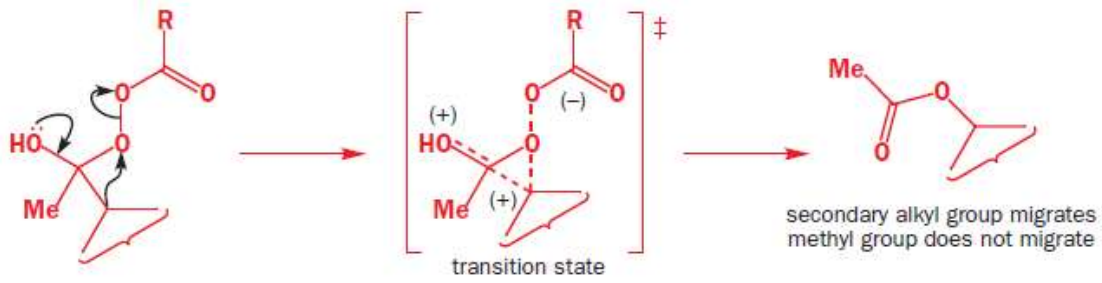
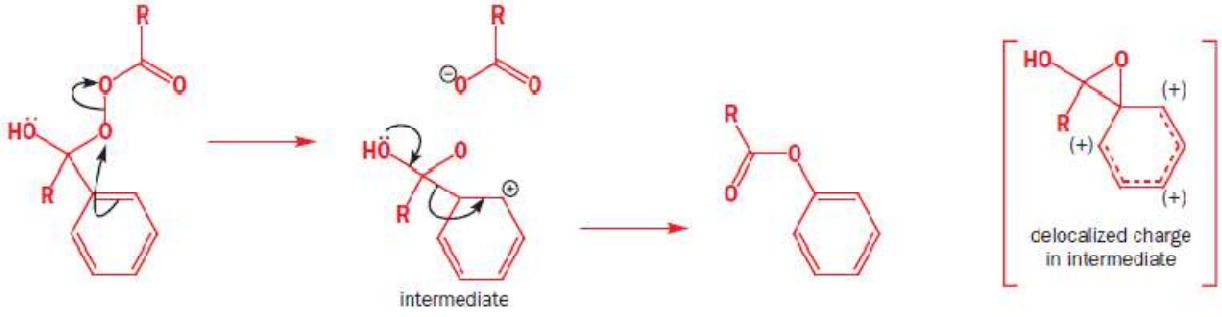
2- **The more substituted group migrates in the Baeyer–Villiger reaction:**

Because the **transition state has a positive charge spread out over the molecule as the carboxylate leaves as an anion**. If the migrating group can take some responsibility for the positive charge the **transition state will be more stable**. **The more stable the charge, the faster the rearrangement**.

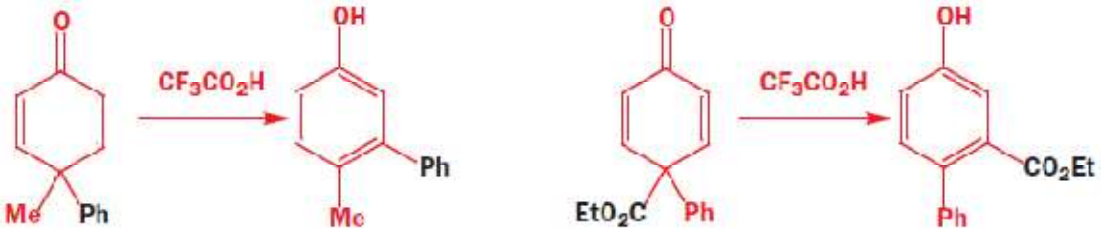


When a benzene ring migrates, **π participation is involved as the benzene ring acts as a nucleophile and the positive charge can be spread out even further**. Note that the Ph is stabilizing the charge here in the way that it stabilizes the intermediate in an electrophilic aromatic substitution reaction like a pentadienyl cation rather than like a benzylic cation. What was a transition state in alkyl migration becomes an intermediate in phenyl migration.

