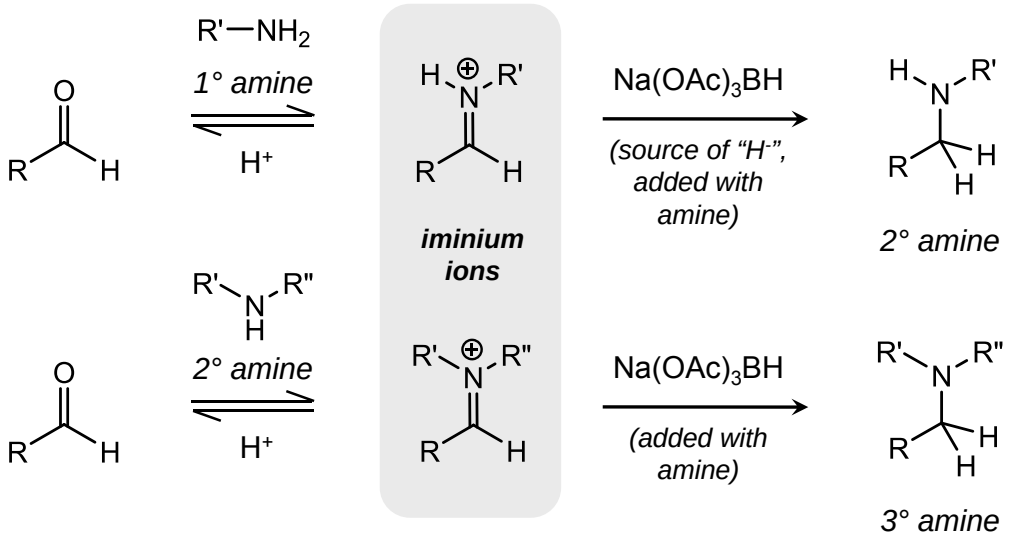


phthalimide



Again, yields primary amines without multiple alkylation.

Secondary and Tertiary Amines from Iminium Salts



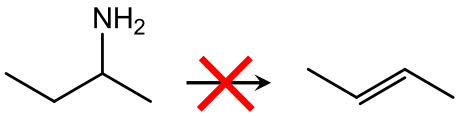
Successful even if iminium ion is unstable.

Requires reducing agent strong enough to reduce imine/iminium, but not strong enough to reduce initial aldehyde or ketone.

Converting Amines to Alkenes: Hofmann Elimination

Amines aren't eliminated directly by E2 or E1; $^{-}NH_2$ and NH_3 are both poor leaving groups.

But, amines can be *converted* into good leaving groups for elimination.



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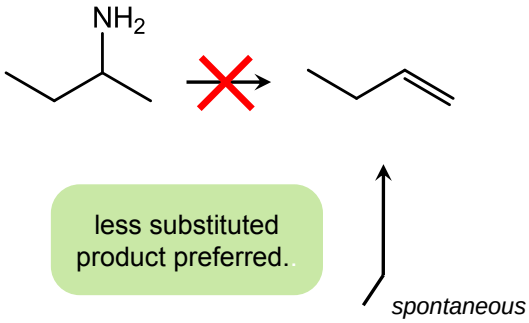

Hofmann elimination: