MARUDHAR KESARI JAIN COLLEGE FOR WOMEN, VANIYAMBADI
PG DEPARTMENT OF CHEMISTRY

CLASS B **:**II M.Sc CHEMISTRY

SUBJECT CODE : GCH41

SUBJECT NAME :ORGANIC CHEMISTRY-IV

UNIT-IV
SYLLABUS

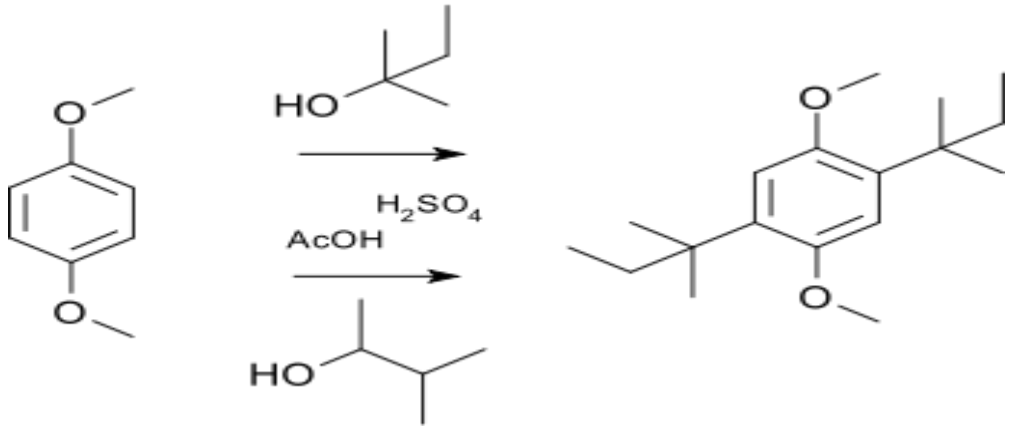
MOLECULARREARRANGEMENTS

A detailed study with suitable examples of the mechanism of the following rearrangements:Wagner - Meerwein, Pinacol- Pinacolone, Demjanov, Dienone - phenol,Favorskii,Baeyer-Villiger,Wolff, Hofmann-Lofler-Freytag–Sommlet-Hauser-Stevens and Von Richter rearrangements.

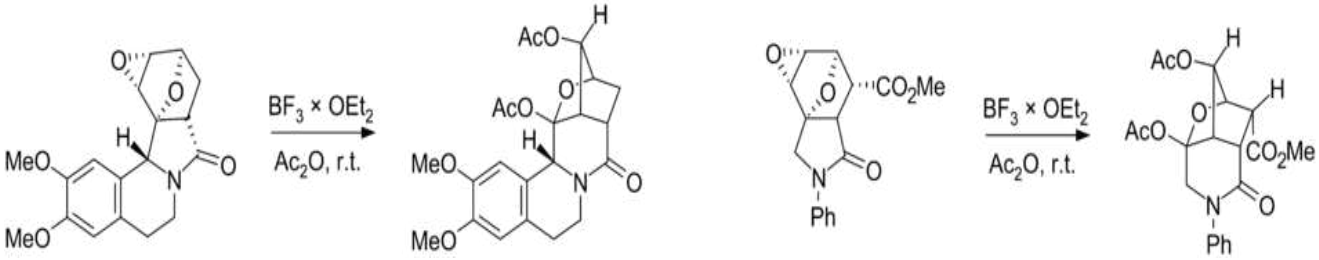
Wagner - Meerwein

The story of the rearrangement reveals that many scientist swerepuzzled with this and related reactions and its close relationship to the discovery of carbocations as intermediates.

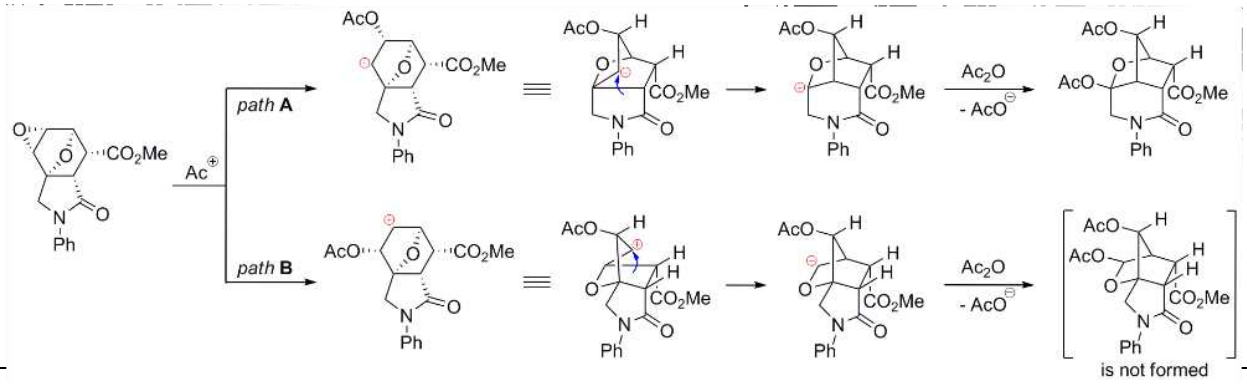
In a simple demonstration reaction of 1,4-dimethoxybenzene with either 2-methyl-2-butanolor3-methyl-2-butanolinsulfuricacidand aceticacid yield sthesamedi substituted product, the latter via a hydride shift of the cationic intermediate:



Currently, there are work srelating to the use of skeletal rearrangement in the synthesis of bridged azaheterocycles.



Plausible mechanisms of the Wagner–Meerwein rearrangement of diepoxyisoindoles

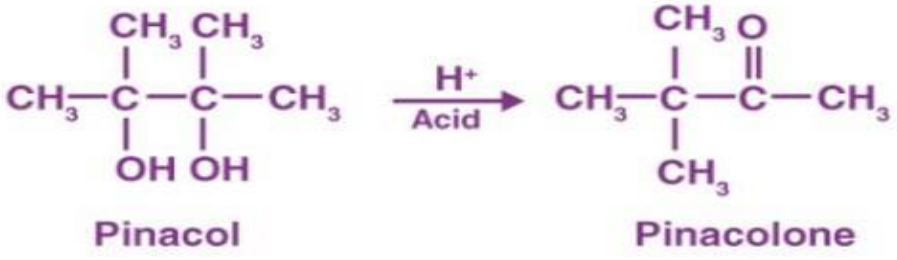


Pinacol–Pinacolone

Pinacol Pinacolone rearrangement is a very important process in organic chemistry for the conversionof1,2diolsinto carbonyl compounds containing a carbonoxygen double bond. This is done via a 1,2-migration which takes place under acyl conditions.

Pinacol Pinacolone Rearrangement Process

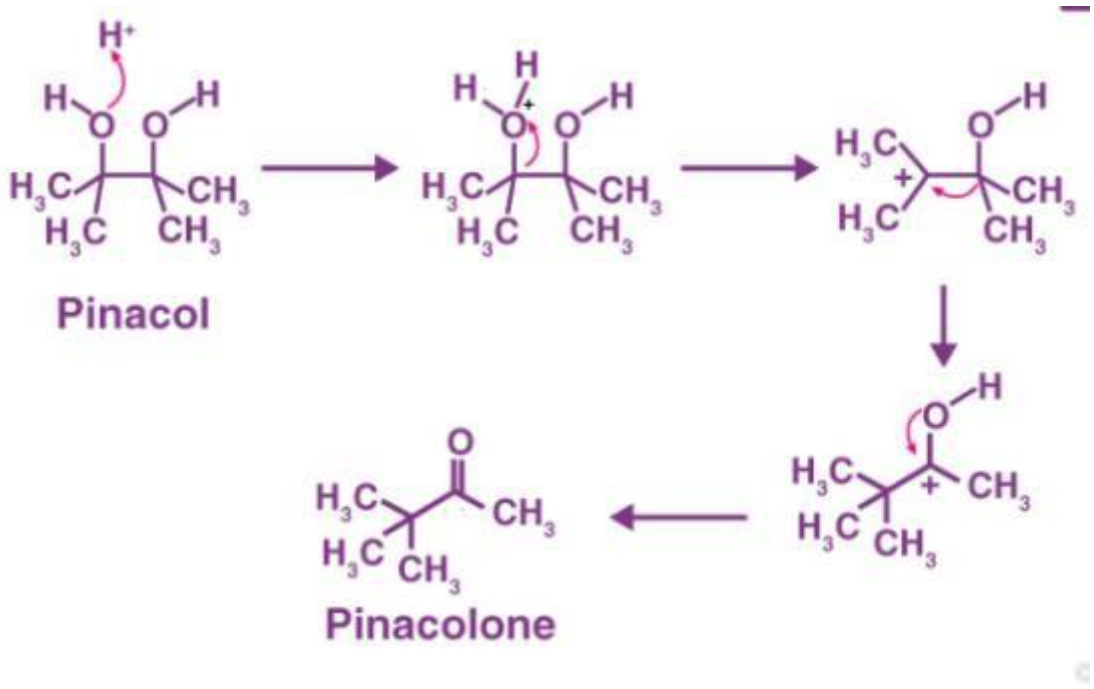
- The pinacol pinacolone rearrangement process takes place via a 1,2-rearrangementasdiscussedearlier. This rearrangement in volves the shift of two adjacent atoms. This reaction is a result of the work of the German chemist William Rudolph Fittig who first described it in the year 1860.
- Pinacolin a compound which has two hydroxyl groups,each attached to a vicinal carbon atom. It is a solid organic compound which is white.
- TheIUPACnameofPinacoloneis3,3-dimethyl-2-butanone.Pinacoloneisavery important ketone. It has a peppermint like or camphor like odour and appears to be a colourless liquid.
- The pinacol pinacolone rearrangement proceeds through the formation of an intermediate which is positive lycharged. The methylgroupinth is intermediate proceeds to migrate from one carbon to another. This reaction can be given by



