MOLECULAR REARRANGEMENT REACTIONS

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DEFINITION

- When a chemical unit an atom or an ion or a group of atoms, migrate from one atom to another in the same species or in another species of the same kind and develops a new species, the reaction is called a **rearrangement reaction**.
- The atom from which the gp migrates is called **migration origin**.
- The atom to which the gp migrates is called **migration terminus.**

INTRAMOLECULAR AND INTERMOLECULAR REARRANGEMENT

- **Intramolecular_** migration of a gp from one atom to another within the same molecule.
- **Intermolecular** _ migration of a gp from an atom of one molecule to atom of another molecule of the same kind.
- **Cross over experiment** _ is used to determine whether a rearrangement is intermolecular or Intamolecular.

- A mixture of two structurally related substrates, G- A- B and X- A- Y is subjected to a rearrangement in cross over experiment
- Product is a mixture of four different species, the reaction is **intermolecular.**
- A-B-G, A-Y-X, A-B-X and A-Y-G.
- Product is a mixture of two species, the reaction is **intramolecular.**
- A-B-G and A-Y-X are intramolecular products and A-B-X and A-Y-G are cross over products.

CLASSIFICATION

- Anionotropic Rearrangement
- Cationotropic Rearrangement
- Free Radical Rearrangement-

- **Anionotropic rearrangements-** migration of an anion to electron deficient migration terminus.
- **Migrating gps** – alkyl , aryl, ring residue, - H atom, - OH or –NH_2 gp
- **Electron deficient centres** – C , N , or O eg. Pinacol Pinacolone Rearrangement

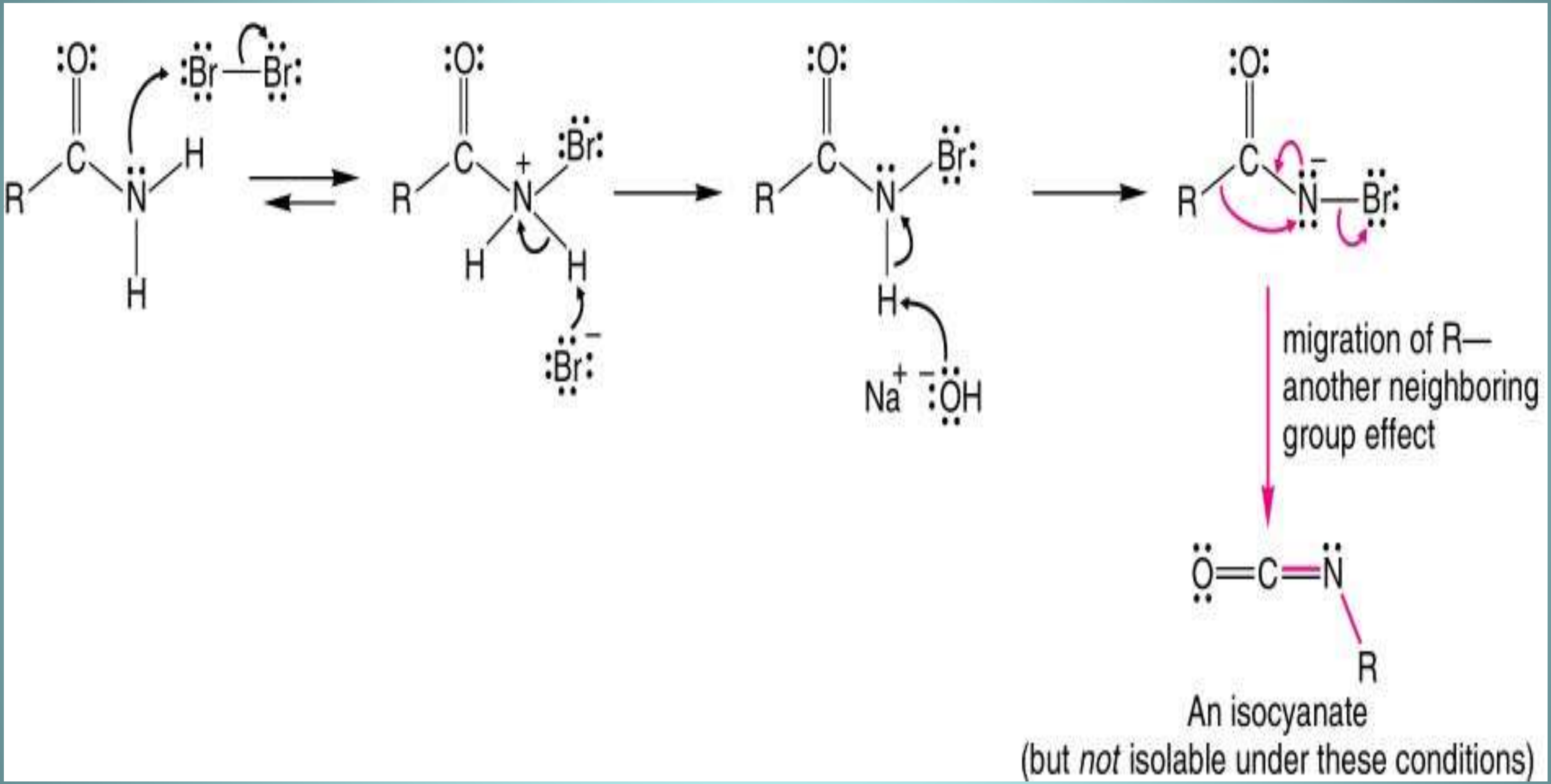
- **C to C migration------ Pinacol Pinacolone.**

- **C to N migration-----Hoffman Curtius**

- **C to O migration -----Baeyer Williger Oxidation.**

- Cationotropic rearrangement - migration of a gp without its electron pair to electron rich centre.

- O to C migration - Fries Rearrangement

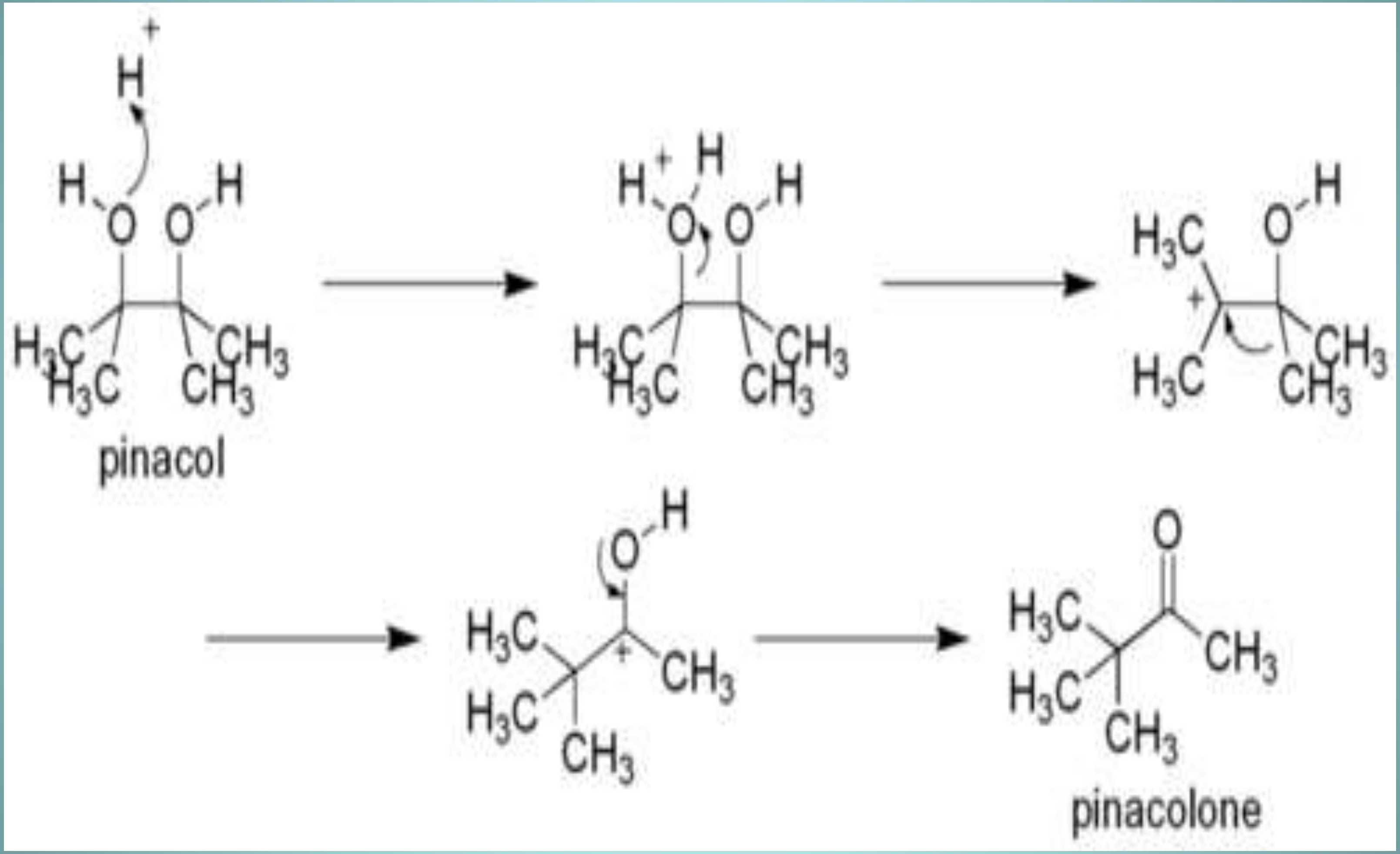

migration of R—
another neighboring
group effect
An isocyanate
(but *not* isolable under these conditions)

PINACOL REARRANGEMENT

- The **pinacol rearrangement** or **pinacol-pinacolone rearrangement** is a method for converting a 1,2-diol to a carbonyl compound in organic chemistry. This rearrangement takes place under acidic conditions. The name of the reaction comes from the rearrangement of pinacol to pinacolone.
- This reaction was first described by Wilhelm Rudolph Fittig in 1860.

MECHANISM OF REACTION

- In the course of this **organic reaction**, protonation of one of the -OH groups occurs and a **carbocation** is formed. If both the -OH groups are not alike, then the one which yields a more stable carbocation participates in the reaction.
- Subsequently, an **alkyl** group from the adjacent carbon migrates to the **carbocation** center.


pinacol
pinacolone

- The driving force for this rearrangement step is believed to be the relative stability of the resultant oxonium ion, which has complete octet configuration at all centers (as opposed to the preceding carbocation).
- The migration of alkyl groups in this reaction occurs in accordance with their usual **migratory aptitude**, i.e. Ph- > 3-alkyl > 2-alkyl >1-alkyl> H .

In case of unsymmetrically substituted glycols the +ve charge is generated on that carbon which is best able to support it eg .carbonium ion is produced on phenylated carbon rather than methylated because of resonance stabilization.

- In α β diol esters the carbonyl carbon of the ester gp is partially +ve and it prevents generation of carbonium ion at α carbon

The +ve charge can be forced to develop at a C by stabilizing it over a ph substituent together with increasing the energy of alternate β C+ making it a primary one.

Carbonium ion is produced on β carbon when both H atoms are substituted by methyl gps indicating that a tertiary carbonium ion is more stable than a benzylic carbonium ion adjacent to a carboethoxy gp.

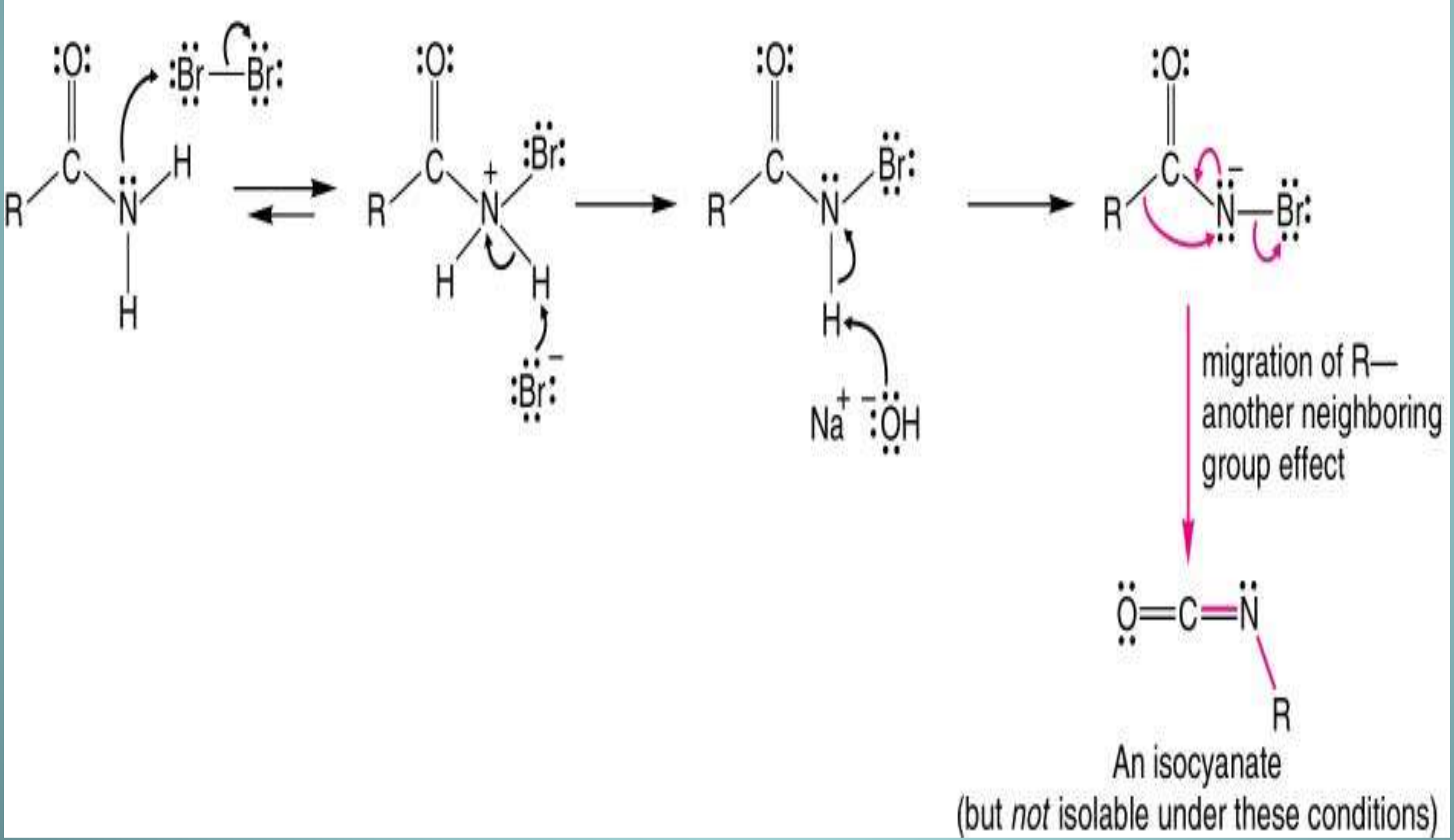
HOFFMAN REARRANGEMENT

- The reaction involves the conversion of an amide into a primary amine with one carbon less than the parent amide, by the action of sodium hypo bromite (Br_2 and NaOH).

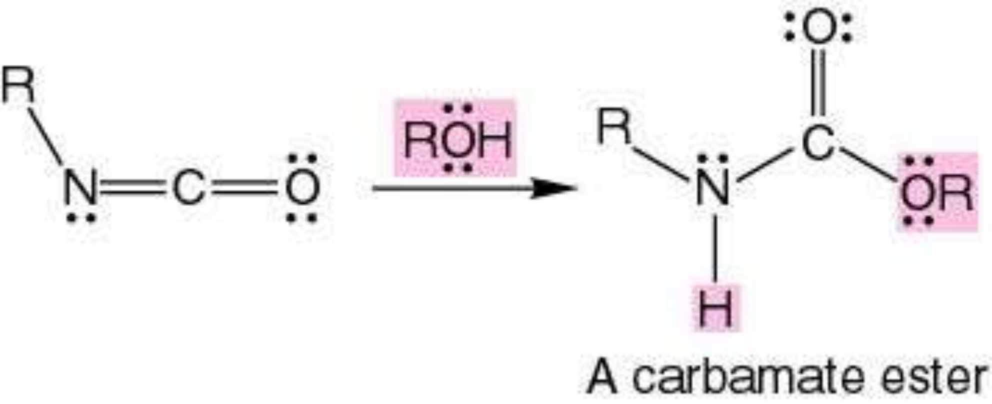
$RCONH2 + Br2 + 4NaOH \longrightarrow RNH_2 + 2NaBr +$