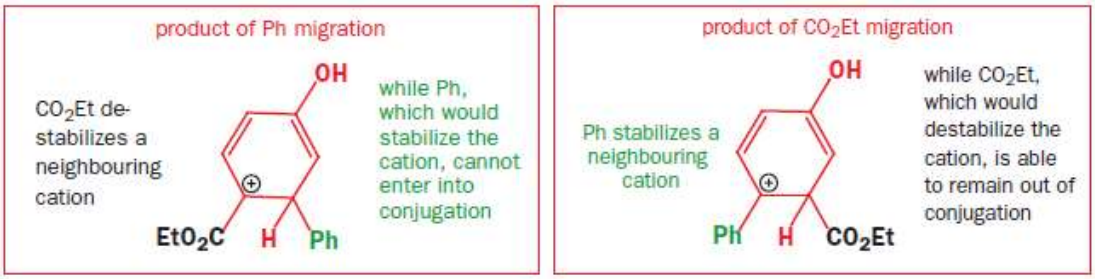


The situation in other rearrangements is much more complicated. Like in **the dienone–phenol rearrangement, when found competition between two different migrating groups**. As in the Baeyer–Villiger reaction, **the transition state is cationic**, so you would **expect cation-stabilizing groups to migrate more readily**. This appears to be true for **Ph versus Me** but is most definitely not true for **Ph versus CO_2Et**. **The cation-destabilizing group CO_2Et migrates even though Ph is much better at stabilizing a positive charge**.

Examples:



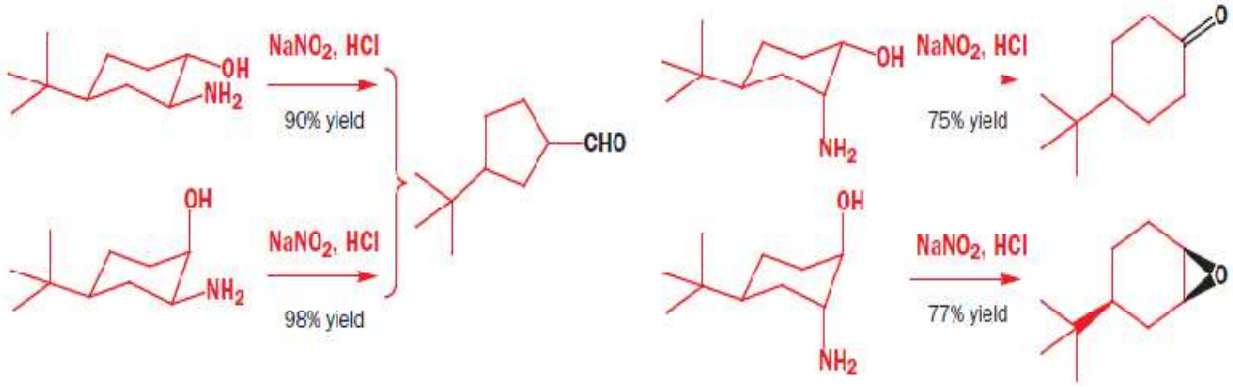
The reason is that **CO_2Et is so cation-destabilizing that it prefers to migrate rather than be left behind next door to a cation**. **It is the cation-stabilizing ability of the group that does not migrate that matters most**.