Mechanism

- The Pinacol Pinacolone rearrangement mechanism proceeds via four steps. Each of these steps is explained below.
- Step1:Since the reactionis carriedout in an acidic medium, the hydroxide group of the pinacol is protonated by the acid.
- Step2:Water is now removed from the compound, leaving behind a carbocation. This carbocation is tertiary and therefore stable.
- Step3:The methyl group shifts to the positively charged carbonina rearrangement of the compound.

- Step4:Theoxygenatomwhichisdoublybondedtothecarbonisnowdeprotonated, giving rise to the required pinacolone.



UsesofPinacolone

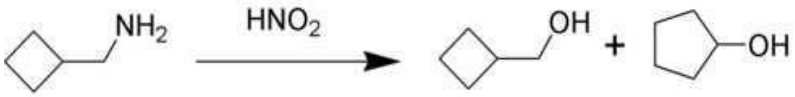
The use soft the pinacolone product produced from the pinacol pinacolone rearrangement include:

- Pinacolone isuse din Pesticides, Fungicides, and Herbicides.
- Pinacolone isused to prepare the cyano guanidine drug– pinacidil.
- Pinacolone isusedto producetriadimefonwhichisusedtocontrolfungaldiseasesin agriculture.

Theprimaryapplicationsofpinacoloneareinthedrug industry.

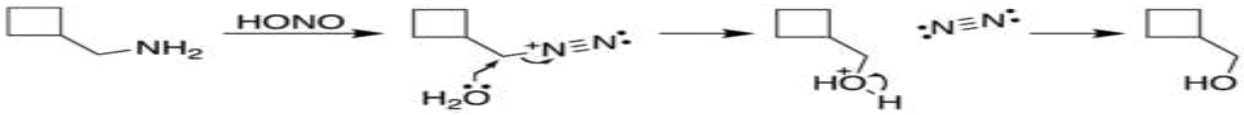
DemjanovReaction

TheDemjanovrearrangement isthechemicalreactionofprimaryamineswithnitrousacid to give rearranged alcohols. It involves substitution by a hydroxyl group with a possible ringexpansion. It is named after the Russianchemist NikolaiJakovlevichDemjanov (Dem'anov, Demianov)



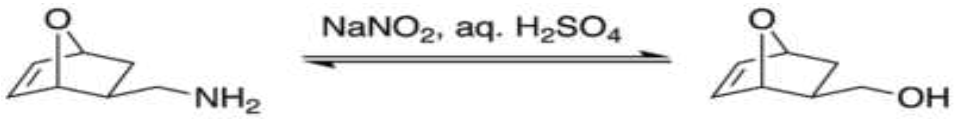
The reaction process begins with diazotization of the amine by nitrous acid. The diazonium groupisagoodleavinggroup,forming nitrogengaswhendisplaced fromtheorganicstructure. Thisdisplacement canoccurviaarearrangement (pathA),inwhichoneofthe sigmabonds adjacent to the diazo group migrates.

This migrationresults inanexpansionofthering. Theresultingcarbocation isthenattackedbya molecule ofwater. Alternately, the diazo groupcanbe displaced directly bya molecule ofwater in an S_N2 reaction (path B). Both routes lead to formation of an alcohol



TheDemjanovrearrangement isa methodtoproducea1-carbonringenlargement infour,fiveor six membered rings. The resulting five, six, and seven-membered rings can then be used in further synthetic reactions.

