

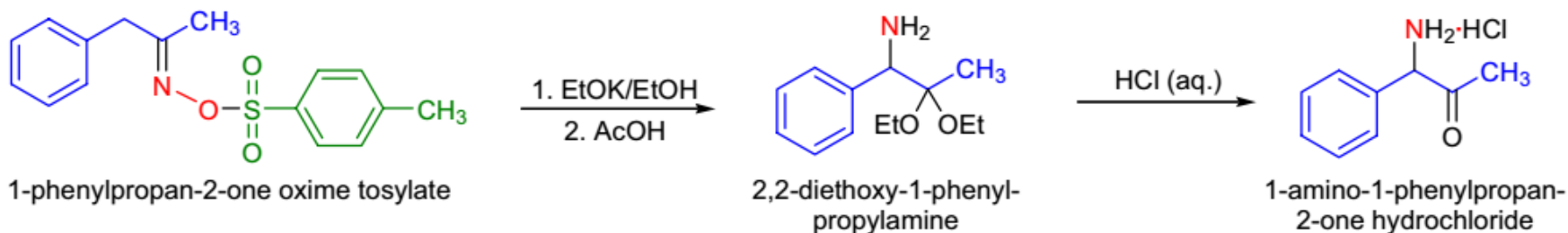
NEBER REARRANGEMENT

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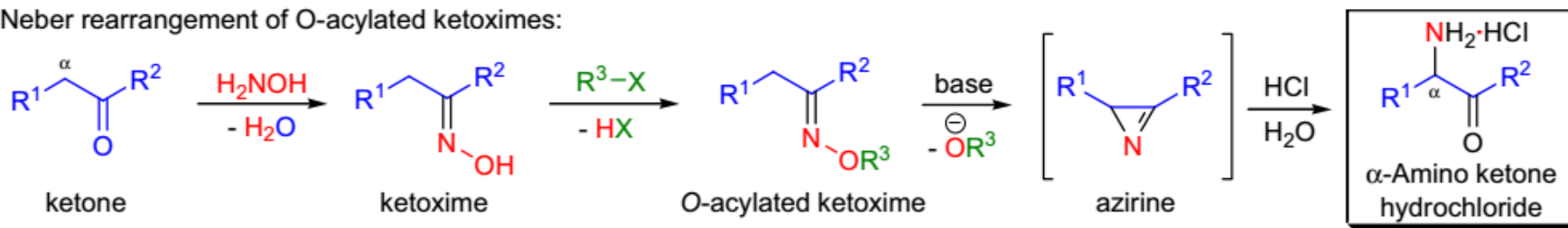
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Discovery of Neber Rearrangement

Rearrangement of ketoxime tosylates (Neber, 1926):