3- **Stereochemistry:**

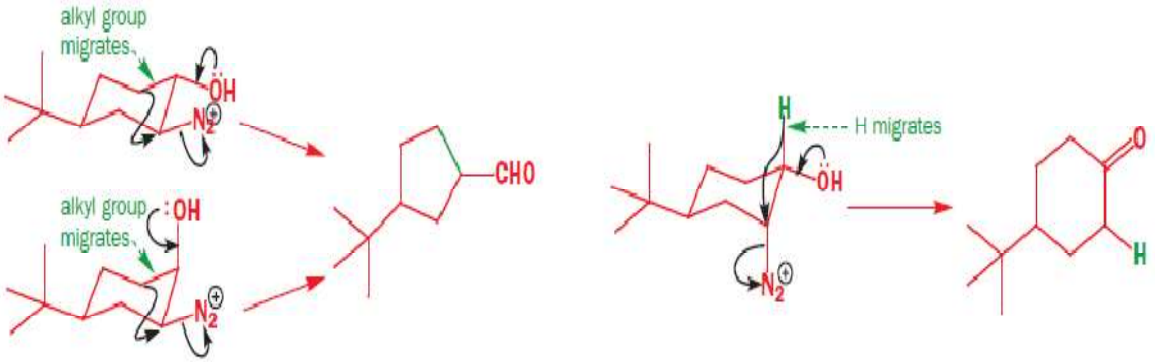
Stereochemistry matters to Selectivity in rearrangement reactions is **affected by the electronic nature of both the group that migrates and the group that is left behind, and Stereochemistry** is important too. The outcome of **diazotization and semipinacol rearrangement (Tiffeneau–Demjanov rearrangement) of this amino-alcohol depends entirely on the diastereoisomer you start with**. There are **four diastereoisomers, and the reaction of each one with the t-butyl group equatorial**.

Examples:



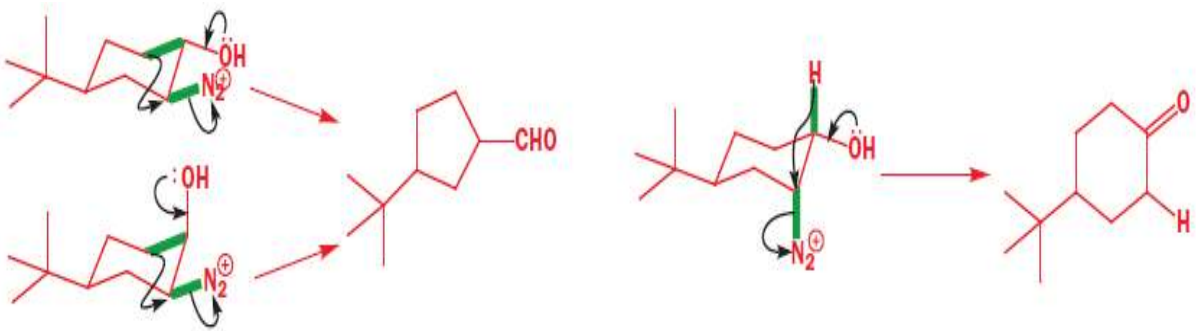
In **all of these reactions**, the **OH group provides the electronic 'push'**. In the **first two reactions, the ring contracts by an alkyl migration from the secondary alcohol, while in the third it is H that migrates from the same position**.

Mechanism:

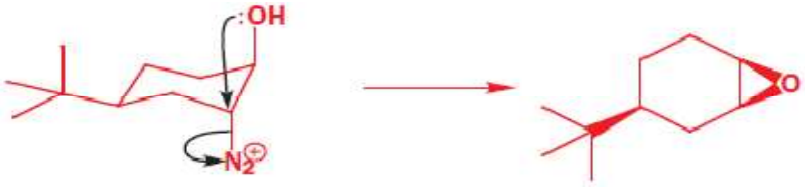


The only **difference between the compounds is stereochemistry** and, if we look at the **orbitals involved in the reactions**. As the **N_2 leaving group departs, electrons in the bond to the migrating group have to flow into the C–N σ* orbital**. And the fact that the **best overlap between these two orbitals (σ and σ*) occurs if they are anti-periplanar to one another just as in an E_2 elimination reaction**.

For the **first two compounds**, with the **$-N_2^+$ group equatorial, the group best placed to migrate is the alkyl group that forms the ring**; for the **third reaction**, there is a **hydrogen atom anti-periplanar to the leaving group, so H migrates**.



The **fourth reaction** has, rather than a group that might migrate, **the hydroxyl group ideally placed to displace N_2 and form an epoxide another example of participation**.



