MOLECULAR REARRANGEMENTS

Key words: rearrangement reactions, migration to electron deficient nitrogen, electron deficient oxygen, electron deficient carbon. Migratory aptitude, cross-over experiments

Module Introduction

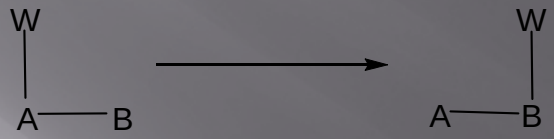
Rearrangment reactions are an interesting class of reactions wherein a group or an atom migration during the course of the reaction. While most of the rearrangements are designed in that fashion, it can also be undesirable in some cases. Depending on the reaction conditions, the nature of rearrangement (and the product) could also change.

In this module, various rearrangement reactions are presented. These are classified with respect the the migration origin and migration terminus.

Emphasis has been placed on examples involving skeletal rearrangements that are practically used in day-to-day organic synthesis.

I. *Introduction*

*Rearrangement reactions involve the migration of a group or an atom from one center (**migration origin**) to another (**migration terminus**) within the same molecule.*



In the above-mentioned generalized representation, atom-A is migration origin from where the migrating group "W" moves to atom-B (migration terminus)

These rearrangements can be roughly classified on the basis of the nature of the migrating group/atom,

i.Nucleophilic or Anionotropic: migrating group migrates with its electron pair.

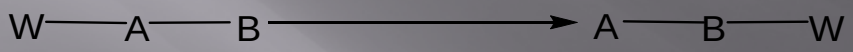
ii.Electrophilic or cationotropic: migrating group migrates without its electron pair.

iii.Free radical: migrating group migrates with only one electron.

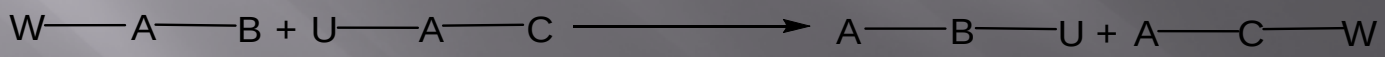
Of these most commonly found are nucleophilic one.

These rearrangements can take place in two possible modes,

i.Intramolecular : In these migrating group do not completely detach from the migration origin and occurs within the same molecule.



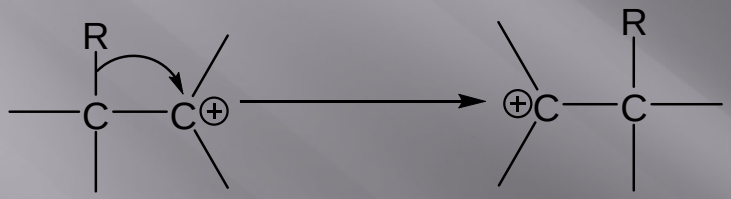
ii. Intermolecular : In these migrating group is detached from the migration origin. In this case, migration of a group/atom can take place to different molecule.



II. *Origin of* 1,2-*rearrangement*

Different pathways through which 1,2-*rearrangement takes place are given below. Examples 1-3 involve electron deficient carbon atoms*

1.



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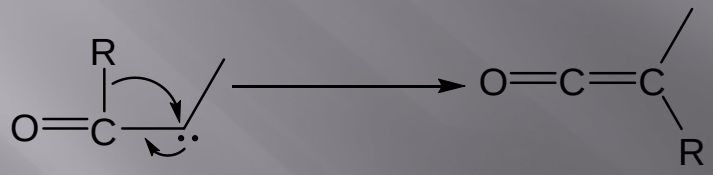

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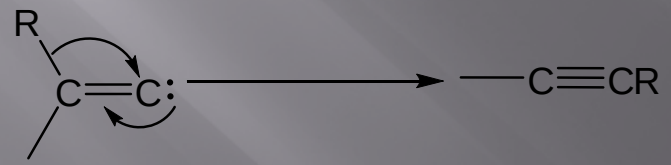

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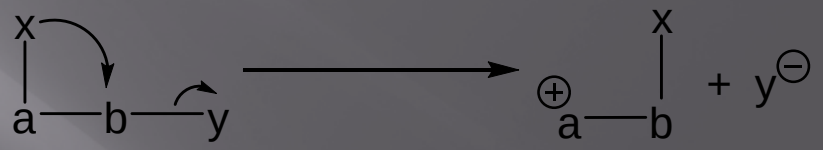

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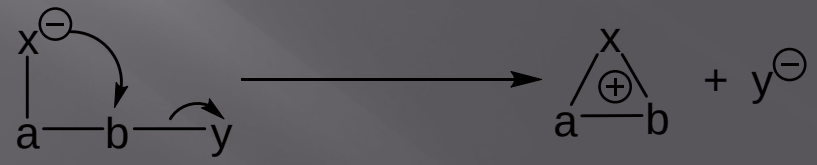


A key driving force in such rearrangement reactions comes from the conversion from a sextet to octet electronic configuration

Some General features of 1,2-rearrangement reactions

Reactions 1 *to* 3, a species with *valence electron sextet either carbocation or carbenium ion is involved. Thermodynamic driving force for an* 1,2-*rearrangement will be significant if rearrangement leads to a structure with octet on all atoms or generates some other more stable carbocation [reaction* 1*] i.e. if newly generated carbocation is stabilized electronically by its substituents than its preceding carbocation. Alternatively, reduction in angle strain can also provide the driving force.*

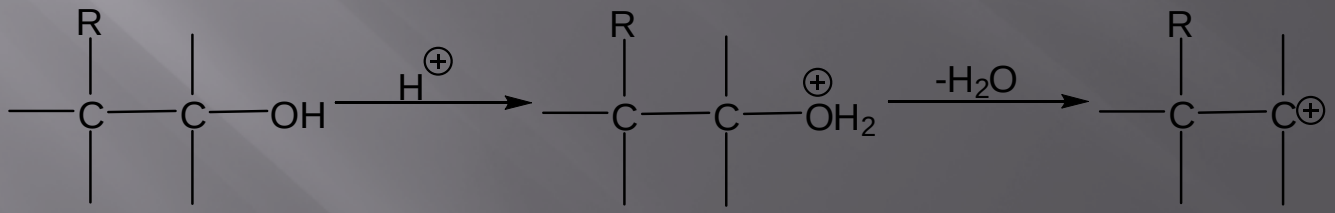
Reaction 4 *&* 5 *show second cause for occurrence of rearrangement. In reactions 4 and 5, atom* b *is bound to a good leaving group. Heterolysis of such a bond would provide a carbocation. Departure of the leaving group is then assisted by neighboring group. This sometimes gives a positively charged three membered ring I(as in reaction* 5*). Rearrangement in such reactions is possible only if group* x *is present at new position in product than in the reactant*

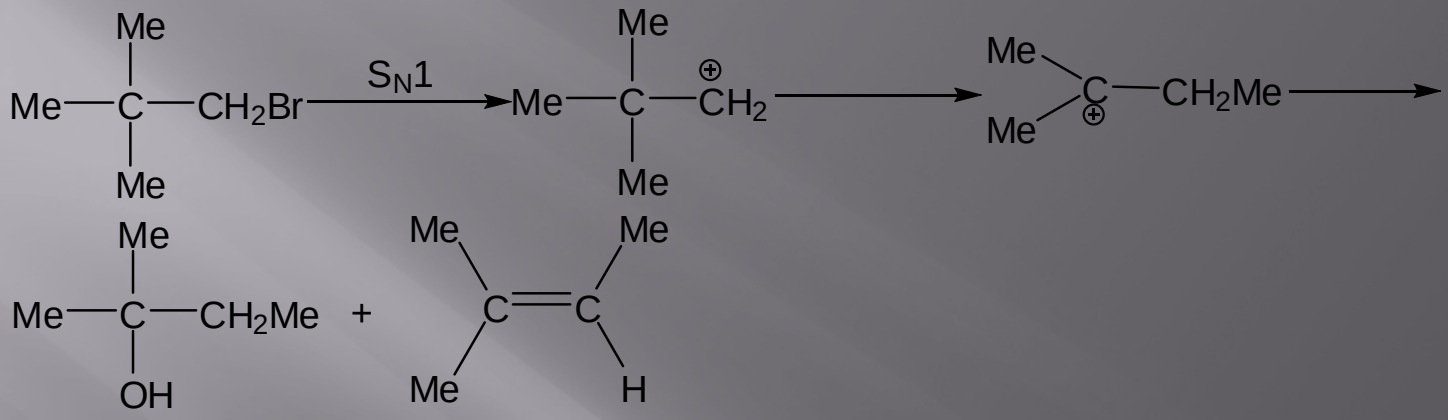
III. *Mechanism of nucleophilic rearrangement*

Broadly these reactions consists of three steps;

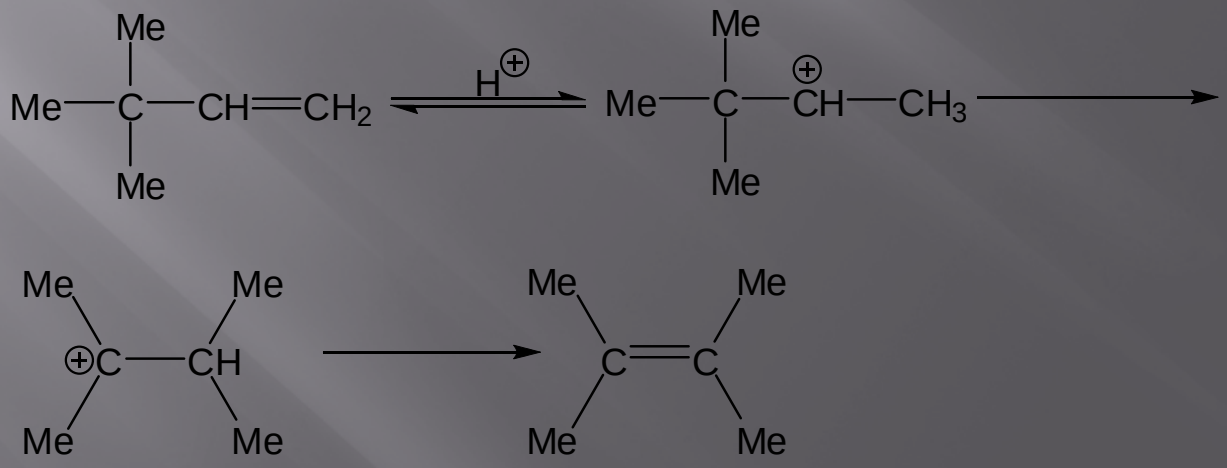
a)First step is ***generation of electron deficient centre*** *in the molecule. As the migrating group migrates with electron pair, the migration terminus must have an incomplete octet. This can be obtained in two ways ,*

i. Through carbocation: Carbocations can be formed in various ways. The most common being dehydration of alcohol. This step is similar to that of S_N1 *or* E1 *reaction.*

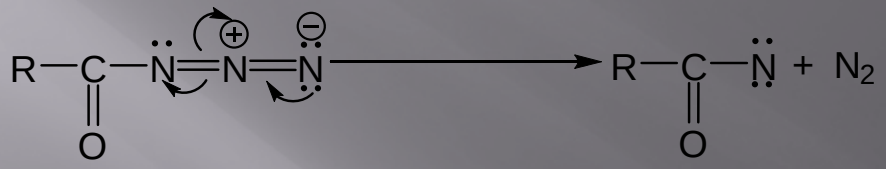




Rearrangement of carbocation is very important reaction in cracking of petroleum products.



ii. Through nitrenes : nitrenes can be formed by decomposition of acyl azides.



b) Migration: *Migrating group migrates to the electron deficient centre with its electron pair creating new electron deficient centre.*

c) In third step, newly formed electron deficient centre acquires octet either by accepting a nucleophile or excluding proton.

It is observed in many cases that either two or all three steps take place simultaneously. As seen in many cases S_N1 type of first step is commonly followed by rearrangement to give a more stable carbocation.

It is proved by the fact that the rate of reaction increases with the ionizing power of solvent and it is unaffected by concentration of base.

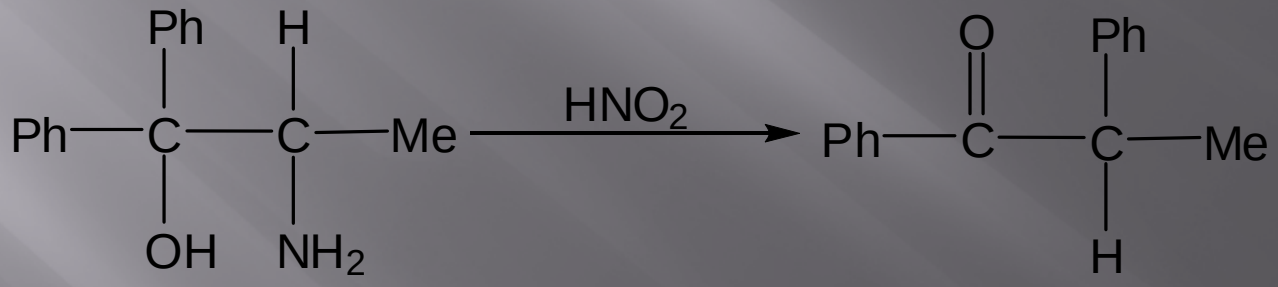
It has been shown that the rate of migration increases with degree of electron deficiency at migration terminus.

IV. *Nature of migration*

Majority of rearrangements are intramolecular.

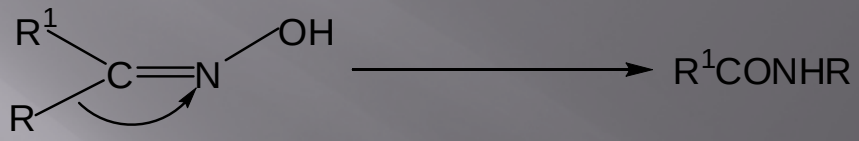
Cross-over experiments *are useful tools to establish the nature of rearrangement.*

Another form of evidence can be gathered by using a chiral migrating group. If the configuration at the migrating group is retained in the product, it is quite likely that the rearrangement is intramolecular.

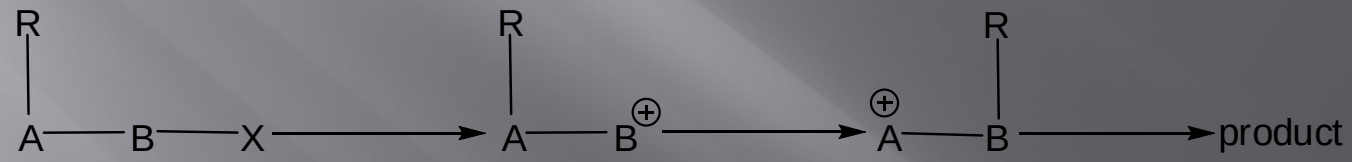


In this example inversion at the migration terminus takes place. The reaction involves diazotization and intramolecular 1,2-phenyl migration.

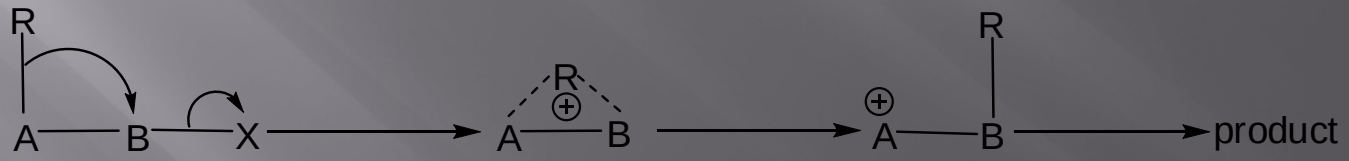
*Eg. In Beckmann rearrangement, only group **anti** to the hydroxyl migrates. This shows the concertedness of the reaction*



So, if racemisation is noticed, then it is probable that the first step takes place before the second step, as in S_N1 reaction.



And, if inversion occurs, then two steps might be concerted, as in S_N2.



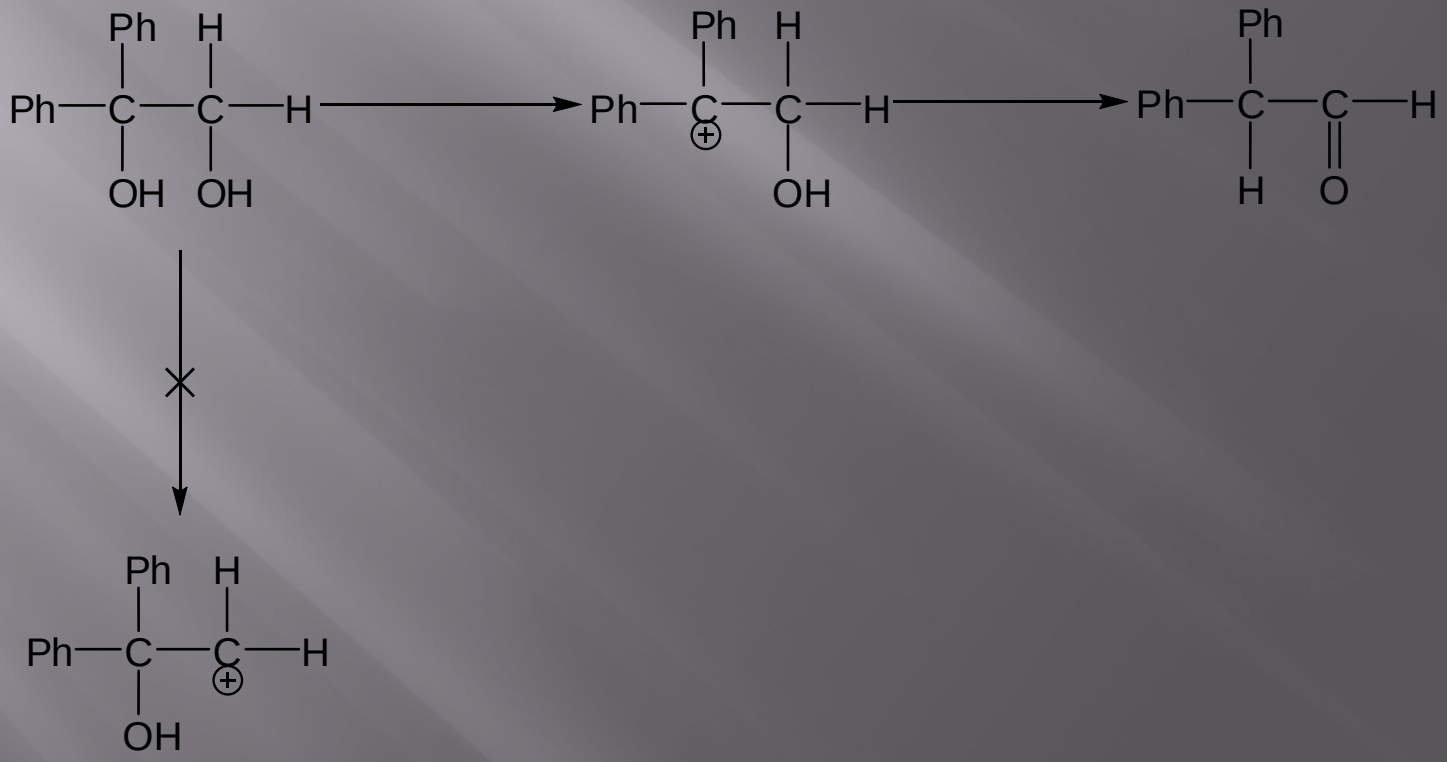
In this case, the neighboring group assists the departure of the leaving group, which in turn can increase the rate of reaction

V. Migratory aptitude

*In many reactions like **Hofmann**, **Curtis** (see later) etc., identity of the group that migrates is quite clear. However, in certain other reactions like **Beckman** rearrangement, there are more than one choice. In such situations the question of which group migrates depends on several factors (such as the geometry of molecule).*

*In the case of **Wagner-Meerwein** and **Pinacol** rearrangement, there are many choices, as substrate contains several groups, that have similar propensity for migration. Such reactions are used for the study of **relative migratory aptitude**.*

** In this example, hydroxyl group is lost from carbon bearing two phenyl groups as it provides a more stable carbocation. The stability of the carbocation is enhanced by group in the order aryl > alkyl >* H.

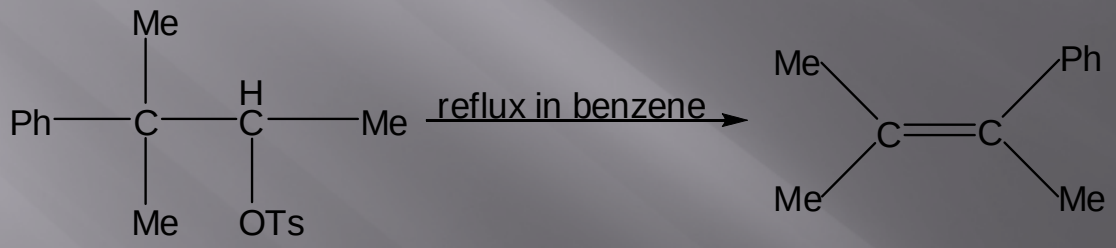


In order to study migratory aptitudes, the substrate should furnish same type of carbocation wherein the migration occurs.

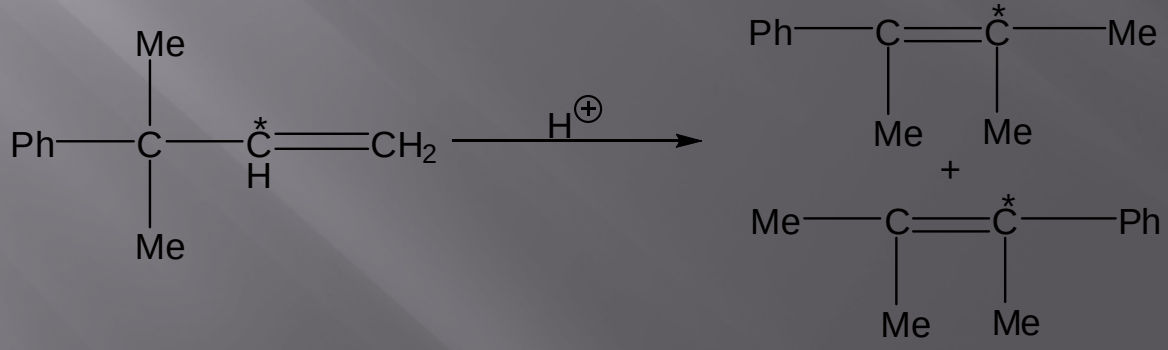
Many factors control migratory aptitude. These are (a) conformational features, (b) relative ability of the groups at the migration origin that can stabilize the developing positive charge.

In the following example, involving the decomposition of tosylate, only phenyl group migrates

The phenyl group in the following example assists the departure of the tosyl group



In a related alkene, upon treatment an acid, a competitive migration of the methyl and the phenyl groups are noticed



Some general trends in the migrating aptitude of different groups

Aryl groups exhibits higher propensity for migration than that of alkyl groups.

Migratory aptitude of hydrogen is unpredictable. Hence, mixture of migrated products are obtained.

In the case of aryl groups, those with electron donating substituents at the meta or para positions migrates preferentially over those containing substituents at the ortho position.

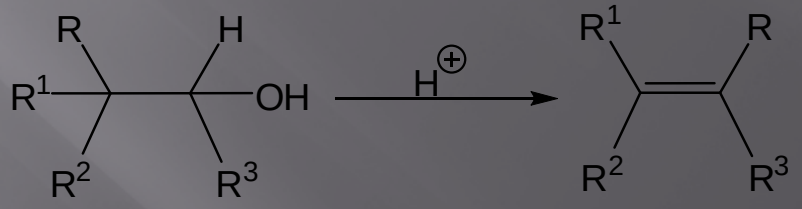
Aryl group containing electron withdrawing groups show reduced

migratory aptitude.

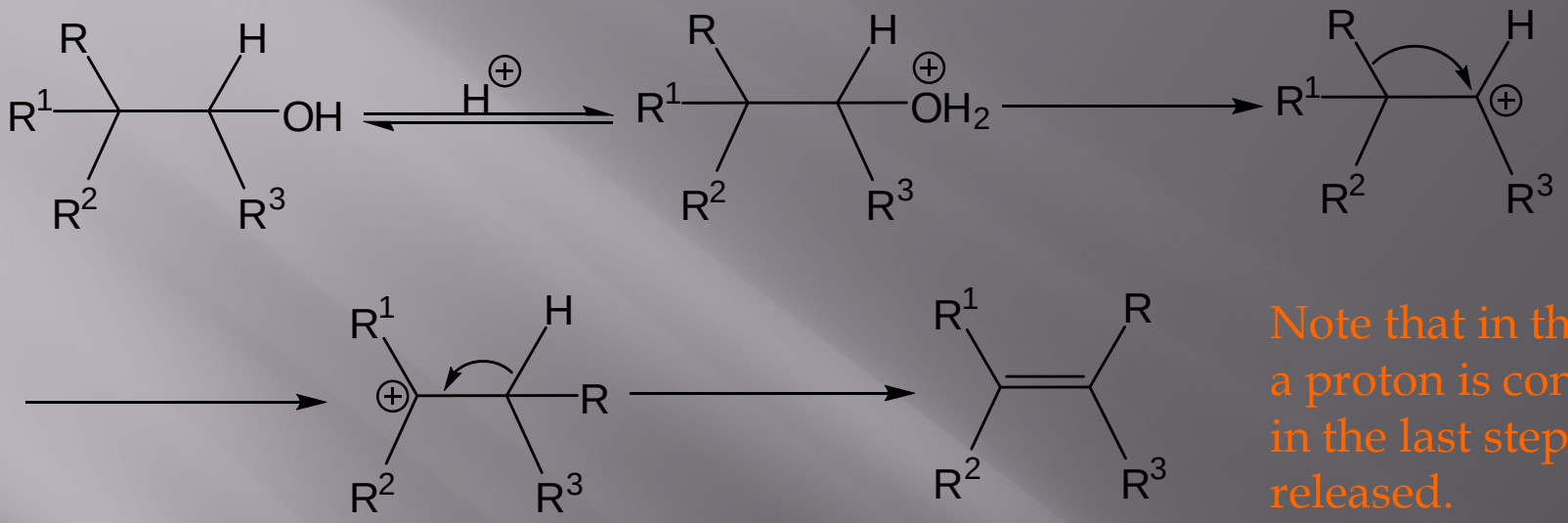
VI. *Reactions involving carbocations*

A. Wagner-Meerwein rearrangement:

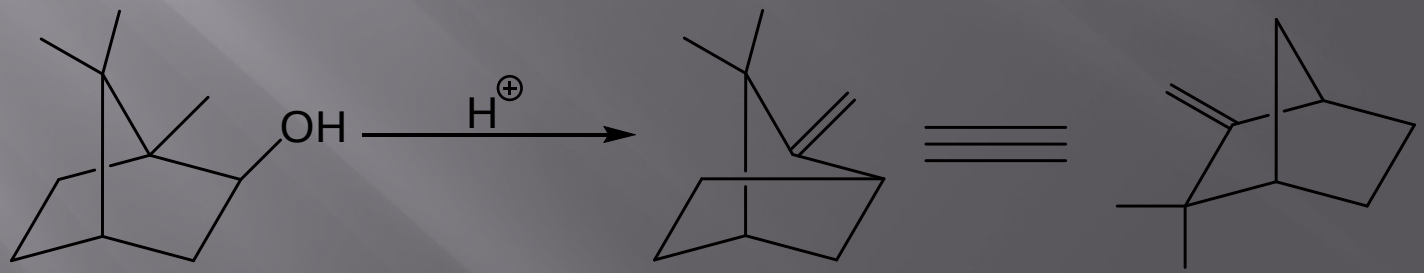
When alcohol containing more than two alkyl or aryl group on β carbon are treated with acid, the product formed is generally a rearranged product, rather than simple substitution or elimination product. This reaction is called Wagner-Meerwein rearrangement. Newly generated carbocation is stabilized generally by loss of a proton to give olefin (and less often by nucleophilic substitution or loss of some other positive group).