IthasbeenshownthattheDemjanovreactionissusceptibleto regioselectivity. Oneexampleof this is a study conducted by D. Fattori looking at the regioselectivity of the Demjanov rearrangement in one-carbon enlargements of naked sugars.[6] It showed that when anexo methylamineunderwent Demjanovnitrousaciddeamination,ringenlargement wasnot produced.

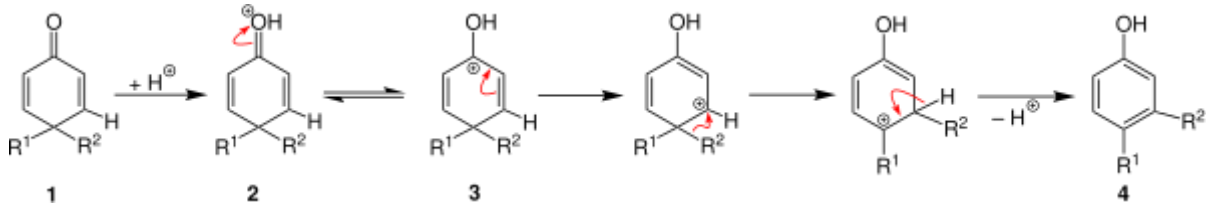


Dienone– phenol

Thedienone–phenolrearrangementisareactioninorganicchemistryfirstreportedin1921 by Karl von Auwers and Karl Ziegler. A common example ofdienone–phenolrearrangement is 4,4-disubstitutedcyclohexadienoneconverting intoastable3,4-disubstitutedphenolinpresence of acid.

A similar rearrangement is possible with 2,2-disubstituted cyclohexadienone to its correspondingdisubstitutedphenol.Usuallythistyperearrangement isaspontaneousunlessthe presence of a dichloromethyl group at 3rd position or 4th position is blocked with any non hydrogen group

Thereactionmechanismof4,4-disubstitutedcyclohexadienonesto 3,4-disubstitutedphenolis illustrated here

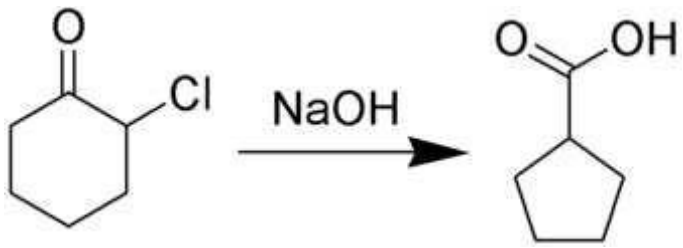


The migrationtendencyforthetwo different groups(R)present at either4,4positionor2,2 position can be determined by comparing the relative stability of intermediateCarbocationformedinthetimeofrearrangement.

FavorskiiReaction&Mechanism

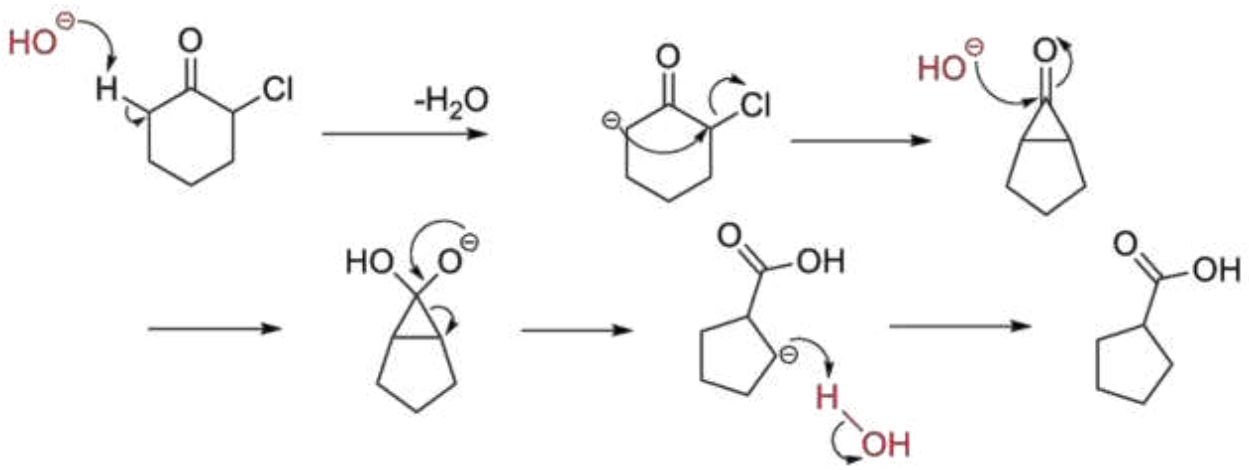
TheFavorskiirearrangement isprincipallyarearrangement ofcyclopropanonesandα-haloketones that leads to carboxylic acid derivatives.