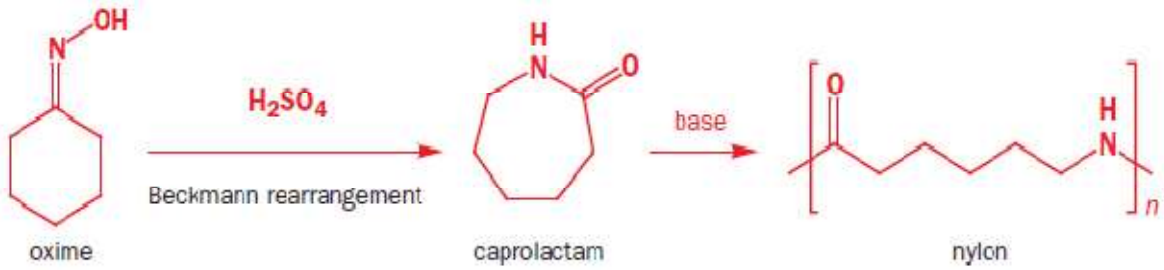
Note: The requirement for the migrating group to be anti-periplanar to the leaving group is quite general in rearrangement reactions.

The Beckmann rearrangement:

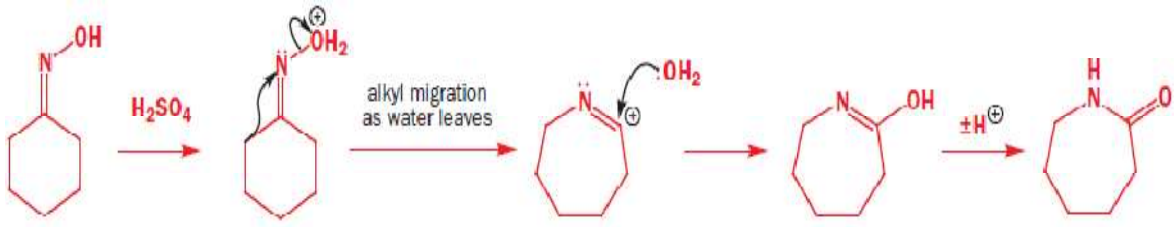
Is the action of sulfuric acid on the oxime of cyclohexanone in a rearrangement to produce caprolactam.

The **industrial manufacture** of **nylon** relies upon the **alkaline polymerization of a cyclic amide** known trivially as **caprolactam**.

Example:



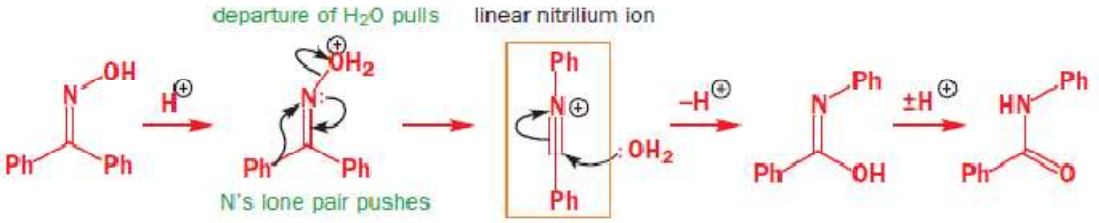
Mechanism: The **acid converts the oxime OH into a leaving group**, and an **alkyl group migrates onto nitrogen as water departs**. The **product cation is then trapped by water to give an amide**.



This **rearrangement** is **not confined to cyclic oximes**, and other ways of **converting OH to a leaving group** also work, such as **PCl_5**, **$SOCl_2$**, and other **acyl or sulfonyl chlorides**. In an **acyclic Beckmann**

rearrangement, the product cation is better represented as this nitrilium ion. When we write **the mechanism we can then involve the nitrogen's lone pair to 'push' the migrating group back onto N**, **a linear system like this was impossible in the seven-membered ring** of the last example.

