

Hoffmann- Bromamide Rearrangement

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Introduction:

The reaction involves the **conversion of an amide into a primary amine with one carbon less**, by the action of alkaline hypohalite (NaOH solution + Br₂ or Cl₂). The overall reaction is:

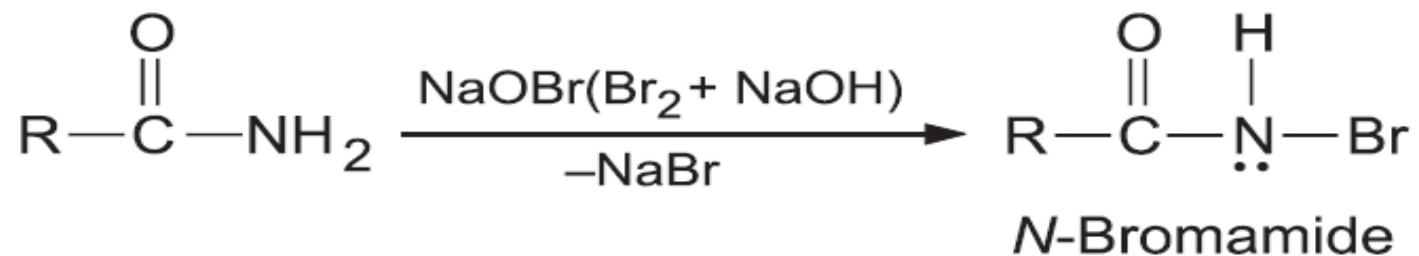


where R may be aliphatic, aromatic or heterocyclic.

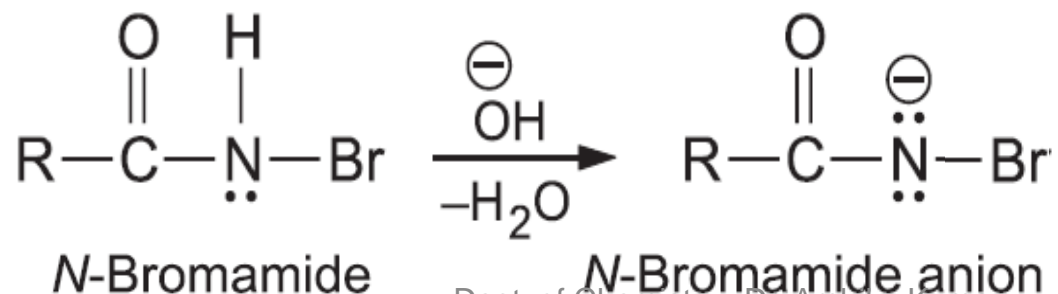
Mechanism:

The mechanism has been suggested on the basis of the intermediates isolated during the course of reaction.

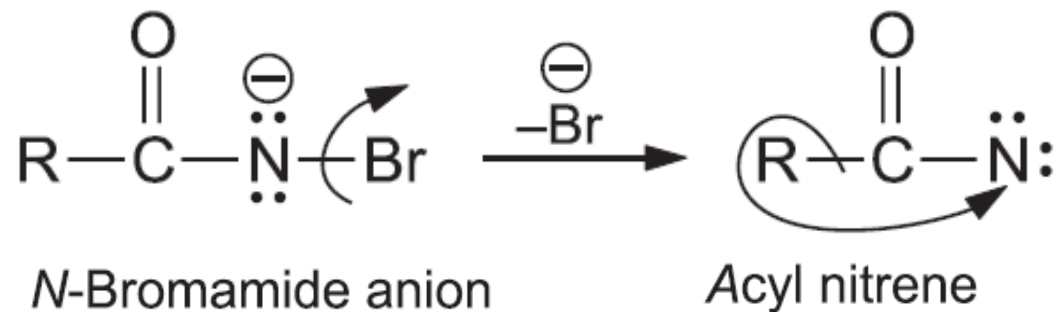
- In the first step *N*-bromamide is formed by the usual reaction of hypobromite on primary amines:



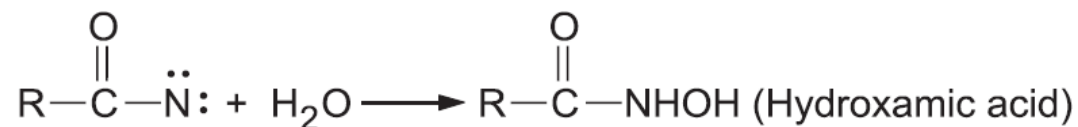
- This follows the removal of the acidic hydrogen from the N-atom by the base to form *N*-bromamide anion in the second step:



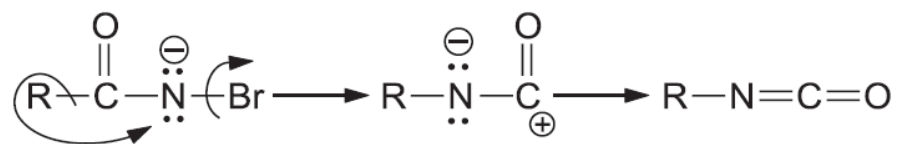
- In the third step (rate determining step) loss of bromine results in the formation of the highly reactive **acyl nitrene**.