Inthecaseofcyclicα-halo ketones,theFavorskiirearrangement constitutesaringcontraction. This rearrangement takes place in the presence of a base, sometimes hydroxide, to yield a carboxylic acid but most ofthe time either an alkoxide base or an amine to yield an ester or anamide, respectively. α,α'-DihaloketoneseliminateHXunderthereactionconditionstogive α,β-unsaturatedcarbonylcompounds



Thereactionmechanism isthoughttoinvolvethe formationofanenolateonthesideof the ketone away from the chlorine atom.

Thisenolatecyclizestoa cyclopropanone intermediatewhichisthenattackedbythe hydroxide nucleophile.



Thesecondstephasalso beenproposedto bestepwiseprocess,withchlorideanionleaving first to produce a zwitterionic oxyallyl cation before a disrotatory electrocyclic ring closure takes place to afford the cyclopropanone intermediate.

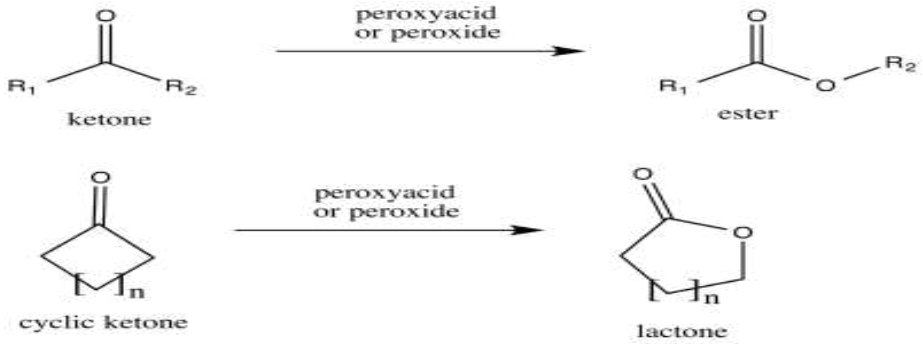
Usageofalkoxideanionssuchassodiummethoxide,insteadofsodiumhydroxide, yieldsthe ring-contracted ester product.

Whenenolateformationis impossible, theFavorskiirearrangementtakesplace byanalternate mechanism, in which addition to hydroxide to the ketone takes place, followed by concerted collapse of the tetrahedral intermediate and migration of the neighboring carbon with displacement of the halide.

Thisissometimesknownasthepseudo-Favorskiirearrangement,althoughprevioustolabeling studies, it was thought that all Favorskii rearrangements proceeded through this mechanism.

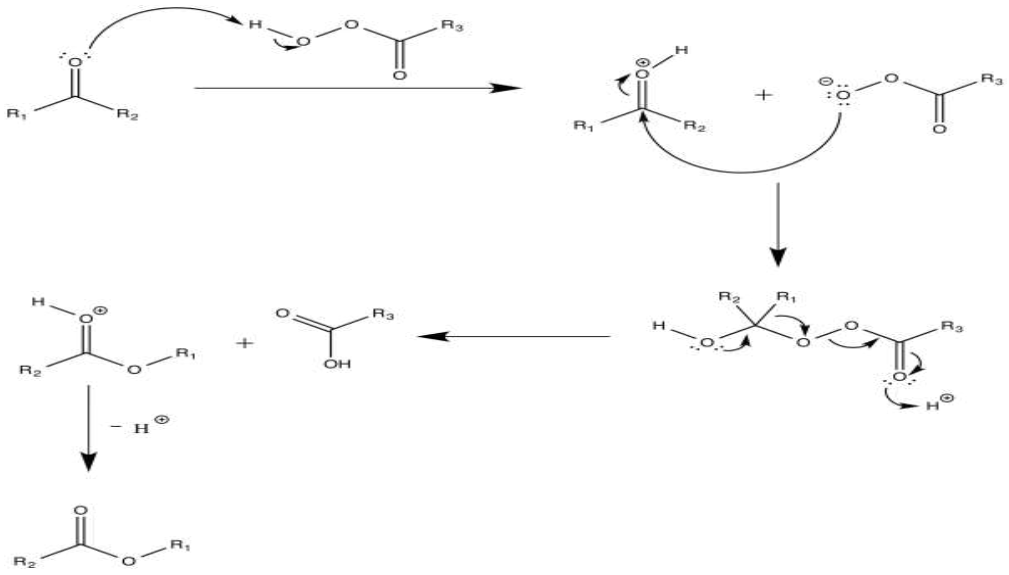
Baeyer– VilligerReaction &Mechanism

The Baeyer–Villiger oxidation is anorganic reactionthat forms anester froma ketone or a lactonefromacyclicketone, usingperoxyacidsorperoxidesastheoxidant.Thereactionis named after Adolf von Baeyer and Victor Villiger who first reported the reaction in 1899.