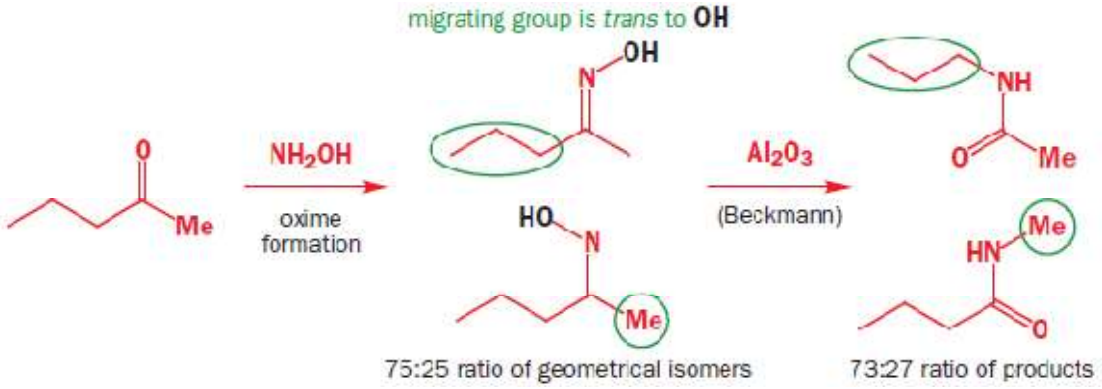
Mechanism:



The Beckmann rearrangement in the unsymmetrical ketones:

In the Beckmann rearrangement of **unsymmetrical ketones**, there are **two groups that could migrate**.

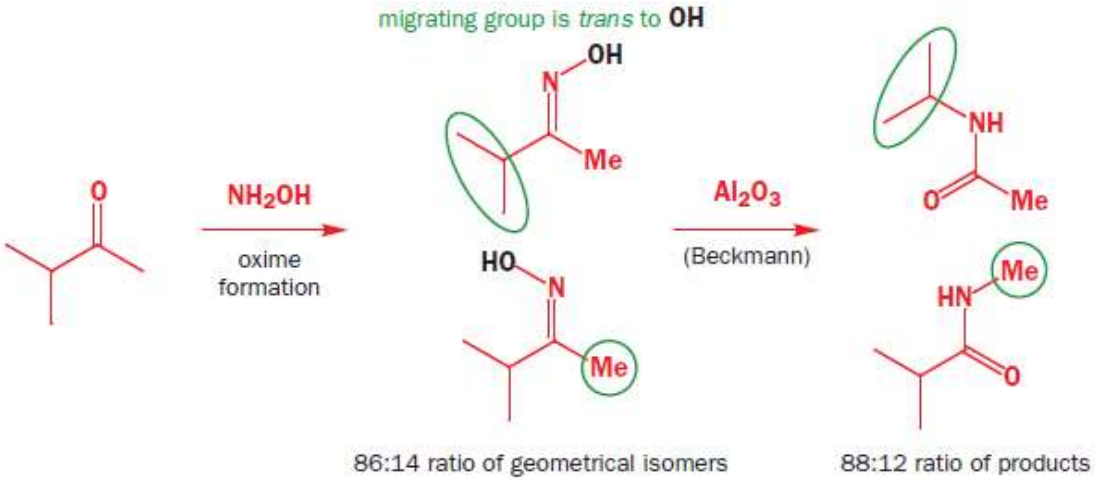
There are also **two possible geometrical isomers** of an **unsymmetrical oxime**: **C=N** double bonds can exhibit **cis/trans isomerism** just as **C=C double bonds** can. **When mixtures of geometrical isomers of oximes are rearranged, mixtures of products result, but the ratio of products mirrors exactly the ratio of geometrical isomers in the starting materials the group that has migrated is in each case the group trans to the OH in the starting material**.



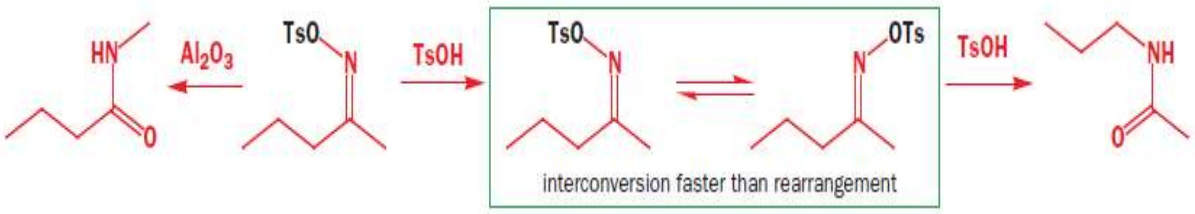
For migration to occur, a **migrating group has to be able to interact with the σ* of the bond to the leaving group**, and this is the reason for the specificity here.

