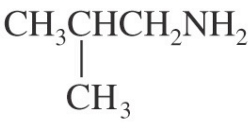
Aminak

♦ Nomenklatura

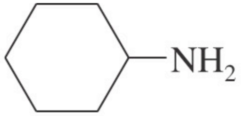
- ➨ *Amina primarioak* izendatzerakoan alkonaren –O atzizkia kendu eta –AMINA eransten da
- ➨ Izenda daitezke baita ere *alkil amina* bezela

CH_3NH_2
Methylamine
(methanamine)

$CH_3CH_2NH_2$
Ethylamine
(ethanamine)



$CH_3\underset{\substack{|\\ CH_3}}{C}HCH_2NH_2$
Isobutylamine
(2-methyl-1-propanamine)



Cyclohexylamine
(cyclohexanamine)

- ➨ *Amina sekundario* eta *tertziarioetan* erradikal organikoari *amina* atzizkia eransten zaio; batzuetan *N*-aurrizkia erabiliz

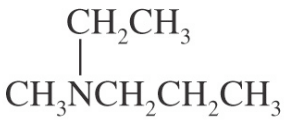
$CH_3NHCH_2CH_3$
Ethylmethylamine
(*N*-methylethanamine)

$(CH_3CH_2)_2NH$
Diethylamine
(*N*-ethylethanamine)

$(CH_3CH_2)_3N$

Triethylamine

(*N*,*N*-diethylethanamine)



$CH_3N(CH_2CH_3)CH_2CH_2CH_3$

Ethylmethylpropylamine

(*N*-ethyl-*N*-methyl-1-propanamine)

➡ **IUPAC-en arabera -NH_2 taldeari *amino* deitzen zaio ordezkatzaile moduan**

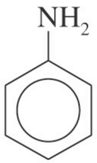
$H_2NCH_2CH_2OH$

2-Aminoethanol

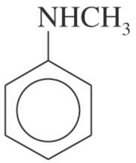
$H_2NCH_2CH_2COOH$

3-Aminopropanoic acid

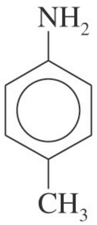
- **Aril Aminak**



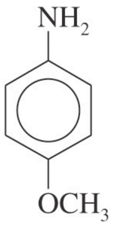
Aniline
(benzenamine)



***N*-Methylaniline**
(*N*-methyl-benzenamine)

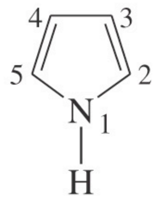


***p*-Toluidine**
(4-methyl-benzenamine)

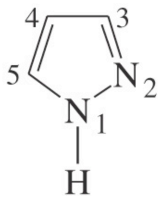


***p*-Anisidine**
(4-methoxy-benzenamine)

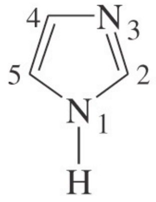
- **Amina Heteroziklikoak**



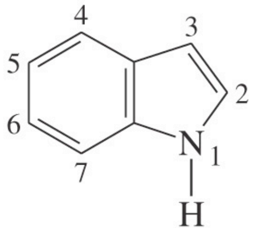
Pyrrole
(1-azacyclopenta-2,4-diene)



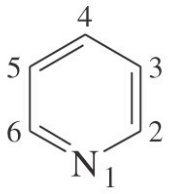
Pyrazole
(1,2-diazacyclopenta-2,4-diene)



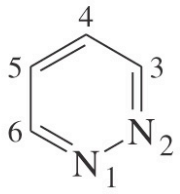
Imidazole
(1,3-diazacyclopenta-2,4-diene)



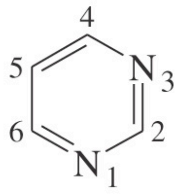
Indole
(1-azaindene)



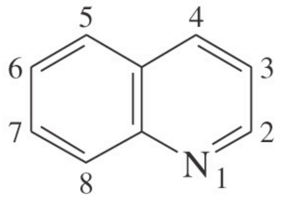
Pyridine
(azabenzene)



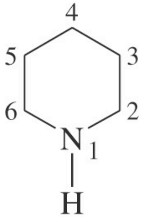
Pyridazine
(1,2-diazabenzene)



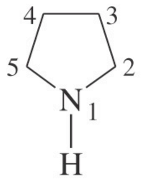
Pyrimidine
(1,3-diazabenzene)



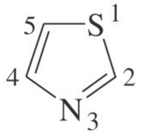
Quinoline
(1-azanaphthalene)



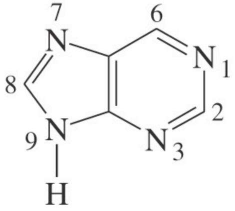
Piperidine
(azacyclohexane)



Pyrrolidine
(azacyclopentane)



Thiazole
(1-thia-3-azacyclopenta-2,4-diene)



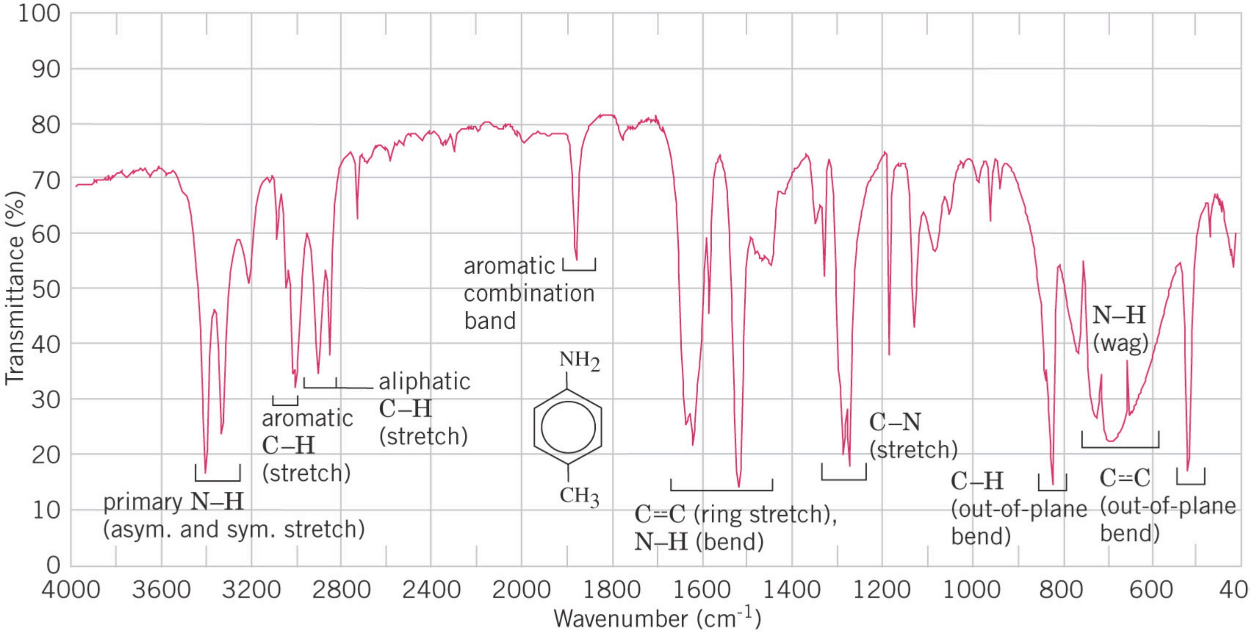
Purine

♦ Aminen Propietate Fisikoak

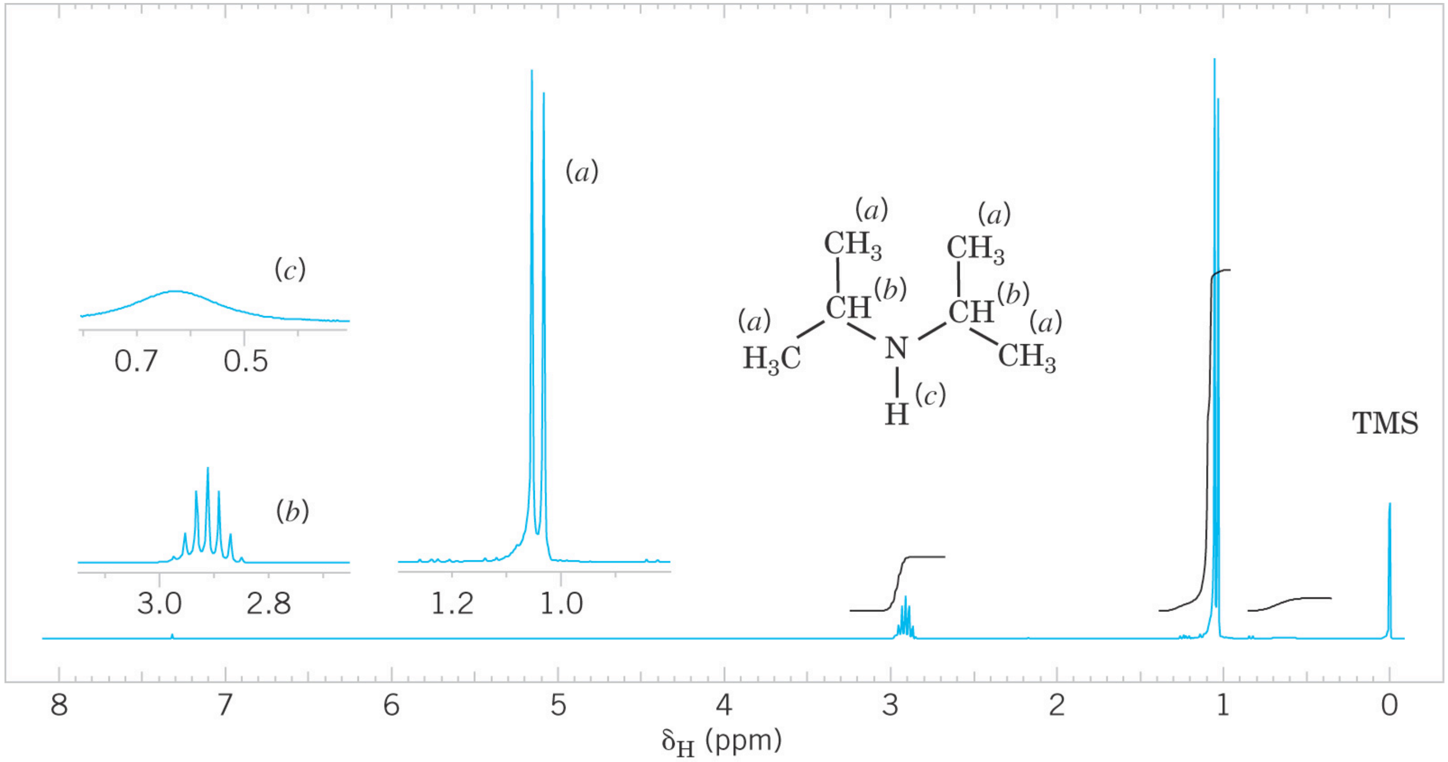
- ➡ Primarioek eta sekundarioek hidrogeno-loturak ematen dituzte
- ➡ Tertziarioek ere eman ditzateke, baina hartzaile bezela bakarrik, urarekin adibidez
- ➡ Pisu molekular bajukoak uretan nahaskorrak dira