$2Na_2CO3 + 2H_2O$

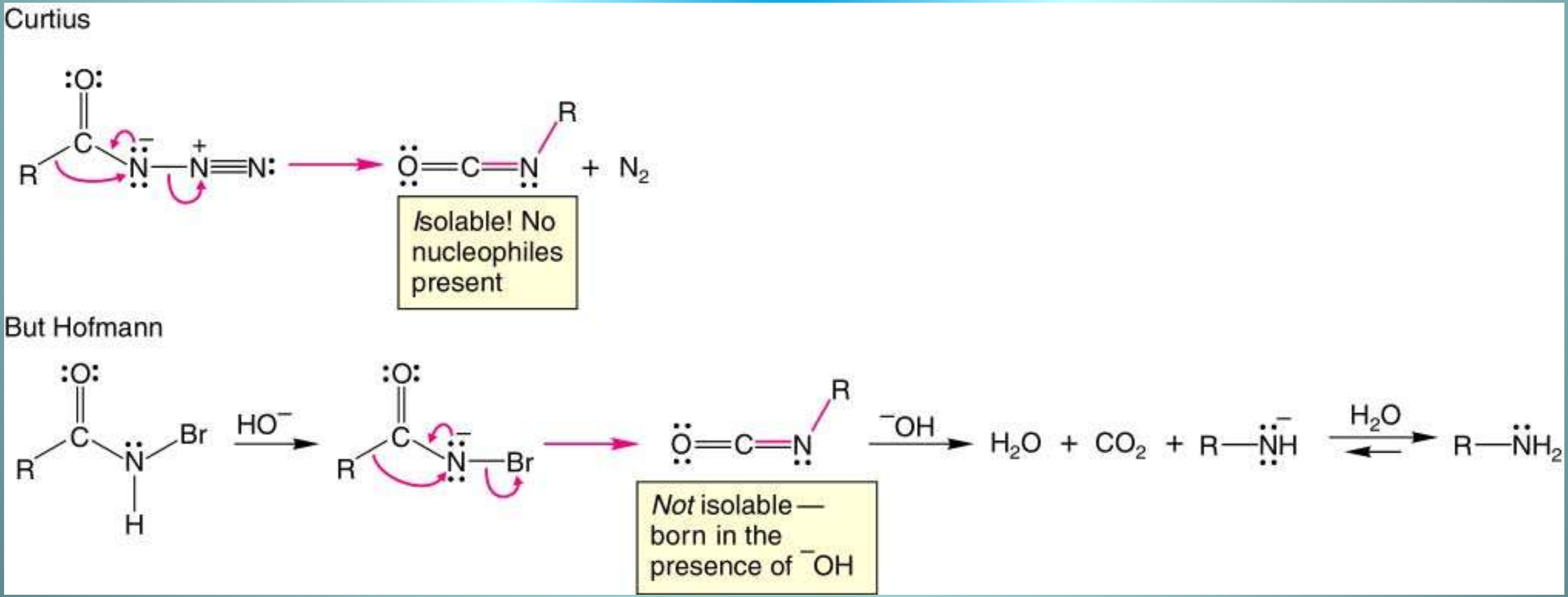
MECHANISM



An isocyanate
(but *not* isolable under these conditions)