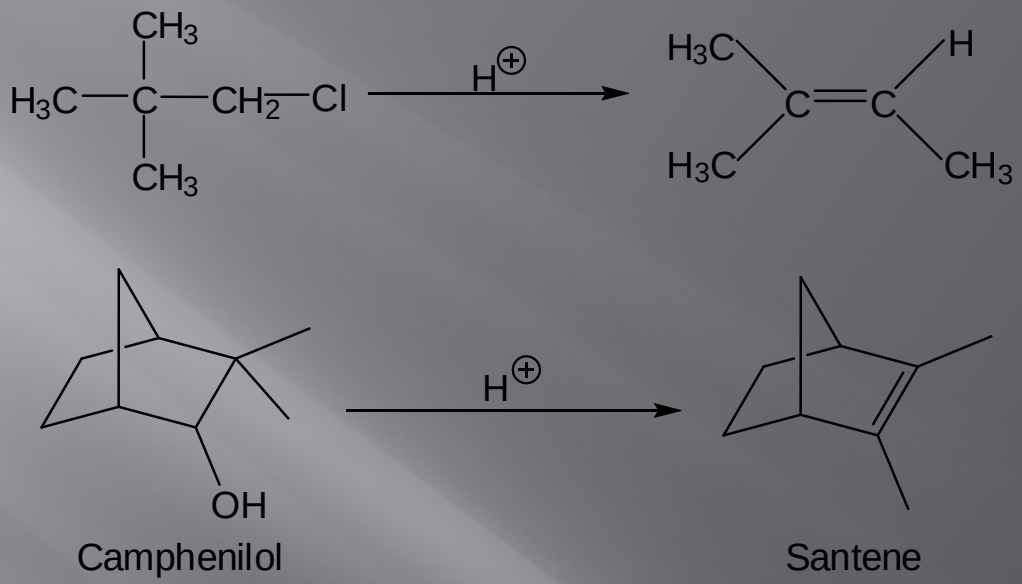


Mechanism involves rearrangement of the carbocation intermediate.



The earliest examples of Wagner-Meerwein rearrangement was noticed in bicyclic terpenes.



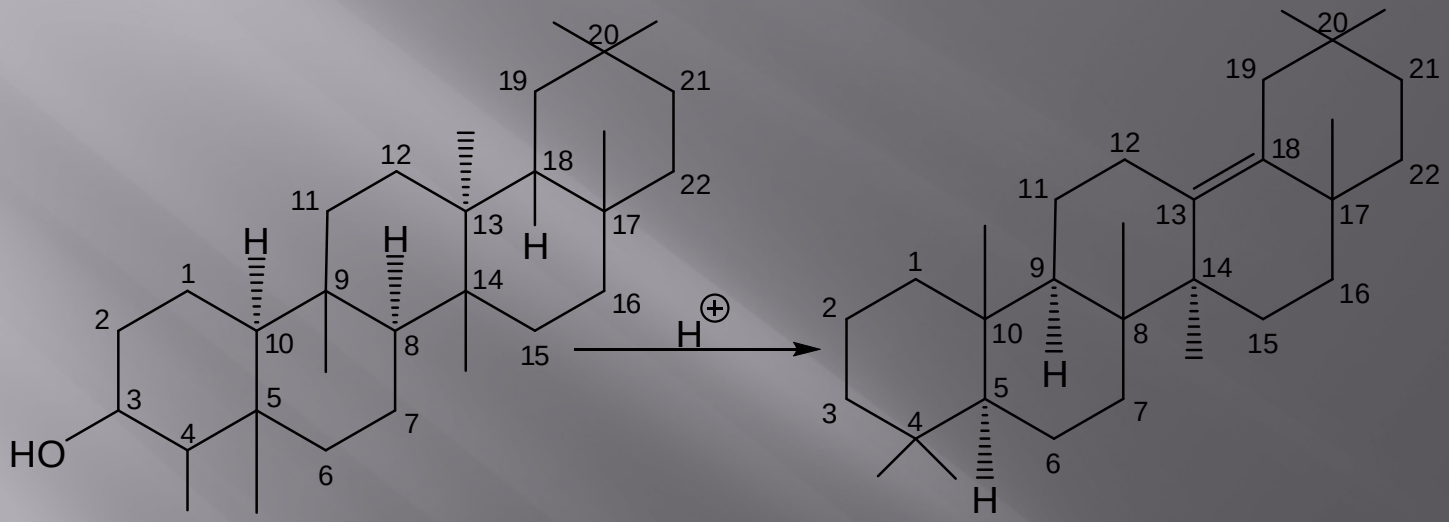


Camphenilol

Santene

In these reactions, double bond is formed according to Zaitsev rule. Leaving group in this reaction can be hydroxyl or other leaving groups (like chloride) which renders carbocationic character to carbon atom. Direction of rearrangement is usually $3^0 > 2^0 > 1^0$.

There are interesting examples where a series of rearrangements occur simultaneously. One example shown below involves a triterpene, 3- β-friedelanol. This compound on treating with acid, 13(8)-oleanene is formed by seven successive 1,2 shifts. [Home work: how?]



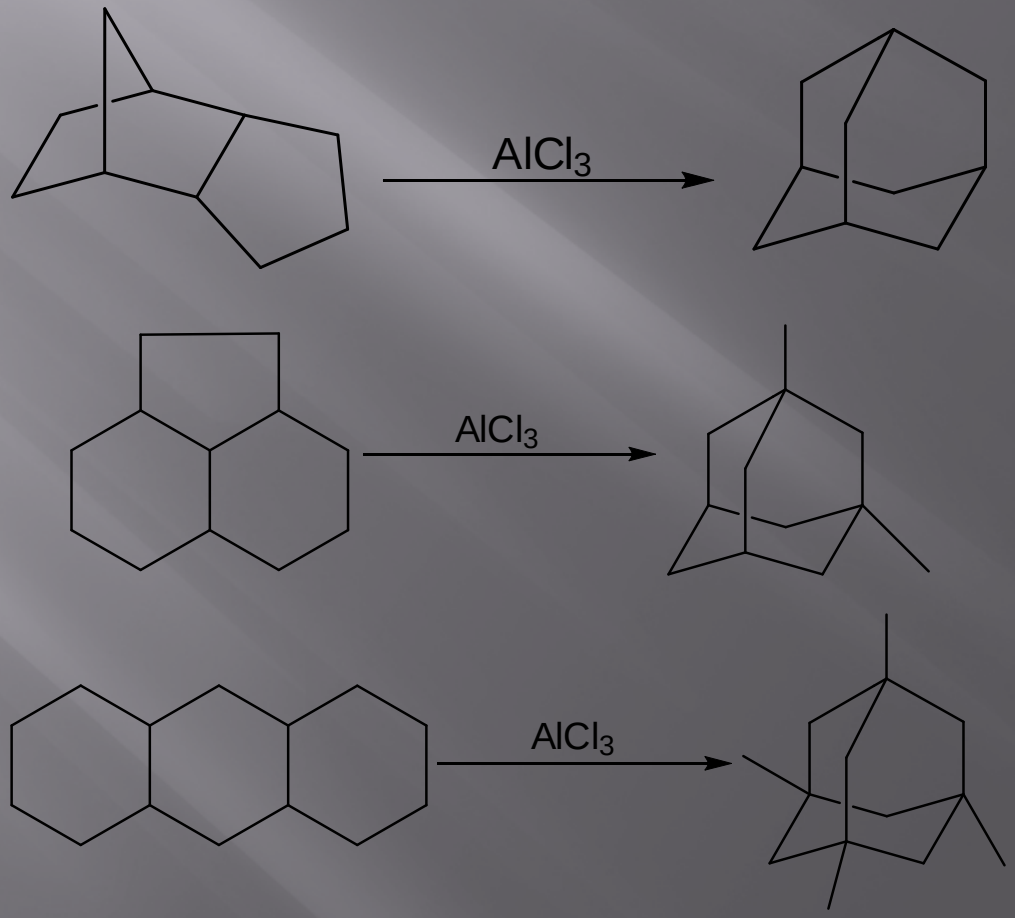
3-friedelanol

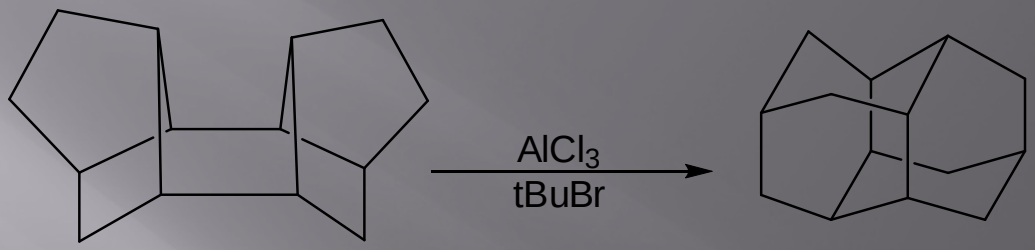
13(18)-oleanene

Textual description of the mechanism*: A carbocation is first generated at* C-3*, which triggers a cascade of rearrangements. Hydride shift from C-*4 *to C-*3*; methyl shift from C-*5 *to C-*4*; hydride shift from C-*10 *to C-*5*; methyl shift from C-*9 *to C-*10*; hydride shift from C-*8 *to C-*9*; methyl shift from C-*14 *to C-*8 *and hydride shift from C-*13 *to C-*14 *takes place, generating carbocation at* C-13*, which is stabilized by loss of proton from* C-18 *to give olefin All these shifts are stereospecific.*

Alkanes, in the presence of Lewis acid or other suitable initiators, can also undergo Wagner-Meerwein rearrangement.

In the following tricyclic molecules consisting of 10 carbon atoms upon a series of rearrangements, provides adamantane(s). The steps are (a) successive 1,2 *and* 1,3 *hydride shifts and alkyl group migration.*

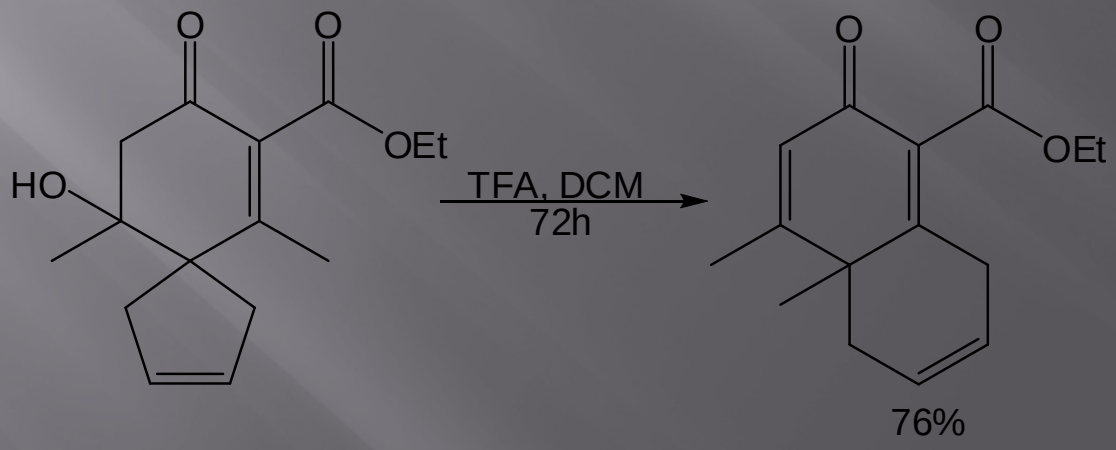




These reactions take place due to the thermodynamic stability

of adamantane, diamentane and similar diamond molecules formed as a result of the rearrangements.

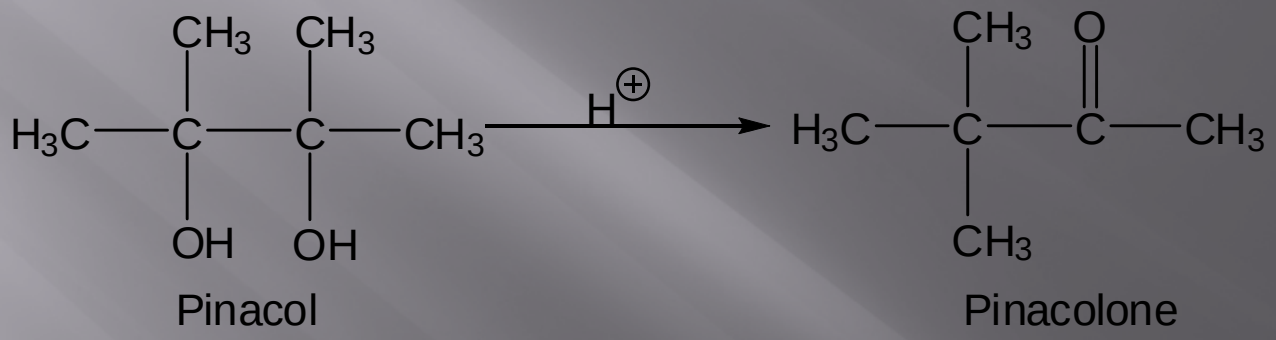
Some ***other kinds of examples*** *for Wagner-Meerwein rearrangement are given below.*



B. Pinacol rearrangement:

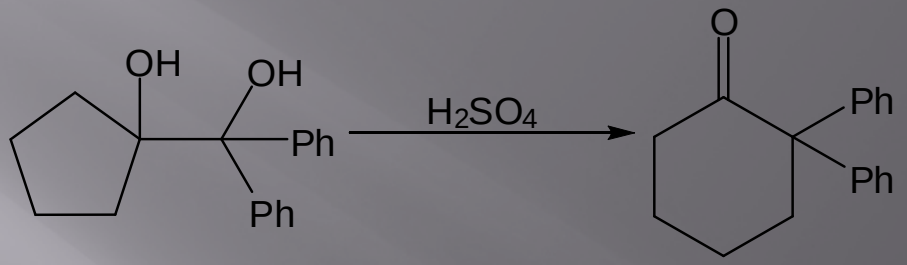
When vicinal diol (also known as pinacol) is treated with acids, it rearranges to give aldehyde or ketone. This reaction is called as Pinacol rearrangement.

E.g.,



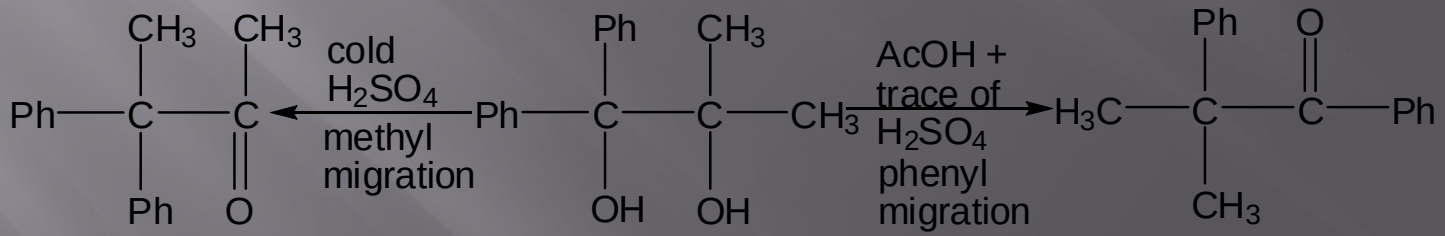
The migrating group can be alkyl, aryl, hydrogen or ethoxycarbonyl.

In the case of unsymmetrical diols, which one of the hydroxy group gets protonated it is important. As seen earlier in this module, in general, the hydroxyl group that can generate a more stabilized carbocation is the one which gets protonated.



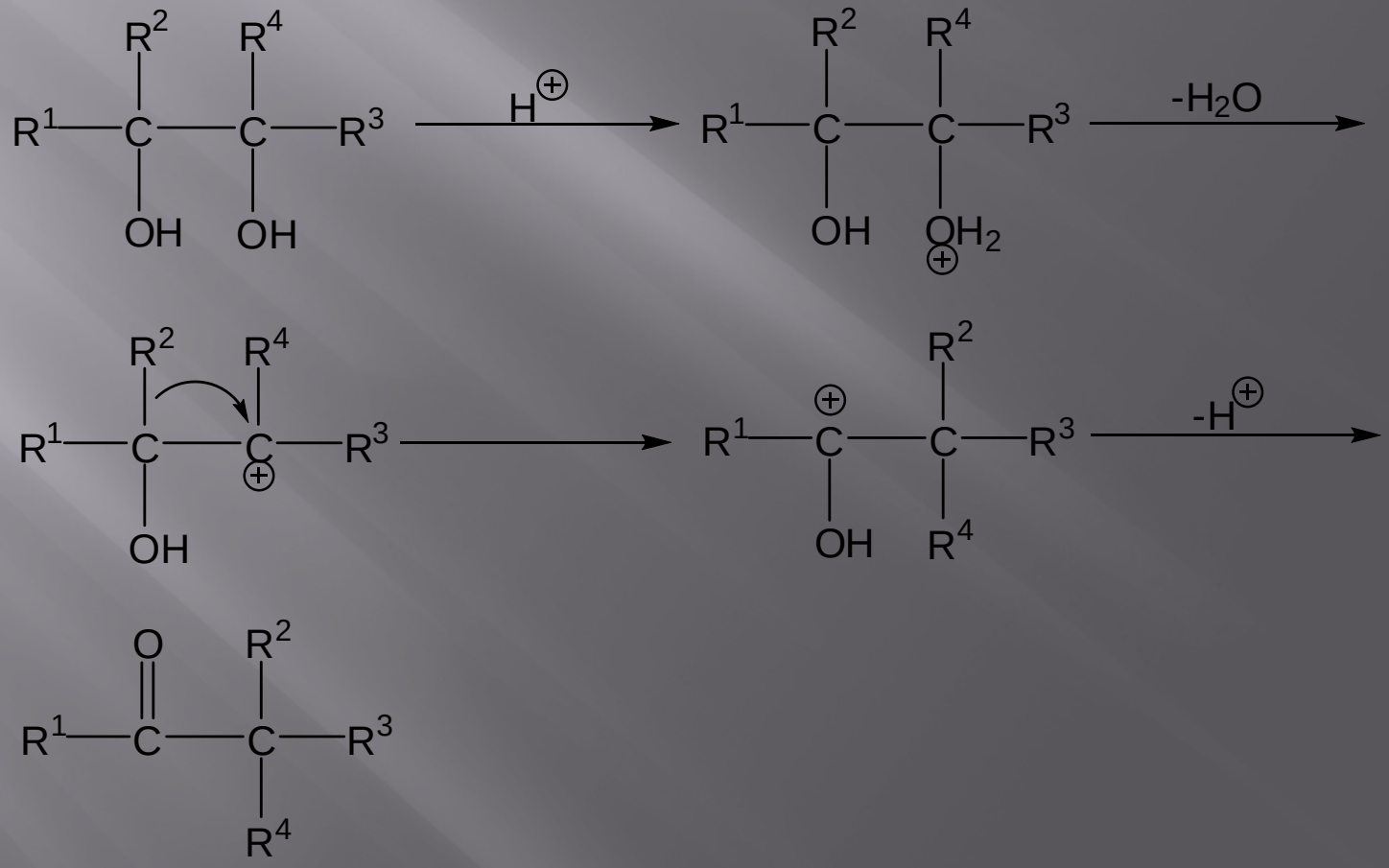
In this reaction, the hydroxyl group on carbon bearing two phenyl groups will be protonated faster to form a more stable benzylic carbocation.

When tri or tetra substituted glycol is used, different products depending upon reaction condition is obtained. It also depends upon migratory aptitude of different groups, as discussed earlier.



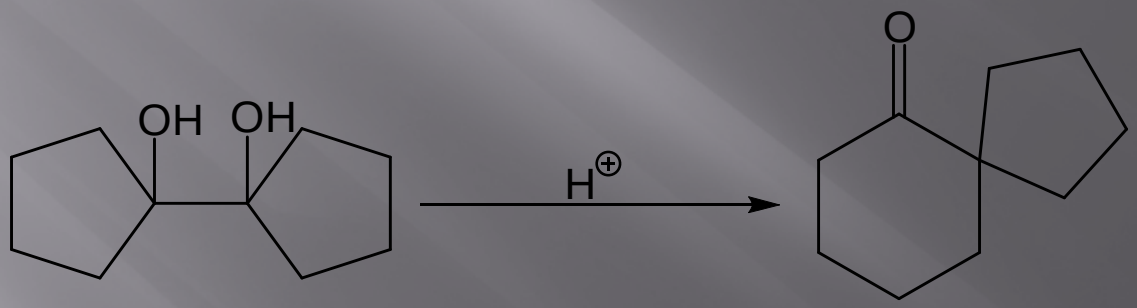
When, at least one of the groups in the glycol is hydrogen (R1 = H, in the following example), aldehyde are produced along with ketone. This can be achieved using weak acids, low temperature etc.,.

A plausible mechanism can be represented as follows;



The driving force for the migration of alkyl group from the initially formed carbocation come from the increased stability of tertiary carbocation.

The first example (given below) involves ring expansion.



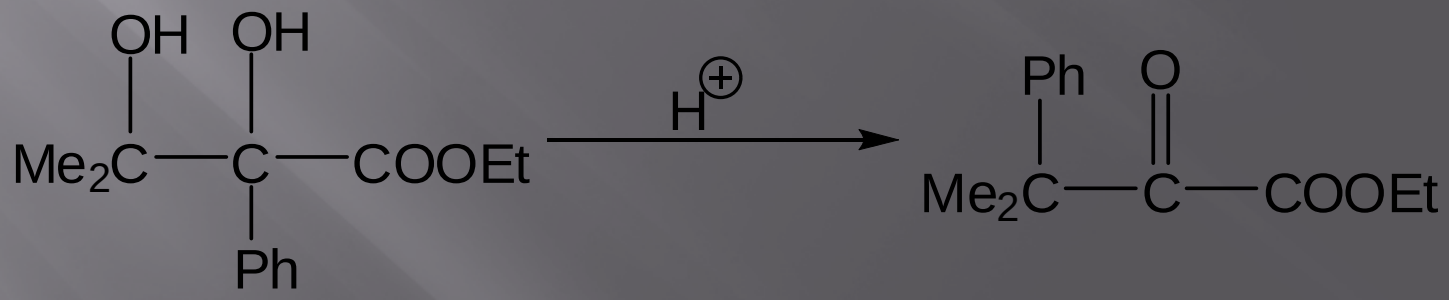
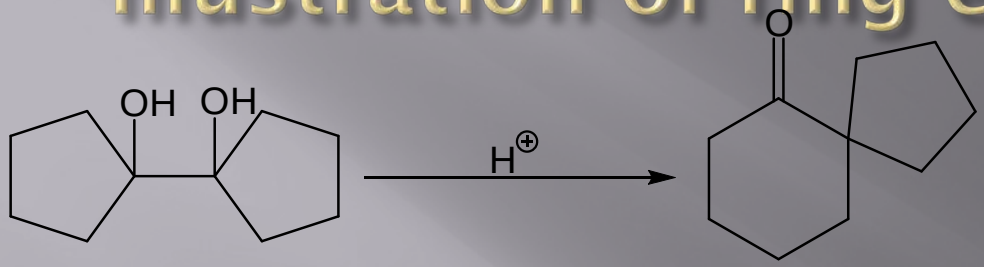
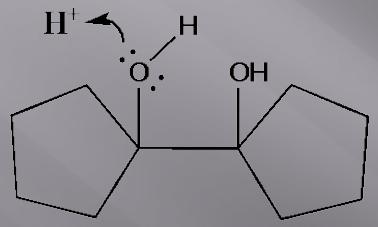


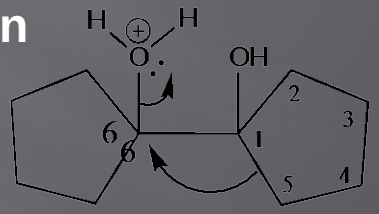
Illustration of ring expansion



Protonation:

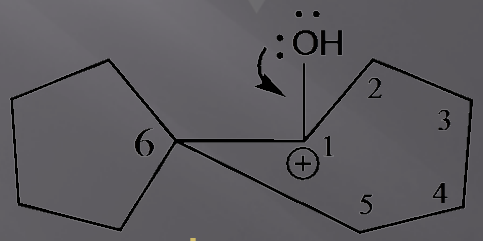


Ring expansion

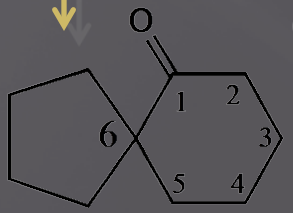


Here the C1-C5 bond of the five membered ring cleaves heterolytically and migrate to the electron deficient migration terminus (C6). Note that in this process C1 of the five-membered ring develops a carbocationic center

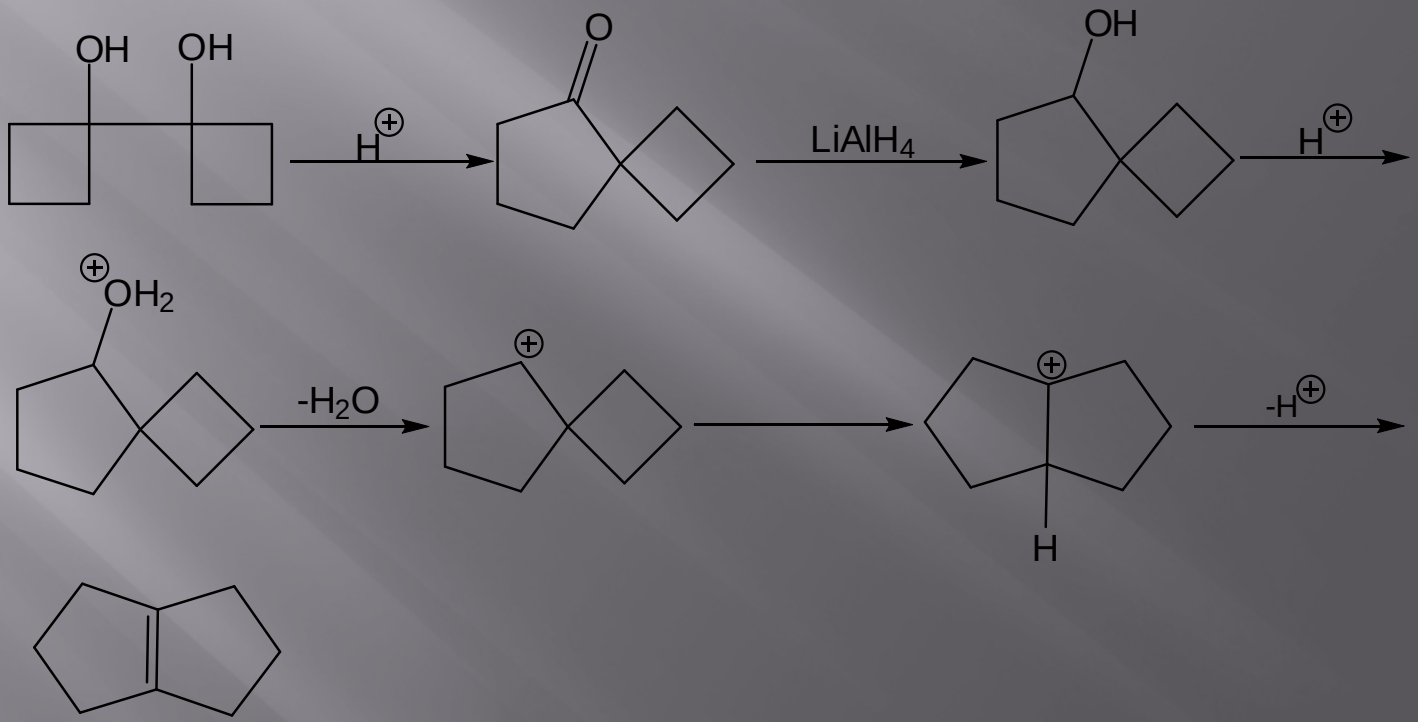
The resulting product is shown here with the similar arrangement as in the reactant so that the process is easy to understand. Student is expected to convert this into a proper structure once the concept is clear



deprotonation:



More useful and synthetically useful example of pinacol rearrangement reaction that are employed is the syntheses of bridged bicyclic compound from a diol are given below.