Inthefirst stepofthe reactionmechanism, theperoxyacid protonatestheoxygenofthe carbonylgroup. This makes the carbonylgroup more susceptible to be attacked bythe peroxyacid. Next, the peroxyacid attacks the carbon of the carbonyl group forming what is known as the Criegeeintermediate.

Through a concerted mechanism, one of the substituents on the ketone group migrates to the oxygenoftheperoxidegroupwhileacarboxylicacid leaves. Thismigrationstep isthoughttobe the rate determining step. Finally, deprotonation of the oxocarbenium ion produces the ester.



WolffReaction&Mechanism

TheWolffrearrangement isareactioninorganicchemistryinwhichanα-diazocarbonyl compound is converted into a ketene by loss of dinitrogen with accompanying 1,2-rearrangement.

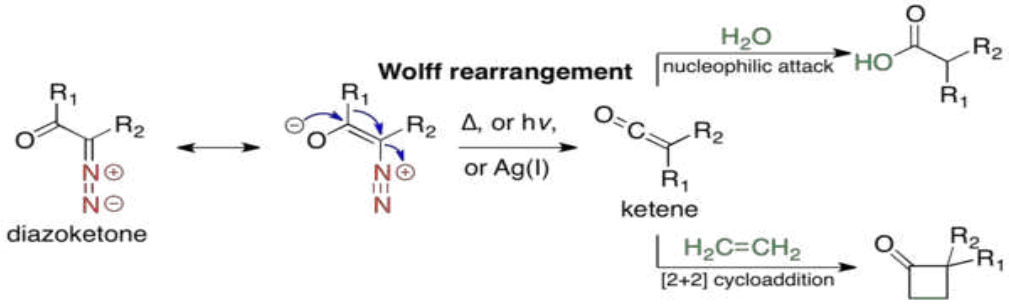
The Wolff rearrangement yields a ketene as an intermediate product, which can undergo nucleophilicattackwithweaklyacidicnucleophilessuchaswater,alcohols, andamines, to

generatecarboxylicacidderivativesorundergo[2+2]cycloadditionreactionstoformfour- membered rings.

The mechanismoftheWolffrearrangement hasbeenthesubject ofdebatesince itsfirst use.No single mechanism sufficiently describes the reaction, and there are often competing concerted and carbene-mediated pathways; for simplicity, only the textbook, concerted mechanism is shown below.

The reaction was discovered by Ludwig Wolff in 1902. The Wolff rearrangement has great syntheticutilitydueto theaccessibilityofα-diazocarbonylcompounds, varietyofreactions from the ketene intermediate, and stereochemical retention of the migrating group.

However,theWolffrearrangement has limitations duetothehighlyreactivenatureofα-diazocarbonyl compounds, which can undergo a variety of competing reactions.



TheWolffrearrangement canbeinducedvia thermolysis,photolysis,ortransitionmetal catalysis.

In this last case, the reaction is sensitive to the transition metal; silver (I) oxide or other Ag(I) catalystsworkwellandaregenerallyused. TheWolffrearrangement has beenused inmany totalsyntheses; the most common use is trapping the ketene intermediate with nucleophiles to form carboxylic acid derivatives.

TheArndt-Eisterthomologation isaspecificexampleofthisuse,whereina carboxylicacid may be elongated bya methylene unit. Another common use is in ring-contraction methods ifthe α- diazo ketone is cyclic, the Wolff rearrangement results in a ring-contracted product.

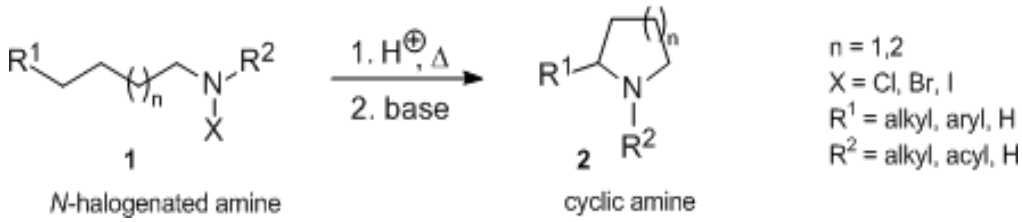
TheWolffrearrangement workswellingenerating ring-strainedsystems,whereotherreactions may fail.