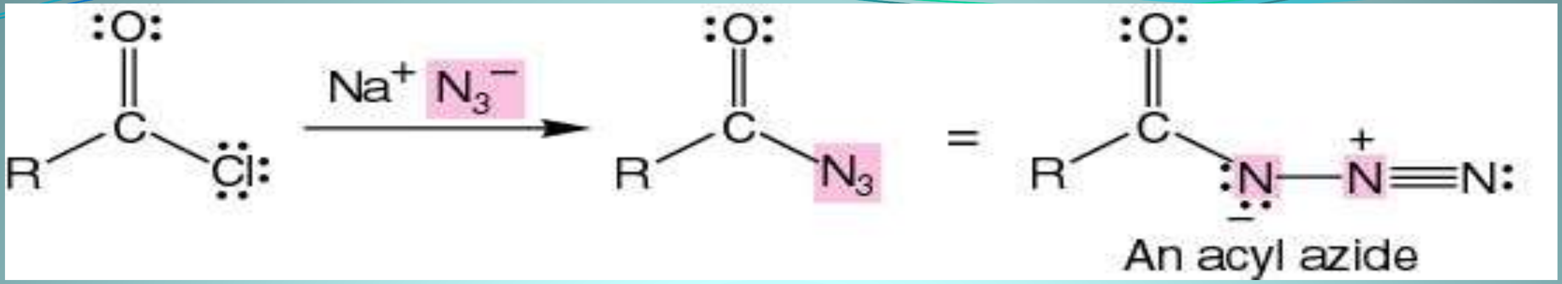


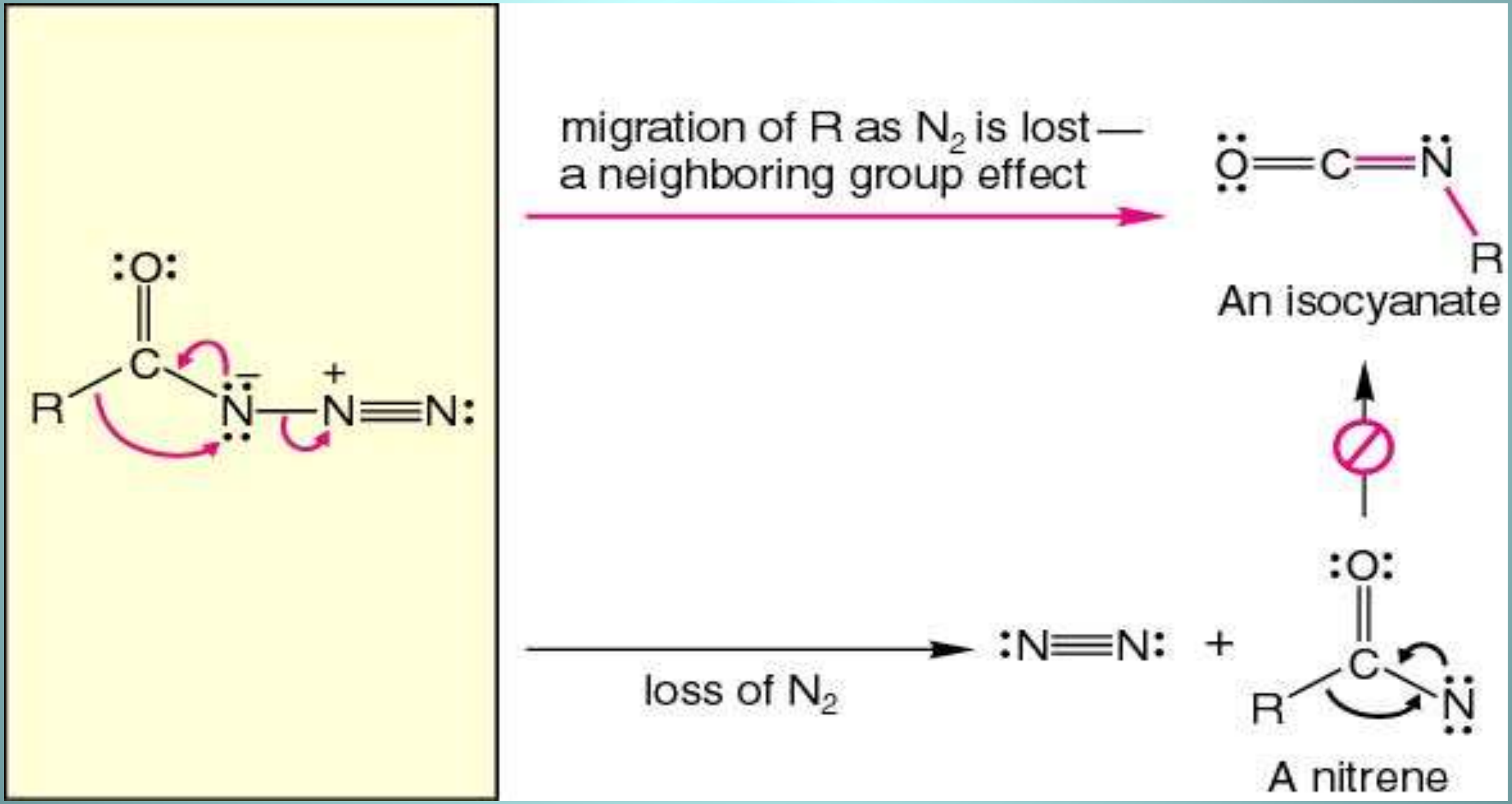
A carbamate ester



*I*solable! No nucleophiles present

Not isolable — born in the presence of ^-OH


$Na^+ N_3^-$
N_3
An acyl azide


migration of R as N_2 is lost— a neighboring group effect
An isocyanate
loss of N_2
A nitrene

- **Ist step**- N Bromamide is formed by the usual reaction of the +ve halogen atom at the N atom of the amide which abstracts a proton
- **2nd step**- Removal of the acidic hydrogen from the N atom by the base to form N-bromamide anion

3rd step- Loss of bromine results in the formation of highly reactive acyl nitrene.