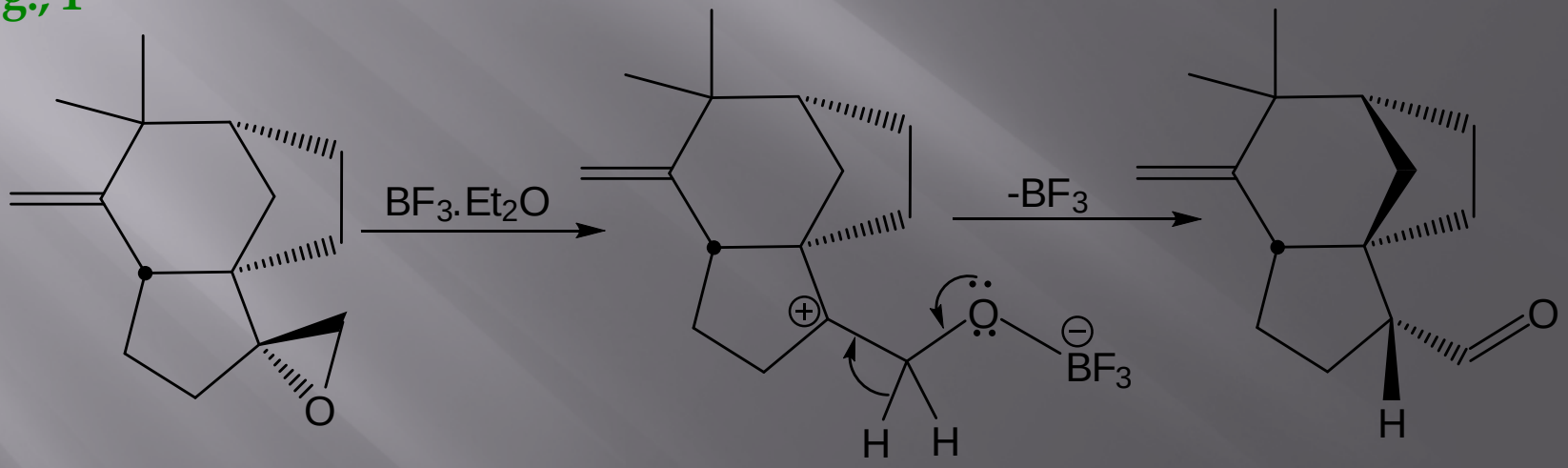


Similar type of reaction is also shown by compounds containing different groups other than hydroxyl group.

This reaction is known as ***Semipinacol rearrangement*** *and involves*

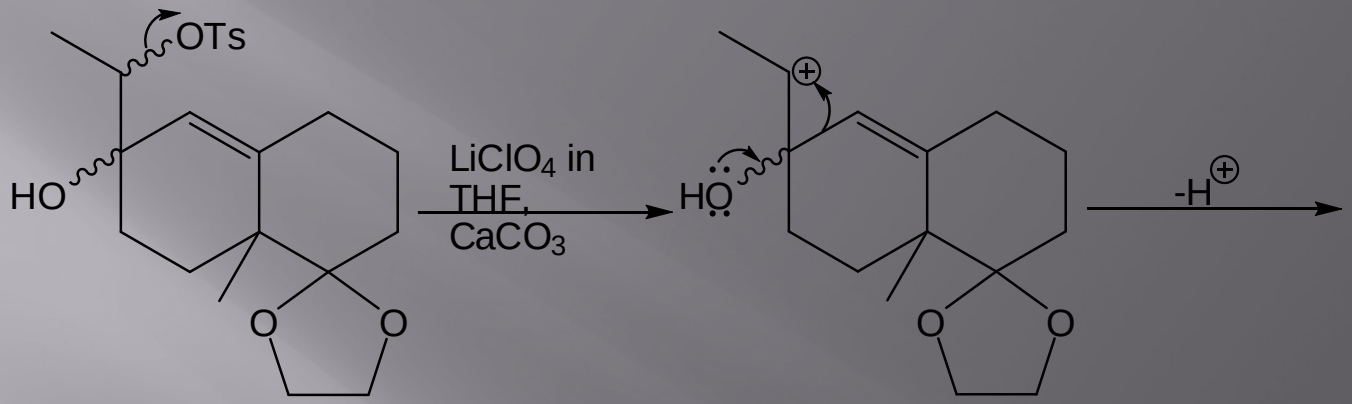
1,2 *shift of* H *or alkyl group from oxygenated carbon atom to neighboring* carbon *atom (i.e. conversion of carbocation to carboxonium ion)*

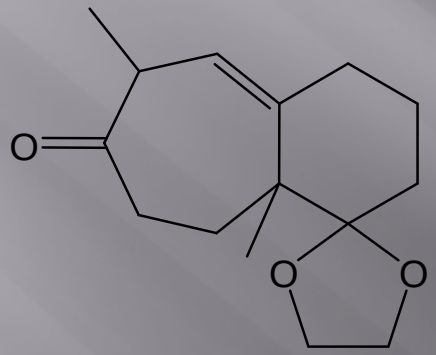
E.g., 1



Description: Here BF3 is a Lewis acid that coordinates to the epoxide oxygen first and opens up the ring to generate the secondary carbocation as shown in the second structure.

E.g., 2

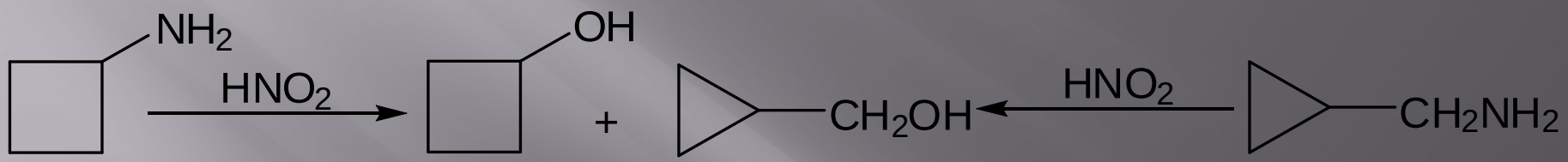


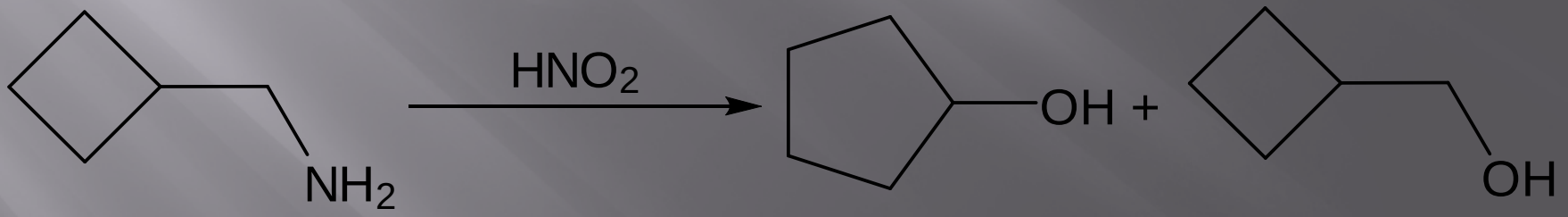


Note that these examples involve ring-expansion

C. Expansion and contraction of rings using molecular rearrangement:

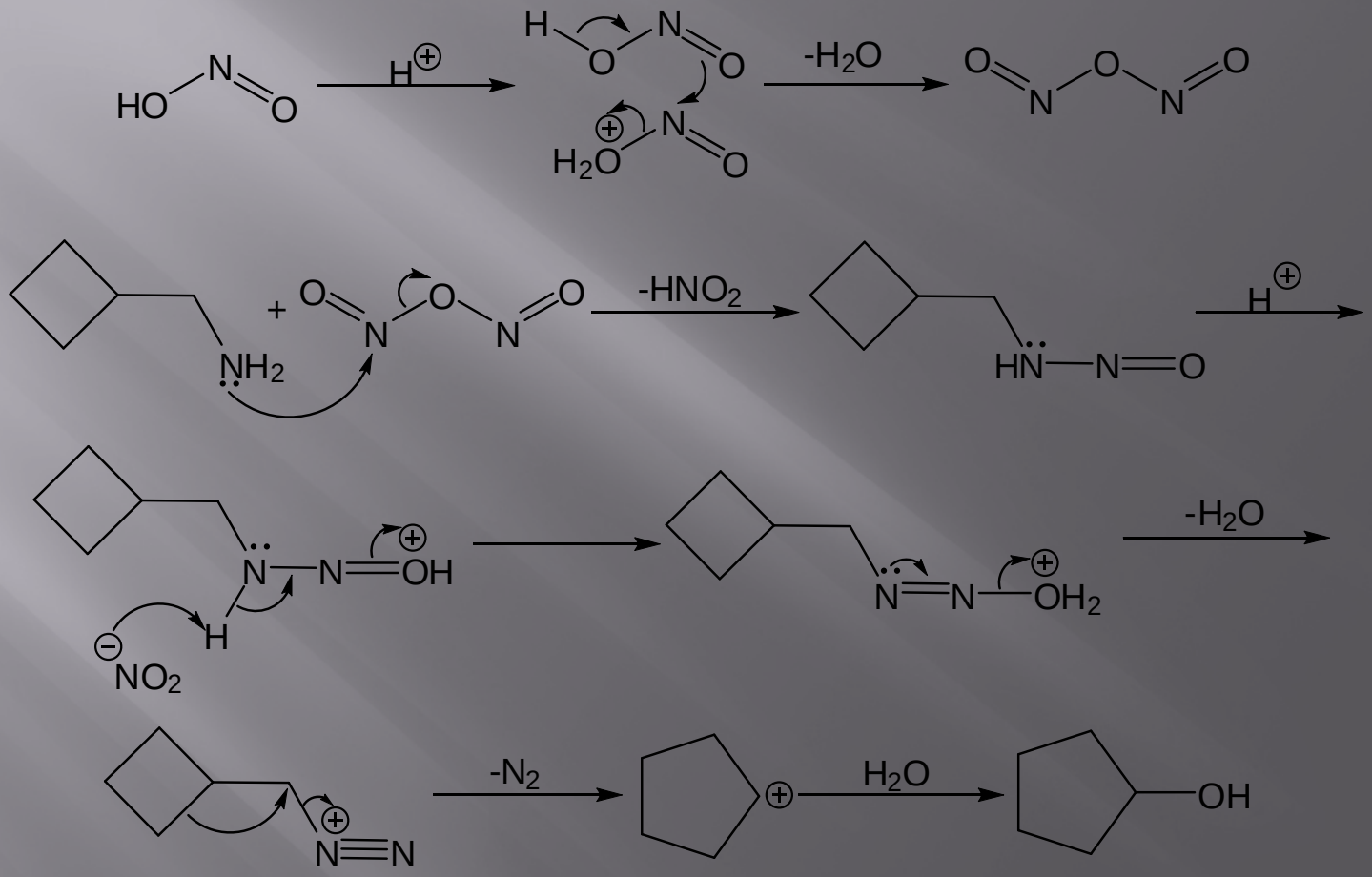
The following reaction represents a special case of Wagner-Meerwein rearrangement. Generally, a mixture of rearranged and non-rearranged products is formed.



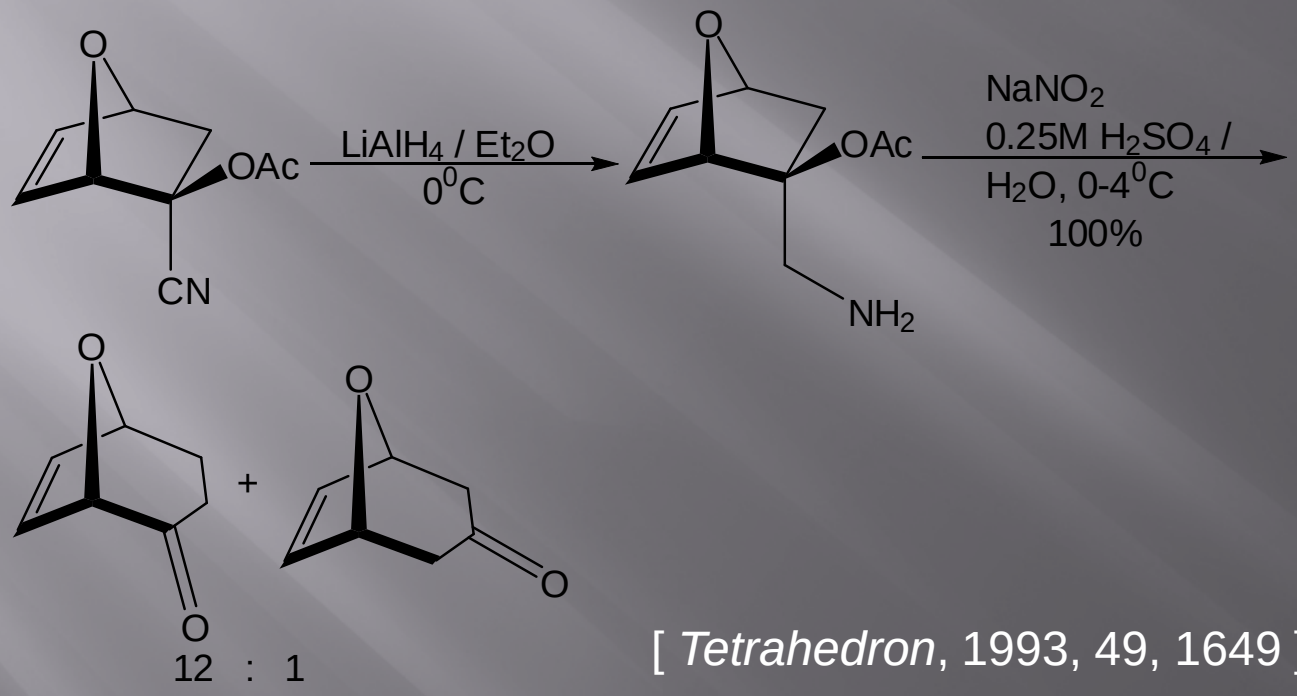


These reactions in which a carbocation is generated by diazotization is called Demjanov reaction

Mechanism is as follows.



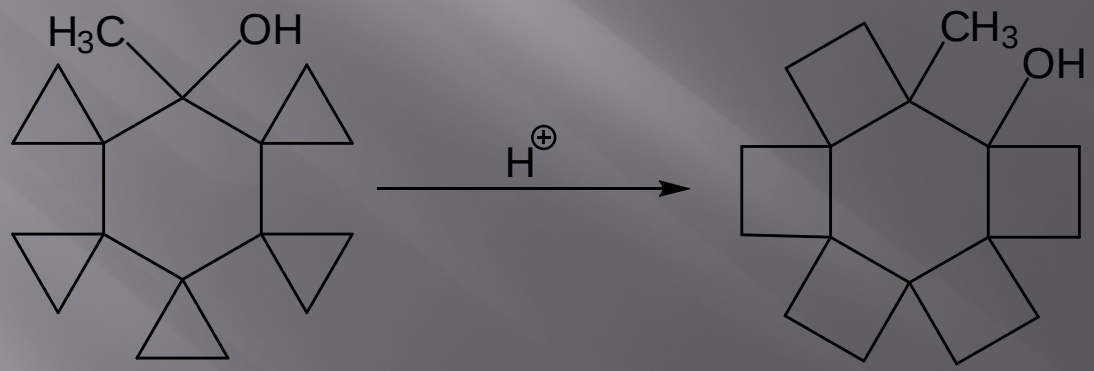
More examples



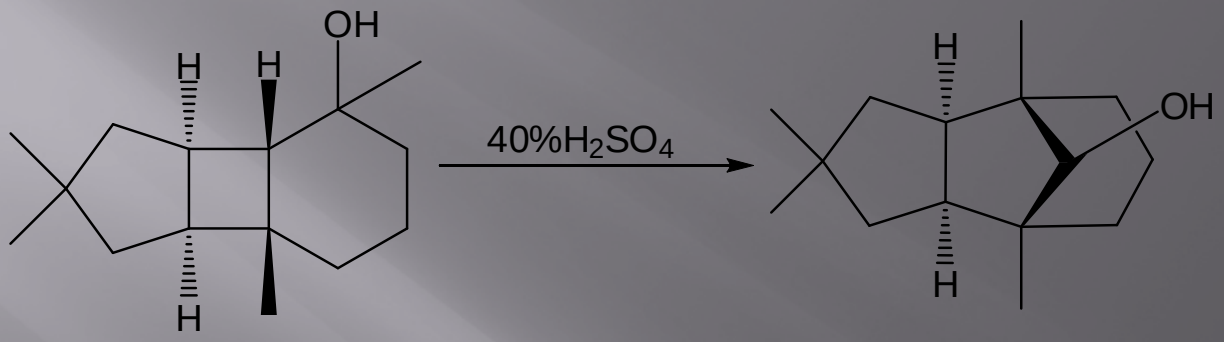
[*Tetrahedron*, 1993, 49, 1649]

It is found that, ring-expansion reactions can give good yields with smaller rings systems, wherein the ring-expansion relieves higher angle strain. Ring-contraction reactions give good yields except for cyclopentyl cation.

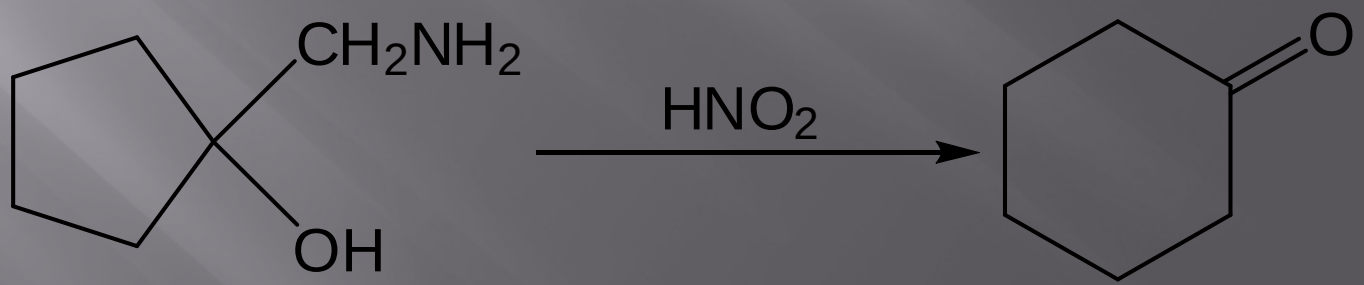
An example of such ring expansion is given below, which involves a series of ring expansions (cascade of ring-exapnsions)



Additional information: Name of the reactant and products are respectively16-methylpentaspiro[2.0.2.0.2.0.2.0.2.1]hexadecan-16-ol *and* 2-methylhexacyclo[12.2.0.0^{2,5}.0^{5,8}.0^{8,11}.0^{11,14}]hexadecan-1-ol.

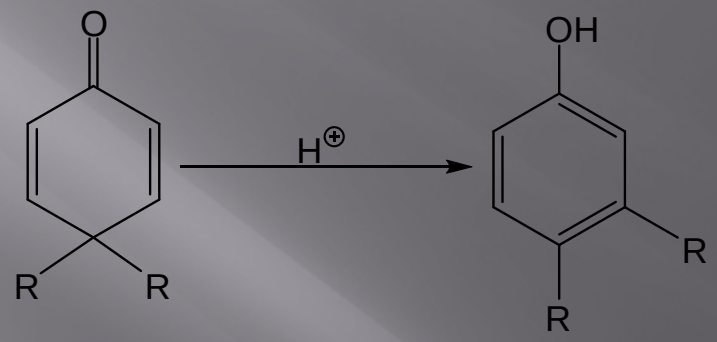


*Reaction of certain **amino alcohols** give analogous reaction to semipinacol rearrangement. The following is one such example known **as Tiffeneau-Demjanov rearrangement**.*

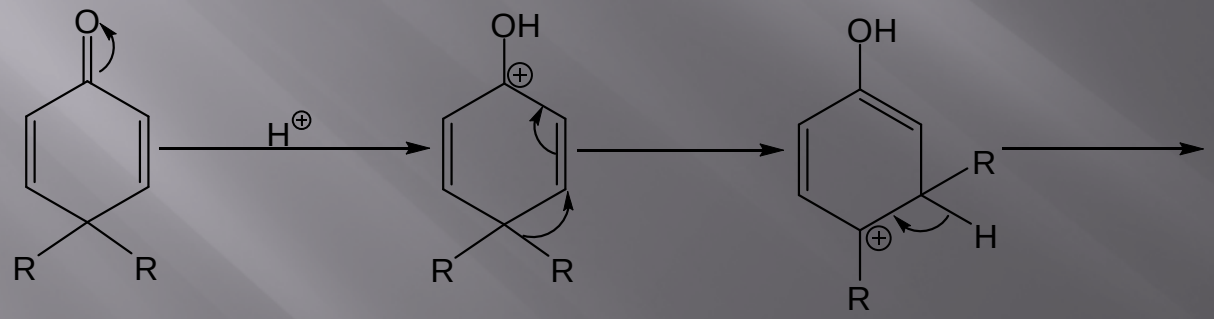


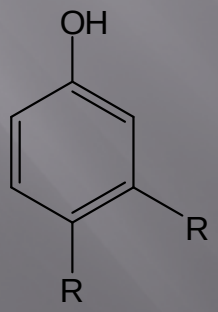
These reactions are known to work better with four to eight membered ring systems as compared to the analogous Demjanov rearrangement.

D. Dienone-phenol rearrangement : *Cyclohexadienone containing C2 or C4 alkyl groups, treatment with acid undergoes 1,2-shift of one of these alkyl groups, to a disubstituted phenol. Driving force for this reaction comes from aromatization of the ring.*

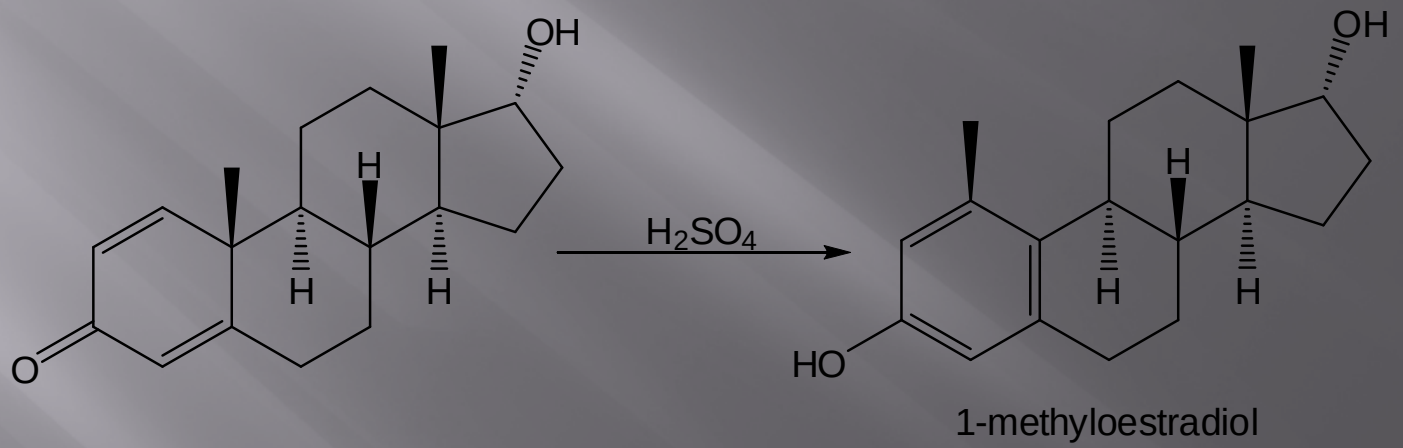


Mechanism





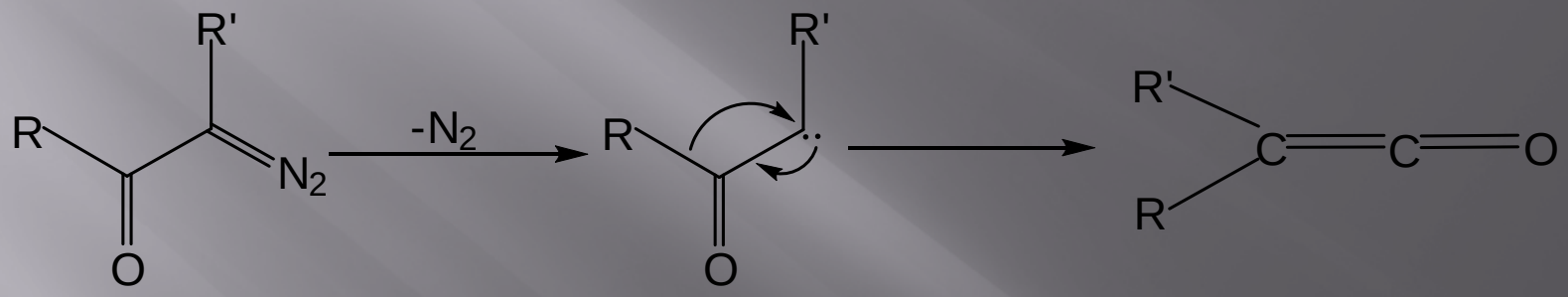
A particularly useful example of dienone-phenol rearrangement can be found in the syntheses of steroidal compound as shown below.