Hofmann-LoflerReaction&Mechanism

TheHofmann–reaction(alsoreferredtoasHofmann–Freytagreactio–Freytagreaction,Löffler–Hofmannreaction, as wellas Löffler's method) is anorganic reaction inwhicha cyclic amine 2 (pyrrolidine or, in some cases, piperidine) is generated by thermal or photochemical

decompositionofN-halogenatedamine1 inthepresenceofastrongacid(concentrated sulfuricacid or concentrated CF_3CO_2H).

TheHofmann–Löffler–Freytagreactionproceedsviaanintramolecularhydrogenatomtransfer to a nitrogen-centered radical and is an example of a remote intramolecular free radical C–H functionalization.



1 *N*-halogenated amine

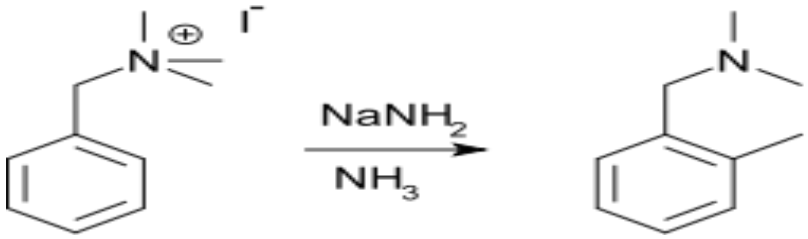
2 cyclic amine

Sommlet-Hauser-Stevens

TheSommelet–Hauserrearrangement (namedafterM.SommeletandCharlesR.Hauser)is a rearrangement reaction of certain benzylquaternary ammonium salts.

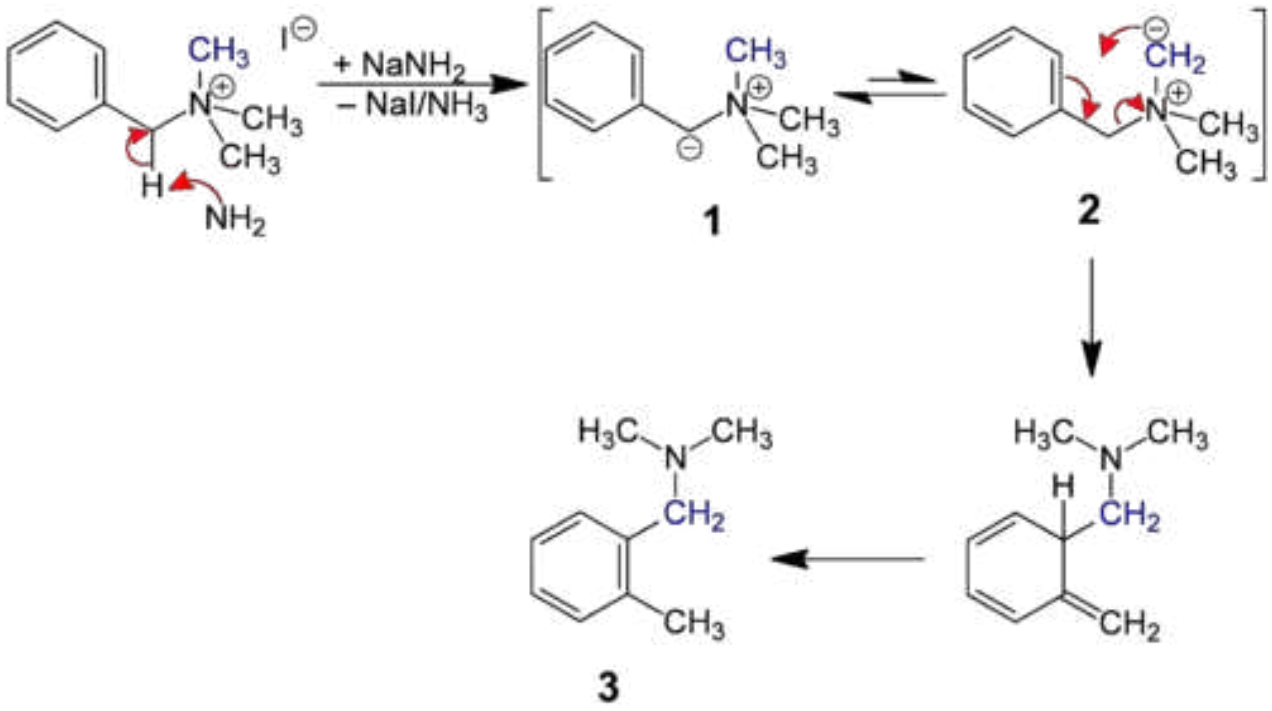
Thereagent issodiumamideoranotheralkalimetalamideandthereactionproducta N,N- dialkylbenzylamine with a new alkyl group in the aromatic ortho position.