Name	Structure	mp (°C)	bp (°C)	Water Solubility (25°C) (g 100 mL^{-1})	pK_a (aminium ion)
Primary Amines					
Methylamine	CH_3NH_2	−94	−6	Very soluble	10.64
Ethylamine	$CH_3CH_2NH_2$	−81	17	Very soluble	10.75
Propylamine	$CH_3CH_2CH_2NH_2$	−83	49	Very soluble	10.67
Isopropylamine	$(CH_3)_2CHNH_2$	−101	33	Very soluble	10.73
Butylamine	$CH_3(CH_2)_2CH_2NH_2$	−51	78	Very soluble	10.61
Isobutylamine	$(CH_3)_2CHCH_2NH_2$	−86	68	Very soluble	10.49
sec-Butylamine	$CH_3CH_2CH(CH_3)NH_2$	−104	63	Very soluble	10.56
tert-Butylamine	$(CH_3)_3CNH_2$	−68	45	Very soluble	10.45
Cyclohexylamine	Cyclo-$C_6H_{11}NH_2$	−18	134	Slightly soluble	10.64
Benzylamine	$C_6H_5CH_2NH_2$	10	185	Slightly soluble	9.30
Aniline	$C_6H_5NH_2$	−6	184	3.7	4.58
p-Toluidine	*p*-$CH_3C_6H_4NH_2$	44	200	Slightly soluble	5.08
p-Anisidine	*p*-$CH_3OC_6H_4NH_2$	57	244	Very slightly soluble	5.30
p-Chloroaniline	*p*-$ClC_6H_4NH_2$	73	232	Insoluble	4.00
p-Nitroaniline	*p*-$NO_2C_6H_4NH_2$	148	332	Insoluble	1.00
Secondary Amines					
Dimethylamine	$(CH_3)_2NH$	−92	7	Very soluble	10.72
Diethylamine	$(CH_3CH_2)_2NH$	−48	56	Very soluble	10.98
Dipropylamine	$(CH_3CH_2CH_2)_2NH$	−40	110	Very soluble	10.98
N-Methylaniline	$C_6H_5NHCH_3$	−57	196	Slightly soluble	4.70
Diphenylamine	$(C_6H_5)_2NH$	53	302	Insoluble	0.80
Tertiary Amines					
Trimethylamine	$(CH_3)_3N$	−117	2.9	Very soluble	9.70
Triethylamine	$(CH_3CH_2)_3N$	−115	90	14	10.76
Tripropylamine	$(CH_3CH_2CH_2)_3N$	−93	156	Slightly soluble	10.64
N,*N*-Dimethylaniline	$C_6H_5N(CH_3)_2$	3	194	Slightly soluble	5.06

- **Analisi Espektroskopikoa**
  - **IG**
    - ★ **Primarioetan eta sekundarioetan N-H dardarketa 3300-3555 cm $^{-1}$ tartean**
    - ★ **Primarioetan 2 (simetrikoa eta asimetrikoa) absortzio; sekundarioetan bakarra**

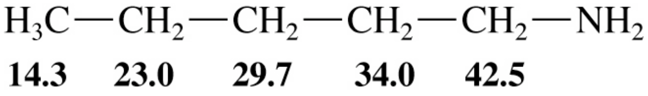


  - **^{1}H EMN**
    - ★ **1° eta 2°: akoplatu gabeko N-H seinale zabala δ 0.5-5 tartean**
    - ★ **N-H protoiek D_2O-rekin H-trukaketa: seinalea desagertuko da ^{1}H espektruan**
    - ★ **Nitrogenoaren alboko karbonoetako protiak δ 2.2-2.9 tartean**



➡ ^{13}C EMN

- ★ **Nitrogenoari lotutako karbonoak δ 20-70 tartean**



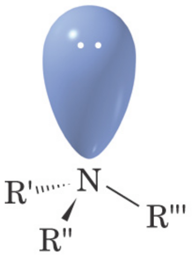
$H_3C-CH_2-CH_2-CH_2-CH_2-NH_2$

^{13}C NMR chemical shifts

♦ Aminen Egitura

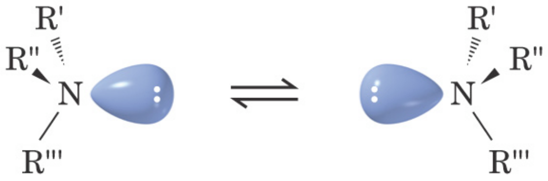
➡ **Nitrogenoak *sp*^{3} hibridazioa du**

- ★ Geometria *tetrahedrikoa* elektroi bikotea kontuan hartuz gero
- ★ Elektroiak ez diren hiru ordezkatzaileak bakarrik kontuan hartuz gero: *trigonal piramidala*
- ★ Karga negatibo partziala elektroi bikotearen inguruan



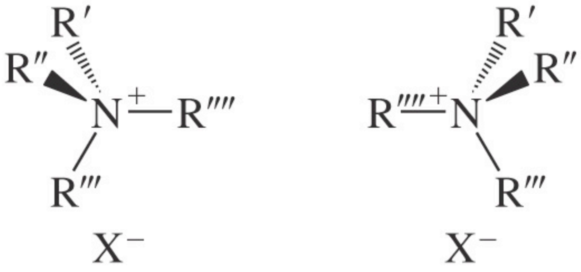
Structure of an amine

➡ **Amina kiralen bi forma enantiomerikoen arteko egitur-trukaketa oso azkarra da giro-tenperaturan (inbertsioa)**



Interconversion of amine enantiomers

- **Amonio gatzen enantiomeroak bai bana daitezke (erresoluzioa)**
  - **Amonio kuaternario gatz kiraletan nitrogenoak ezin du inbertsioa eman, elektroi bikotea falta bait du**



Quaternary ammonium salts such as these can be resolved.

♦ Aminen Basetasuna: Amina Gatzak

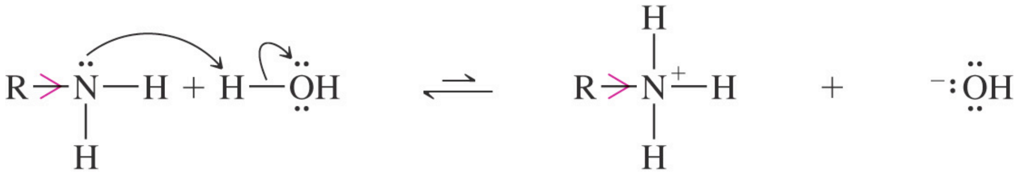
➨ **Aminak base ahulak dira (azido konjokatuak nahiko azidoak)**

$$R\overset{+}{N}H_3 + H_2O \rightleftharpoons RNH_2 + H_3O^+$$

$$K_a = \frac{[RHN_2][H_3O^+]}{[RNH_3{}^+]} \qquad pK_a = -\log K_a$$

➨ **Alkil amina primarioak amoniakoa baino basikoagoak dira**

	$\ddot{N}H_3$	$CH_3\ddot{N}H_2$	$CH_3CH_2\ddot{N}H_2$	$CH_3CH_2CH_2\ddot{N}H_2$
Conjugate acid pK_a	**9.26**	**10.64**	**10.75**	**10.67**



By releasing electrons, R→ stabilizes the alkylaminium ion through dispersal of charge.

- ➡ **Alkilo taldeek iminio katioia egonkortzen dute (gas fasean)**

$$(CH_3)_3N > (CH_3)_2NH > CH_3NH_2 > NH_3$$

- ➡ **Ur-disoluzioetan trimetil amina dimetil amina baino (eta metil amina baino) base ahulagoa da**
  - ★ **Iminio katioiak urarekin hidrogeno-loturak ematen ditu, egonkortuz**
  - ★ **Trimetiliminio katioiak hidrogeno bakar bat dauka hidrogeno-loturak eman ditzakena, eta beraz eraginkortasun gutxiagoz solbatatzen da**

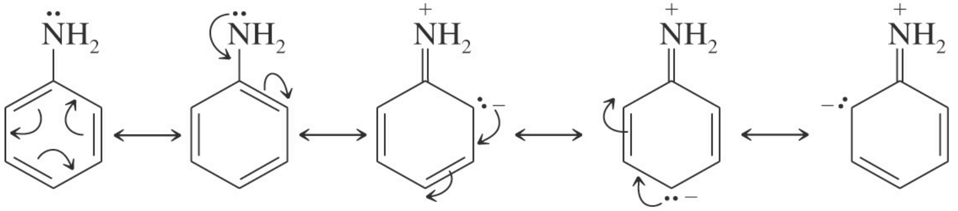
$$(CH_3)_2NH > CH_3NH_2 > (CH_3)_3N > NH_3$$

- # Aril Aminen Basetasuna

➡ Dagokien alkil aminekin alderatuz, base ahulagoak dira

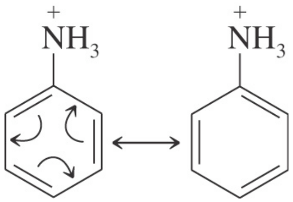
	Cyclo-$C_6H_{11}NH_2$	$C_6H_5NH_2$	*p*-$CH_3C_6H_4NH_2$
Conjugate acid pK_a	10.64	4.58	5.08

➡ Nitrogenoaren elektroi-bikotea eraztun aromatikoan zehar delokalizatu egiten da, eta protoia hartzeko joera gutxiago du