1-methyloestradiol

E. Wolff rearrangement :

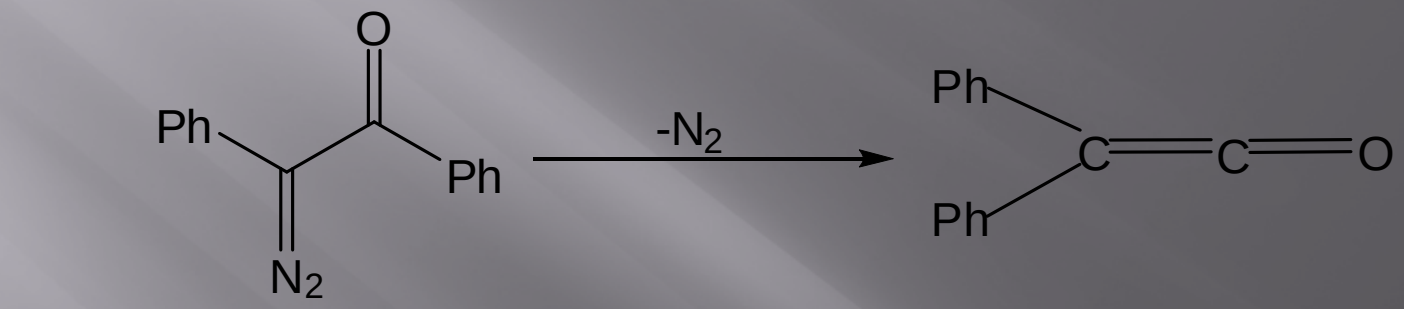
Wolff rearrangement is rearrangement reaction, in which a ***diazo ketone*** *is converted into ketene.*

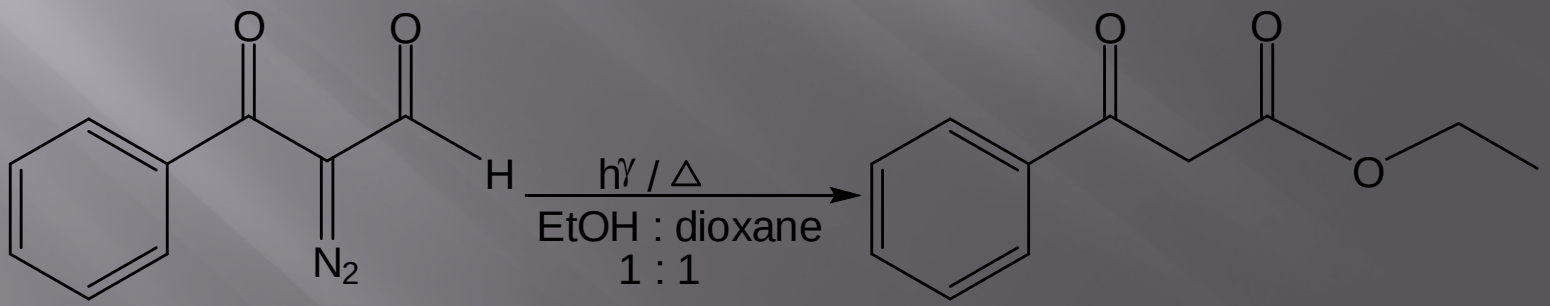


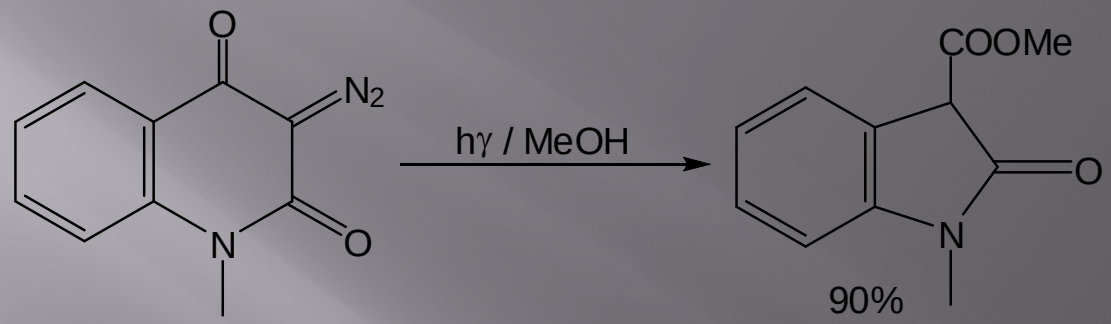
This reaction takes place in the presence of light, heat or transition metal catalyst such as Ag_2O.

The mechanism is suggested to proceed through the involvement of a carbene in presence of heat or light. It may also proceed through a concerted Pathway in the presence of Ag_2O with out carbene.

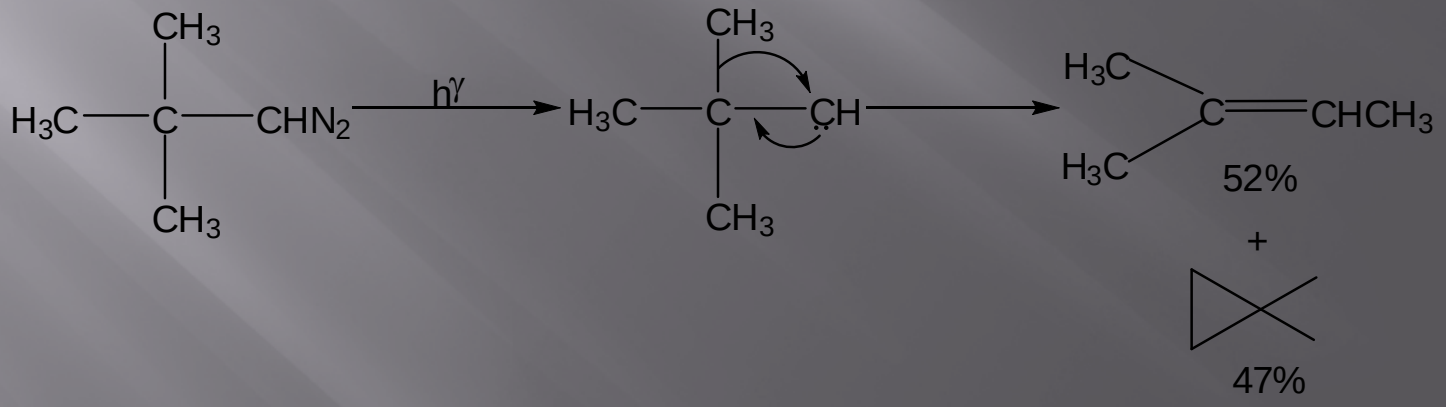
Migratory aptitude is found to vary depending on whether the reaction is carried out under thermal or photochemical route. In the photochemical pathway methyl is migrates preferentially while in thermal pathway phenyl group migrates.





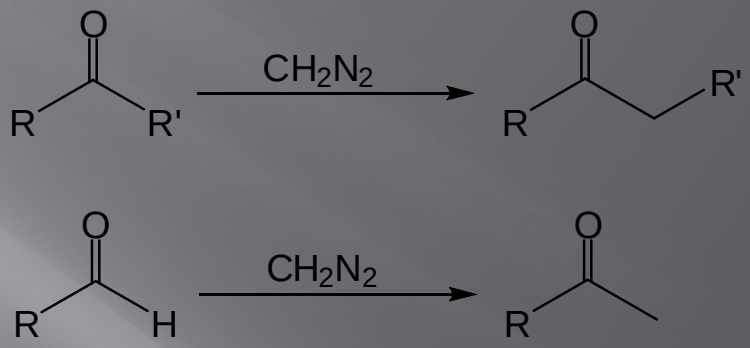


Other 1,2 migrations to carbene are also known.

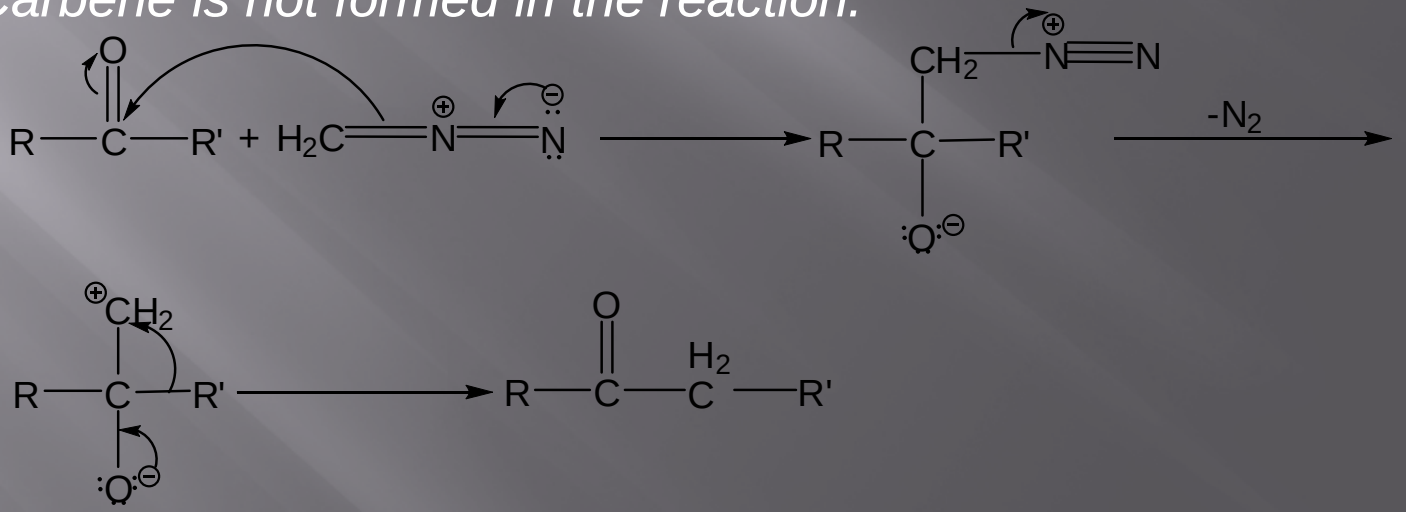


F. Homologation of aldehyde or ketone :

Aldehyde or ketone can be converted to their higher analogs on treatment with diazomethane.

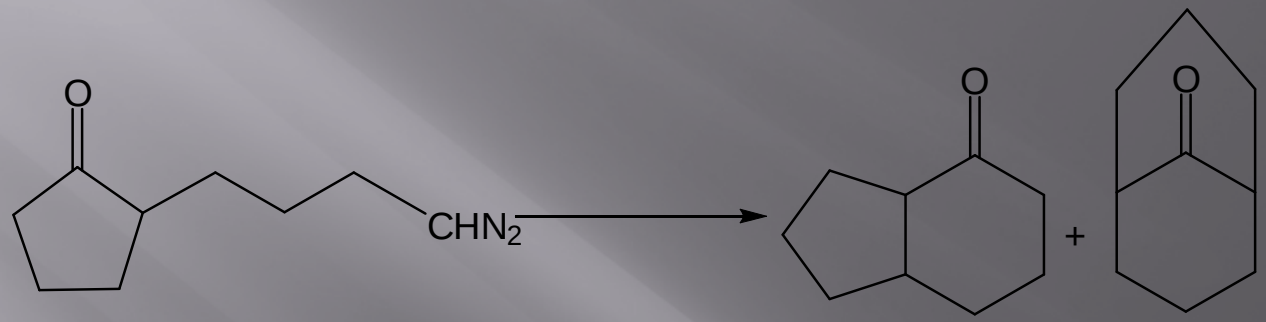


Though, it appears to be an insertion reaction, it is purely rearrangement reaction. Carbene is not formed in the reaction.



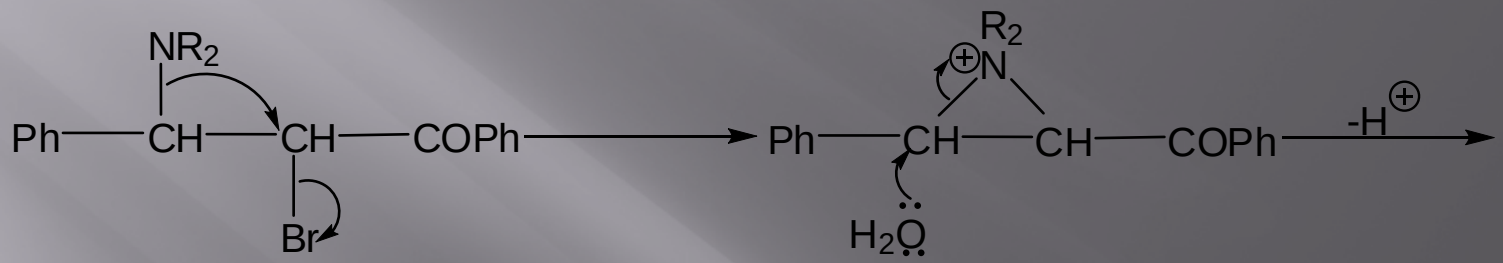
In case of aldehyde, hydrogen migrates preferentially which is evident from good yields of methyl ketone

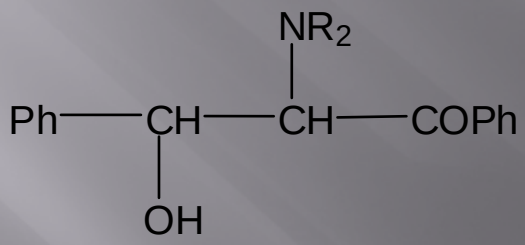
Another interesting application of Wulfs reaction can be found in the preparation of bicyclic ring compounds from alicyclic diazo compounds.

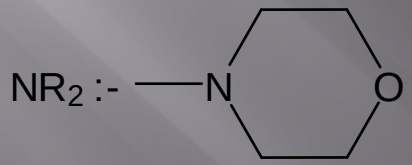


G. Neighboring group participation:

Several rearrangements involve NGP*, wherein the group responsible for anchimeric assistance undergoes 1,2 migration.*





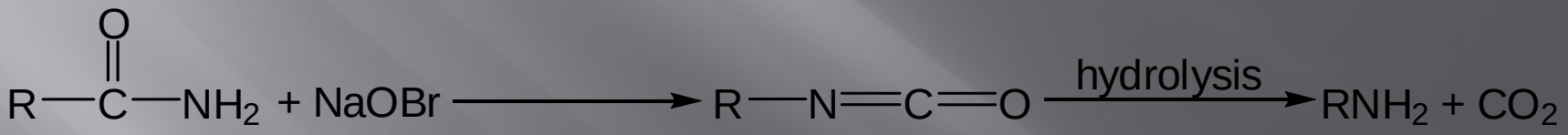


In this reaction, anchimeric assistance is offered by the morpholino group.

VII. *Rearrangement Reactions Involving Electron Deficient Nitrogen*

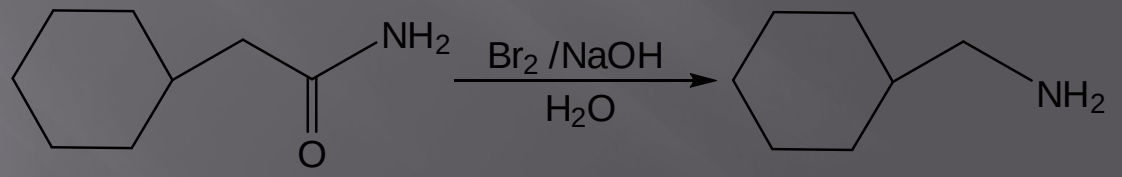
A. Hofmann rearrangement:

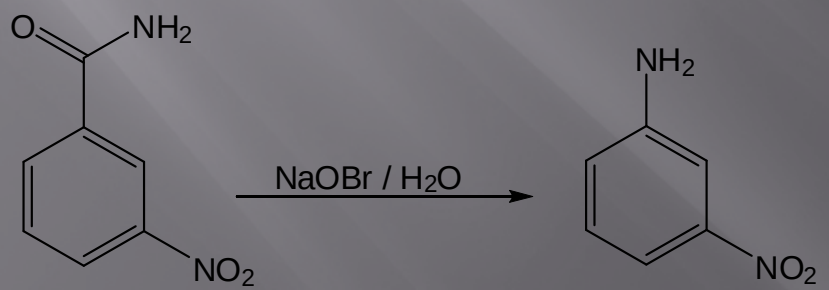
When an unsubstituted amide is treated with sodium hypobromite, corresponding primary amine with one carbon less is produced. This reaction involves Hofmann rearrangement.



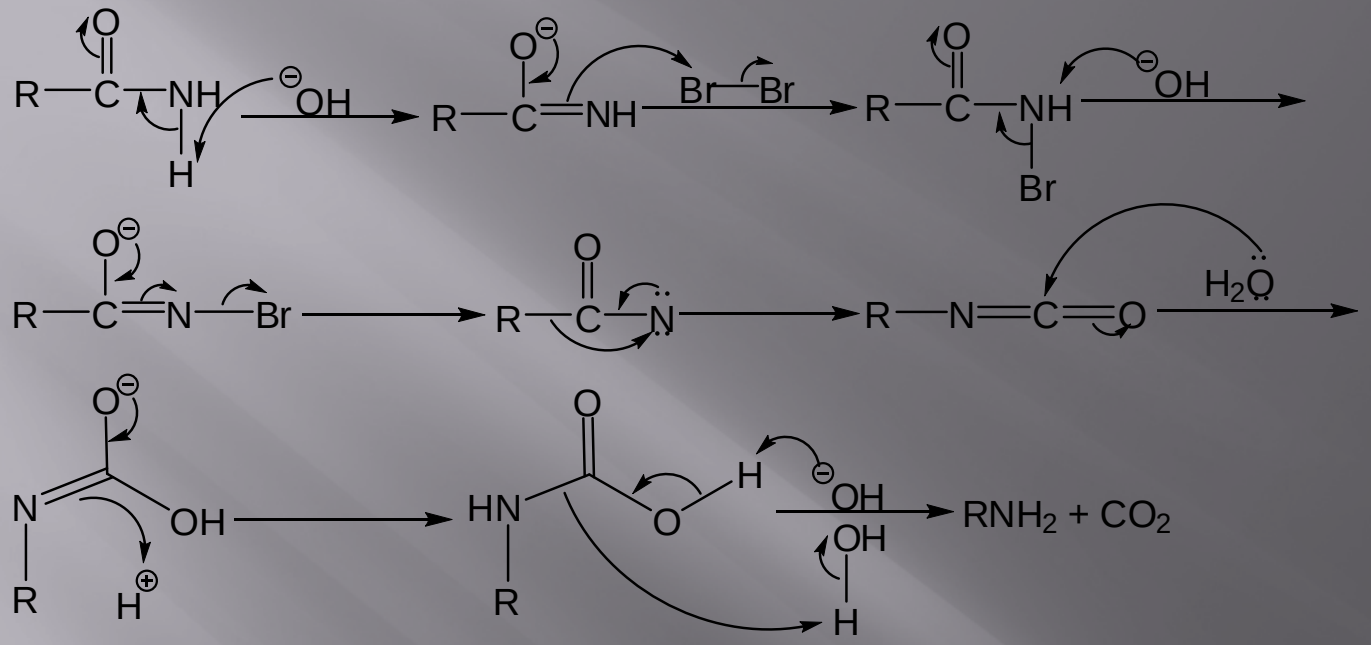
R *in this reaction can be alkyl or aryl.*

Examples





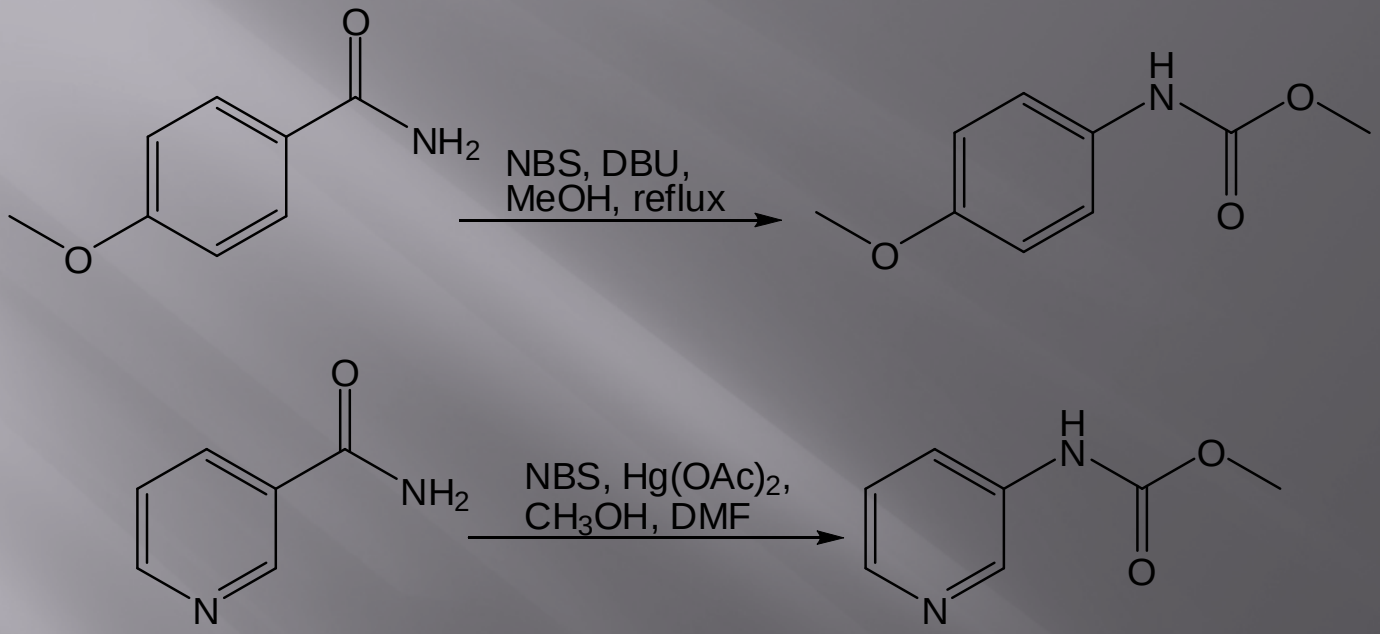
Mechanism of reaction is as follows,



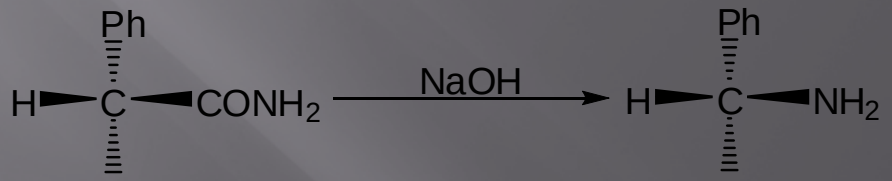
description

In the first step, base removes a proton from amide. The conjugate base of amide thus formed reacts with bromine to give N*-bromoamide. Acidity of proton on nitrogen is increased by this bromine atom and its removal becomes easy toward generating nitrene intermediate (in which nitrogen is electron deficient). 1,2-shift of alkyl group in this nitrene intermediate gives corresponding isocyanate. This isocyanate on hydrolysis gives primary amine with one carbon less than starting material.*

When methanol is used as a solvent instead of water, then the corresponding carbamate ester can be obtained.

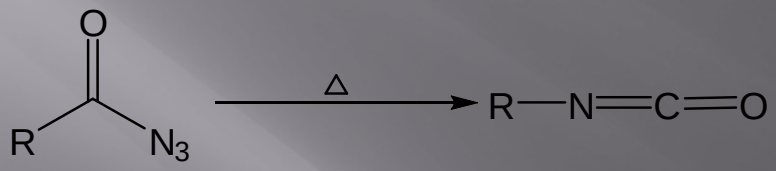


When optically active α-phenylpropionamide undergoes Hofmann degradation, α-phenylethylamine of same configuration and optical purity is obtained i.e. rearrangement proceeds with ***retention of configuration****.*



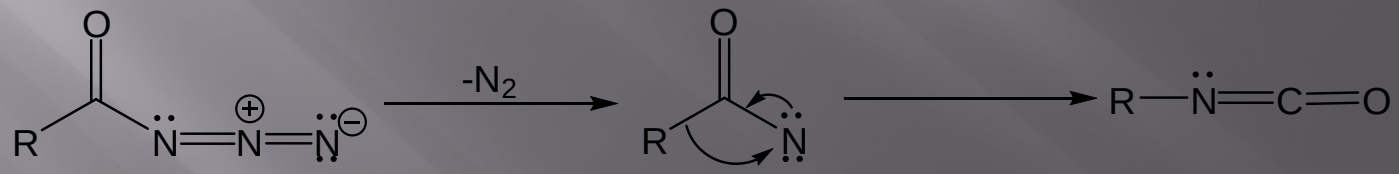
B. Curtius rearrangement:

*In Curtius rearrangement, **acyl azide are pyrolysed** into isocynate which can be hydrolyzed to corresponding amines.*

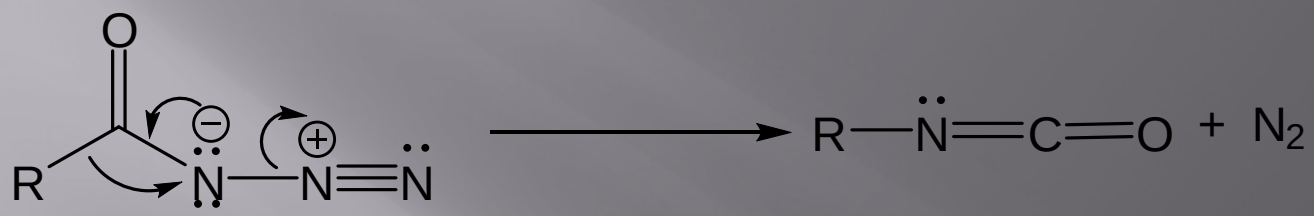


Curtius rearrangement is catalyzed by protic or Lewis acids.

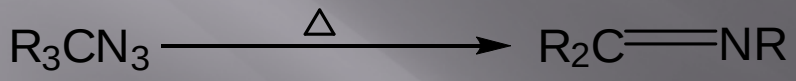
Mechanism is similar to that of Hofmann rearrangement.



However, there is no evidence of existence of free nitrene. These two steps may be concerted.

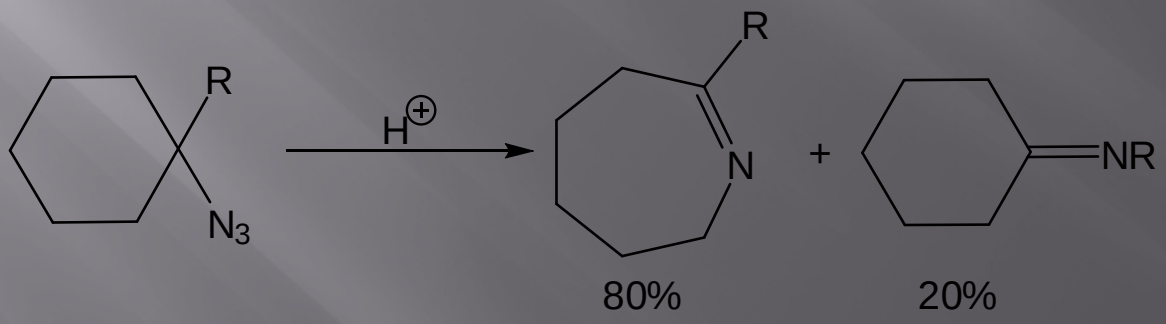


In a similar reaction, alkyl azides provide imines.

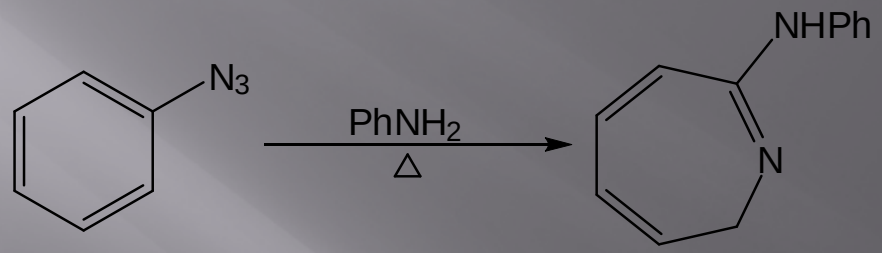


R *may be alkyl, aryl or hydrogen. In the case of tert alkyl azides, there is evidence of existence of nitrene.*

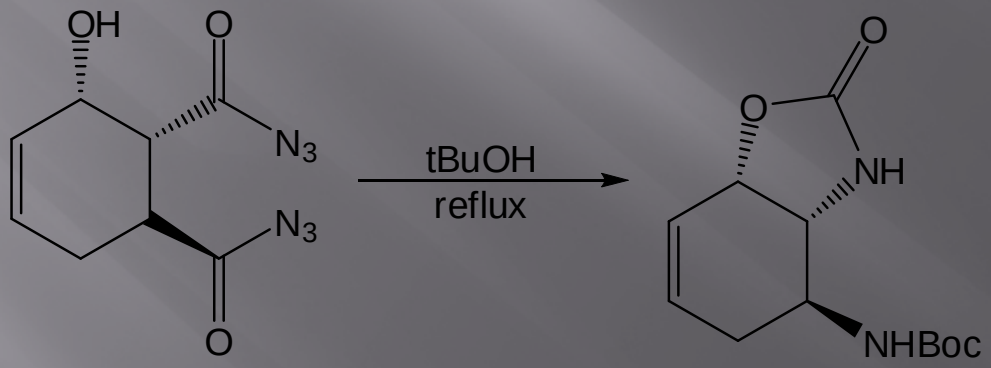
Cycloalkyl azides can yield ring expansion.