Here it is the C=N double bond that provides the constraint. If one of the alkyl chains is branched, more of the oxime with the OH group anti to

that chain will be formed and correspondingly more of the branched group will migrate.



Conditions that allow those double isomers to interconvert can allow either group to migrate. Most **protic acids allow the oxime isomers to equilibrate** so, for example, **this tosylated oxime rearranges with full stereospecificity in Al_2O_3 (the anti methyl group migrates)**, but with **TsOH**, **equilibration of the oxime geometrical isomers means that either group could migrate in the event**, the **propyl group (which is more able to support a positive charge) migrates faster**.



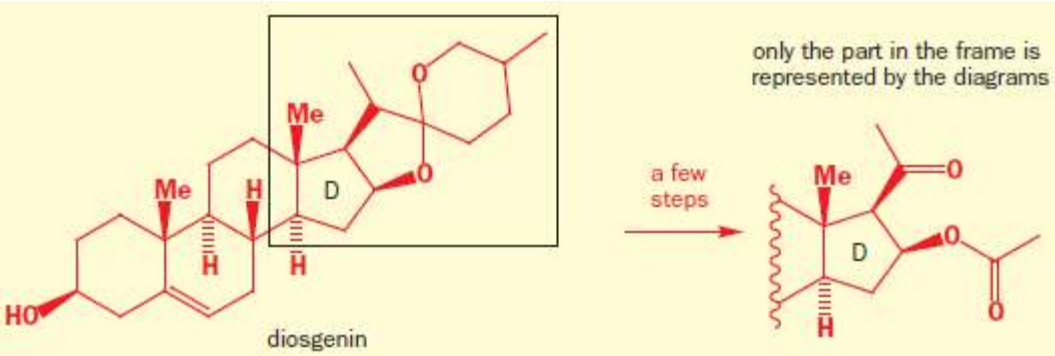
Note: That the **effect of the Beckmann rearrangement is to insert a nitrogen atom next to the carbonyl group**. It forms a useful trio with **the Baeyer–Villiger oxygen insertion** and the **diazoalkane carbon insertion**.

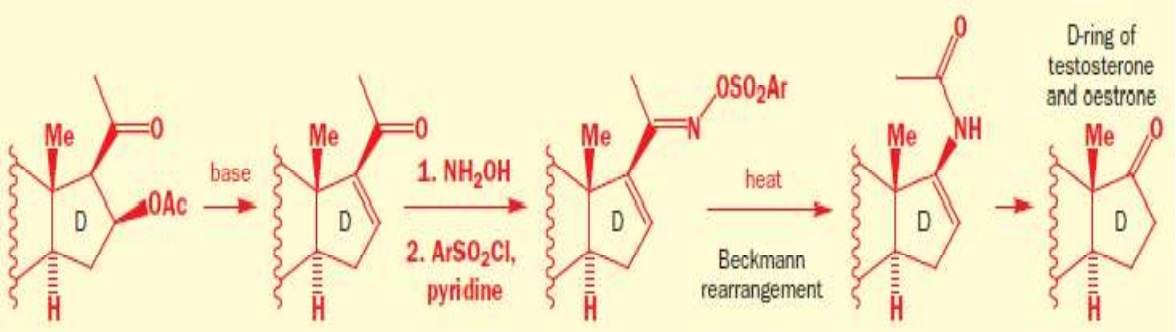
Example: The diosgenin use: steroids from vegetables

Many of the **human steroid hormones are available by semisynthesis**, **synthesis starting from a natural product similar in structure to the** target molecule. **One very important starting material for semisynthesis routes to these hormones is diosgenin**, a **plant sterod** which makes up 5% of the dry mass of the roots of Mexican yams. Most of the chemical manipulation necessary to turn diosgenin into human

steroids concerns the top right **five-membered ring** (the 'D' ring). A few steps **convert the acetal group of the natural product into a simpler methyl ketone**, present in **cortisone and progesterone**.