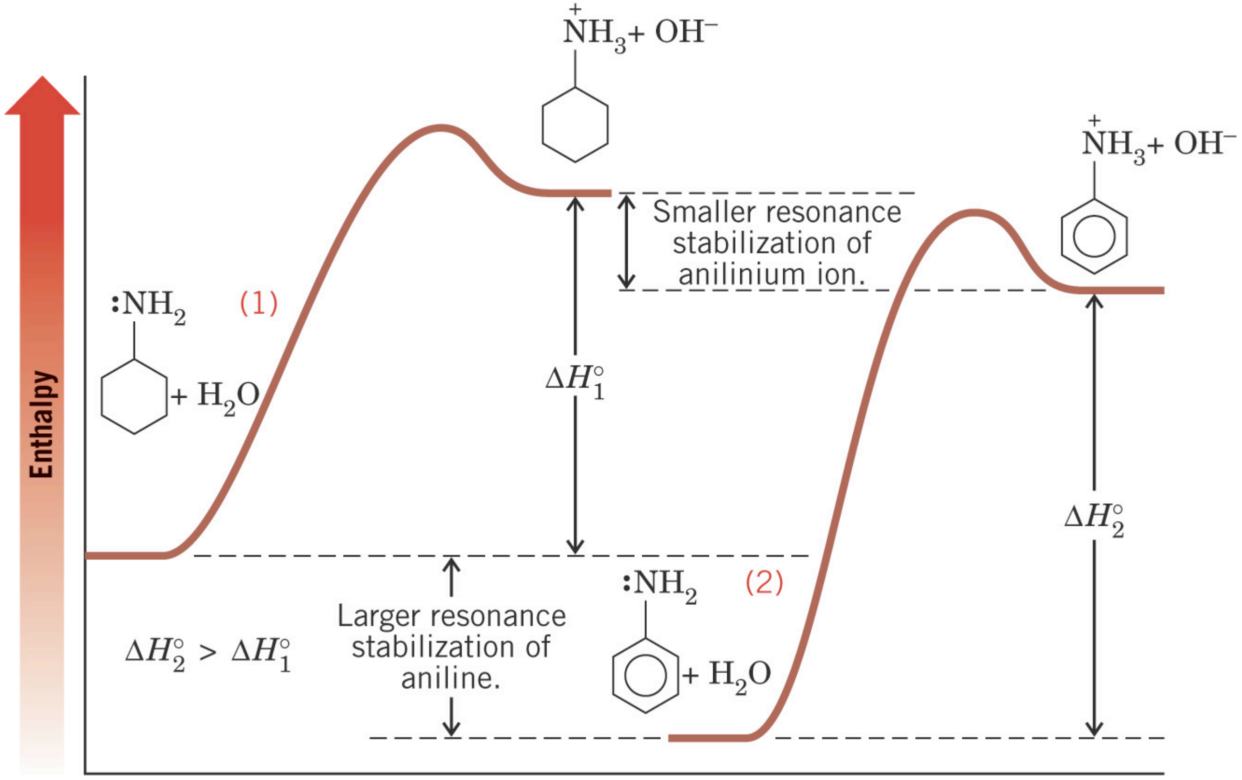


1 2 3 4 5

➡ Anilina protonatzea ere zailagoa da, behin protonatu ondoren aromatikoak diren bi erresonantzi egitura bakarrik ditu

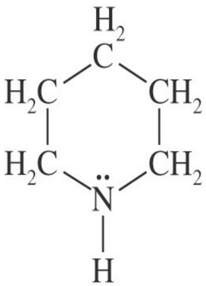
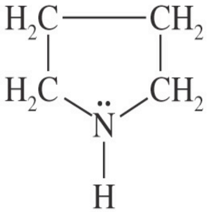
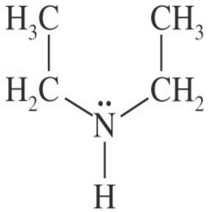


➡ Δ*H*º Balioak alderatuz anilina eta ziklohexil aminaren protonazioarentzat

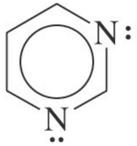
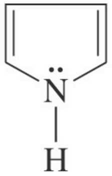
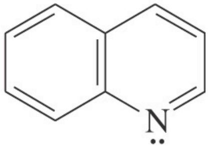


Amina Heteroziklikoen Basetasuna

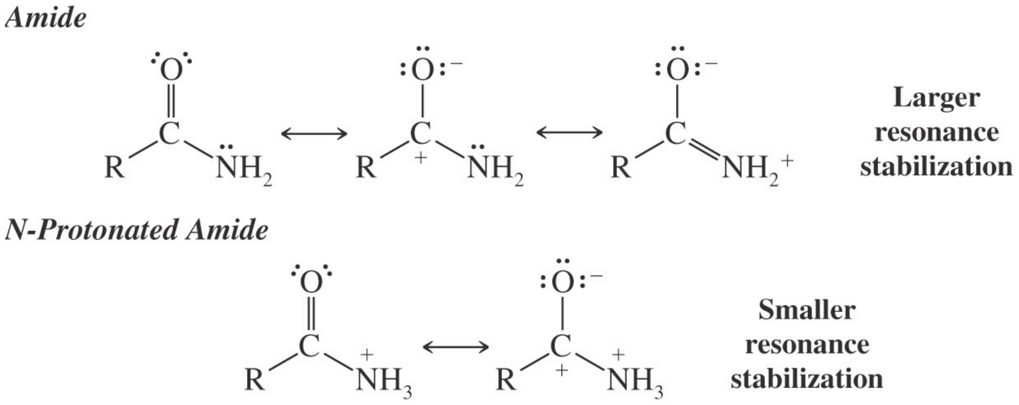
➡ Ez-aromatikoak (aziklikoen antzekoa)

			
	Piperidine	**Pyrrolidine**	**Diethylamine**
Conjugate acid pK_a	$pK_a = 11.20$	$pK_a = 11.11$	$pK_a = 10.98$

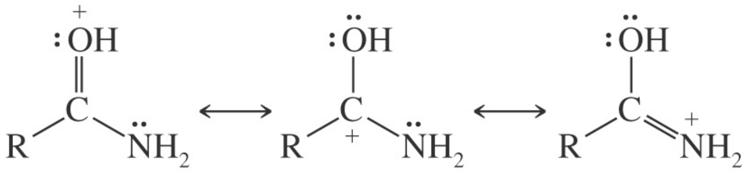
➡ Aromatikoak (ahulagoa)

				
	Pyridine	**Pyrimidine**	**Pyrrole**	**Quinoline**
Conjugate acid pK_a	$pK_a = 5.23$	$pK_a = 2.70$	$pK_a = 0.40$	$pK_a = 4.5$

- **Aminak versus Amidak**
  - ➡ **Amidak askoz ere base ahulagoak dira (*pKa* ia 0)**
  - ➡ **Amidak erresonantzi-egonkortzea dauka, protonatu ondoren ez**



  - ➡ **Amidetan, nitrogenoaren elektroi-bikotea delokalizaturik dago. Protonazioa oxigenoan ematen da**



Aminium Gaztak eta Amonio Kuaternarioak

- **Aminen protonazioz aminio gatzak sortzen dira**
  - **Aminium gatzak gutxienez hidrogeno bat daramate nitogenongan**

$$CH_3CH_2\ddot{N}H_2 + HCl \xrightarrow[H_2O]{} CH_3CH_2\overset{+}{N}H_3\ Cl^-$$

Ethylaminium chloride
(an aminium salt)

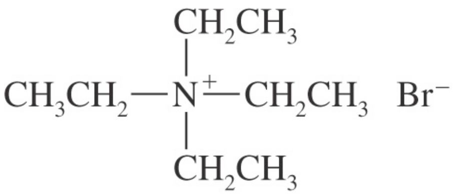
$$(CH_3CH_2)_2\ddot{N}H + HBr \xrightarrow[H_2O]{} (CH_3CH_2)_2\overset{+}{N}H_2\ Br^-$$

Diethylaminium bromide

$$(CH_3CH_2)_3\ddot{N} + HI \xrightarrow[H_2O]{} (CH_3CH_2)_3\overset{+}{N}H\ I^-$$

Triethylaminium iodide

- **Amonio kuaternarioek lau talde dauzkate nitrogenongan (hidrogenorik ez)**



$$CH_3CH_2-\overset{CH_2CH_3}{\underset{CH_2CH_3}{N^+}}-CH_2CH_3\quad Br^-$$

Tetraethylammonium bromide
(a quaternary ammonium salt)

- **Amonio kuaternarioen haluroak ez dira azidoak.**
- **Amonio kuaternarioen hidroxidoak basikoak dira, hidroxiloa dutelako**

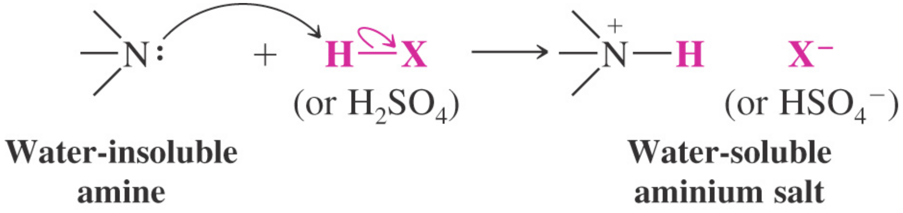
$(CH_3CH_2)_4N\,Br^-$

Tetraethylammonium bromide
(does not undergo reaction with acid)

$$(CH_3)_4\overset{+}{N}\,OH^- + HCl \longrightarrow (CH_3)_4\overset{+}{N}\,Cl^- + H_2O$$

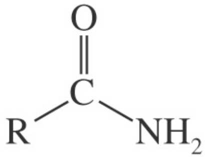
Uretako Disolbagarritasuna

- Hainbat aminio kloruro, bromuro, ioduro eta sulfato disolbagarriak dira
  - Uretan disolbatzen ez diren aminak sarritan azido diluituan disolbagarriak dira



- Erabilera azido/base erauzketetan

- Amidak, baseak ez direnez, normalean ez dira disolbagarriak azido diluituetan



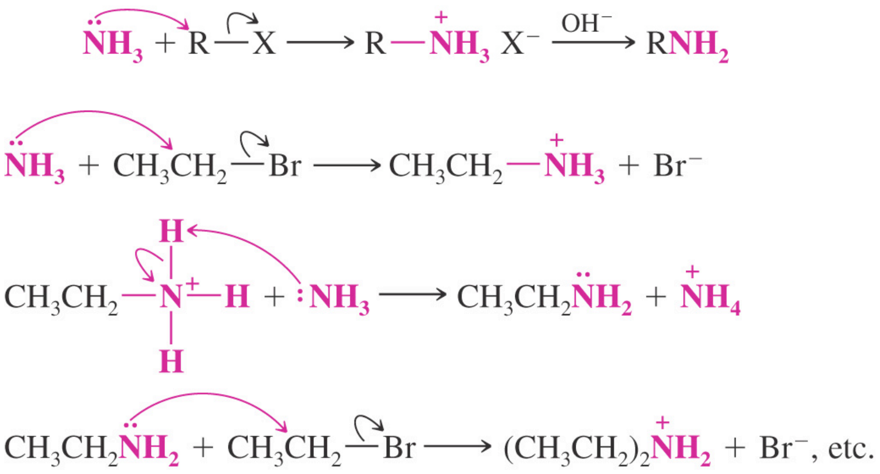
Water-insoluble amide
(not soluble in aqueous acids)

♦ Aminen Lorpena

● Ordezkapen Nukleozaleren Bidez

➡ Amoniakoren alkilazioa

- ★ **Mugak: polialkilazio nahasteak**



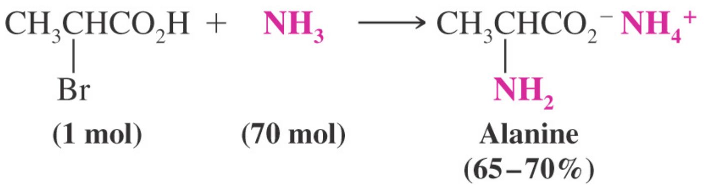
$$\ddot{N}H_3 + R{-}X \longrightarrow R{-}\overset{+}{N}H_3\ X^- \xrightarrow{OH^-} RNH_2$$

$$\ddot{N}H_3 + CH_3CH_2{-}Br \longrightarrow CH_3CH_2{-}\overset{+}{N}H_3 + Br^-$$

$$CH_3CH_2{-}\overset{+}{N}H_3 + :NH_3 \longrightarrow CH_3CH_2\ddot{N}H_2 + \overset{+}{N}H_4$$