Aryl azides can also give ring expansion on heating.



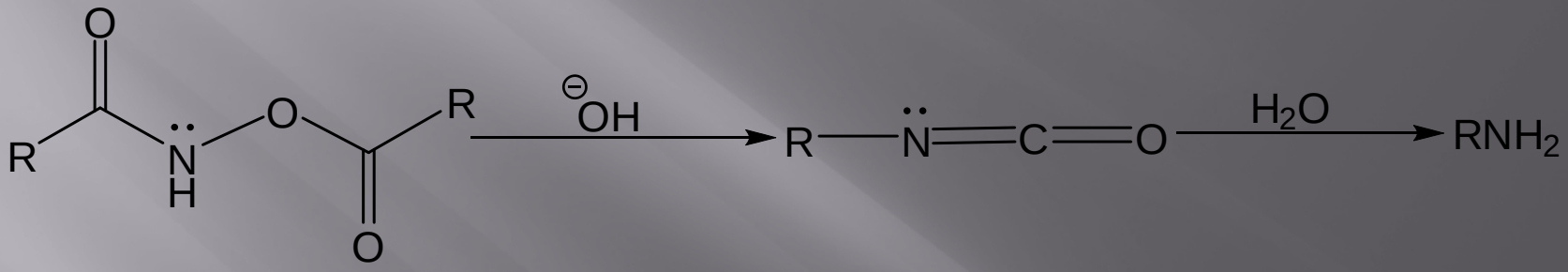
Home work: (Propose a mechanism for the following reaction)



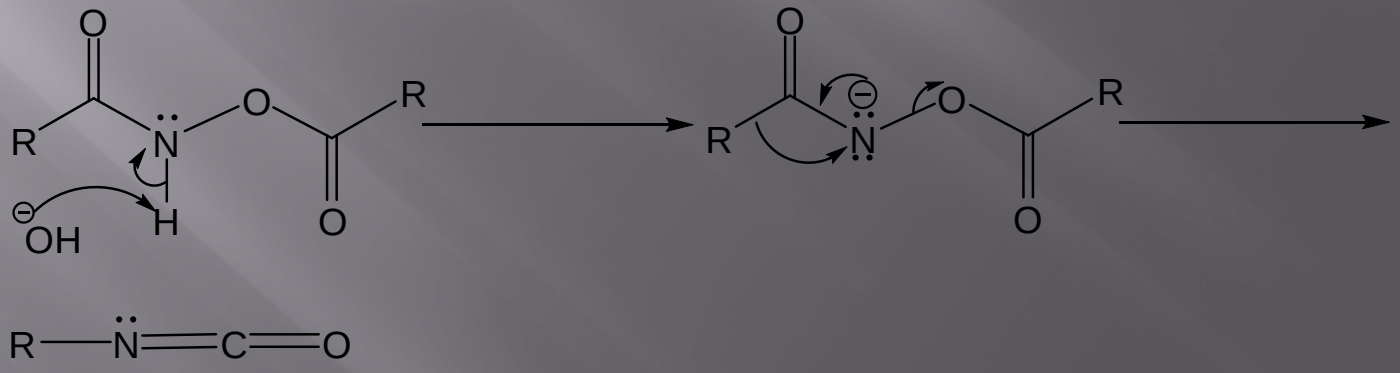
[*Tet. Lett*., 19 Feb 2007, Vol.48, Issue 8, 1403]

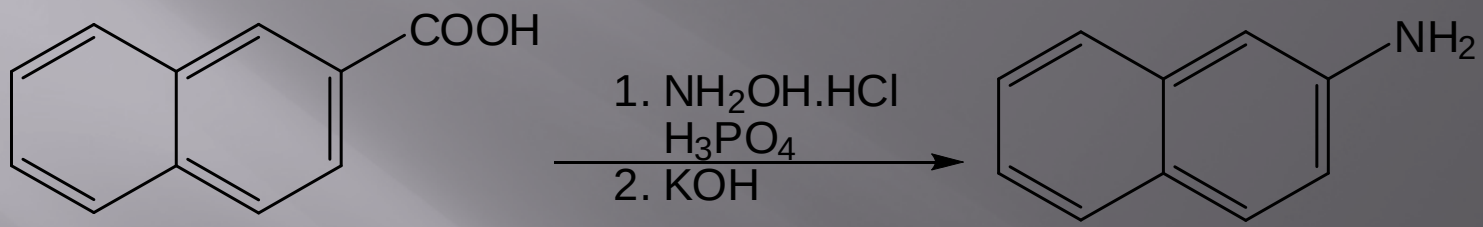
C.Lossen rearrangement:

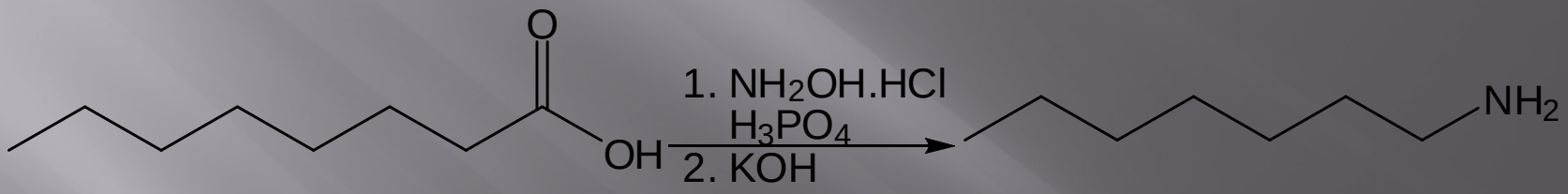
O-acyl derivatives of hydroxamic acids *on heating with a base concerts to the corresponding isocyanate. This reaction is known as Lossen rearrangement. The isocyanate thus produced can be further hydrolyzed to corresponding amines.*



Mechanism





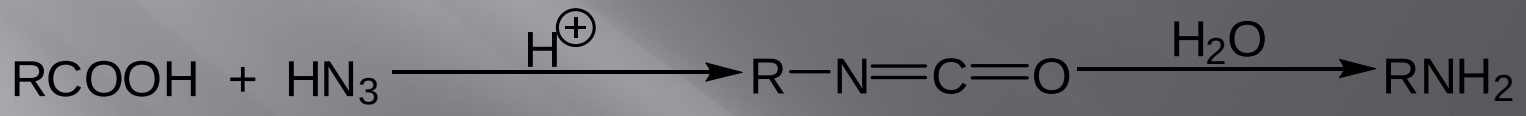


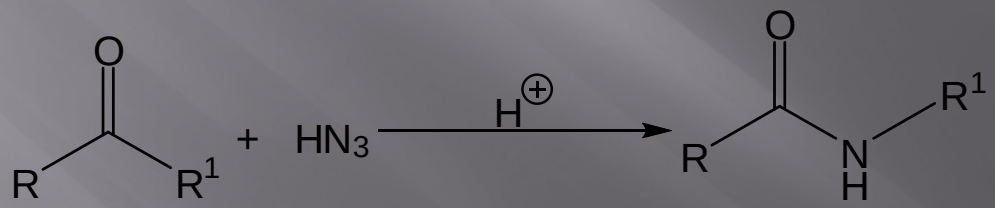
[*JACS*, 1953, 75, 2014]

D. Schmidt rearrangement :

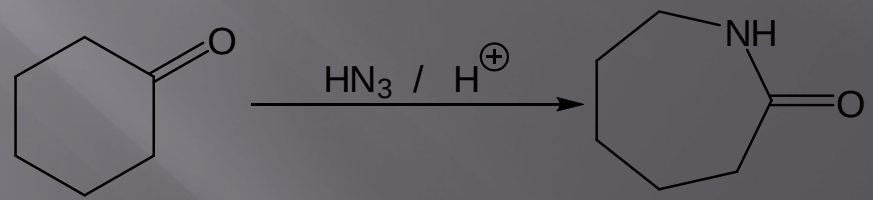
Reaction of carboxylic acid or aldehyde or ketone with ***hydrazoic acid***

in the presence of mineral or Lewis acid to give corresponding primary amine or amide is known as Schmidt rearrangement.

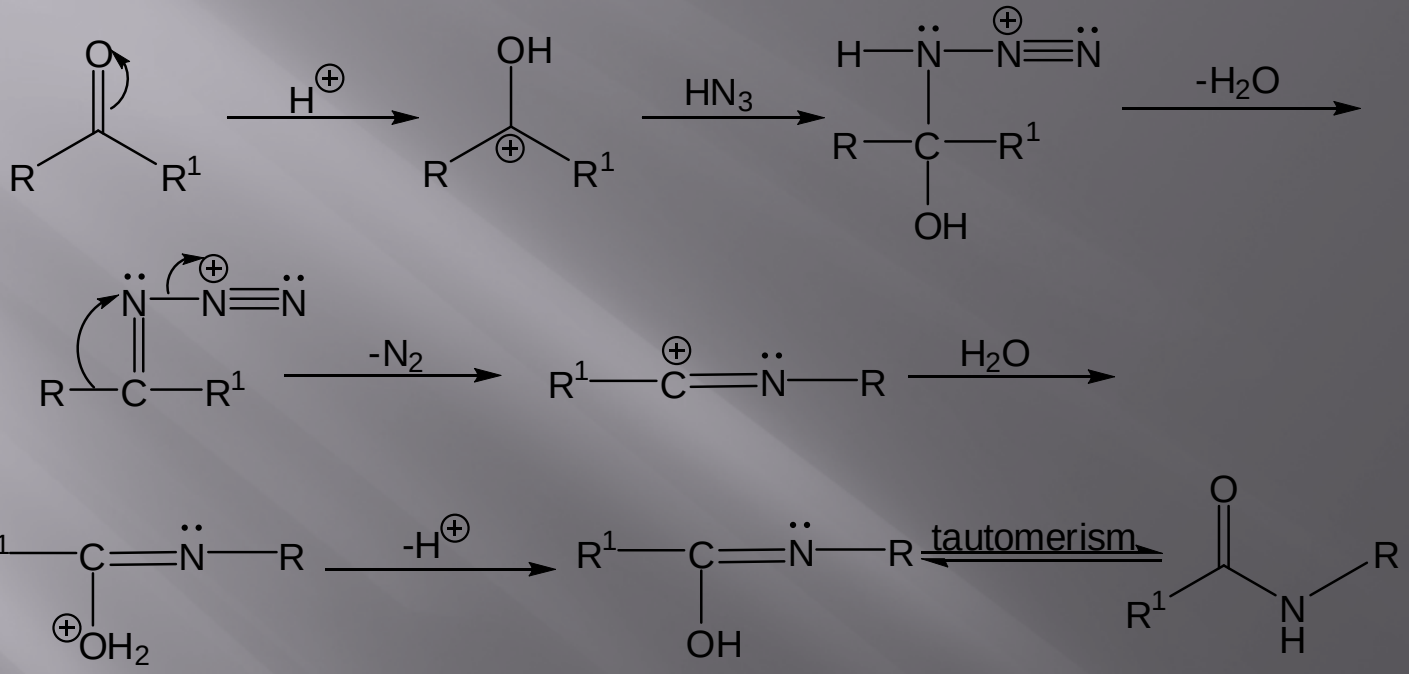




Cyclic ketones give lactams.



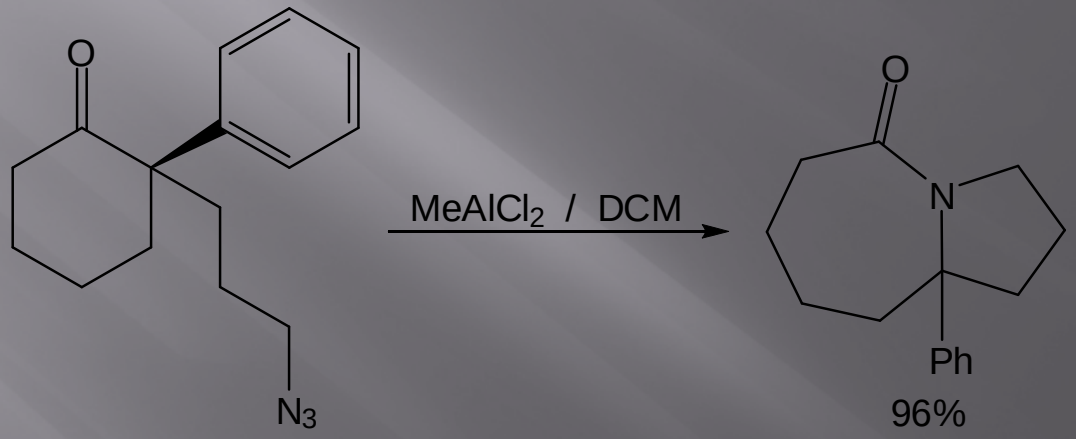
Mechanism is similar to that of Curtius rearrangement, except that protonated azide undergoes molecular rearrangement.

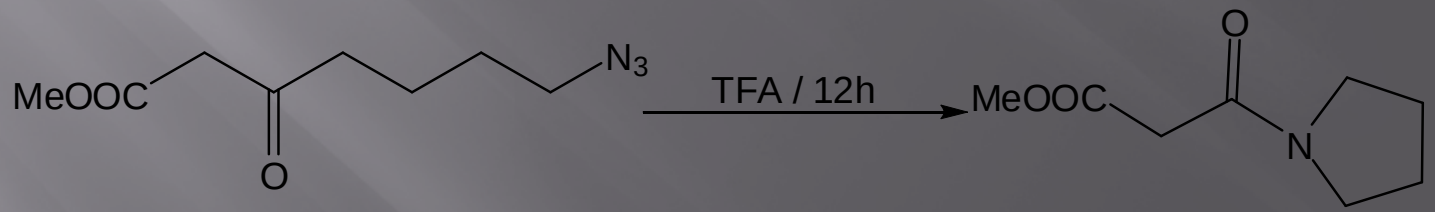


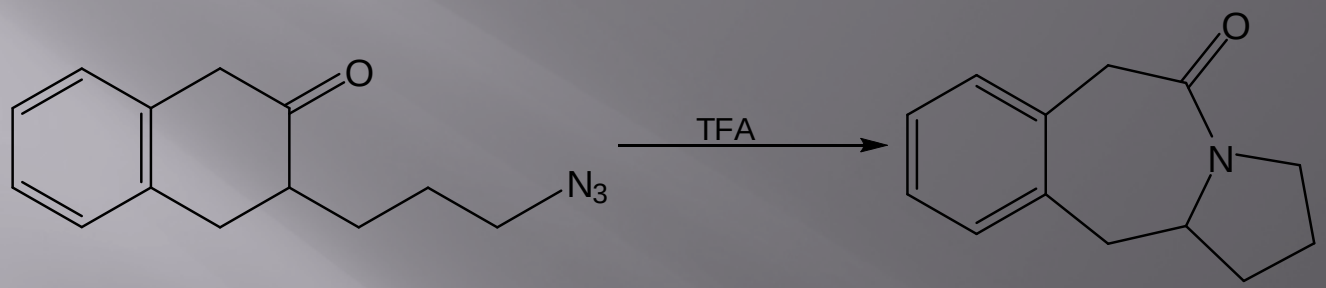
In reaction with ketone, ketone is activated by protonation for nucleophilic addition of azide group to it.

In the case of alkyl aryl ketone, the aryl group migrates preferentially except for bulky alkyl group.

Intramolecular Schmidt reaction can be used for the preparation of bicyclic lactams.



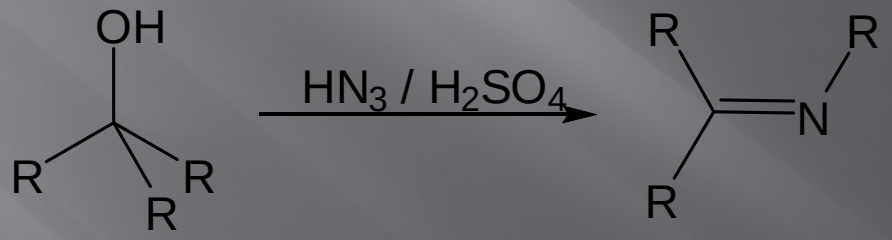




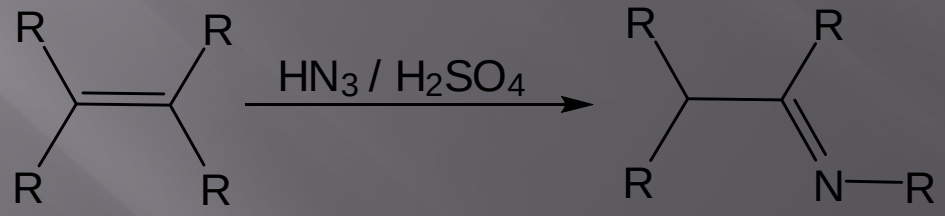
[*Org. Syn*., 2007, 84, 347]

Reaction of tert-alcohol (e.g.1) or olefin (e.g., 2) with hydrazoic acid under acidic condition to give substituted imines is also a form of Schmidt rearrangement.

E.g.,1

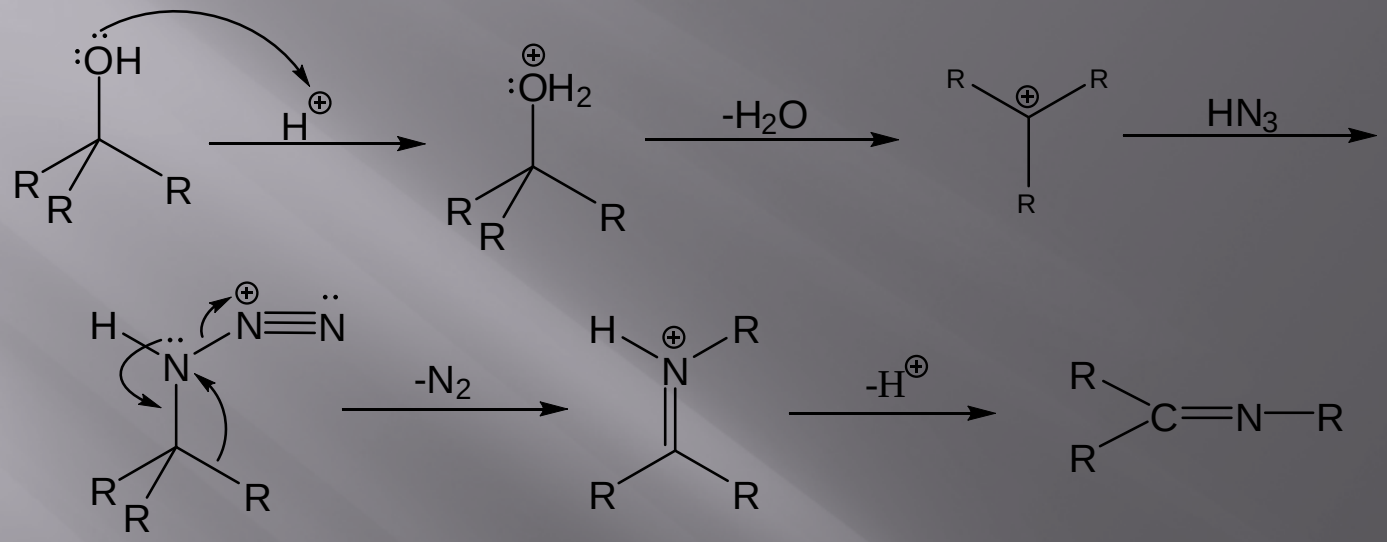


E.g.,2

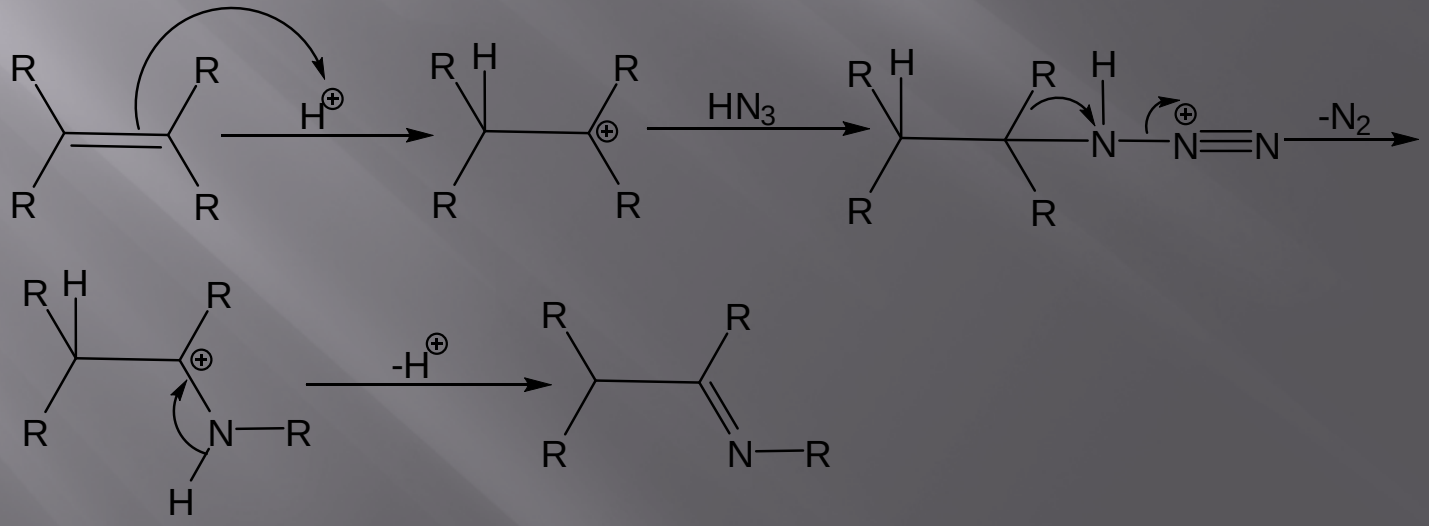


Mechanism of the reaction is as follows.

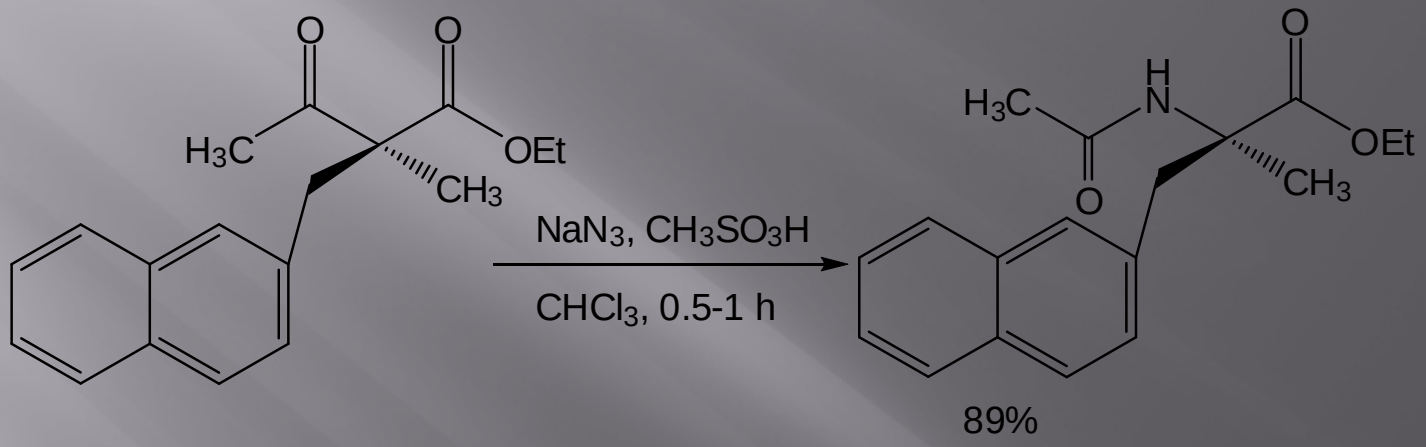
tert-alcohol



olefin



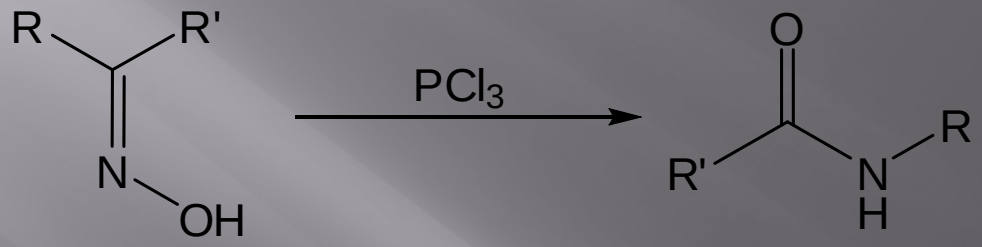
A more recent example on the use for Schimdt rearrangement



[*Tet. Lett.*, 1988, 29, 403]

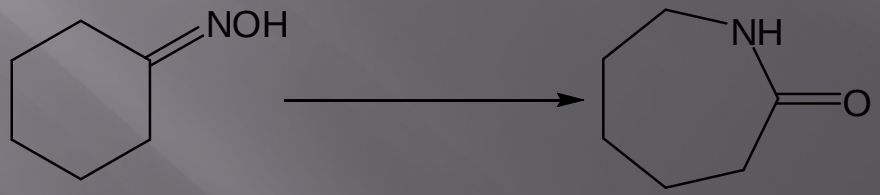
E.Beckmann rearrangement :

Oximes on treatment with Lewis acid or protic acid rearrange to give substituted amides. This reaction is called as Beckmann rearrangement.*



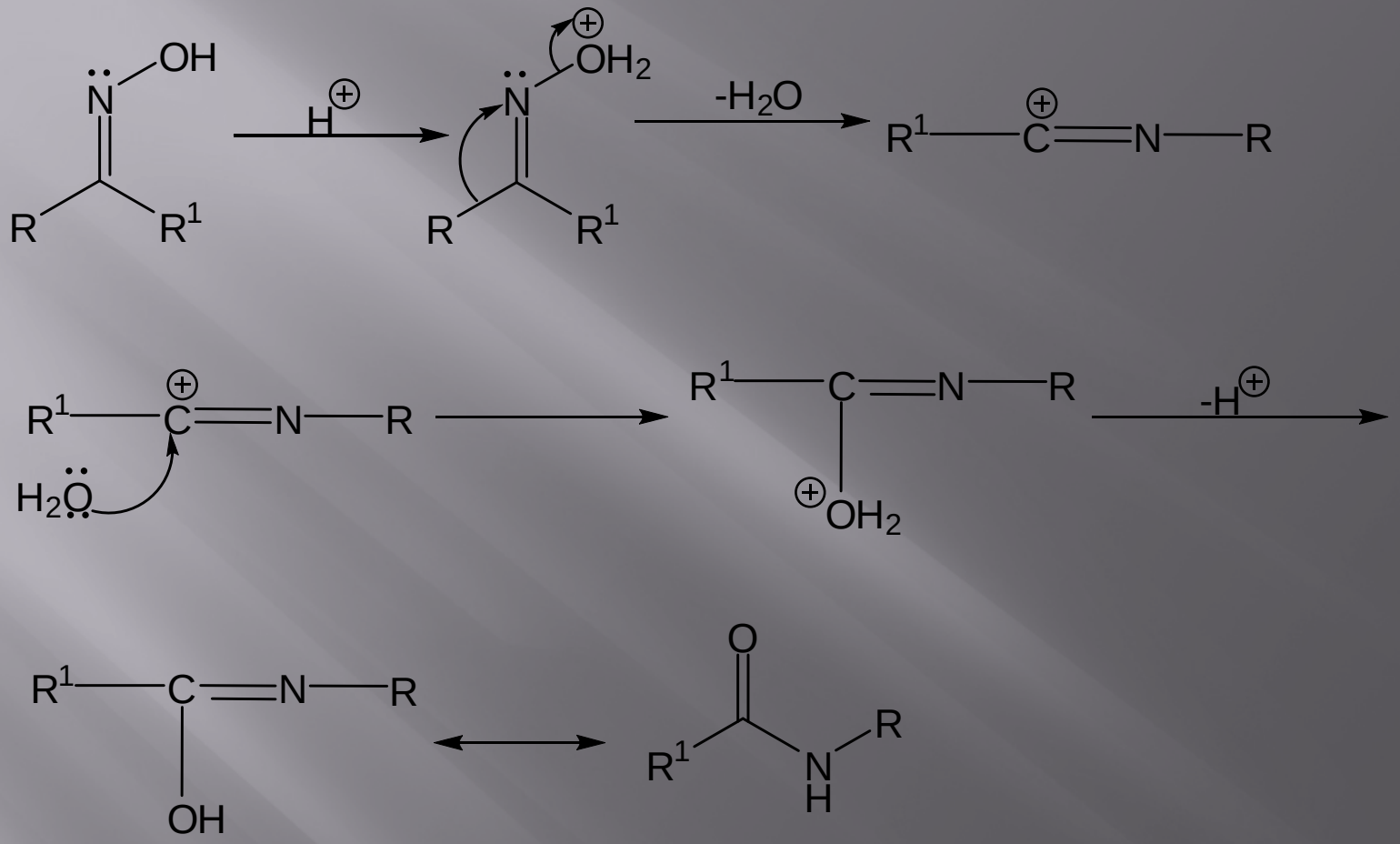
Generally group anti to hydroxyl migrates. However, there are several exception reported. R *and* R' *can be alkyl, aryl or hydrogen. (Hydrogen does not migrate under normal reaction conditions, but it migrates when the reaction is carried out with nickel acetate under neutral conditions.)*

Like Schmidt rearrangement, oximes of cyclic ketones give ring-expansion.



