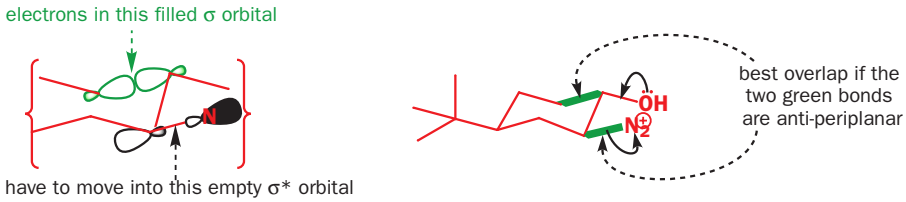
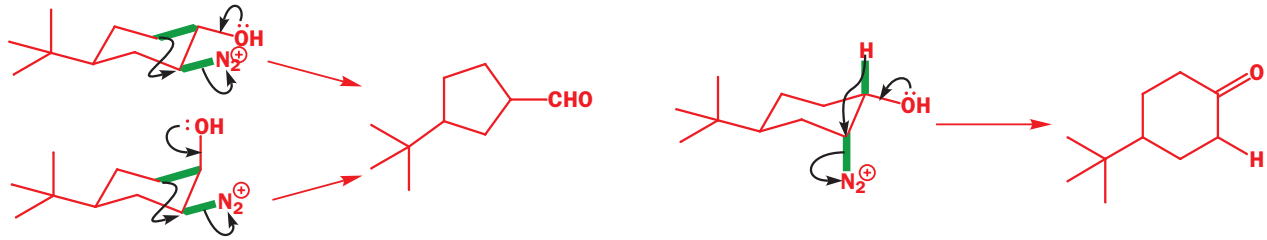
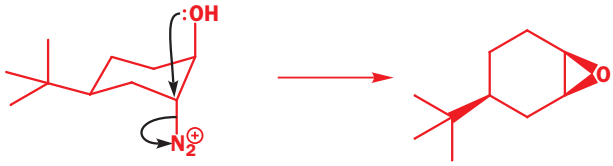
p. 000. But what we didn't talk about then was the fact that best overlap between these two orbitals (σ and σ*) occurs if they are anti-periplanar to one another—just as in an E2 elimination reaction.



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.



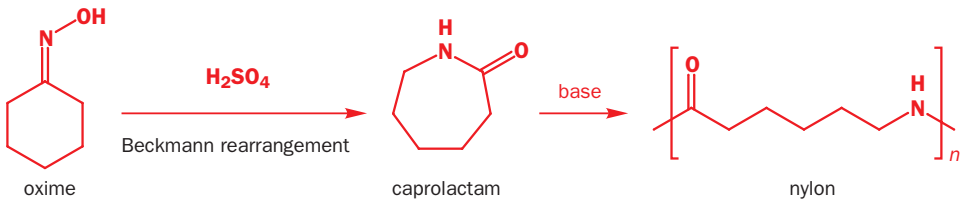
The fourth reaction has, rather than a group that might migrate, the hydroxyl group ideally placed to displace N_2 and form an epoxide—another example of participation.



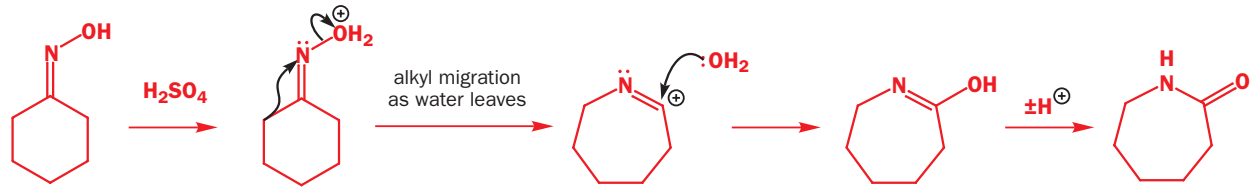
The requirement for the migrating group to be anti-periplanar to the leaving group is quite general in rearrangement reactions. The reason we haven't noticed its effect before is that most of the compounds we have considered have not been conformationally constrained in the way that these are. Free rotation means that the right geometry for rearrangement is always obtainable—stereochemistry is not a factor in the Baeyer–Villiger reaction, for example. We will come back to some more aspects of stereochemical control in the next chapter, on fragmentation reactions. Before then, we will consider one last rearrangement reaction, in which stereochemistry again plays an important controlling role.