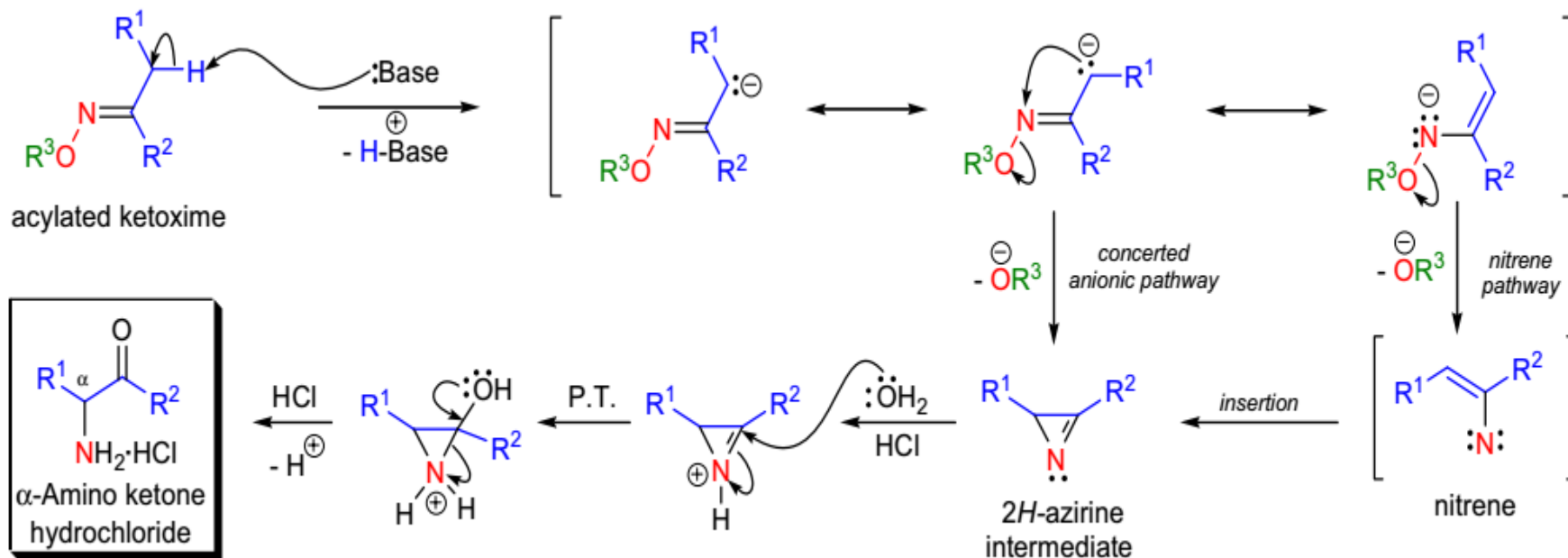
Neber rearrangement of O-acylated ketoximes:



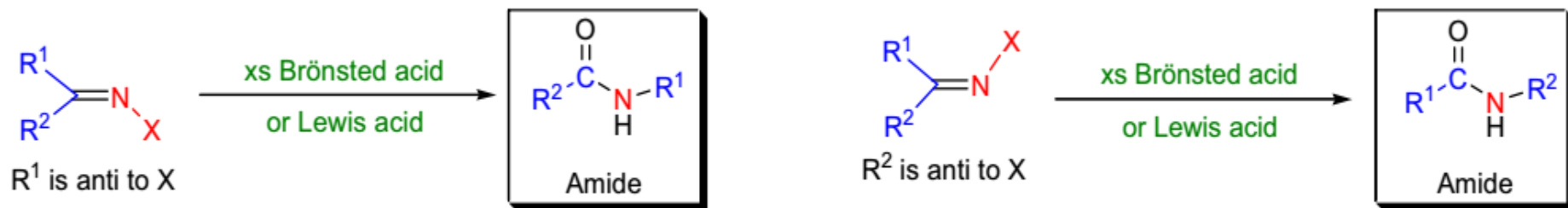
R^1 = H, alkyl, aryl; R^2 = alkyl, aryl, O-alkyl, NH_2 , NH-alkyl; R^3 = $\text{SO}_2\text{C}_6\text{H}_4\text{CH}_3$, SO_2CH_3 ; base: NaOEt, KOEt

The base-induced rearrangement of O-acylated ketoximes to the corresponding α -amino ketones is known as the Neber rearrangement.