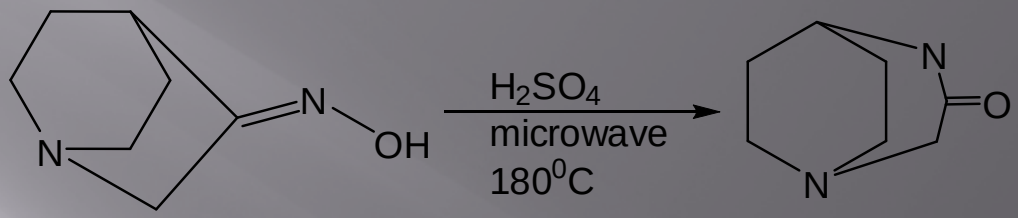
* Oximes are condensation product between hydroxylamine and an aldehydes/ketones

Mechanism of reaction



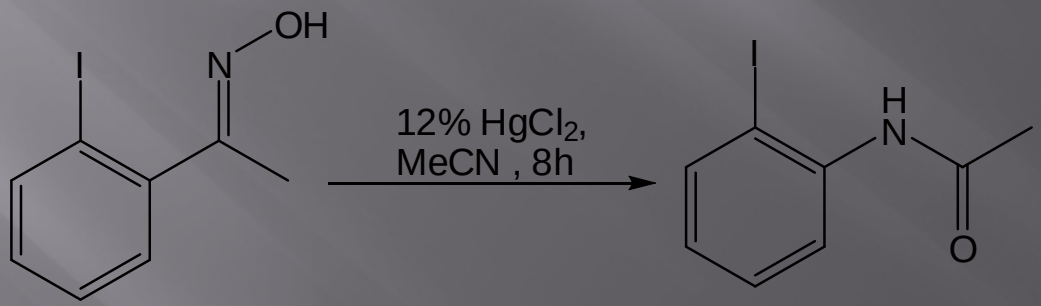
The proposed mechanism is supported by detection of nitrillium ion by NMR and UV spectroscopy.

Examples



[*Syn. Comm.,* 2006, 36, 321]

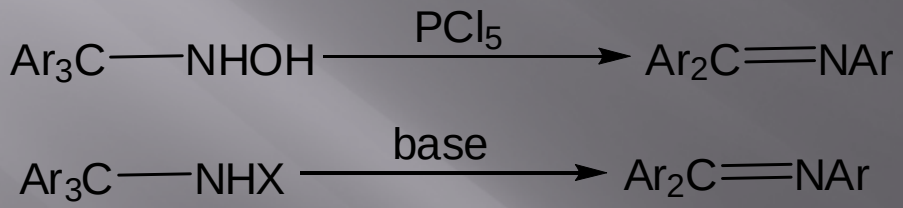
[*J. Org. Chem.*, 2002, 67, 6272]



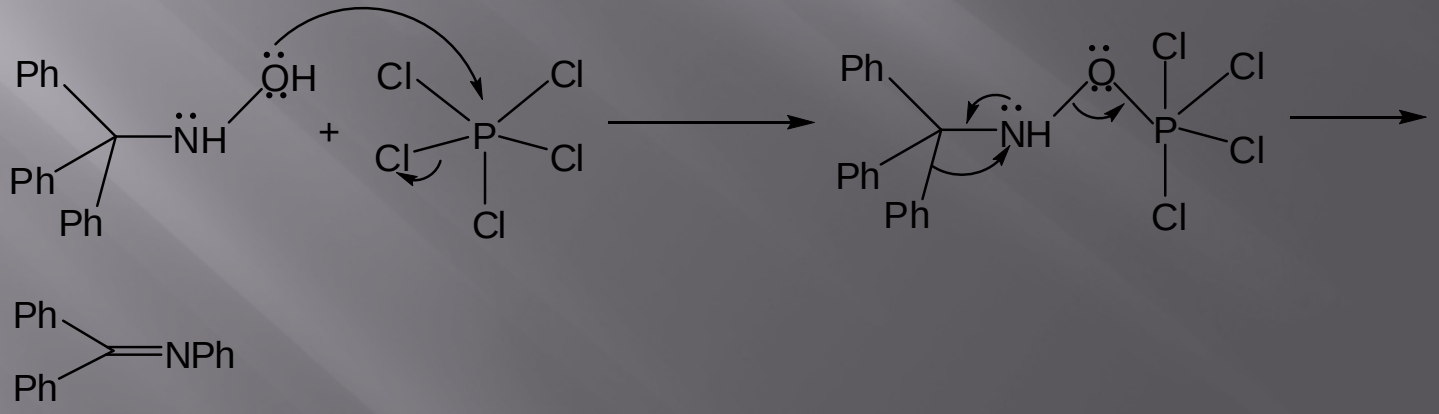
[*J. Org. Chem.*, 2007, 72, 4536]

F. Stieglitz rearrangement:

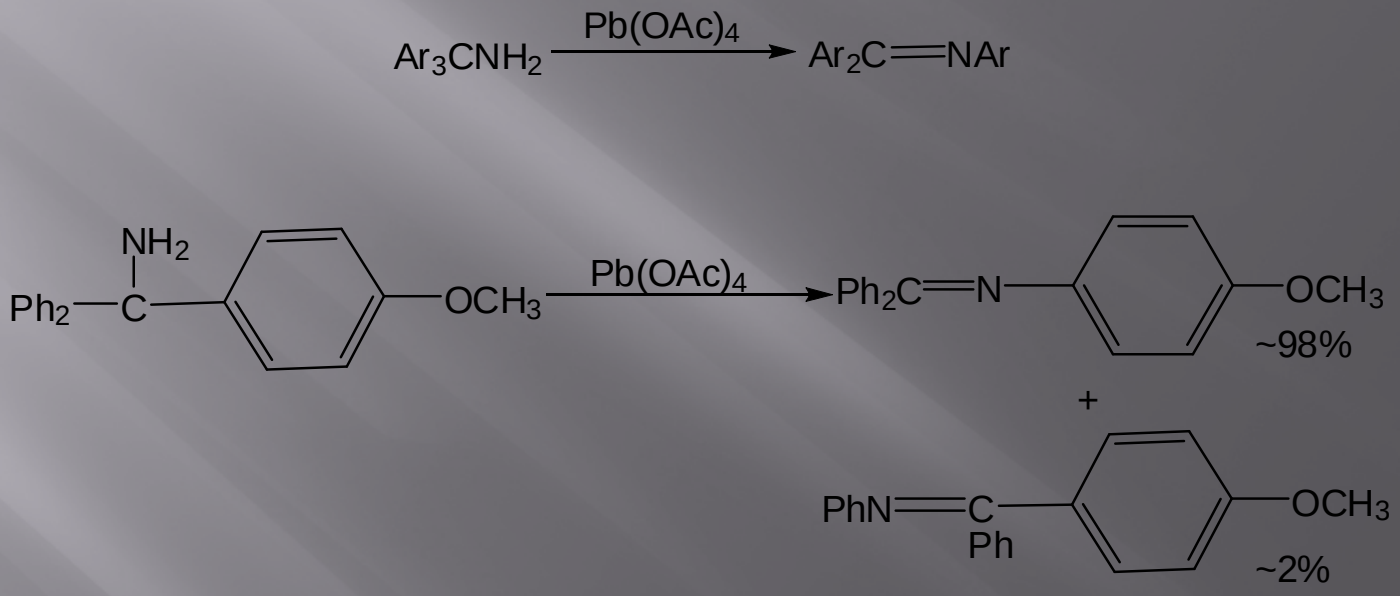
*Stieglitz rearrangement is a general term applied for rearrangement reactions of trityl-*N*-haloamines and hydroxylamines to trityl imine.*



Mechanism is as follows,



Stieglitz reaction can also be facilited by treatment with lead tetraacetate.

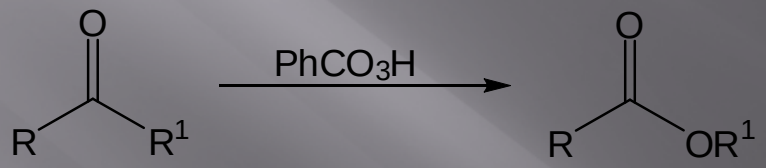


[*J. Org. Chem.*, **1974**, *39*, 3932]

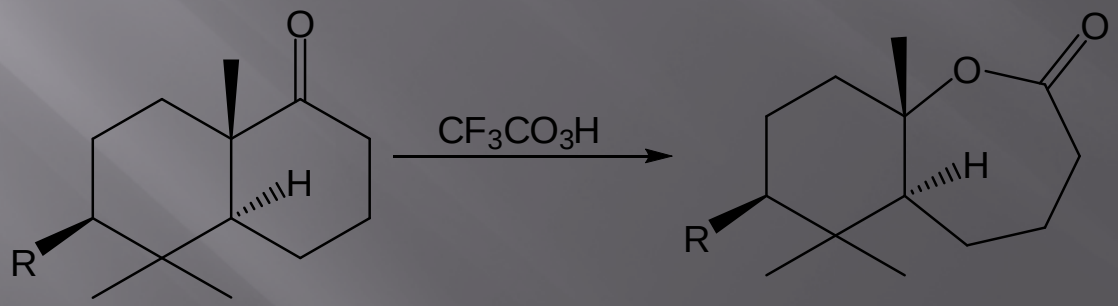
VIII. *Rearrangement reactions involving electron deficient oxygen*

A. Baeyer-Villiger rearrangement :

In Baeyer-Villiger rearrangement, ketone on treatment with peracid gives ester by oxyinsertion. Reaction is catalyzed by presence of acid catalyst.

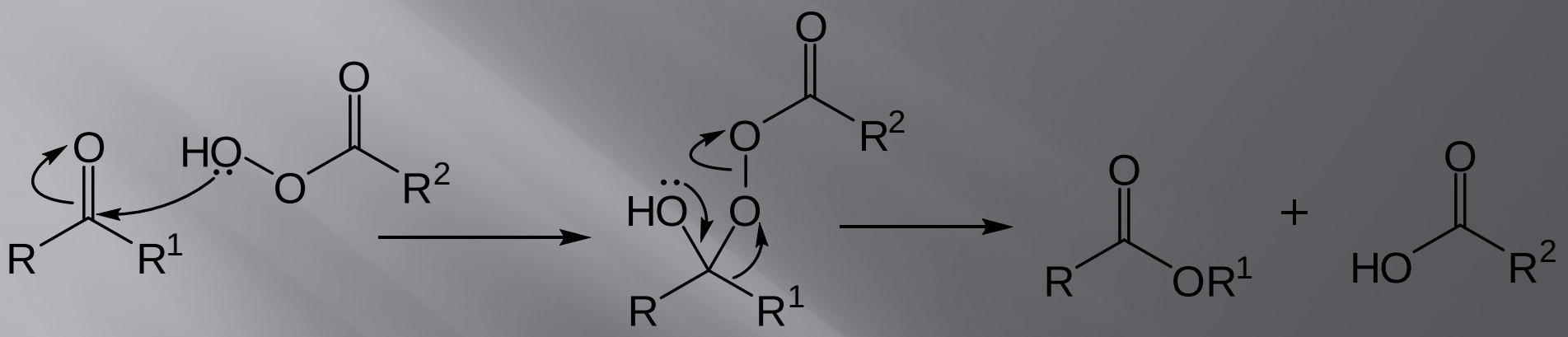


Reaction is particularly useful for synthesis of lactones.



R : H, OAc, OCOPh *etc.*

Mechanism is as follows,



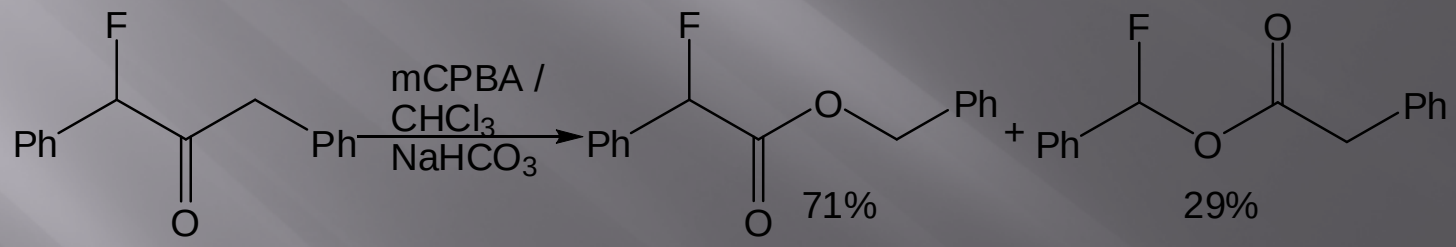
First step is the addition of peroxy acid to the carbonyl carbon leading to a tetrahedral intermediate. In next step, a concerted migration of the migrating group and loss of carboxylic acid provides the product.

The mechanism is supported by fact that oxidation of $Ph_2C^{18}O$ *yields only* $PhC^{18}OOPh$ (*i.e. there is no scrambling of* ^{18}O *label in the product Ester.)*

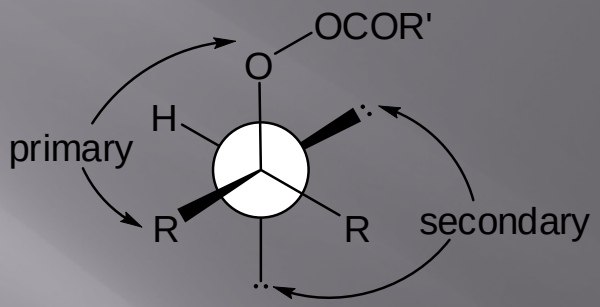
The ***loss of carboxylates and migration of*** **R** ***is concerted****, as the reaction is known to be faster when electron withdrawing substituents are present in the leaving group and electron donating substituents in migrating group.*

If the migrating group is chiral then its ***stereochemistry is retained****.*

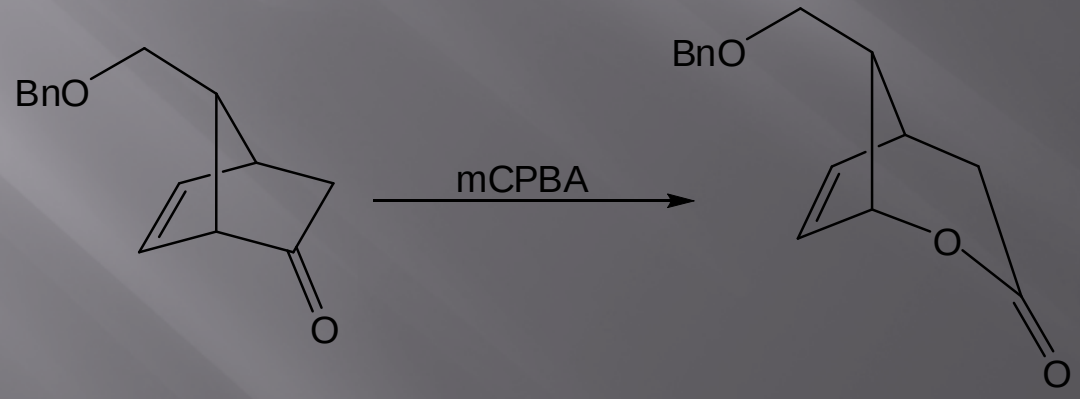
Migratory aptitude in unsymmetrical ketones is as, H > 3^0 > cyclohexyl > 2^0 > benzyl > aryl > 1^0 > methyl*. In case of aryl group, migrating ability is increased by electron donating groups present on ring.*



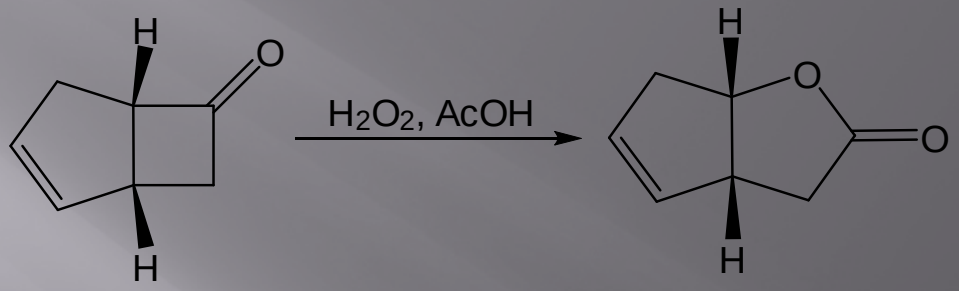
Migration is favored when migrating group is antiperiplanar to the O-O *bond of leaving group. This is known as primary stereoelectronic effect. Antiperiplanar alignment of lone pair of electrons on* O_2 *with migrating group is termed as secondary stereoelectronic effect.*



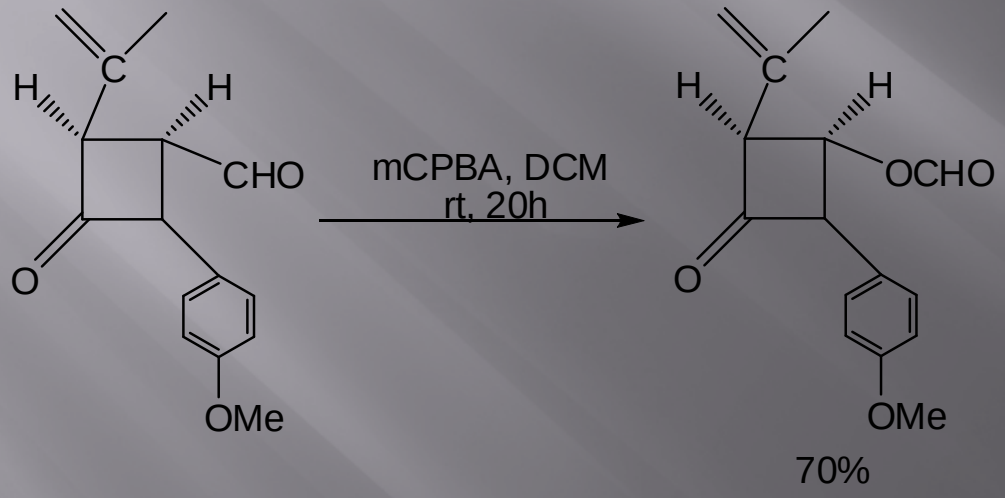
In the case of unsaturated ketones epoxidation is likely to be a competitive reaction. But, Baeyer-Villiger rearrangement is favored because ring strain can be relieved by oxy insertion and ring expansion.

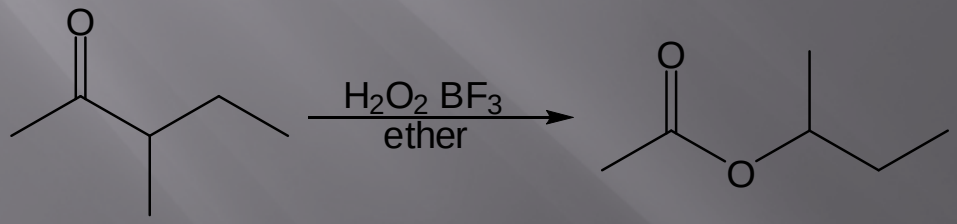


More examples



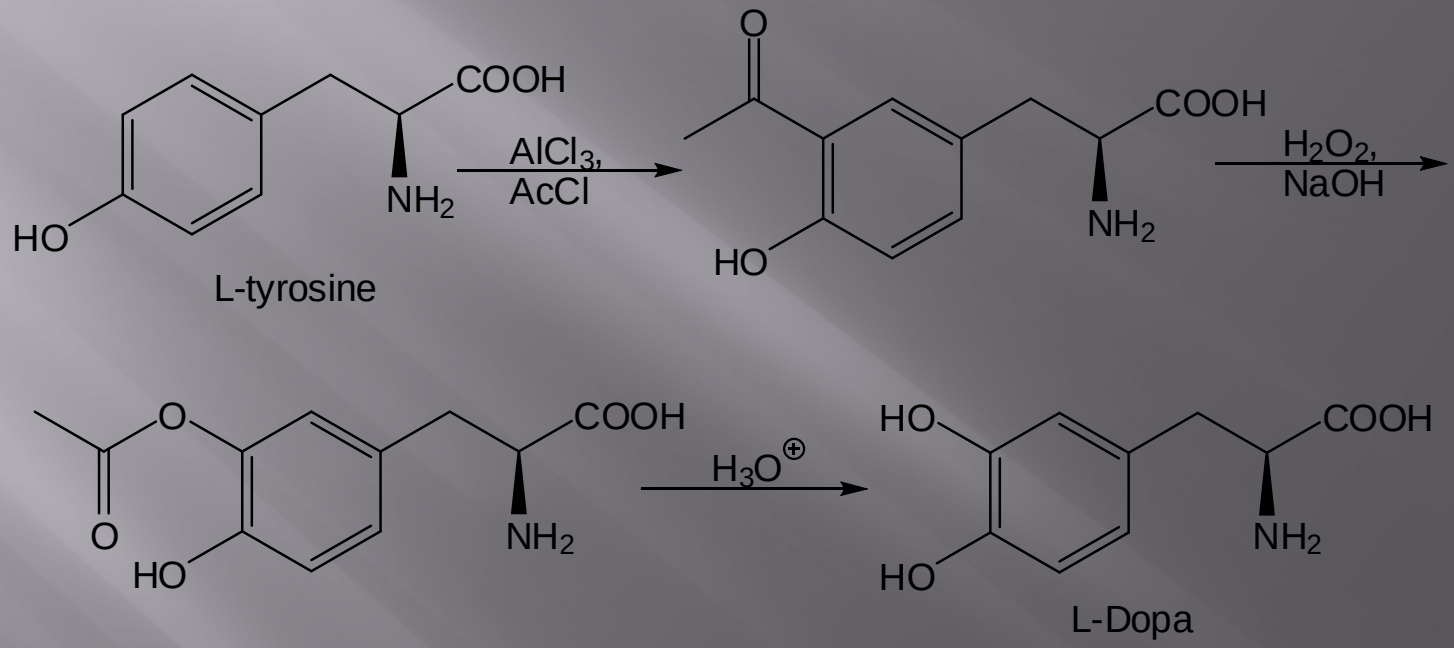
Chemoselective oxidation of β-lactum aldehyde has been achieved with mCPBA *in DCM where only formates are formed in better yields.*





[*JOC*,1962, 27, 24]

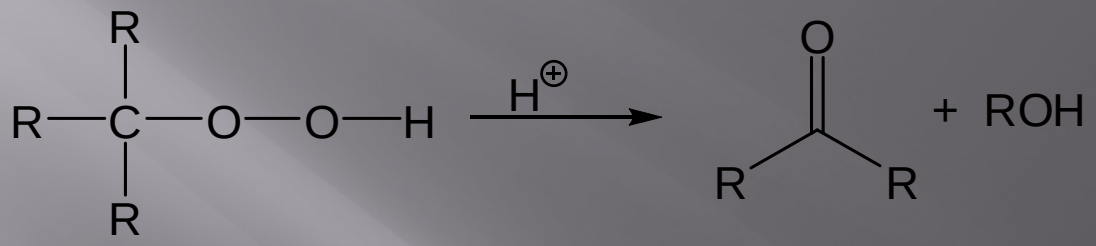
One of the most important synthetic use of BV reaction is found in the syntheses of L-*Dopa (a drug used in the treatment Parkinson's disease).*



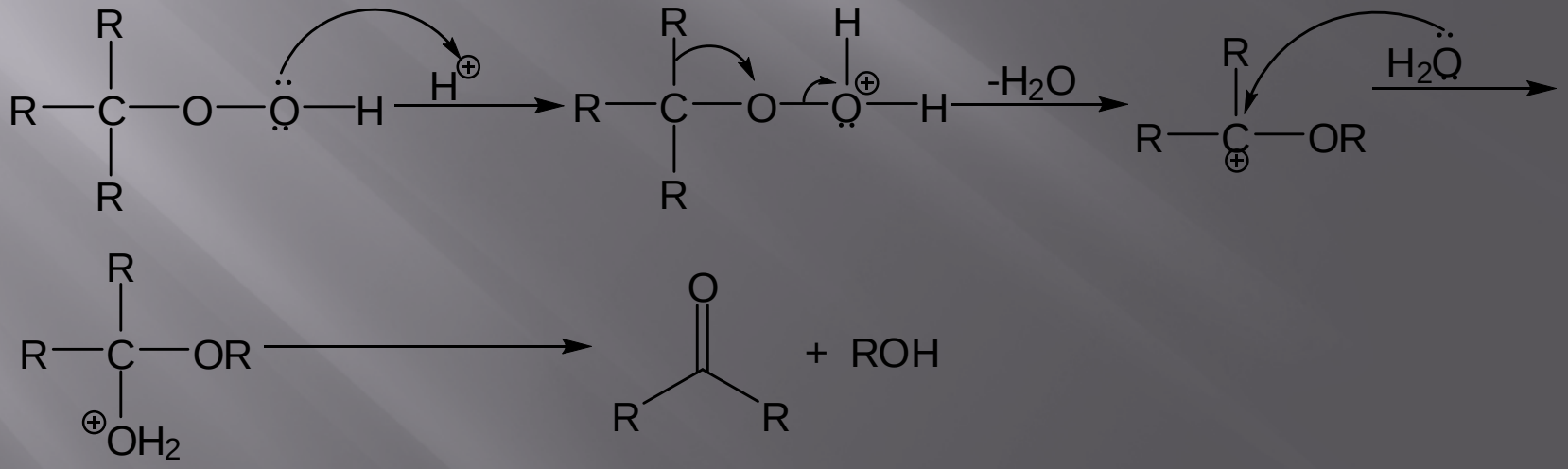
B. Rearrangement of hydroperoxide :

Hydroperoxides can be cleaved in the presence of protic or Lewis acid.