The Beckmann rearrangement

The industrial manufacture of nylon relies upon the alkaline polymerization of a cyclic amide known trivially as caprolactam. Caprolactam can be produced by the action of sulfuric acid on the oxime of cyclohexanone in a rearrangement known as the **Beckmann rearrangement**.

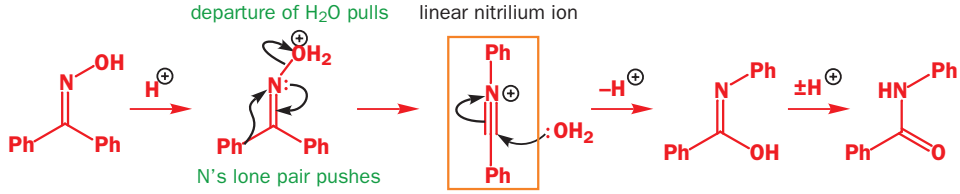


The mechanism of the Beckman rearrangement follows the same pattern as a pinacol or Baeyer–Villiger reaction—acid converts the oxime OH into a leaving group, and an alkyl group migrates on to nitrogen as water departs. The product cation is then trapped by water to give an amide.



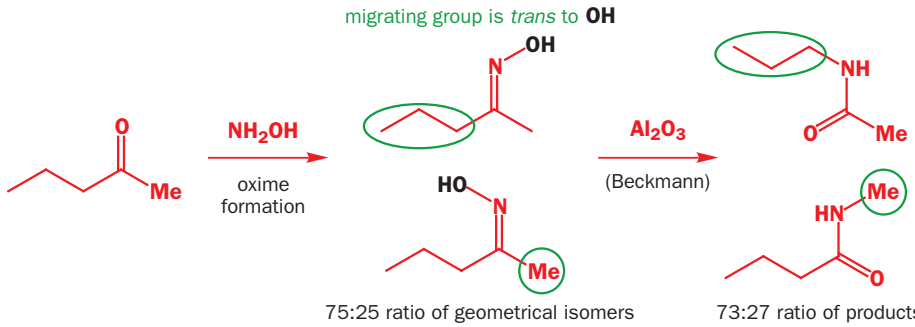
▶ A linear system like this was impossible in the seven-membered ring of the last example.

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 on to N.

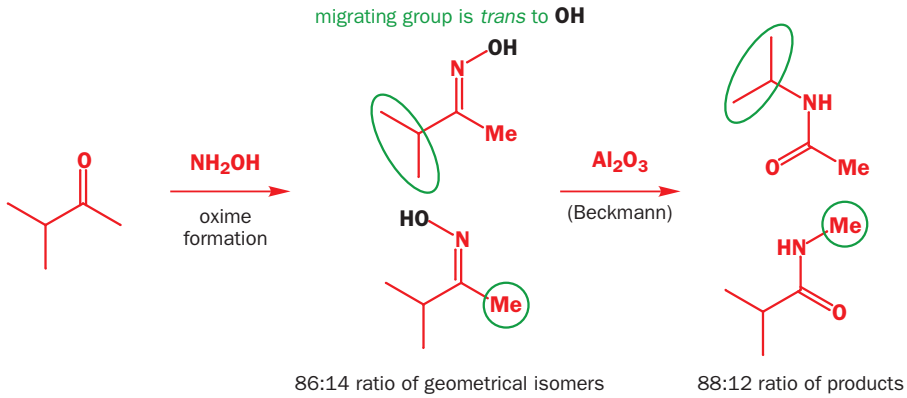


Which group migrates in the Beckmann rearrangement?

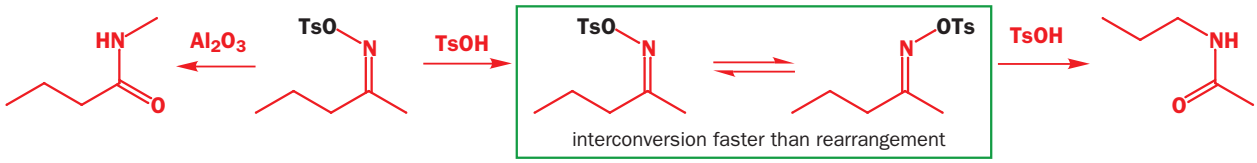
In the Beckmann rearrangement of unsymmetrical ketones there are two groups that could migrate. There are also two possible geometrical isomers of an unsymmetrical oxime: C=N double bonds can exhibit *cis/trans* isomerism just as C=C double bonds can. When mixtures of geometrical isomers of oximes are 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.