Bur for hormones such as **oestrone and testerone two carbon atoms need removing to make a cyclopentanone**. This is accomplished **using a Beckmann rearrangement**. The **oxine forms with the OH group trans to the more bulky cyclic substituent**. **Tosylation and Beckmann's rearrangement give an acetylated enamine which hydrolysis to the required cyclopentanone**.

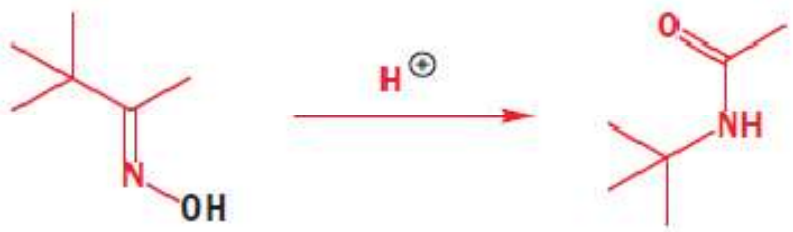




The Beckmann fragmentation:

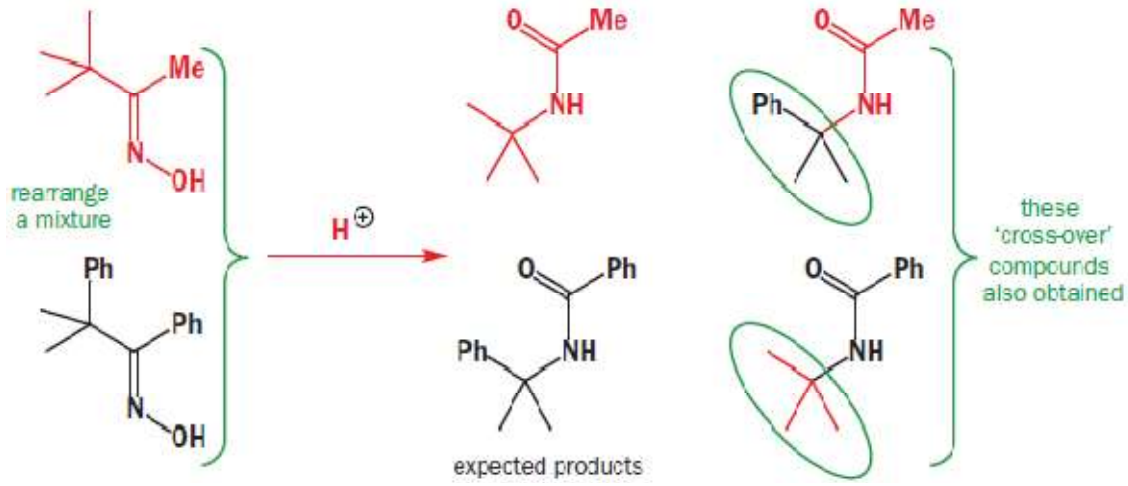
***t*-Butyl groups migrate** well in **the Baeyer–Villiger reaction** and, **Beckmann rearrangement** of this compound appears to be quite normal too.

Example:



But, when this **compound and another compound with a tertiary center next to the oxime are mixed together and treated with acid, it becomes apparent that what is happening is not an intramolecular reaction**.

Example:



Mechanism: Each **migrating tertiary group must have lost contact with the amide fragment** it started out with. Each **molecule falls to bits to give a *t*-alkyl cation and a nitrile**: the **Beckmann rearrangement now goes via a fragmentation mechanism**. **Migrating groups have to provide some degree of cation stabilization**. **But if they stabilize a cation too well there is a good chance that fragmentation will occur and the 'migrating group' will be lost as a carbocation**.