- **4th step**- Migration of R takes place to the electron deficient N atom to form isocyanate
- **5th step**- Isocyanate reacts with water to give carbamic acid which eliminates carbon dioxide to give amine.

- The intermediates , N- bromamide, its anion and iso-cyanate (in aprotic solvent) have been isolated.
- The possibility of formation of acyl nitrene has been rejected, for if it is formed it would react with water to give hydroxamic acid which is not detected.
  - ..

$RCON: + H_2O =$ RCONHOH (hydroxamic acid)

Hence the loss of Br and migration of R occur in concerted step

- Since no cross over product is obtained when two different amides are rearranged, hence rearrangment is intramolecular and the migratng gp never completely separates during migration.

- The rate of reaction increases when the migrating gp is more electron donating and decreases when electron withdrawing.

APPLICATIONS

- **Acids and amides to amines**

$$RCOOH \xrightarrow{NH_4OH} RCONH_2 \xrightarrow{Br_2 + KOH} RNH_2$$

$$Me_3\,CCH_2CONH_2 \xrightarrow{NaOBr} Me_3CCH_2NH_2$$

- **Higher amides give nitriles which can be reduced to amines.**

- $RCH_2CONH_2 \xrightarrow{Br_2 + KOH} RCH_2CN \xrightarrow{Na + alcohol} RCH_2NH_2$

- **Urea gives Hydrazine**

$$H_2NCONH_2 \xrightarrow{Br_2 + KOH} NH_2NH_2$$

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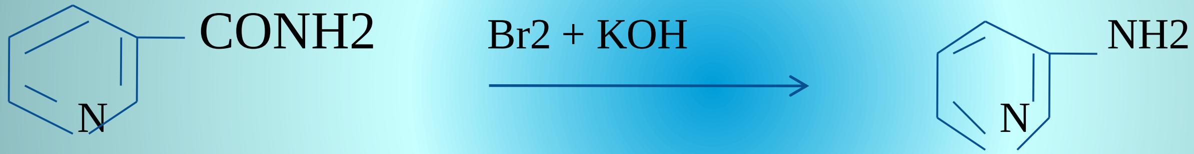
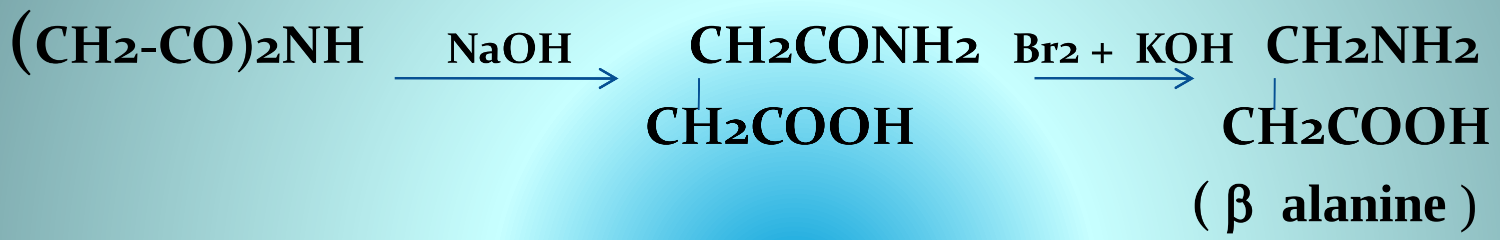
- **Preparation of β amino pyridine from nicotinamide**
- 

- **Preparation of aldehydes**
- $C_6H_5\text{-}CHOH\text{-}CONH_2 \xrightarrow{Br_2 + KOH} C_6H_5CHO + NH_3$
- Synthesis of amino acids



- $$(CH_2\text{-}CO)_2NH \xrightarrow{NaOH} \underset{CH_2COOH}{\underset{|}{CH_2CONH_2}} \xrightarrow{Br_2 + KOH} \underset{CH_2COOH}{\underset{|}{CH_2NH_2}}$$

(β alanine)