We have already touched on the idea that, 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. In the example a couple of pages back the stereospecificity of the reaction was due to the starting material being constrained in a conformationally rigid ring. 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.



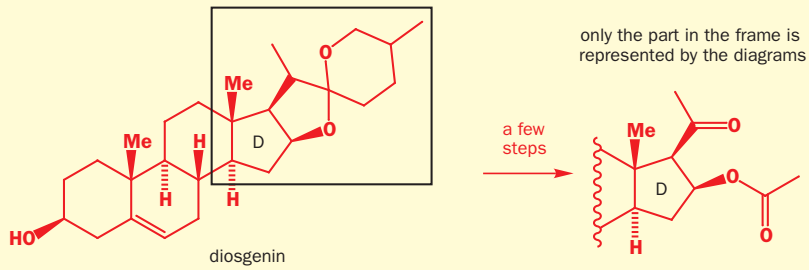
Conditions that allow those double isomers to interconvert can allow either group to migrate—which does so will then be decided, as in the Baeyer–Villiger reaction, by electronic factors. Most protic acids allow the oxime isomers to equilibrate—so, for example, this tosylated oxime rearranges with full 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.



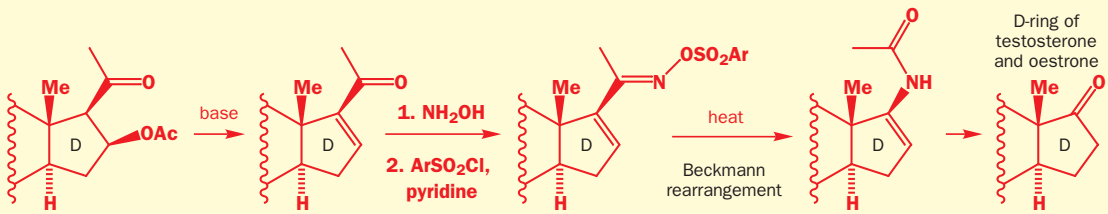
Notice that the effect of the Beckmann rearrangement is to insert a *nitrogen* atom next to the carbonyl group. It forms a useful trio with the Baeyer–Villiger *oxygen* insertion and the diazoalkane *carbon* insertion.

The diosgenin story: steroids from vegetables

Many of the human steroid hormones are available by 'semisynthesis'—in other words 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

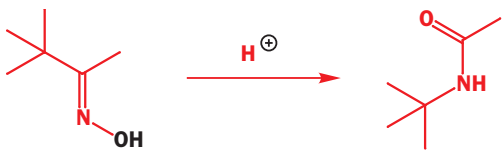


Bur for hormones such as oestrone and testerone two carbon atoms need removing to make a cyclopentanone. This is accomplished using a Beckmann rearrangement. The oxine forms with the OH group trans to the more bulky cyclic substituent. Tosylation and Beckmann rearrangement gives an acetylated enamine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

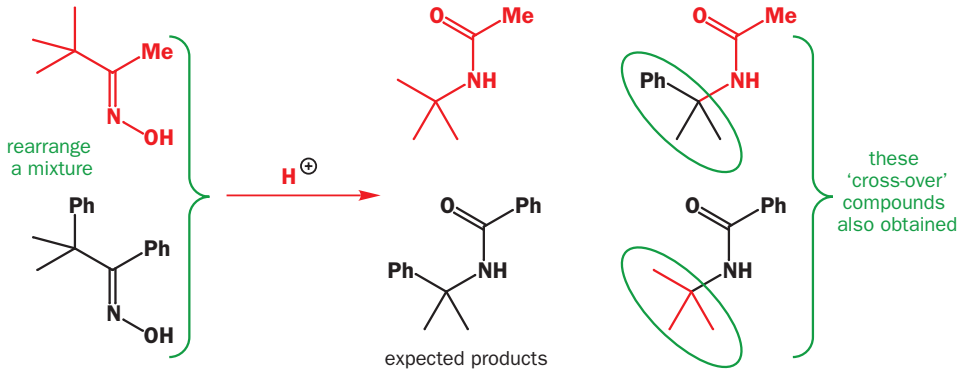


The Beckmann fragmentation

To finish this chapter, a Beckmann rearrangement that is not all that it seems. *t*-Butyl groups migrate well in the Baeyer–Villiger reaction and, indeed, Beckmann rearrangement of this compound appears to be quite normal too.