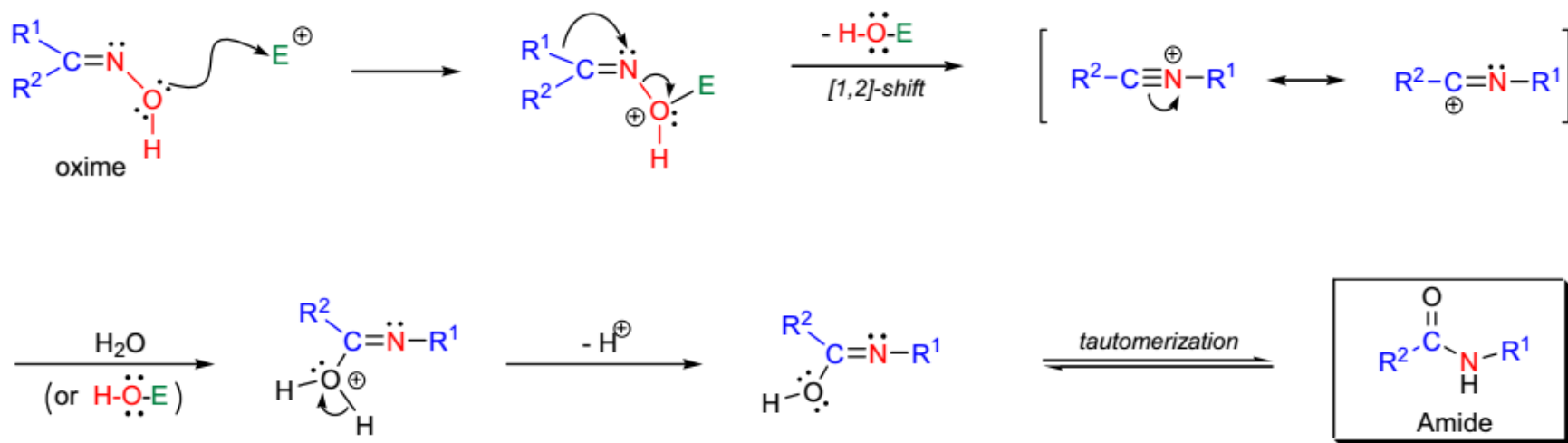
Mechanism of Neber Rearrangement



Mechanism of Beckmann rearrangement



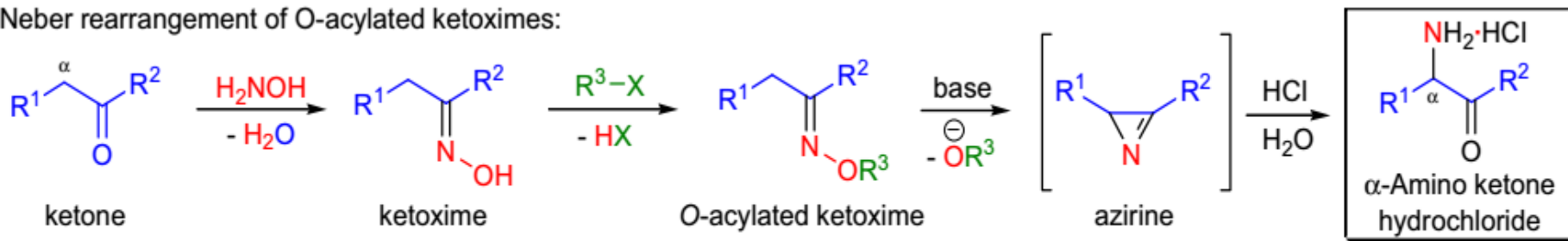
R^1, R^2 = alkyl, aryl, heteroaryl; X = OH, OTs, OMs, Cl



The conversion of aldoximes and ketoximes to the corresponding amides in acidic medium is known as the Beckmann rearrangement

Features of Neber Rearrangement

Neber rearrangement of O-acylated ketoximes:



$R^1 = H, \text{ alkyl, aryl}; R^2 = \text{ alkyl, aryl, O-alkyl, NH}_2, \text{ NH-alkyl}; R^3 = \text{ SO}_2\text{C}_6\text{H}_4\text{CH}_3, \text{ SO}_2\text{CH}_3; \text{ base: NaOEt, KOEt}$

- 1) acylated ketoximes derived from both acyclic and cyclic ketones can be used;
- 2) the required oximes are readily prepared from the ketones by reacting them with hydroxylamine under acidic conditions;
- 3) O-acylation of the oximes is conducted using acyl halides or anhydrides in the presence of a mild base (e.g., pyridine);
- 4) the rearrangement is usually carried out in an alcohol solution containing equimolar quantities of an alkali alkoxide;
- 5) when two methylene groups are available at the α - and α' -positions, the rearrangement mainly gives rise to a product in which the amino group is located on the more electrophilic carbon;
- 6) the rearrangement is not stereospecific, since the stereochemistry of the substrate (syn or anti) usually does not influence the outcome of the reaction, and this is in sharp contrast with the stereospecificity of the Beckmann rearrangement;
- 7) the product amino ketones have a tendency to dimerize, so they often need to be prepared in a protected form as their amino acetals or hydrochloride salts

Synthetic Applications of Neber Rearrangement

