**有机名称反应**

**Arndt-Eistert合成（Wolf重排）**

* Arndt Eistert is a complete set of reactions in which a carboxylic acid is stepped up to its higher homologue.

\[
R\text{C}HO \xrightarrow{SOCl_2} R\text{C}Cl \xrightarrow{2CH_2N_2} [\begin{array}{c} R\text{C}H\text{C}N \text{N} \\ -\text{CH}_3\text{Cl} \\ -\text{N}_2 \end{array}] \xrightarrow{\text{Wolf Rearrangement}} \xrightarrow{(\text{Ag}_2\text{O})} R\text{CH}_2\text{COOH}
\]

* Acid is first converted to acid chloride by reacting with SOCl₂. Then the acid chloride treated with diazomethane to form diazo ketone. The third step is the crucial Wolf rearrangement step. The diazoketone is treated with Ag⁺ catalyst(Ag₂O) in presence of H₂O or ROH or NH₃/RNH₂ to form higher carboxylic acid, or ester or amide respectively.

* Labelled COOH carbon produced the higher acid with the same labelled COOH group, which meant that the alkyl group is bonded to the carbon atom contained in diazomethane.

* During the formation of diazoketone from acid chloride, two moles of diazomethane are required and in this step, CH₃Cl and N₂ are eliminated. In the steps below (–CH₃N₂⁺ and Cl⁻ shown which produce CH₃Cl and N₂)

* The diazoketone on photolysis or pyrolysis or in presence of Ag(I) catalyst(Ag₂O) rearranges with expulsion of N₂ to form a ketene. Note that in the mechanism given above, this step has been shown with the formation of carbene first, which rearranges to ketene. This is correct in some cases. But in other cases, concerted N₂ extrusion from diazoketone forming the ketene has also been observed (see later for general Wolf mechanism). Hence Wolf rearrangement is bit controversial in this respect. Both carbene formation and concerted pathways have been accepted by different authors.

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* Ketene in presence of a nucleophile like H₂O produces the higher carboxylic acid. If there is R’OH or NH₂/RNH₂ in place of water, ester or amides are formed respectively.
(N.B: In the mechanism above for the Wolf step, hv(photolysis) is written. You please write Ag₂O in its place. In fact, photolysis or pyrolysis is also alternative to Ag⁺ catalysed reaction. This has been borrowed from Google search by copy-paste mode. Thanks to Google)

General Wolf Rearrangement Mechanism:
Any diazoketone on photolysis, or pyrolysis or in presence of Ag₂O expels N₂ and forms a ketene.

(N.B: The nucleophile H₂O or ROH or RNH₂ is taken along with Ag₂O in order to form the c.acid or ester or amide respectively. If this is added later after formation of ketene, there is time for independent ketene reactions to give unwanted byproducts.

**Baeyer Villiger Oxidation:**
* Ketones react with peroxy acids like peroxy benzoic acid( Ph–CO–OOH), Caro’s acid(H₂SO₅), m-CPBA( m-Cl-C₆H₄-CO–OOH), H₂O₂/BF₃ etc. to form esters. It is to be viewed as an insertion of -O- adjacent to the carbonyl function. The insertion is preferable towards the more substituted side/longer side.
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Regioselectivity: The major ester formed in which the -O- is inserted on side of carbonyl group which is more substituted i.e having longer and more branched group. (see below for migratory aptitude give below). In the first example, -O- is inserted to cyclohexyl (not to methyl) to form cyclohexyl acetate(not methylcyclohexane carboxylate). In the 2nd example, -O- is inserted to n-hexyl group(not methyl) to form n-hexyl acetate(not methylheptanoatoa). In the 3rd example too, the -O- inserted to the secondary carbon atom having one branch(not the unbranched side). Note that this is the major product in each case. The other minor product is also formed.

* **Mechanism:** The peroxy acid first makes a peroxy acyl bond with the carbonyl carbon with its pi-bond polarized. Next, there is a 1,2- alkyl/ring residue migration from Carbon to Oxygen from among the two groups bonded to the carbonyl group of ketone. This is the rate determining step. The more electron-rich group(having more +I effect) preferentially migrates. However, the migratory aptitude of the alkyl and other groups follow the typical order given below(obtained on experimental basis for this reaction).

* **Migratory Aptitude:** -H > 3° alkyl >cycloalkyl > 2° alkyl > -Ph = allyl > 1° alkyl > -Me

Aldehydes also give this test resulting carboxylic acid due to H- migration.
**Bamberger Rearrangement:**

N-phenylhydroxyl amine on treatment with strong aq. acid (e.g., H₂SO₄) rearranges to p-aminophenol

Mechanism:

Protonation of phenylhydroxy amine and subsequent dehydration produces nitrenium ion (4). Then H₂O makes nucleophilic attack onto para carbon and a proton transfer to N- makes a p-hydroxyamino compound. But still aromatization is left. A para proton expulsion brings about aromatization. The proton transfer to N-atom is not shown and also aromatization not shown. But can you not work it out?