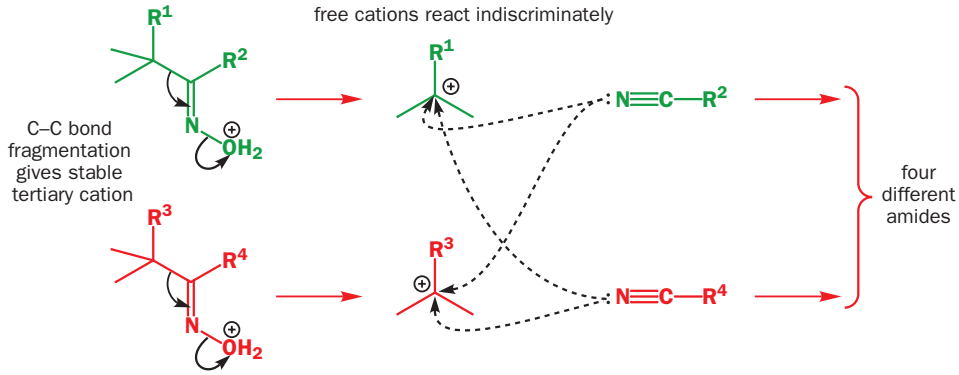


But, when this compound and another compound with a tertiary centre next to the oxime are mixed together and treated with acid, it becomes apparent that what is happening is not an intramolecular reaction.



▶ The recombination step of this reaction is really just a Ritter reaction: reaction of a nitrile with a carbocation. You came across the Ritter reaction on p. 000.

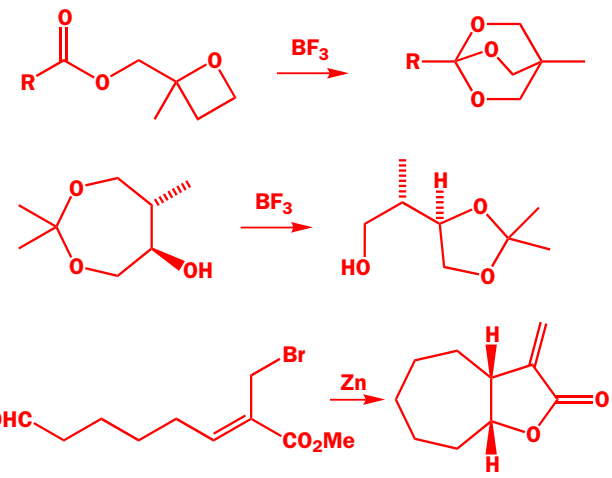
Each migrating tertiary group must have lost contact with the amide fragment it started out with. Each molecule falls to bits to give a *t*-alkyl cation and a nitrile: the Beckmann rearrangement now goes via a **fragmentation** mechanism.



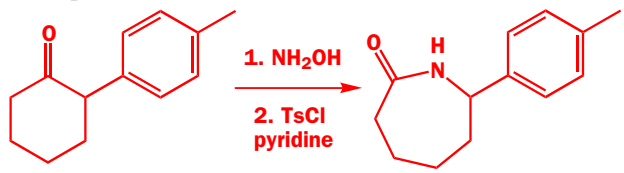
Migrating groups have to provide some degree of cation stabilization. But if they stabilize a cation too well there is a good chance that fragmentation will occur and the 'migrating group' will be lost as a carbocation. It is with this idea that we begin the next chapter.

Problems

1. Rearrangements by numbers. This problem is just to help you acquire the skill of tracking down rearrangements by numbering. There are no complicated new reactions here. Just draw a mechanism.



2. Explain this series of reactions.



3. Draw mechanisms for the reactions and structures for the intermediates. Explain the stereochemistry, especially of the reactions involving boron. Why was 9-BBN chosen as the hydroborating agent?