Forexample,benzyltrimethylammoniumiodide,$[(C_6H_5CH_2)N(CH_3)_3]I$,rearrangesinthe presenceofsodiumamideto yield theo-methylderivativeofN,N-dimethylbenzylamine.



Thebenzylic methyleneprotonisacidicanddeprotonationtakesplaceto producethe benzylic ylide

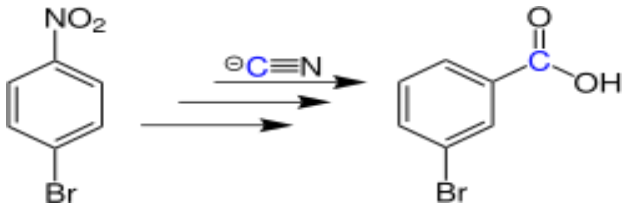
This ylide is inequilibriumwithasecond ylidethat is formedbydeprotonationofone ofthe ammonium methyl groups Thoughthe second ylide is present in much smaller amounts, it undergoes a 2,3-sigmatropic rearrangement because it is more reactive thanthe first one and subsequent aromatization to form the final product



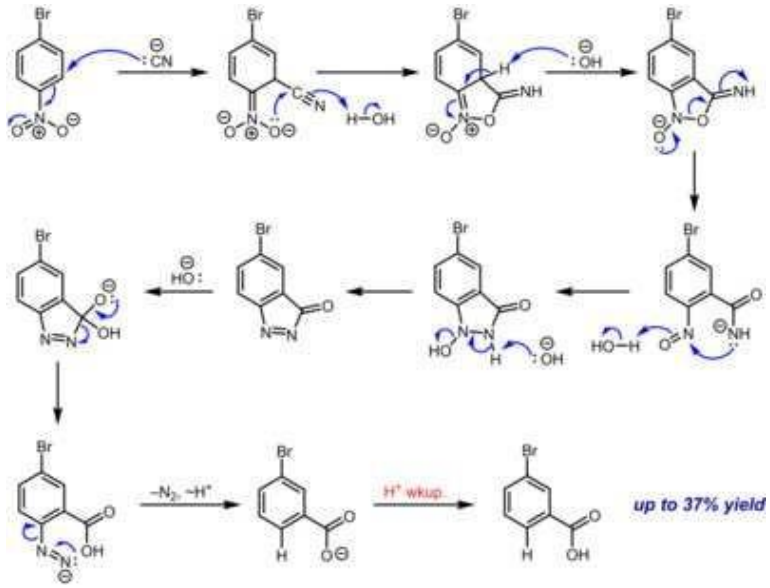
VonRichterrearrangements

Itisthereactionofaromaticnitro compoundswithpotassiumcyanide inaqueousethanoltogive the product of cine substitution (ring substitution resulting in the entering group positioned adjacent to the previous location of the leaving group) by a carboxyl group.

Although it is not generallysyntheticallyusefuldue tothe low chemicalyield and formationof numeroussideproducts,itsmechanismwasofconsiderableinterest,eludingchemistsforalmost 100 years before the currently accepted one was proposed.



Several reasonable mechanisms were proposed and refuted by mechanistic data before the currentlyacceptedone, shownbelow, wasproposedin1960byRosenblumonthebasisof ^{15}N labeling experiments.



First,thecyanideattacksthecarbonorthotothenitrogroup.This is followedbyringclosing via nucleophilic attackon the cyano group, after which the imidate intermediate is rearomatized. Ringopeningvianitrogen–oxygenbondcleavagegivesanortho-nitroso benzamide,

whichrecyclizes to give a compound containing a nitrogen–nitrogenbond. Eliminationofwater givesacyclicazoketone,whichundergoesnucleophilicattackbyhydroxidetogiveatetrahedral intermediate.

This intermediatecollapseswitheliminationoftheazogrouptoyieldanaryldiazenewith an ortho carboxylate group

which extrudes nitrogen gas to afford the anionic form of the observed benzoic acid product, presumablythroughthegenerationand immediateprotonationofanarylanionintermediate. The product is isolated upon acidic workup