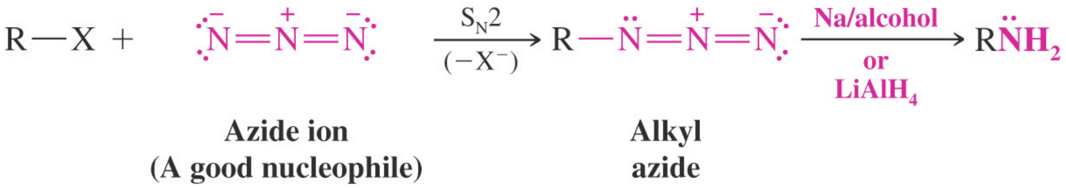
$$CH_3CH_2\ddot{N}H_2 + CH_3CH_2{-}Br \longrightarrow (CH_3CH_2)_2\overset{+}{N}H_2 + Br^-, \text{etc.}$$

- ★ **Amoniakoren soberakin batek laguntzen du polialkilazioa ekiditzen**



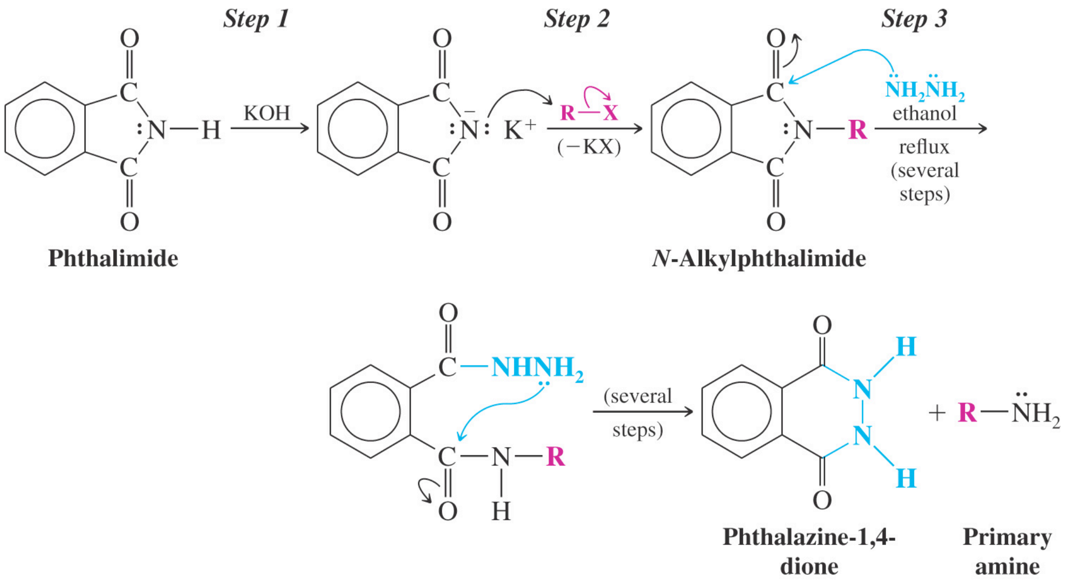
$$\underset{(1\ \text{mol})}{CH_3\underset{Br}{CH}CO_2H} + \underset{(70\ \text{mol})}{NH_3} \longrightarrow \underset{\substack{\textbf{Alanine}\\(65-70\%)}}{CH_3\underset{NH_2}{CH}CO_2^-\ NH_4^+}$$

➡ Azida Ioiaren Alkilazioa + Erredukzioa



➡ Gabriel-en Sintesia

- ★ **1. Urratsa: Potasio ftalimida alkilatu**
- ★ **2. Urratsa: Hidrazinarekin tratatu etanol beroan**



Amina Aromatikoak: Nitrokonposatuen Erredukzioa

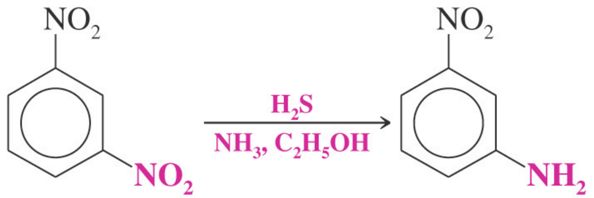
$$Ar{-}H \xrightarrow[H_2SO_4]{HNO_3} Ar{-}NO_2 \xrightarrow{[H]} Ar{-}NH_2$$

General Reaction

$$Ar{-}NO_2 \xrightarrow[\text{or (1) Fe, HCl (2) } OH^-]{H_2\text{, catalyst}} Ar{-}NH_2$$

Specific Example

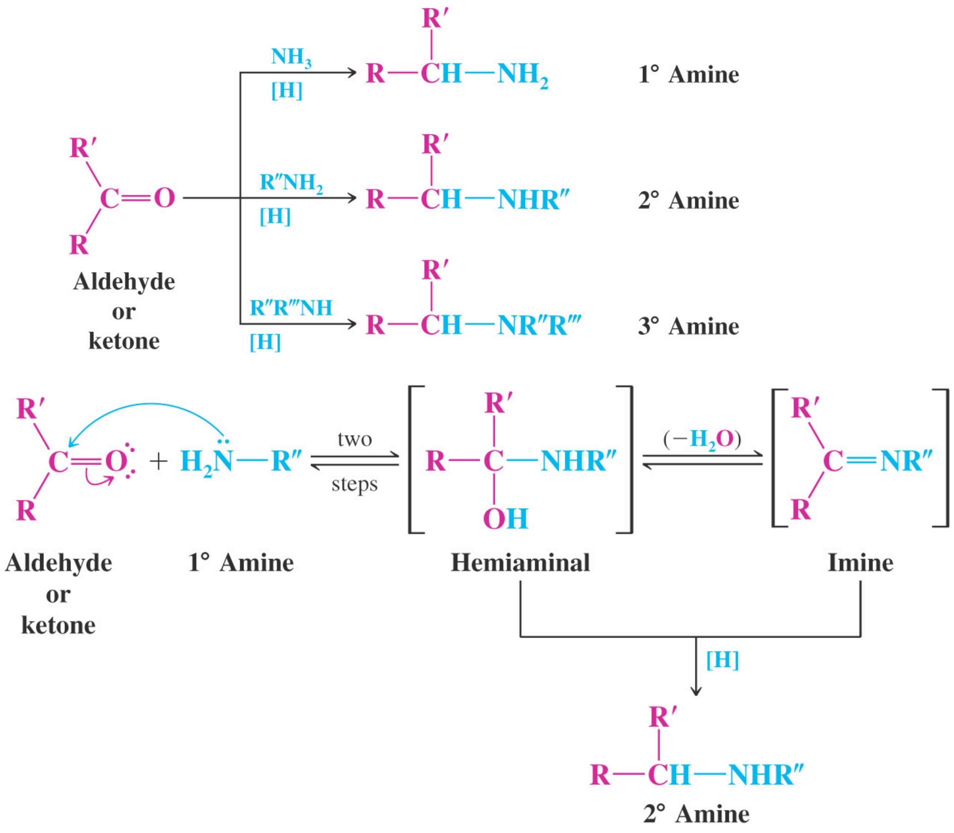
➡ **Bi nitro-tatik bakarra erreduzitu nahi dugunean: hidrogeno sulfurotik baliokide bakarra erabiliz**



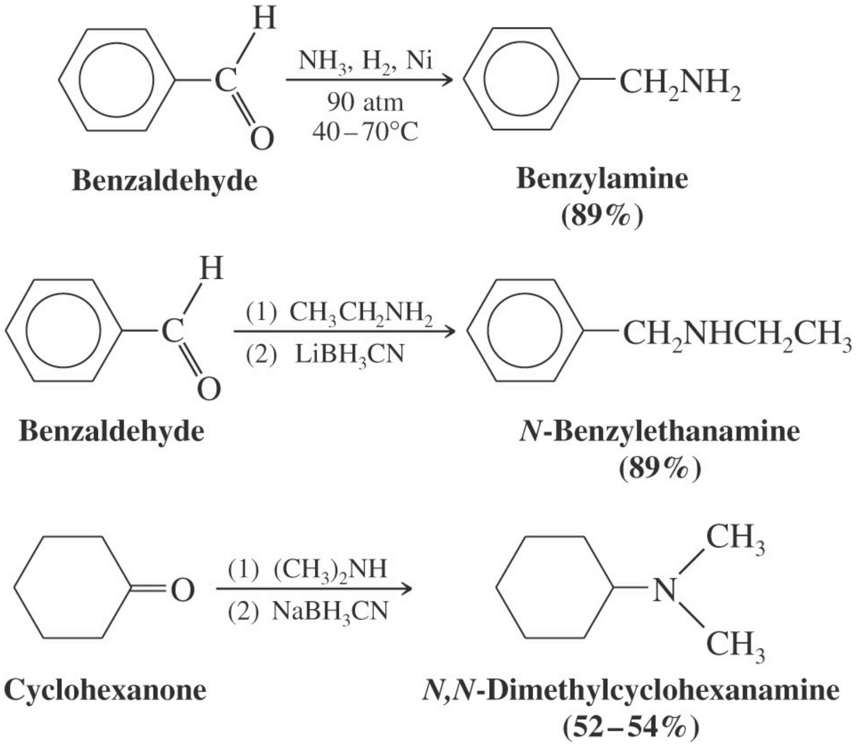
m-Dinitrobenzene

m-Nitroaniline
(70–80%)