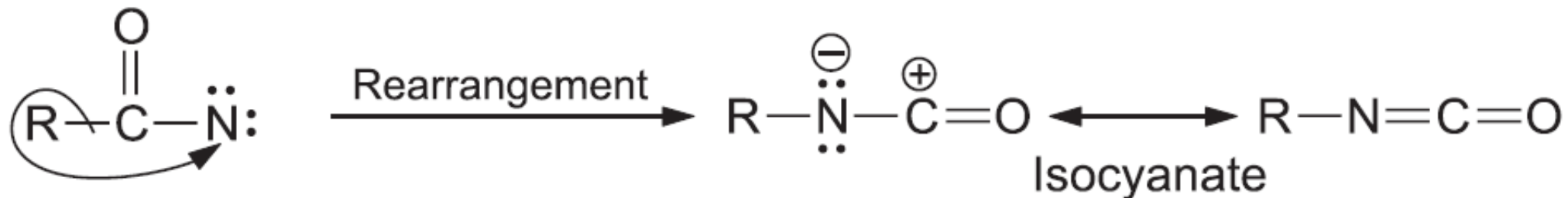
Note: The possibility of the formation of acylnitrene, however, has been rejected, for if it is formed it would react with water to give hydroxamic acid, which has not been detected.



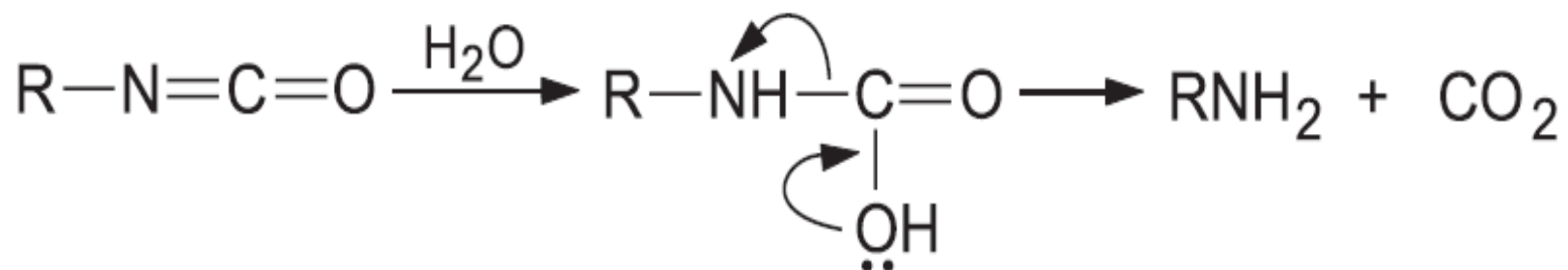
Hence, the loss of Br and the migration of R in N-bromamide anion is suggested to be concerted (since no cross over products are formed and migrating R retains its chirality – if molecule is asymmetric).



- Thus in the fourth step, migration of R to the electron-deficient nitrogen gives the isocyanate.



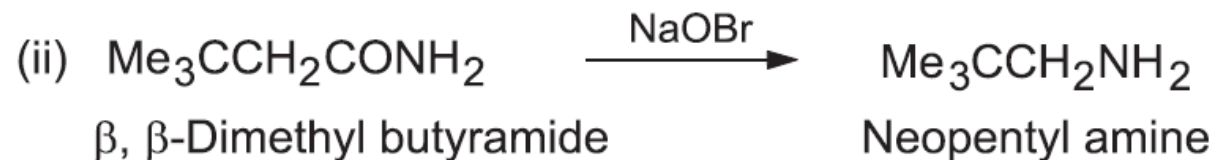
- Formed isocyanate reacts with water to give carbamic acid which spontaneously eliminates carbon dioxide to yield the amine.



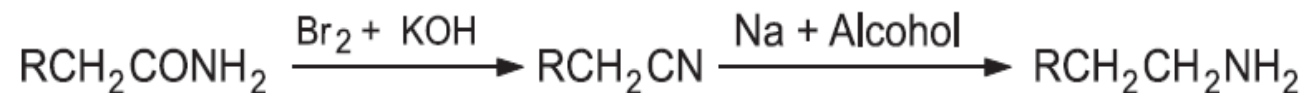
Applications

1. Formation of amines It is a very useful method for the preparation of amines.

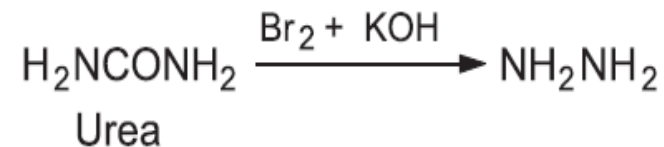
(a) Acids and amides to amines.



(b) Higher amides (with more than eight carbons) give nitriles which can be reduced to amines.