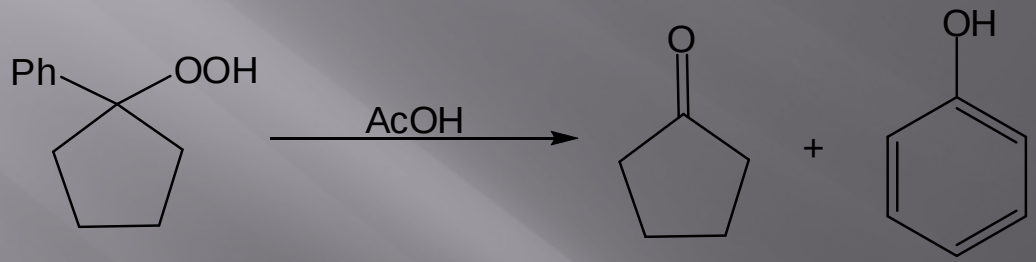
Reaction goes through rearrangement.



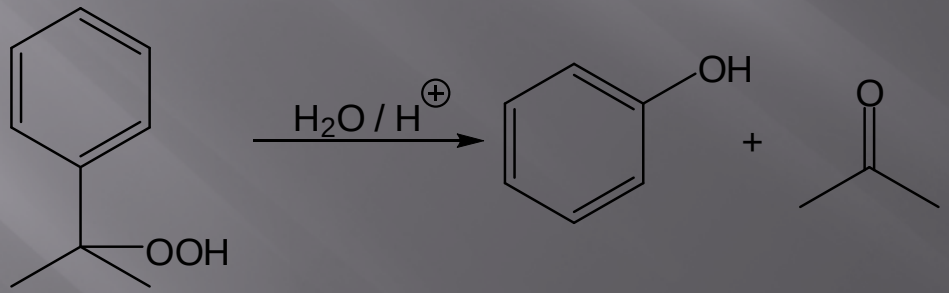
Mechanism is as follows.



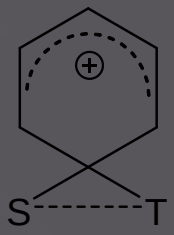
The important steps in the mechanism can be described as follows: (a) Protonation of peroxide and removal of a molecule of water (b) Simultaneous shift of the migrating alkyl group to the electron deficient oxygen to give a rearranged carbocation (b) formation of hemiketal by the reaction of water, which then breaks down to give alcohol and ketone.



Alkyl group must be showing some sort of anchimeric assistance and the rearrangement must be going through benzonium ion.



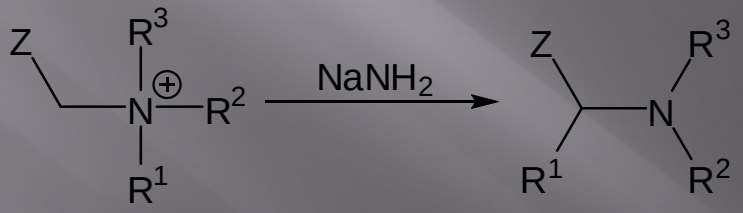
Benzonium ion :



IX. *Migration from nitrogen to carbon*

Stevens rearrangement :

In Stevens rearrangement, quaternary ammonium salt containing electron withdrawing group on α carbon atom when treated with strong base rearrange to give a tertiary amine.

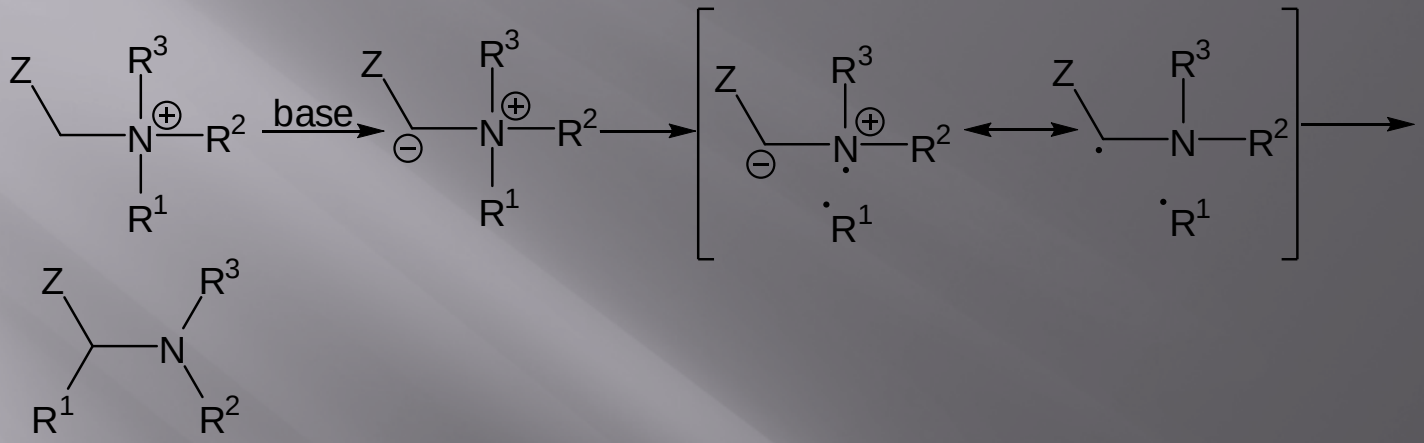


Rearrangement is intramolecular (as shown by cross over experiment).

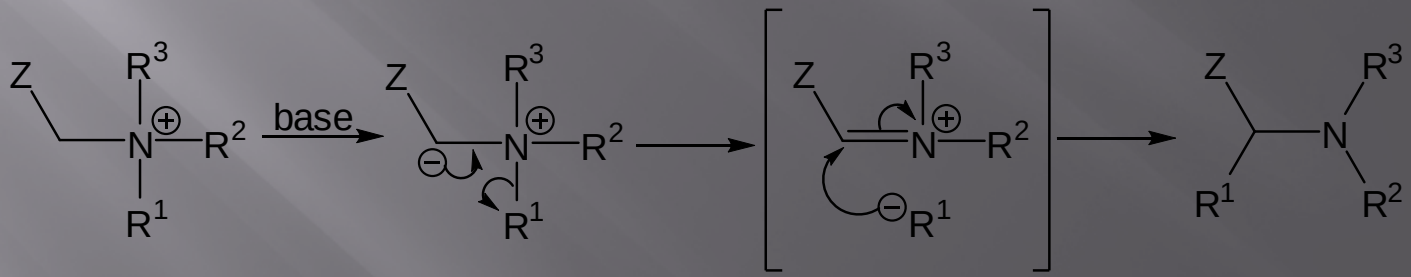
Also, retention of configuration was noticed in the product.

Two mechanistic pathways are possible. One involving radical pair in a solvent cage. Presence of solvent cage is important in order to explain retention of configuration.

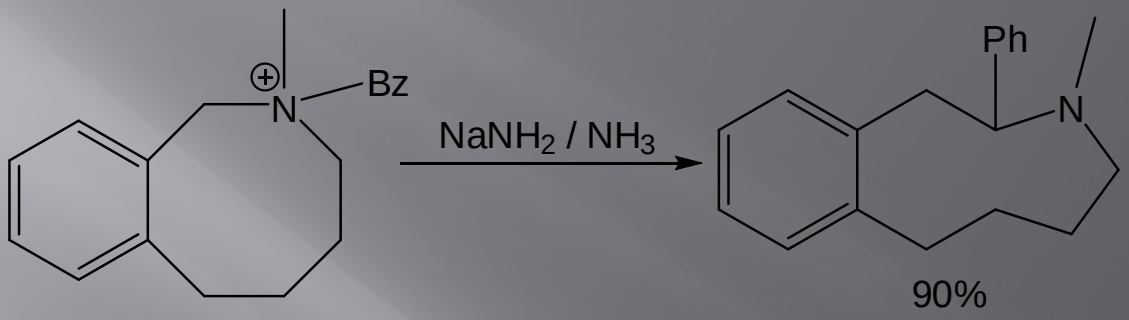
Involving ion pair in solvent cage.



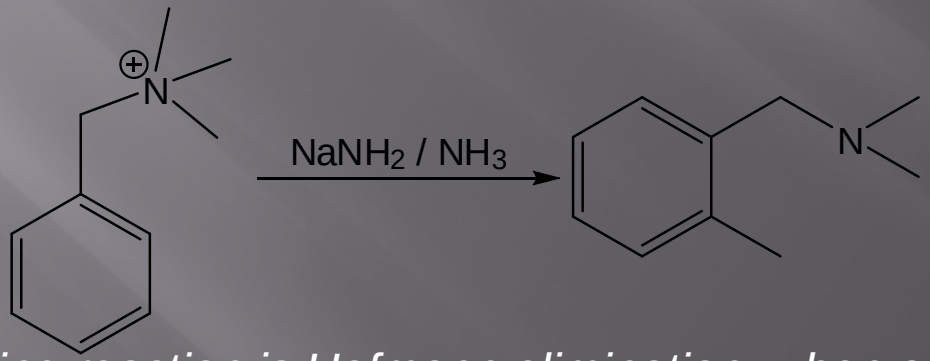
Involving an ionic pathway.



Reaction can be used for ring enlargement.

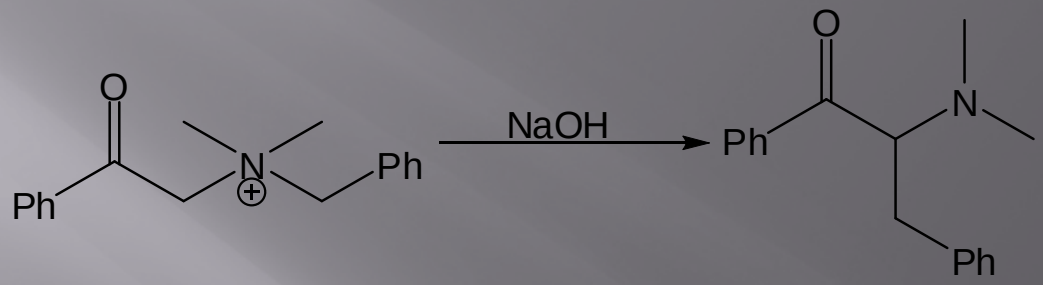


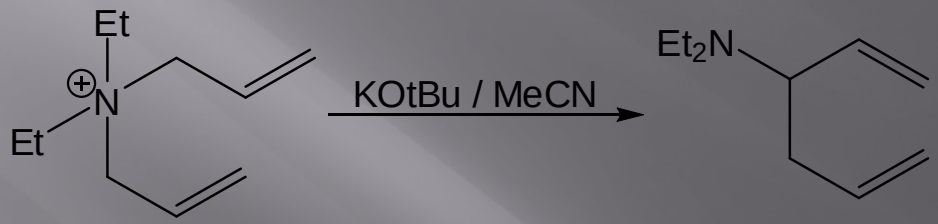
When Z group is an aryl group, the rearrangement is known as ***Sommelet-Hauser rearrangement****, in which reaction of tert-alkyl ammonium salt with* $NaNH_2$ *gives N,N-dialkylbenzylamine with ortho substituted aromatic ring (shown below).*

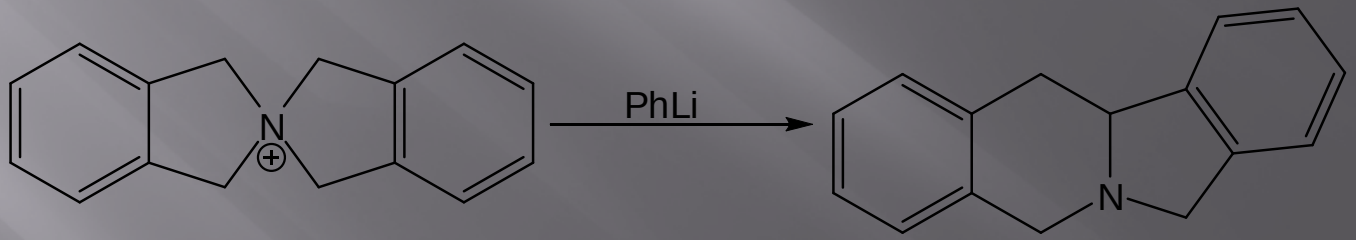


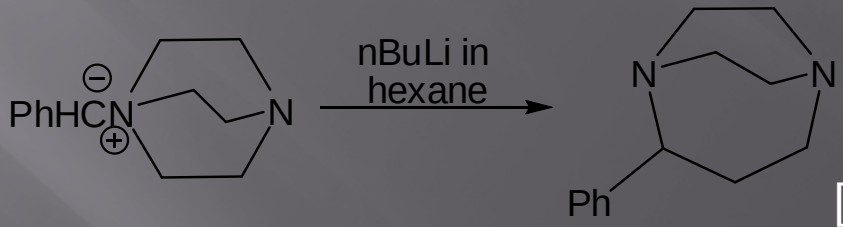
Another competing reaction is Hofmann elimination, when one of the alkyl group contains β *hydrogen atom.*

Some examples of Steven rearrangement are given below.







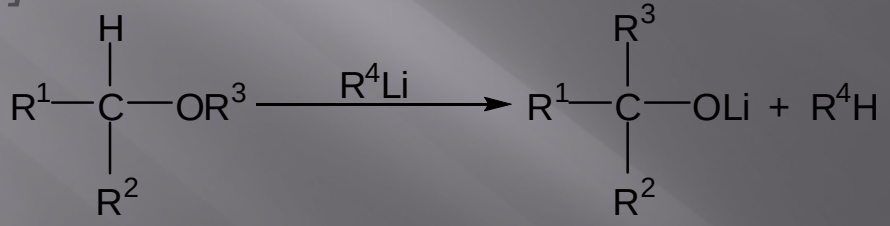


[*JOC*, 1974, 39, 130]

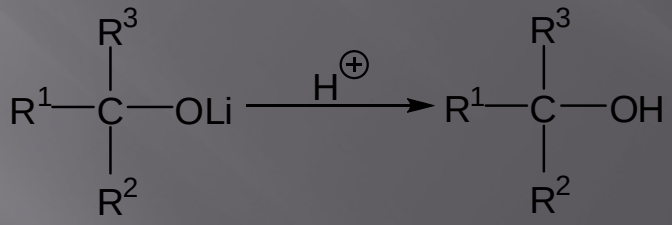
X. Migration from oxygen to carbon

Wittig rearrangement:

Ethers, on reaction with alkyl lithium rearrange in a similar manner to that of Stevens rearrangement to give alkoxy lithium. This reaction is called Wittig rearrangement.[Note: Witting reaction of phosphorous ylides are different]



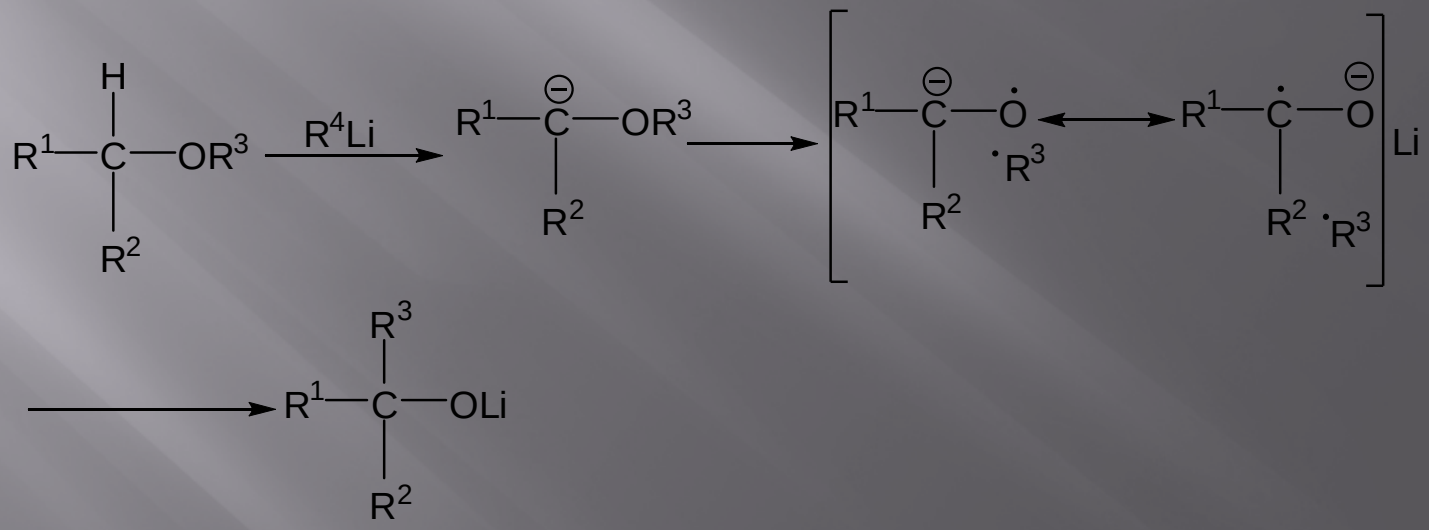
This alkoxy lithium can then be converted to alcohol.



R *may be alkyl, aryl or vinyl group.*

Migratory aptitude are allylic, benzyl>ethyl>methyl>phenyl.

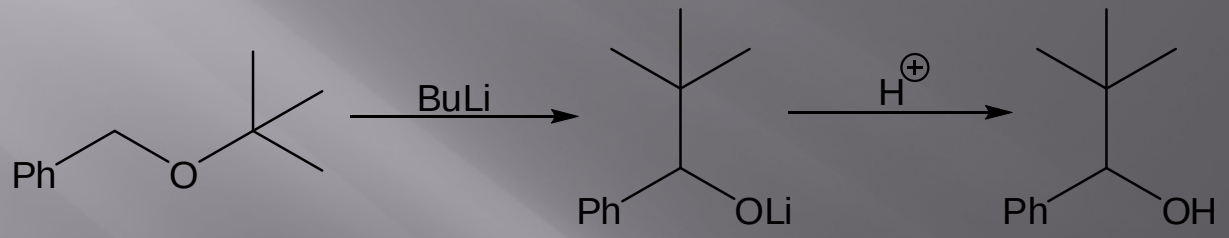
Mechanism is suggested to follow a radical pair pathway.

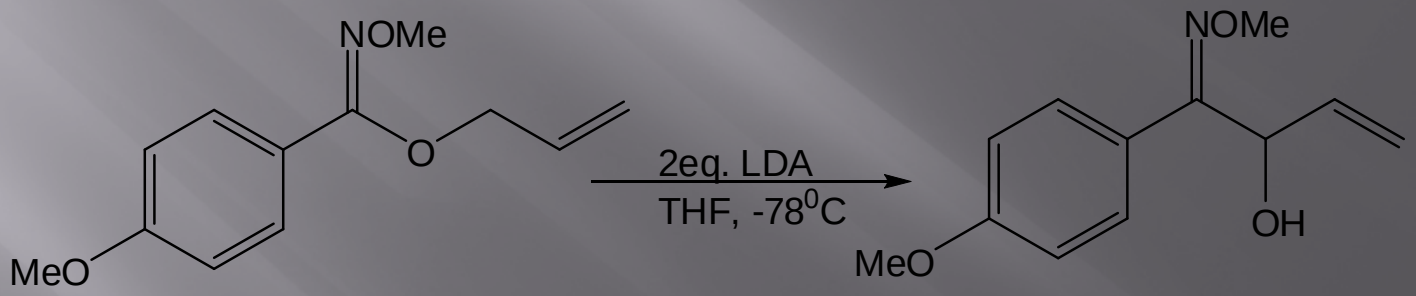


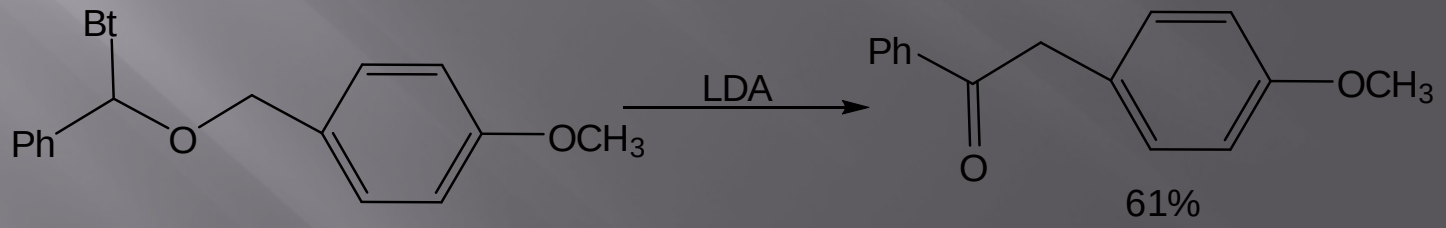
i.Reaction is largely intramolecular

ii.Migratory aptitudes are analogous to free radical mechanism.

iii.Product obtained is with retention of configuration.

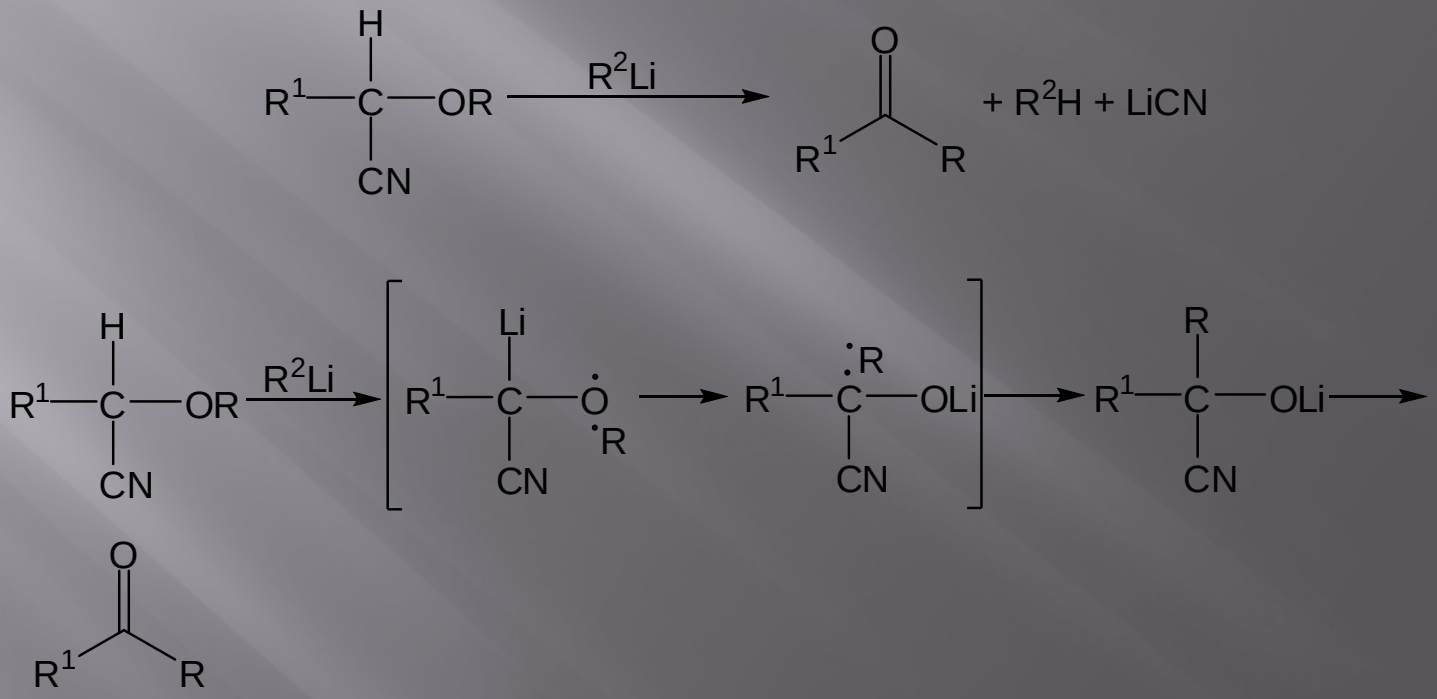






Bt : *benzotriazol-1-yl*

When R^2 *is a good leaving group and electron withdrawing functional group like* CN*, then this group is eliminated and ketone is formed.*



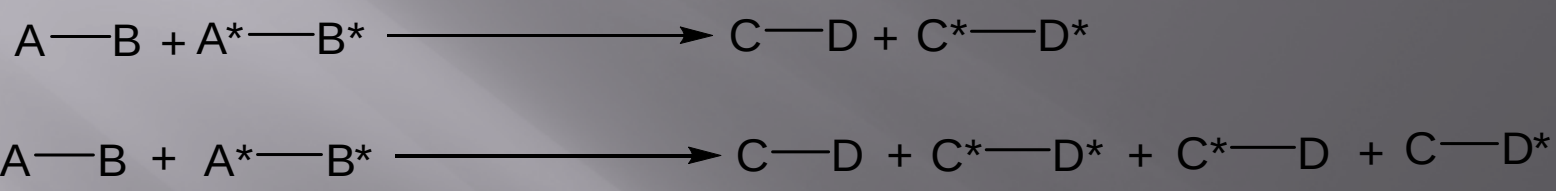
XI. *Crossover experiment*

The purpose of crossover experiment is to determine whether the given reaction takes place intermolecularly or intramolecularly i.e. whether reactant break apart to form intermediates, which diffuse away into solution before they combine to give product.

In this experiment two substrate differing in substituent are mixed together and are reacted under the same reaction condition and the product obtained is analyzed.

Illustration for cross-over experiments:

Consider, a simple reaction in which A-B *reacts to give* C-D.



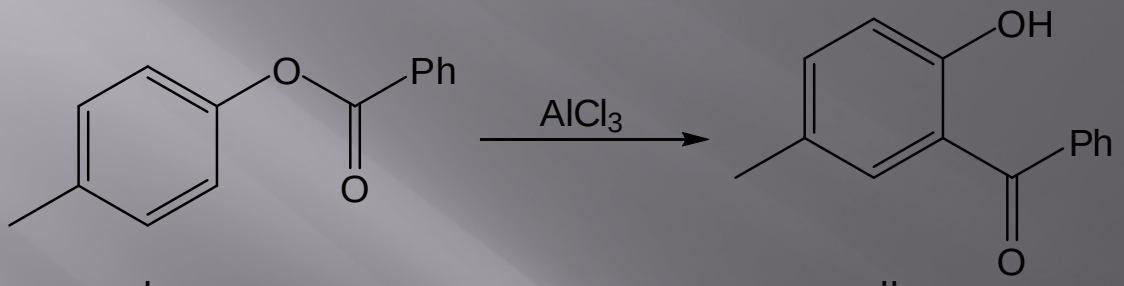
There are two possible of outcomes for the above reaction, as A, A are differently substituted (so are B and B*).*

One in which no crossover of substituent is seen. This is possible if reaction is intramolecular. [The reactant stay connected throughout the course of the reaction]

The other possibility is that a mixture of products are obtained in the crossover reaction. This is possible in the case of ***intermolecular*** *reaction.*

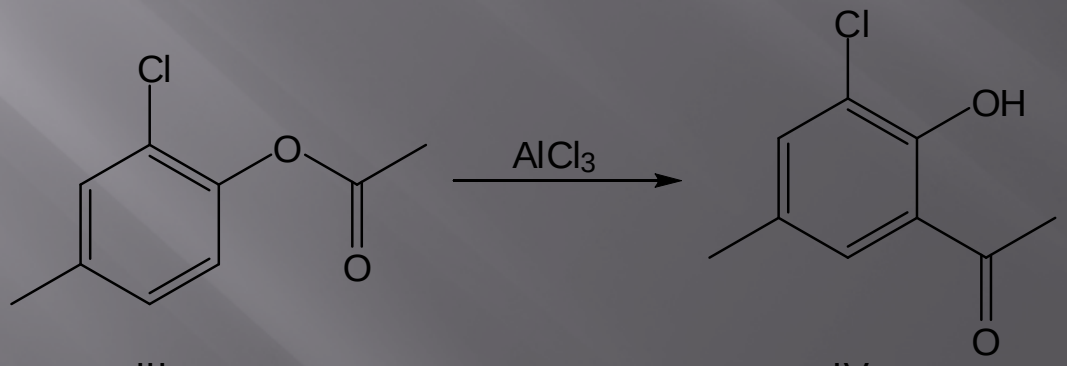
The experiment can be illustrated by considering Fries rearrangement.

p-Tolylbenzoate (I) *on rearrangement gives* 2-hydroxy-5-methylbenzophenone (II).