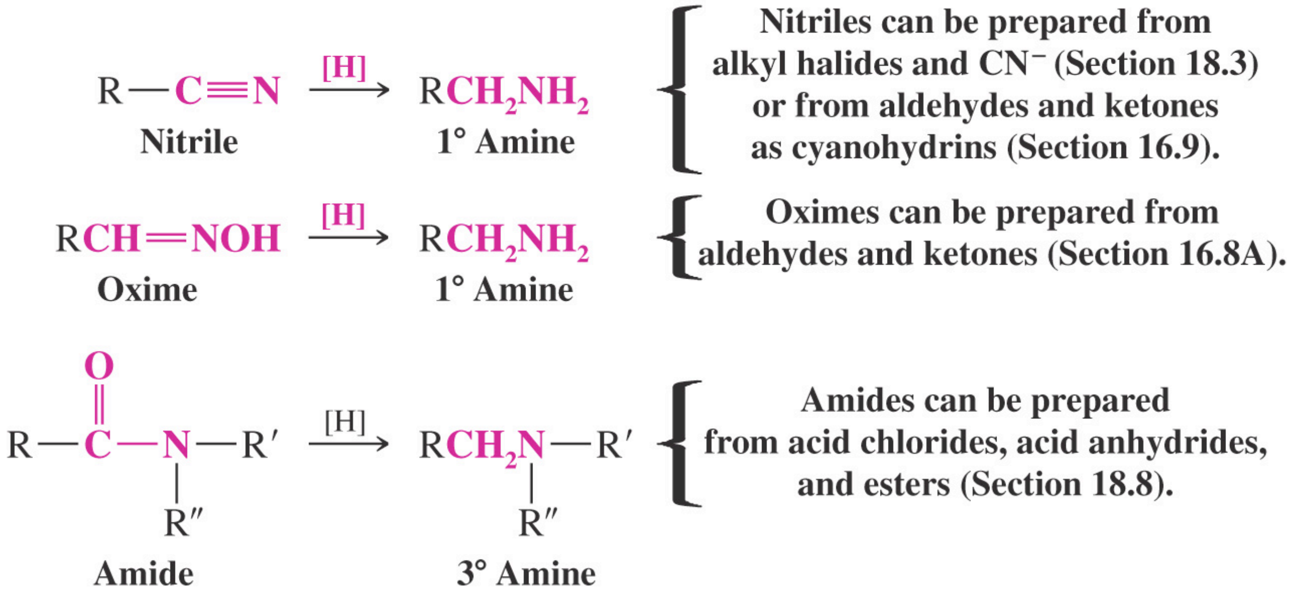
- **Aminazio Erreduzitzailea**
  - ➡ **Lehenik, aldehido edo zetonekin imina edo iminio ioia eman**
  - ➡ **Gero hauek erreduzitu**



- ➡ **Erredukziorako hidrogeno gasa eta katalizatzailea erabil dezakegu, edo-ta erreduzitzaile kimikoa ($NaBH_3CN$, $LiBH_3CN$)**



- **Nitrilo, Oxima eta Amiden Erredukzioz**
  - ➡ **Nitrilo eta oximen erredukzioz amina primarioak**
  - ➡ **Amiden erredukzioz amina primario, sekundario edo tertziarioak**



$$R-C\equiv N \xrightarrow{[H]} RCH_2NH_2$$

Nitrile → 1° Amine

Nitriles can be prepared from alkyl halides and CN^- (Section 18.3) or from aldehydes and ketones as cyanohydrins (Section 16.9).

$$RCH=NOH \xrightarrow{[H]} RCH_2NH_2$$

Oxime → 1° Amine

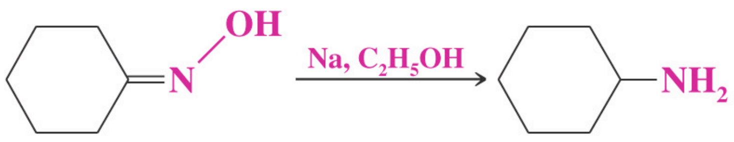
Oximes can be prepared from aldehydes and ketones (Section 16.8A).

$$R-\overset{O}{\overset{\|}{C}}-\underset{R''}{\underset{|}{N}}-R' \xrightarrow{[H]} RCH_2\underset{R''}{\underset{|}{N}}-R'$$

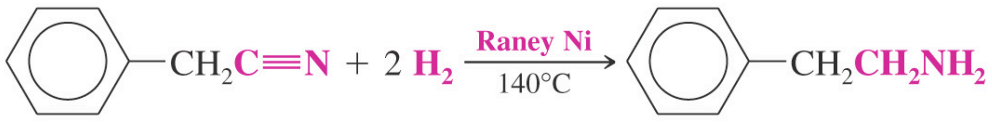
Amide → 3° Amine

Amides can be prepared from acid chlorides, acid anhydrides, and esters (Section 18.8).

- Hidrogenazio katalitikoa, nahiz erredkzio kimikoa ($LiAlH_4$)

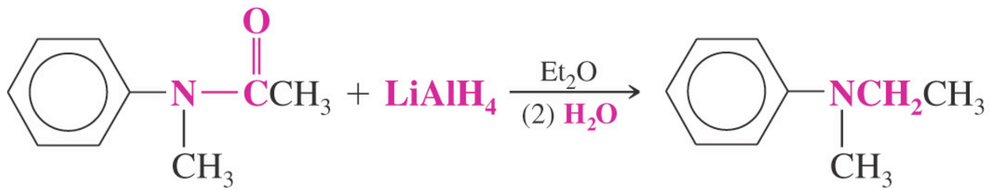


(50–60%)



2-Phenylethanenitrile
(phenylacetonitrile)

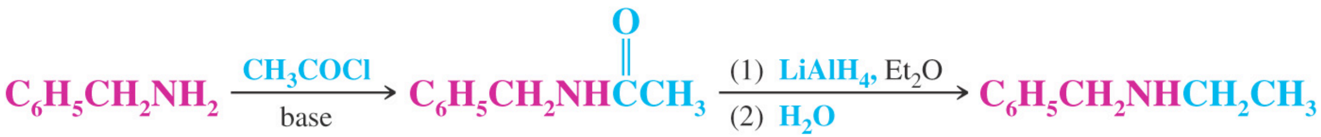
2-Phenylethanamine
(71%)



N-Methylacetanilide

N-Ethyl-*N*-methylaniline

- Amina monoalkilatua lor daiteke azilatuz eta gero amida erreduzituz

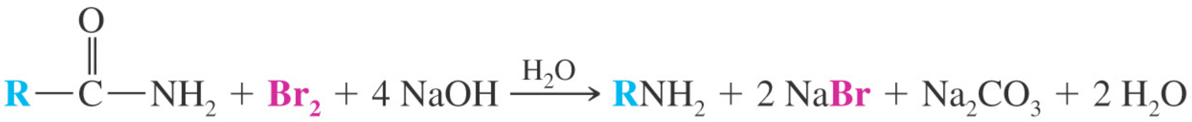


$$C_6H_5CH_2NH_2 \xrightarrow[\text{base}]{CH_3COCl} C_6H_5CH_2NH\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[(2)\ H_2O]{(1)\ LiAlH_4,\ Et_2O} C_6H_5CH_2NHCH_2CH_3$$

Benzylamine

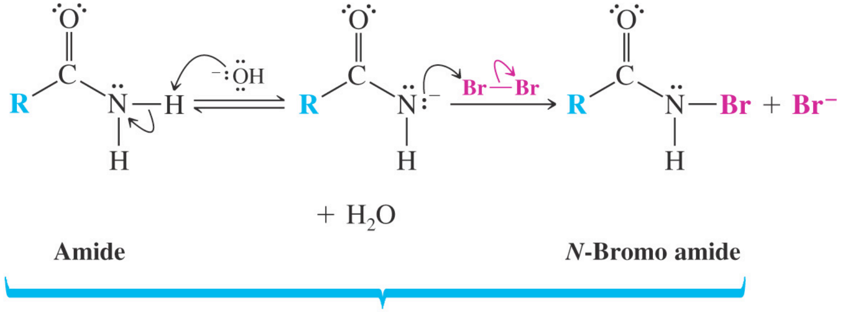
Benzylethylamine

- **Amina Primarioak Hofmann eta Curtius-en Transposizioen Bidez**
  - **Amida ordezkatugabeak karboniloa gal dezake (*Hofmann-en transposizioa edo degradazioa)***

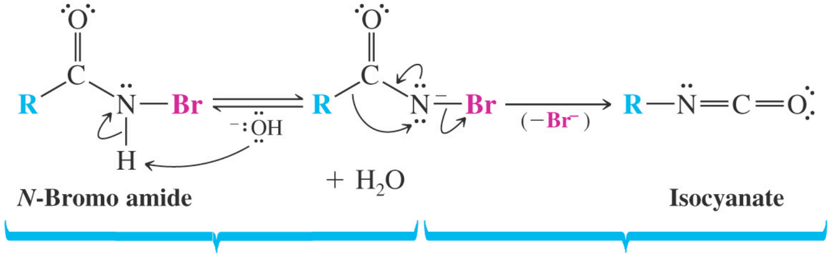


$$\mathrm{R-\overset{O}{\overset{\|}{C}}-NH_2 + Br_2 + 4\,NaOH \xrightarrow{H_2O} RNH_2 + 2\,NaBr + Na_2CO_3 + 2\,H_2O}$$

  - **Lehen urratsean amida *N*-bromatu egiten da**
    - ★ **Gero deprotonatu eta isozianatoa ematen du transposizioz**
    - ★ **Isozianatoa hidrolizatu egiten da karbamatora, eta hau dekarboxilatu**

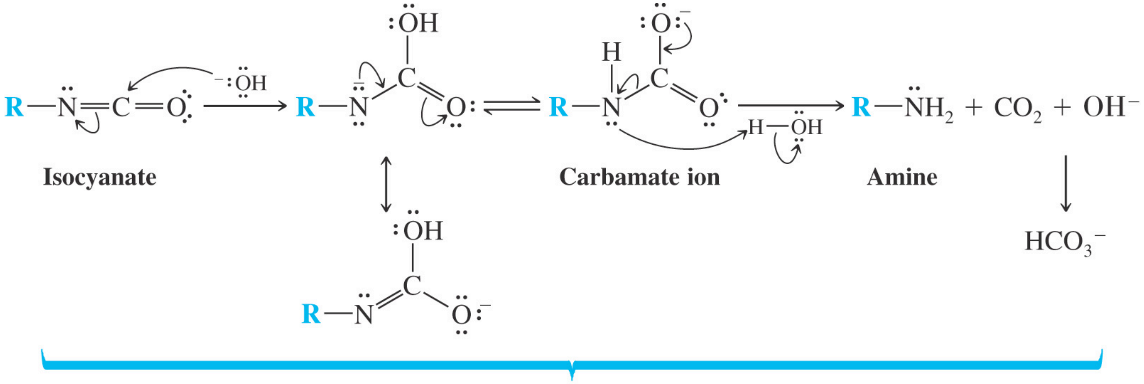


Base-promoted *N*-bromination of the amide occurs.



Base removes a proton from the nitrogen to give a bromo amide anion.

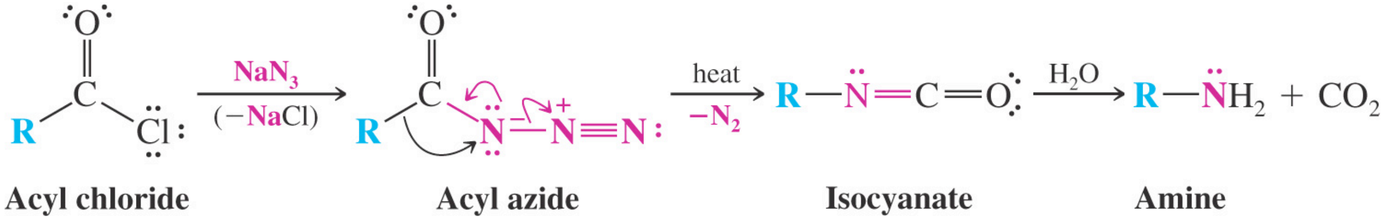
The R— group migrates to the nitrogen as a bromide ion departs. This produces an isocyanate.