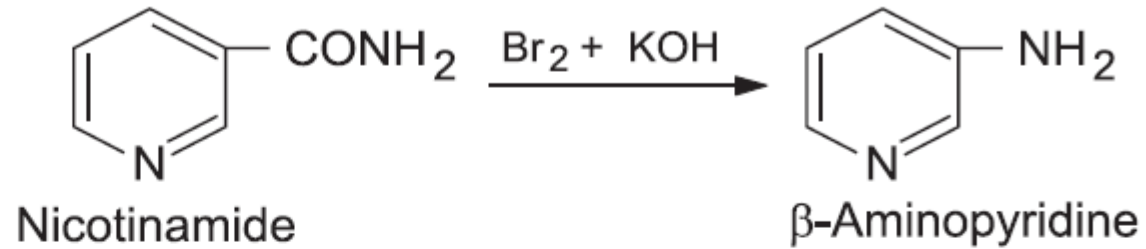


(c) Urea gives the valuable reagent hydrazine.

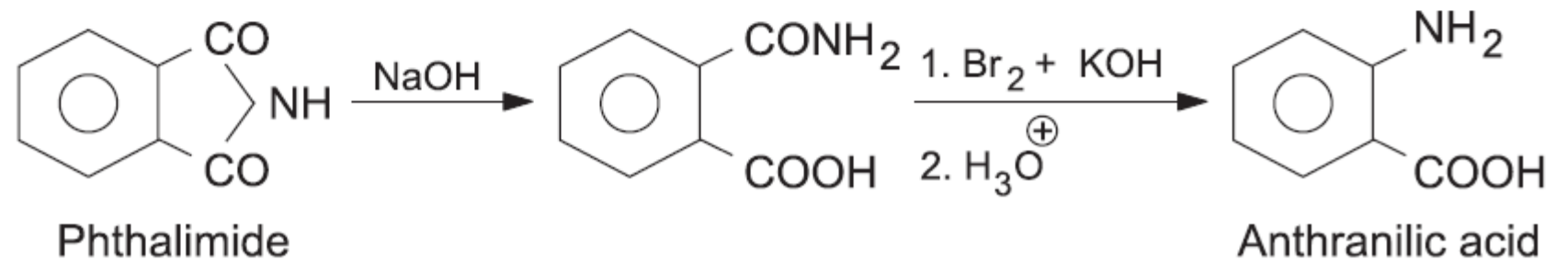
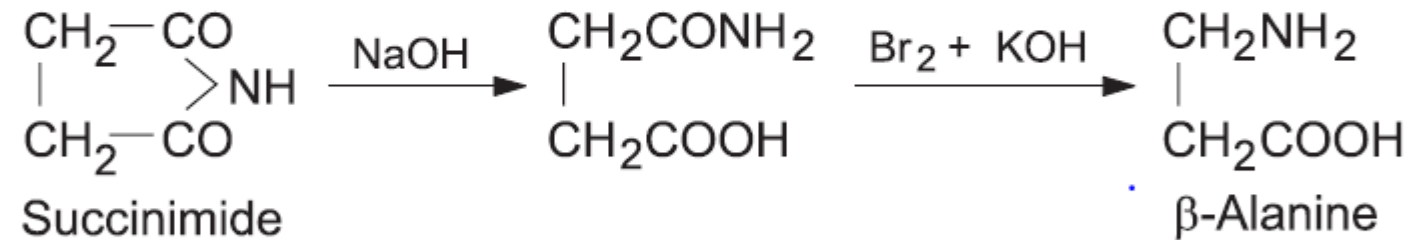


The yield of amines is poor with β , γ -unsaturated acids.

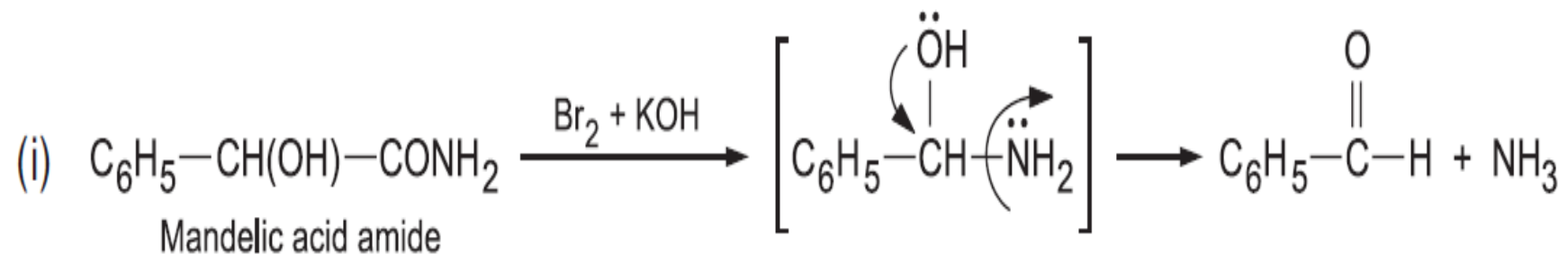
2. Preparation of β -amino pyridine from nicotinamide



3. Synthesis of amino acids



4. Preparation of aldehydes from hydroxyacid amides



(ii) Methanolic α, β -unsaturated acid amides on treatment with NaOCl give urethane which on hydrolysis with HCl gives a good yield of aldehyde.