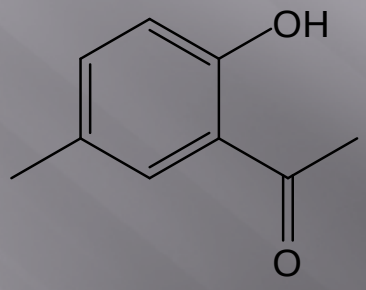
I II

In the similar reaction, o-chloro-p-tolylacetate (III) *give* 2-hydroxy-3-chloro-5-methylacetophenone (IV).

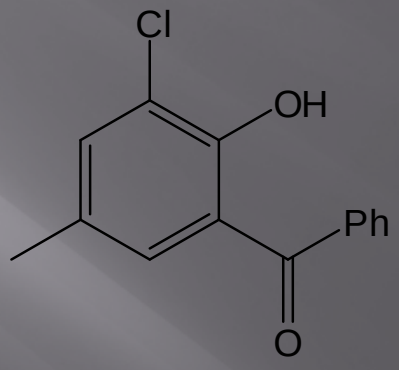


III IV

When I *and* II *are mixed together and product is analyzed,* V *and* VI*, along with* II *and* IV *are obtained.*



V

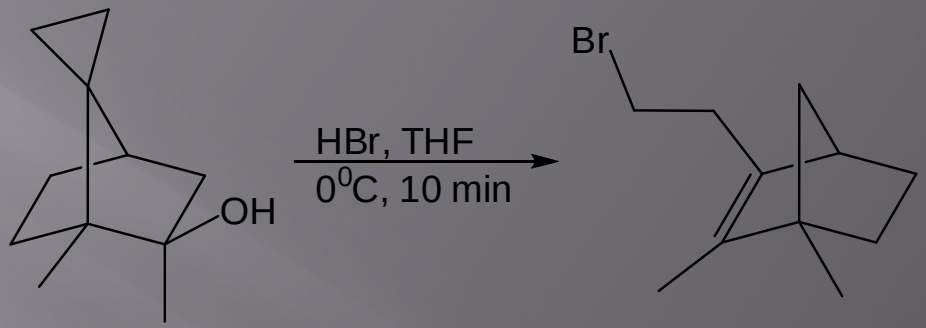


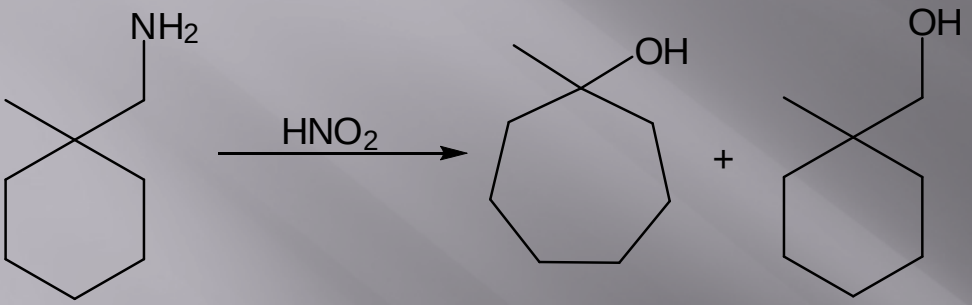
VI

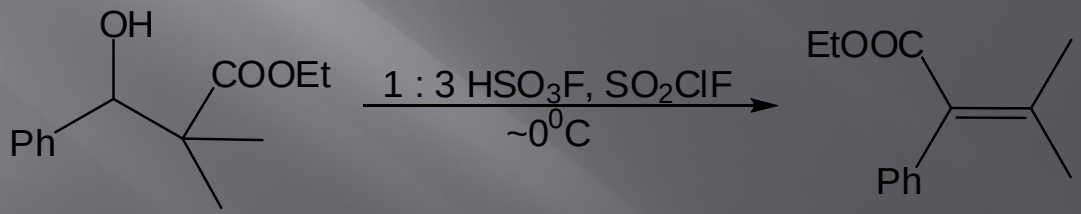
This shows that the reaction proceeds ***intermolecularly*** *and fragments are formed in solution.*

Practice Problems

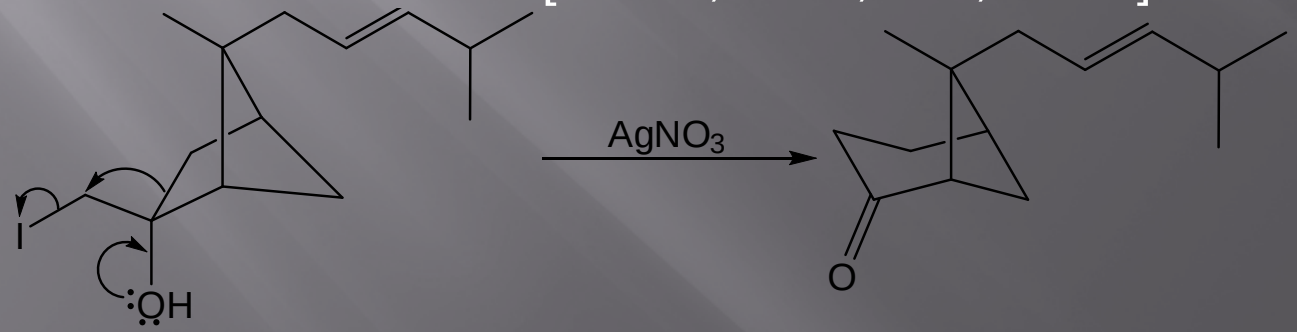
Propose a mechanism for the following examples



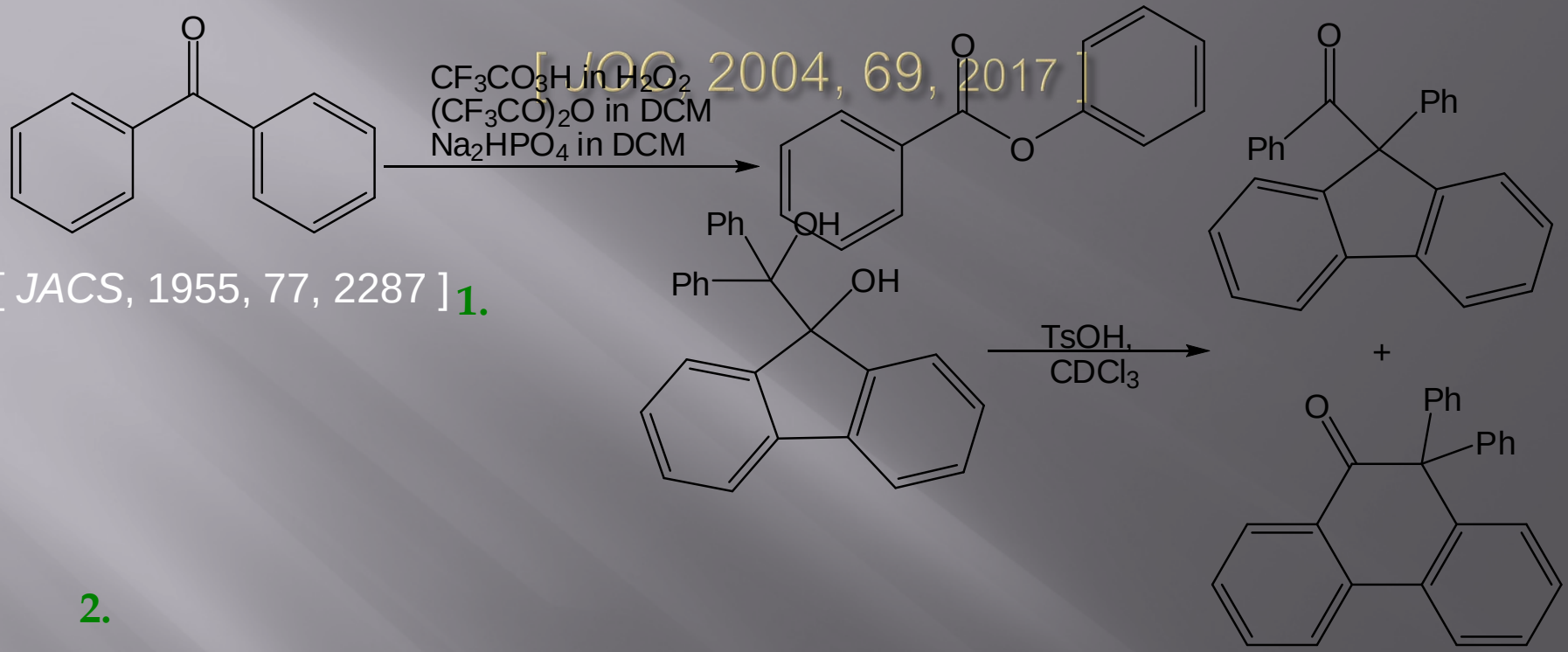




[*JACS*, 1982, 104, 2631]

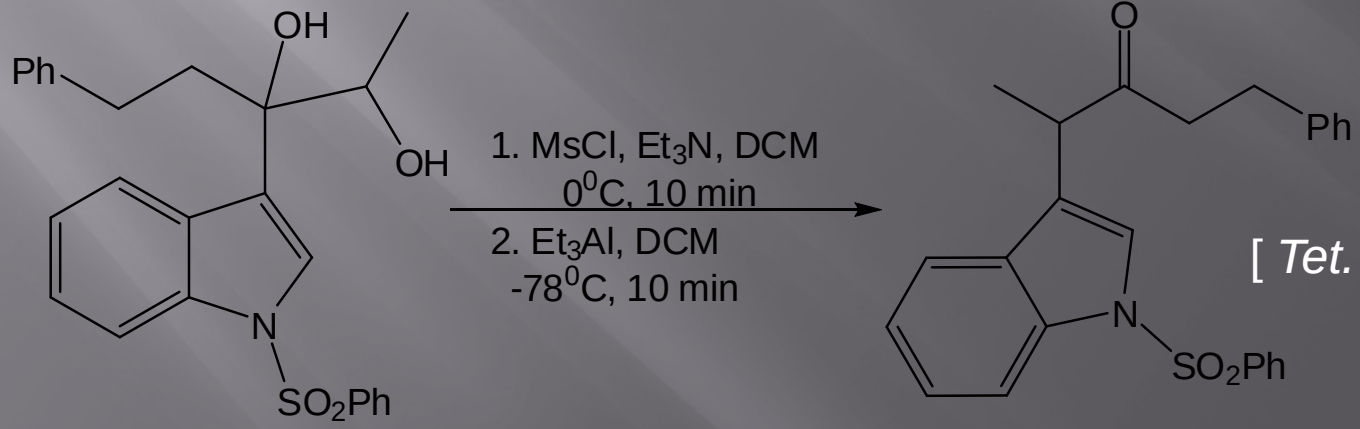


Home work: Propose a mechanism for the following pinacol reaction



[*JACS*, 1955, 77, 2287] **1.**

2.

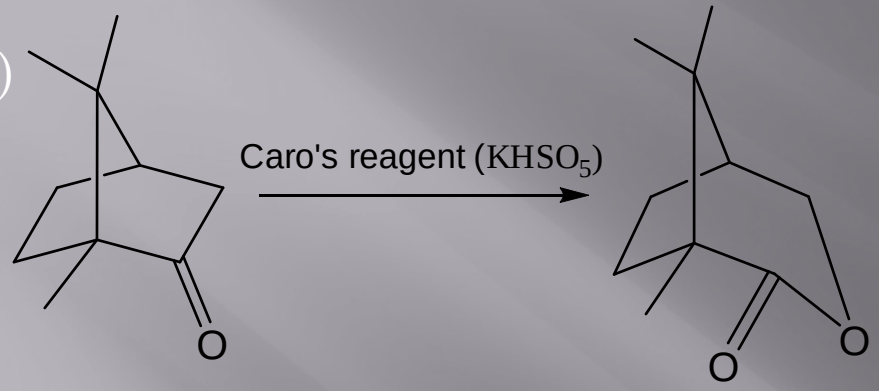


90%

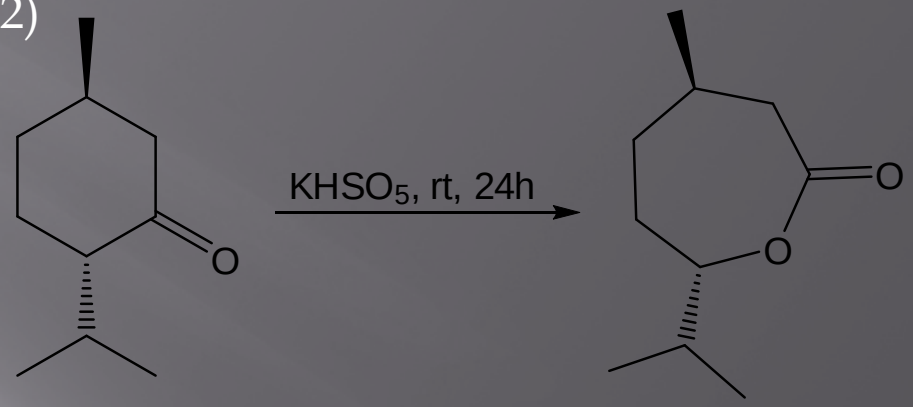
[*Tet. Lett.*, 2002, 43, 6937]

Practice problems/Additional Information on BV reaction

(1)



(2)



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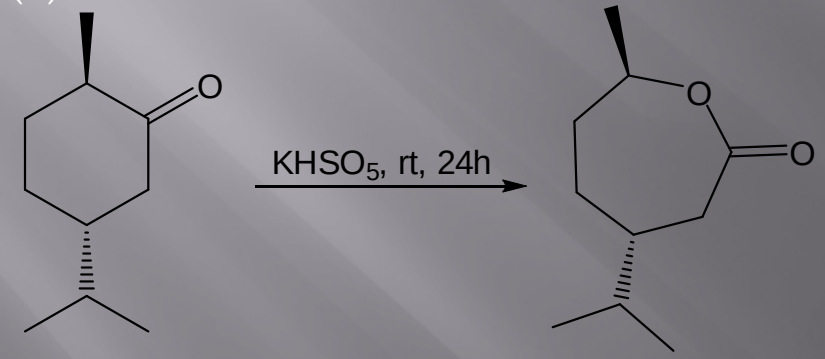

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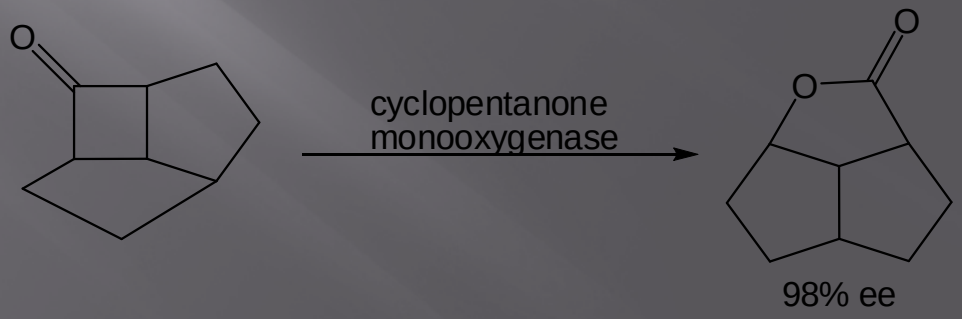
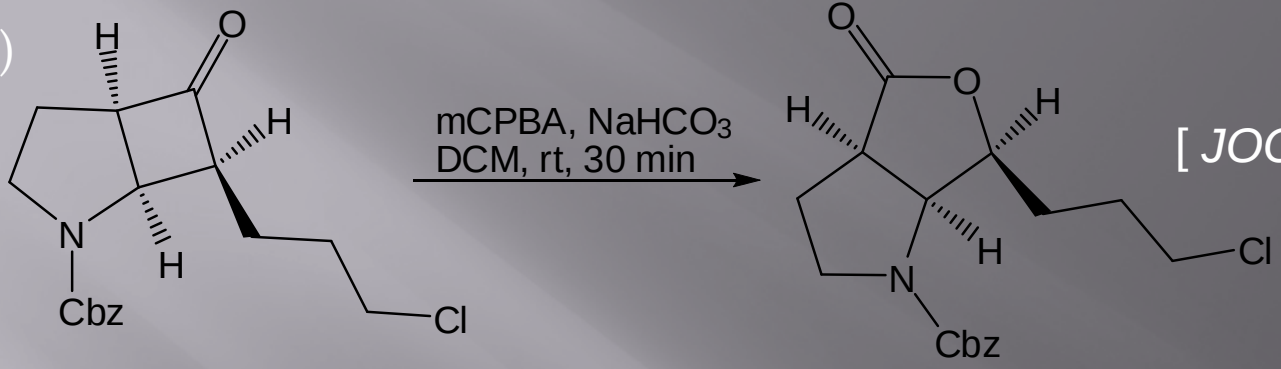


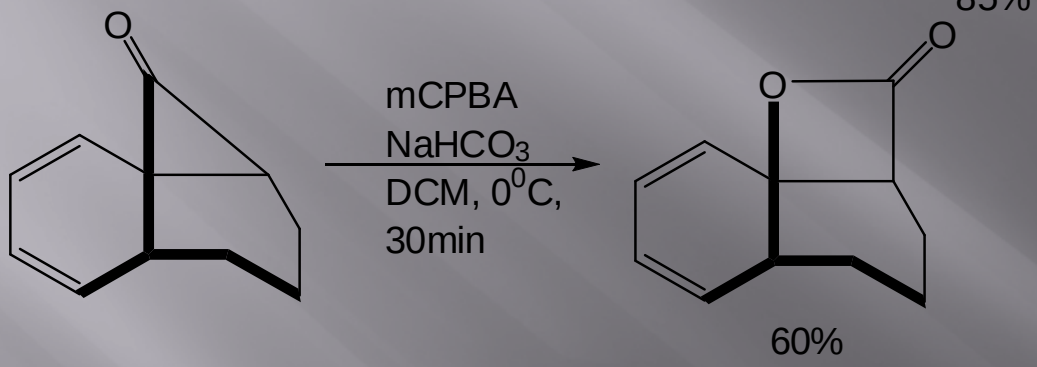
[*Chem.Comm.*, 1996, 2333]

(5)



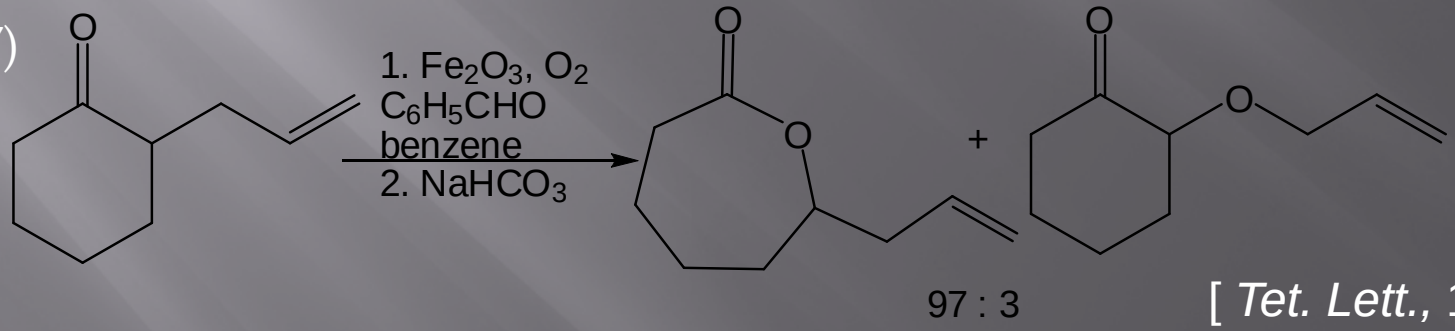
[*JOC,* 2002, 67, 3651]

(6)



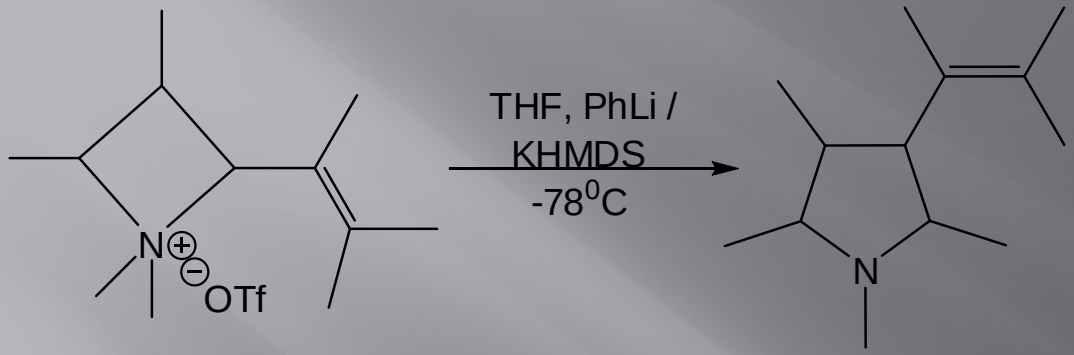
[*Tet. Lett.,* 2009, 50,4519]

(7)

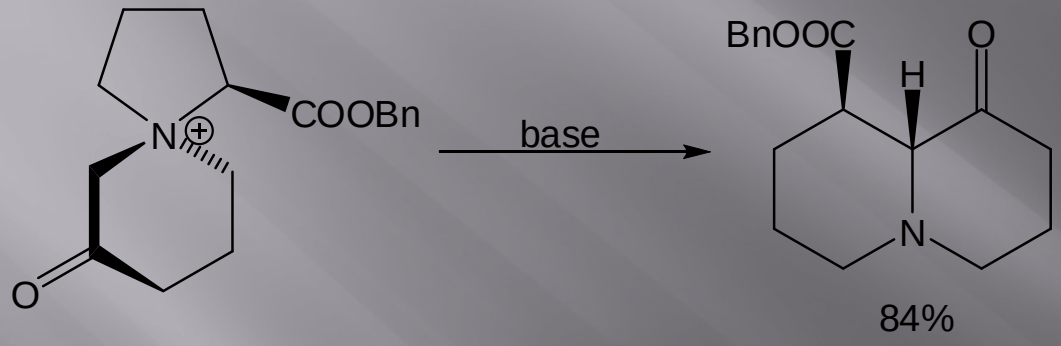


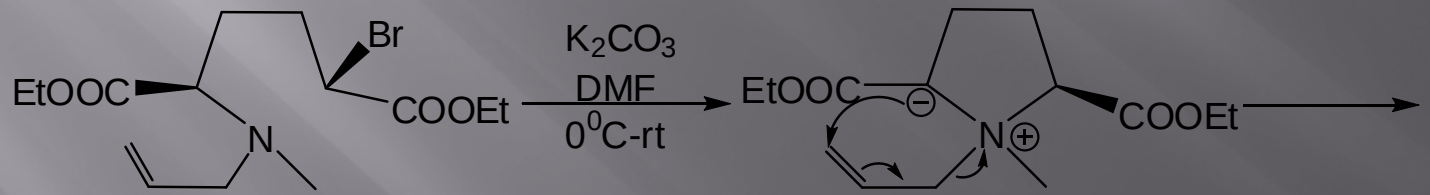
[*Tet. Lett.,* 1992, 33, 7557]

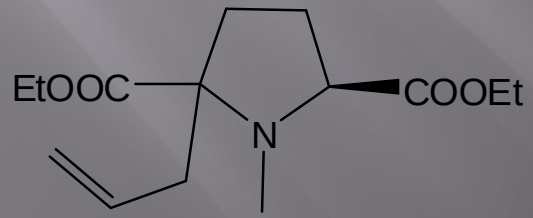
Practice Problems



[*Tet. Lett*., 2004, 45, 7525]



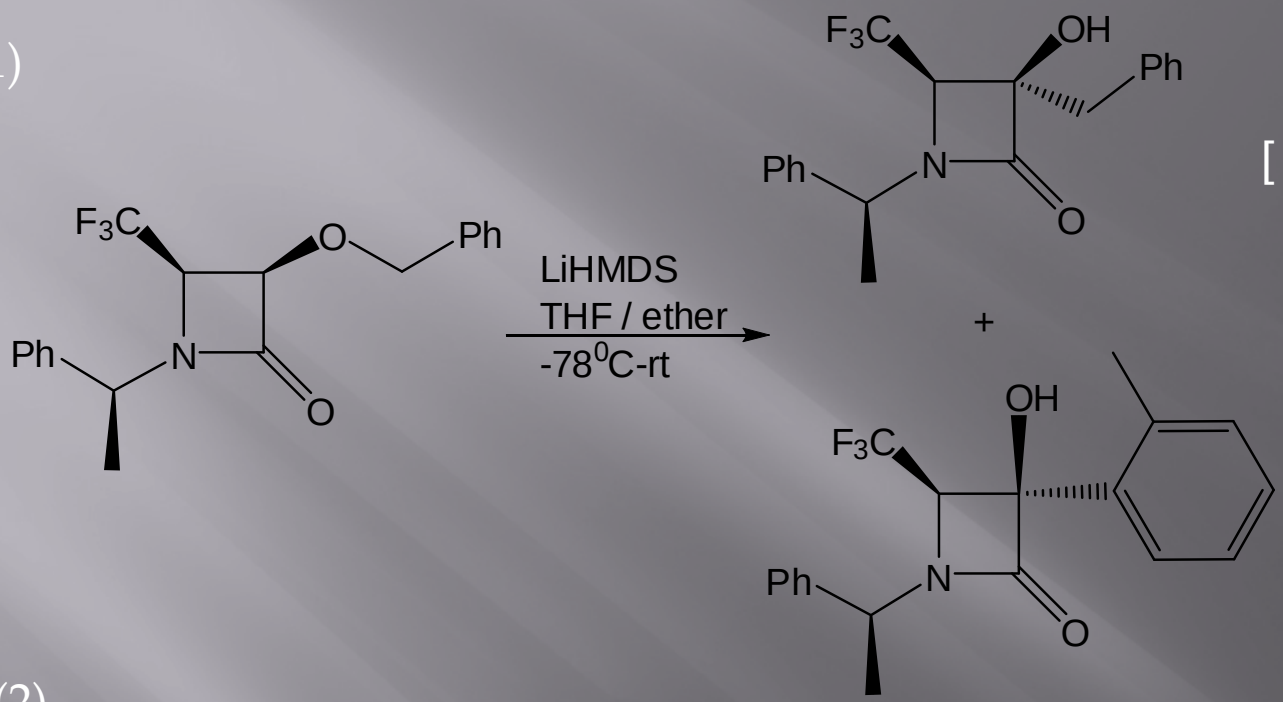




[*Tet. Lett.,* 2002, 43, 899]

Practice Problems

(1)



[*Org. Lett.,* 2001, 3, 2529]

(2)

[*JACS*, 1962, 84, 4295]