The isocyanate undergoes hydrolysis and decarboxylation to produce the amine.

➡ ***Curtius-en transposizioan* azil azida batek hartzen du parte**

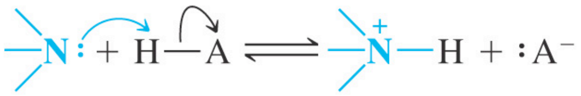
- ★ **Honek N_2 galtzen du eta isozianatoa eman**
- ★ **Azkenik hidrolisia eta dekarboxilazioa**



♦ Aminen Erreakzioak

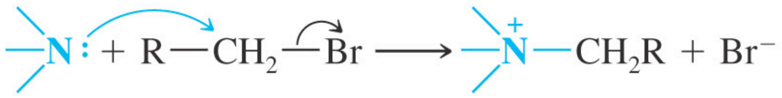
- **Nitrogenongan dagoen elektroi-bikotea da giltza: base izaera, nukleozale izaera**

Acid–Base Reactions



An amine acting as a base

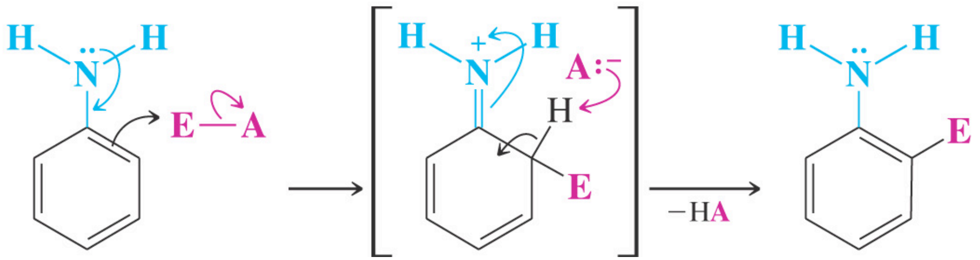
Alkylation

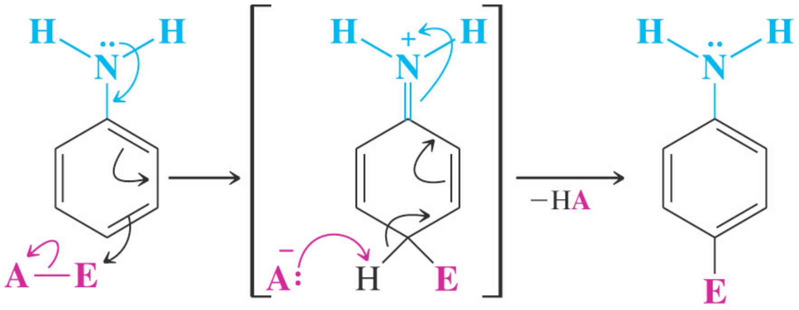


An amine acting as a nucleophile in an alkylation reaction

- **Erresonantziaren eraginez, nukleozalea karbono bat bihur daiteke**

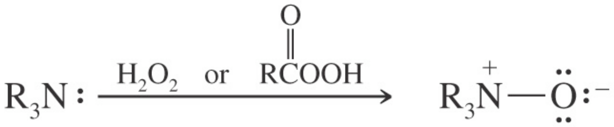
Electrophilic Aromatic Substitution





The amino group acting as an activating group and as an ortho–para director in electrophilic aromatic substitution

- **Aminen Oxidazioa**
  - ➡ **Amina primario eta sekundarioak erraz *N*-oxida daitezke, baina nahasteak lortzen dira eta ez da erabilgarria sintesian**
  - ➡ **Amina tertziarioek *N*-oxidazio garbia ematen dute**



$$R_3N: \xrightarrow{H_2O_2 \text{ or } R\overset{O}{\overset{\|}{C}}OOH} R_3\overset{+}{N}-\ddot{\underset{\cdot\cdot}{O}}:^-$$

A tertiary amine oxide

♦ Aminen Erreakzioa Azido Nitrosorekin

- **Azido nitrosoa (HONO) *in situ* prestatzen da sodio nitrito eta azido sendo batez**

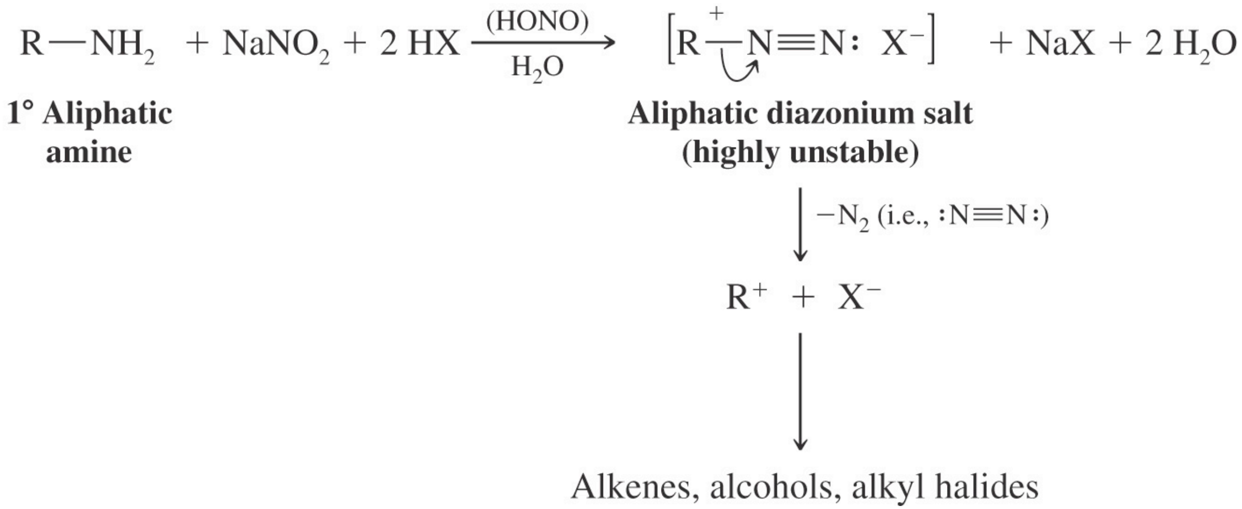
$$HCl_{(aq)} + NaNO_{2(aq)} \longrightarrow HONO_{(aq)} + NaCl_{(aq)}$$

$$H_2SO_4 + 2\ NaNO_{2(aq)} \longrightarrow 2\ HONO_{(aq)} + Na_2SO_{4(aq)}$$

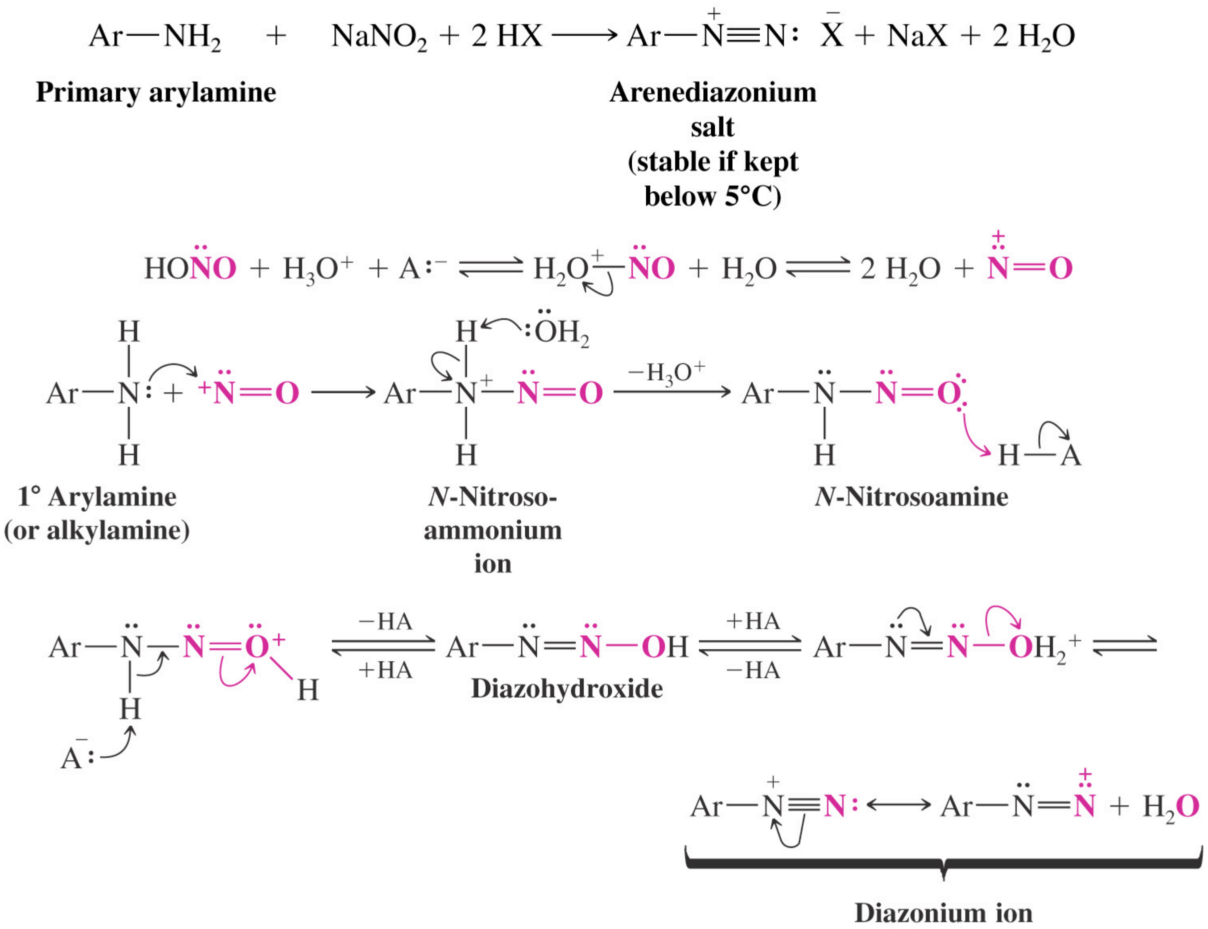
● Amina Primarioak Diazotatu Daitezke

- **Diazonio gatzak ezegonkorrak dira eta karbokatioia emanez dekonposatzen dira**
  - **Karbokatioiak zera eman dezake: alkenoa, alkohola, edo alkil haluroa**

General Reaction

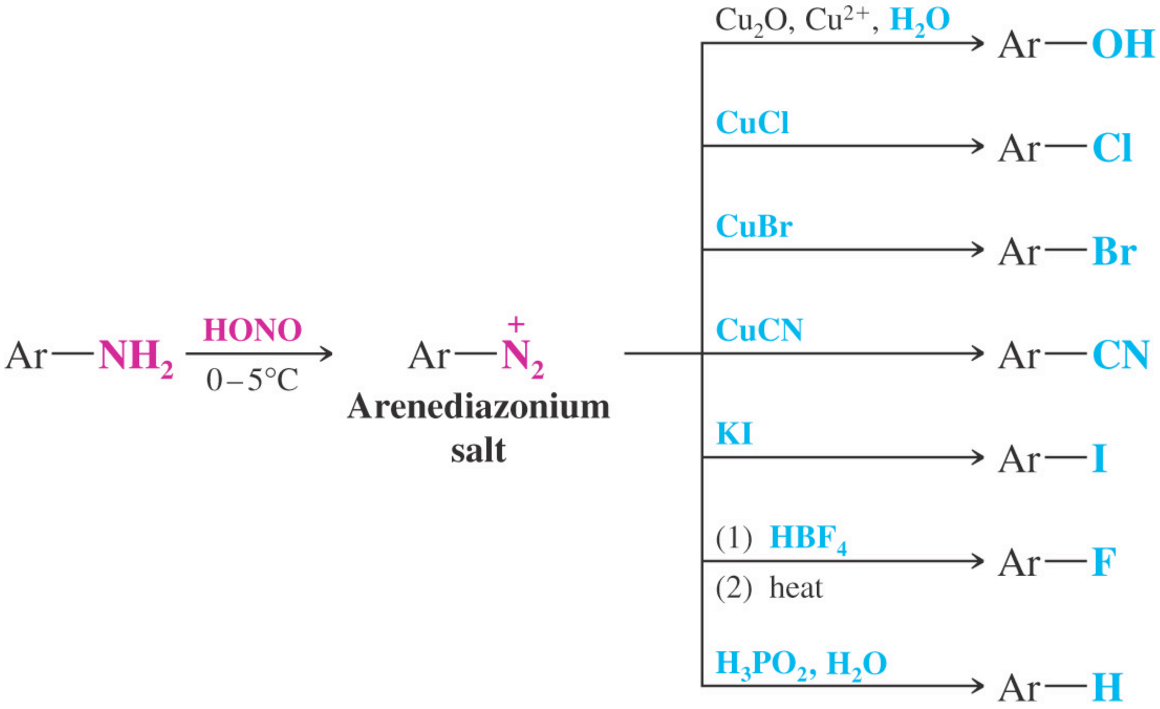


- **Aril Amina Primarioek Diazonio Gatz Egonkorragoak Ematen Dituzte**
  - ★ ***N*-nitrosoamina da sortzen den artekarietako bat**



♦ Arenodiazonio Gatzen Desplazamendu Erreakzioak

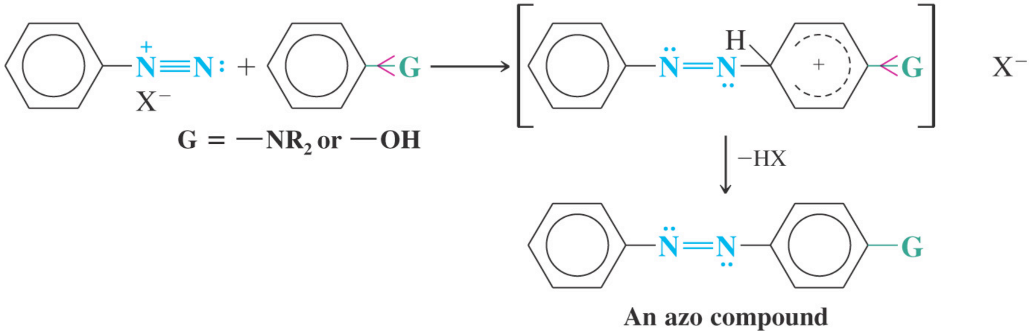
➡ Hainbat nukleozalek N_2+ taldea desplazatu dezake

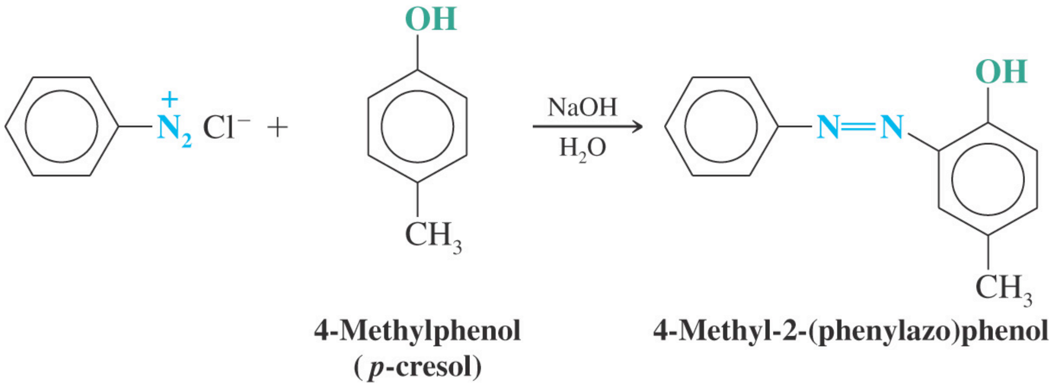


♦ Diazonio Gatzen Akoplamendu Erreakzioak

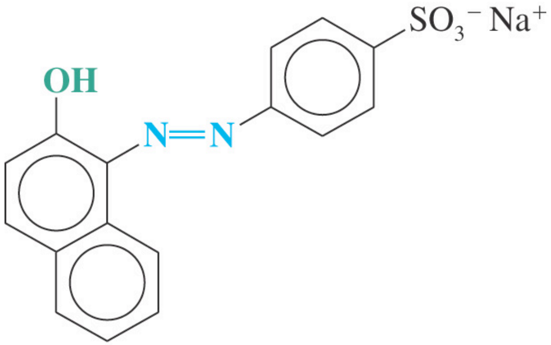
➡ **Gehien bat fenolekin eta aril amina tertziarioekin**

General Reaction





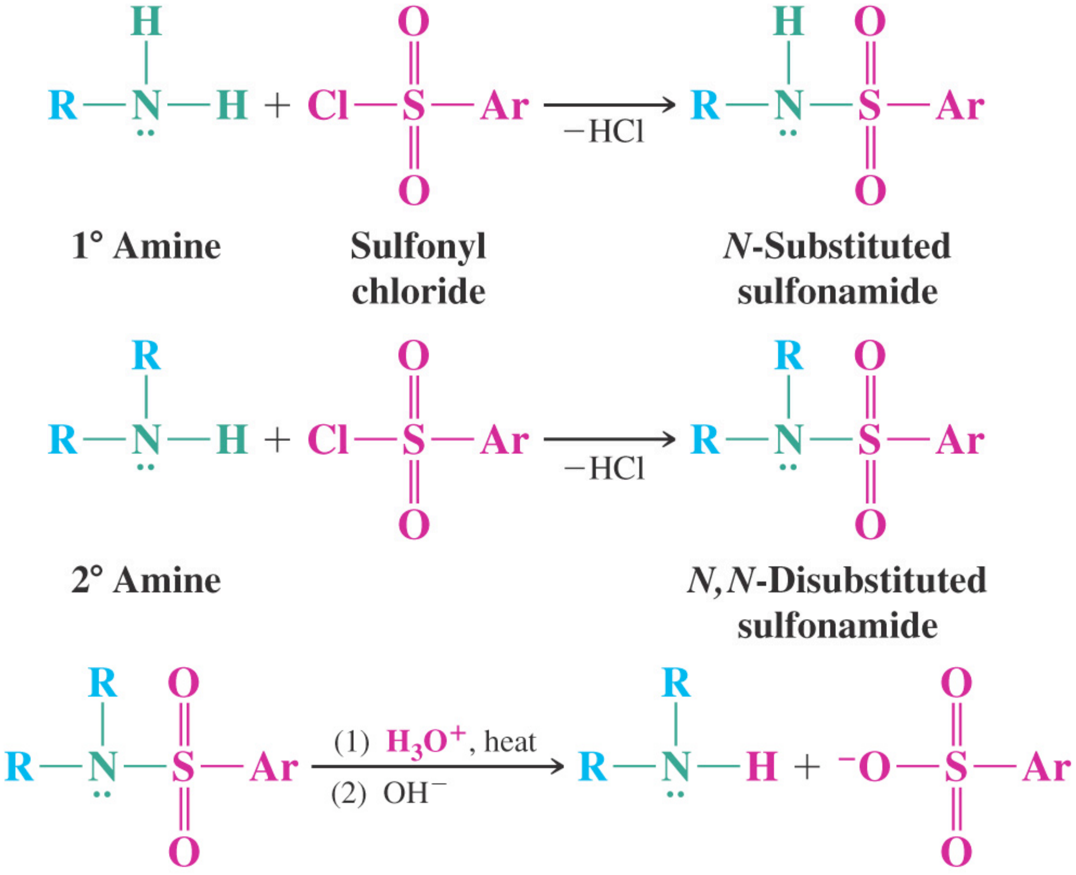
- ➡ Azo konposatuak oso erabiliak dira koloratzaile moduan aintzinatik
  - ★ Azo taldeak konjokazioa luzatzen du eta argiaren absortzio-maiztasuna txikitu
  - ★ $-SO_3^-Na^+$ Taldeak urekiko disolbagarritasuna haunditu eta itsaskortasuna kotoia edo artilea bezalako fibrekiko
  - ★ Adibidez Laranja II koloratzailea 2-naftoletik egiten da



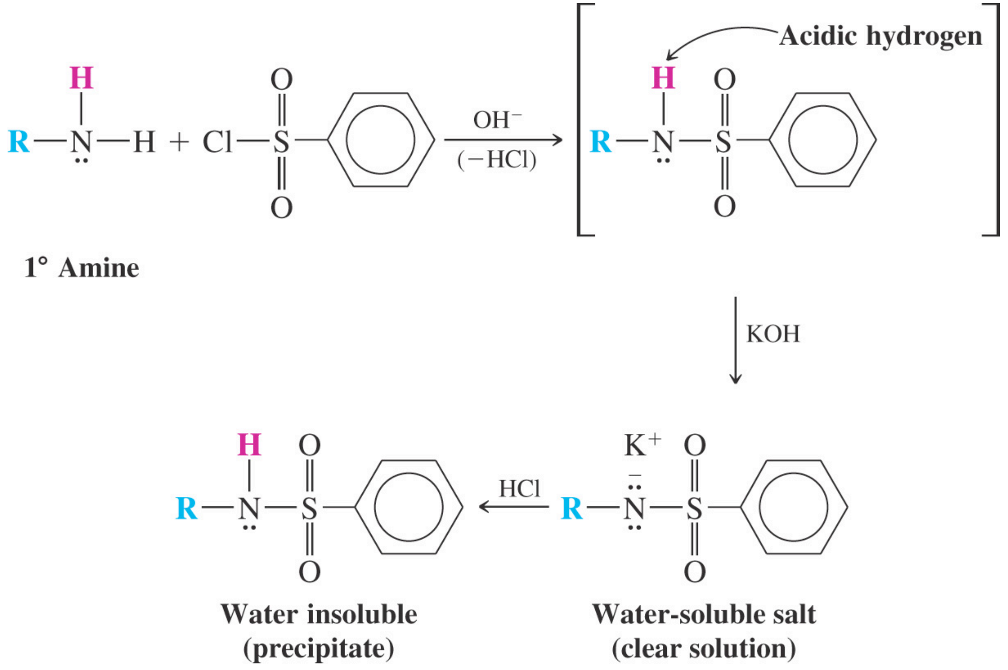
Orange II

◆ Aminen Erreakzioa Sulfonil Kloruroekin

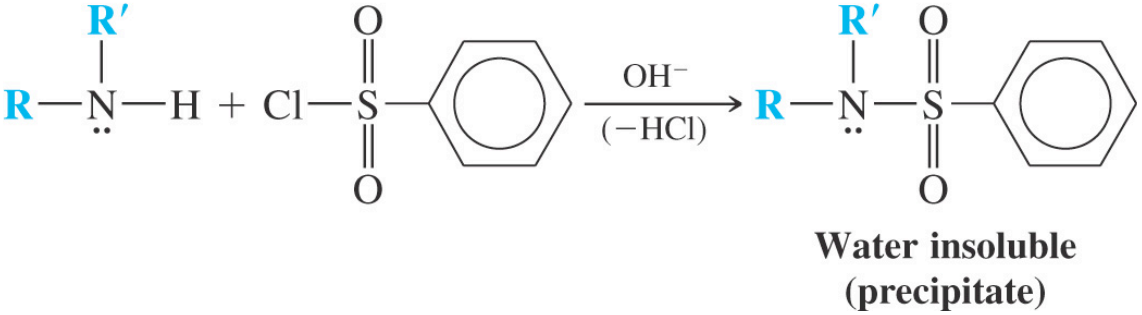
- ➡ **Amina primario zein sekundarioek *sulfonamidak* ematen dituzte**
  - ★ **Sulfonamidak hidrolizatu daitezke berotuz disoluzio azidoan**



- **Hinsberg-en Testa**
  - **Amina 1º, 2º eta 3º bereizteko**
  - **Amina, benzenosulfonil kloruroa eta potasio hidroxidoa nahasten dira uretan; gero azidotu egiten da**
  - **Amina primariotik lortutako bentzenosulfonamida disolbagarria behar du izan disoluzio basikoan, baina hauspeatu egiten du azidoan**



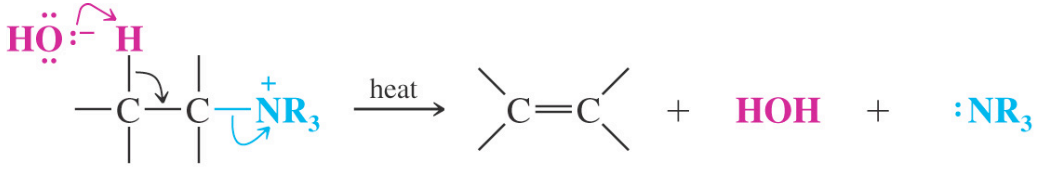
- Amina sekundariotik datorrenak zuzenean hauspeatu egiten du disoluzio basikopean
  - Ez du hidrogeno azidorik



- Amina tertziarioak ezin du sulfonamida eman, ordez disolbatu egingo da azidotzean, iminio gatza emanez

♦ Hofmann-en Eliminazioa

➡ Amonio hidroxido kuaternarioa berotzean E2 motako eliminazioa

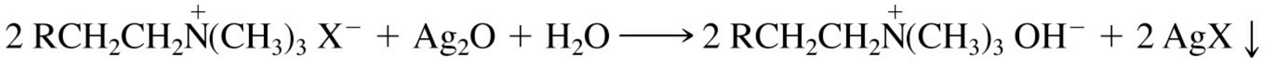


A quaternary ammonium hydroxide

an alkene

a tertiary amine

➡ Amonio hidroxido kuaternarioa halurotik prestatu daiteke zilar oxidoarekin tratatuz

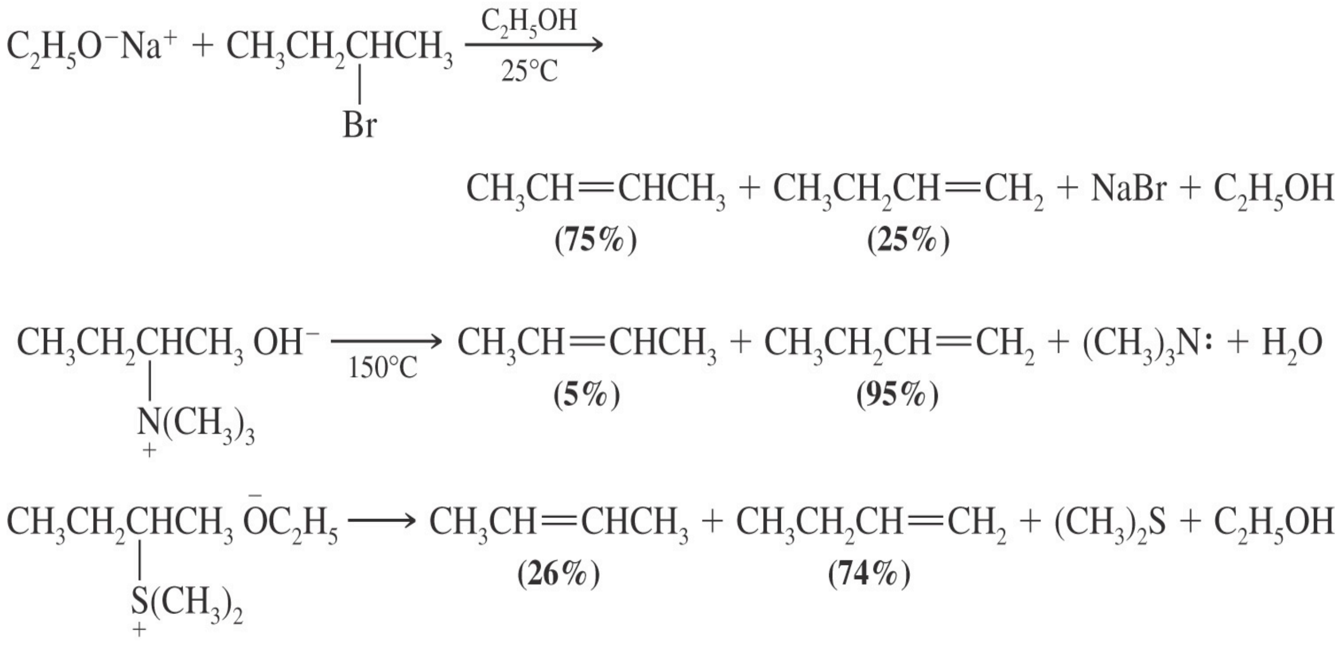


$$2\,RCH_2CH_2\overset{+}{N}(CH_3)_3\;X^- + Ag_2O + H_2O \longrightarrow 2\,RCH_2CH_2\overset{+}{N}(CH_3)_3\;OH^- + 2\,AgX\downarrow$$

A quaternary ammonium halide

A quaternary ammonium hydroxide

- **Hofmann eliminazioan eta beste eliminazio batzutan, non talde aterakorrak karga duen, gutxien ordezkatutako lotura bikoitza sortzen da**
  - **Hofmann-en araua deitzen zaio (Saytsev-en aurkakoa)**

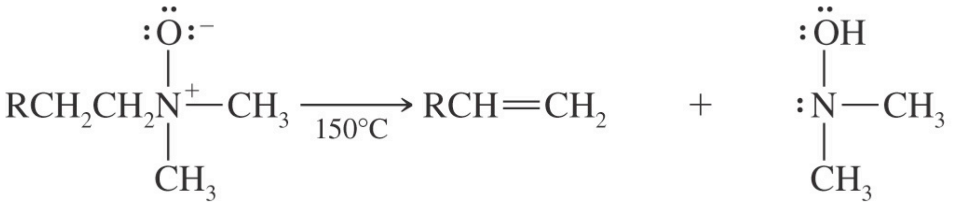


$$C_2H_5O^-Na^+ + CH_3CH_2\underset{\mathrm{Br}}{\underset{|}{C}}HCH_3 \xrightarrow[25^\circ C]{C_2H_5OH} \underset{(75\%)}{CH_3CH{=}CHCH_3} + \underset{(25\%)}{CH_3CH_2CH{=}CH_2} + NaBr + C_2H_5OH$$

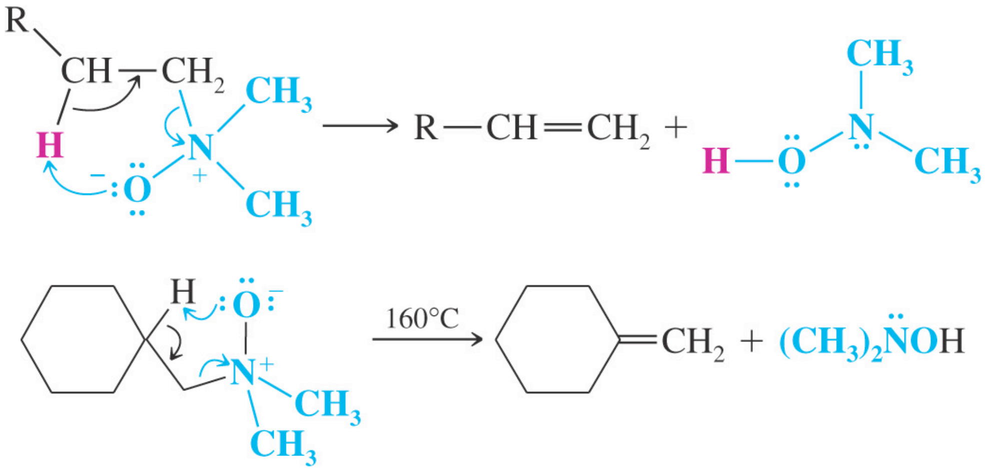
$$CH_3CH_2\underset{\overset{+}{N}(CH_3)_3}{\underset{|}{C}}HCH_3\ OH^- \xrightarrow[150^\circ C]{} \underset{(5\%)}{CH_3CH{=}CHCH_3} + \underset{(95\%)}{CH_3CH_2CH{=}CH_2} + (CH_3)_3N\colon + H_2O$$

$$CH_3CH_2\underset{\overset{+}{S}(CH_3)_2}{\underset{|}{C}}HCH_3\ \overset{-}{O}C_2H_5 \longrightarrow \underset{(26\%)}{CH_3CH{=}CHCH_3} + \underset{(74\%)}{CH_3CH_2CH{=}CH_2} + (CH_3)_2S + C_2H_5OH$$

- ## Cope-ren Eliminazioa
  - ➡ **Amina tertziario baten oxidoa berotzean alkenoa emateko**
    - ★ **Eliminazioa sin-espezifikoa da, eta trantsio-egoera zikliko batetik bideratzen da**



A tertiary amine oxide **An alkene** ***N,N*-Dimethylhydroxylamine**



(98%)