**Beckmann Rearrangement:**

Oximes of carbonyl compound rearrange in presence of acidic compounds like P₂O₅, PCl₅, H₂SO₄, SOCl₂, etc. to form N-substituted amide(2° amide). Other than dil. H₂SO₄, in all other catalyst, use of H₂O is required for the hydrolysis step (explained below).

Stereoselectivity: The substituent located trans(anti) to –OH group of oxime preferentially migrates to form the major product. In other words, trans-migration is KEY to this rearrangement. In the general case shown below, the group anti to –OH is R, which migrates (R¹ is retained the carbon atom)
(Please read the symbol \( \rightleftharpoons \) for the reversible symbol ( \( \rightleftharpoons \) ) in respect of resonance structures shown inside square bracket. It is burrowed by copy-paste mode from Google Search. Thanks to Google).

* The trans group \( R \) migrates with expulsion of \( H_2O \) from the hydrated oxime molecule, thus forming a nitrilium ion, which is stabilised by resonance. This ion on hydrolysis followed by deprotonation form imidol which tautomerises in presence of acid to form sec-amide.

* So the two GIs namely ANTI and SYN oxime forms different amide products.

* Oximes of aldehydes and ketones can be easily prepared by reacting it with hydroxyl amine\((NH_2OH)\) which is \( Ad_\delta \) type of addition followed by dehydration.

* Cyclic ketoximes can be easily converted to cyclic amides called LACTAMs by treating the oxime with acidic catalyst.

\[ \text{Cyclohexanone} \quad \xrightarrow{\text{NH}_2\text{OH}} \quad \text{Caprolactam} \]

* SYN-aldoximes on treatment with \( \text{PCl}_5 \) gives alkyl cyanides. See this example.

\[ \text{C=N} + \text{PCl}_5 \xrightarrow{\text{HCl}} \text{C=N} - \text{POCl}_3 - \text{Cl}^{-} \]

Of course, if this product is hydrolysed then we can get carboxylic acid mostly. So treatment of dil \( \text{H}_2\text{SO}_4 \) or hydrolysis step after \( \text{PCl}_5 \) treatment is avoided in the above case to get alkyl cyanides, which are important compounds for organic synthesis.
The stereoselectivity of trans migration is seen even in cyclic ketoximes. When 2-methylcyclohexanone reacts with NH₂OH, predominantly ANTI oxime product is formed due to steric hindrance for the formation of syn isomer. When we treat the anti isomer with dil H₂SO₄, we get nearly 70% of the lactam in which Me- group is adjacent to -NH- due to migration of the ring residue carrying -Me group(lying trans to -OH group). The other lactam, not shown in the figure below, is due to migration of migration of ring reside which does not carry the -Me group(unsubstituted part).

SAQ: Predict the major product when A and B separately treated with an acidic catalyst.

Solution: A : \[ \text{MeO} \quad \text{C-} \quad \text{N} \quad \text{H} \quad \text{Ar} \]

B: \[ \text{Ar} \quad \text{C-} \quad \text{N} \quad \text{H} \quad \text{OMe} \]

**Benzilic Acid Rearrangement.**

\( \alpha \)-diketones react in presence of strong base to form rearranged \( \alpha \)-hydroxy acids.

The carbonyl group which is more electrophilic is attacked by OH– in the first step and alkyl/aryl group from that carbonyl carbon migrates to the other carbonyl group which polarises.

In the example shown below benzil(1,2-diphenylethanedione) on treatment with KOH followed by acidification gives the conjugate base of benzilic acid which on acidification(not shown) gives benzilic acid.
Example:

\[
\text{Benzidine Rearrangement:}
\]

* Hydrazobenzene (1,2-diphenylhydrazine) i.e. Ph–NH–NH–Ph on treatment with mineral acid catalyst (H₂SO₄) form 4,4’-benzidine (p,p’diaminodiphenyl) as major product. Small amounts of other isomers are also formed.
Mechanism:

**Birch Reduction:**

* The formation of unconjugated diene (1,4-diene) from benzene by reducing it with Na or Li in liq. NH₃ in presence of alcohol like EtOH or t-BuOH is called Birch reduction. Benzene is converted to 1,4-cyclohexadiene.

* If there is a EDG group (+M or +I) in benzene ring, then a more substituted unconjugated hexadiene will be formed, with hydrogenation occurring at ortho and meta positions.

* If there is a EWG group, then the less substituted cyclohexadiene is formed with hydrogenation occurring at ipso and para positions.

Mechanism:

Benzene accepts one electron from Na/liq. ammonia system (blue solution containing ammoniated electron) to form a radical anion. To minimize repulsion between electrons (the anion and the unpaired electron), they are kept farthest apart and hence the 1,4-addition to form 1,4-diene, although 1,3-diene is more stable due to resonance.

- The starting material can be easily obtained from nitrobenzene by selective reduction by using Fe/NaOH or Zn/NaOH (Refer the chapter nitrobenzene for details).
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The radical ion has two more RSs (not shown). The radical accepts one H\(^+\) ion from alcohol to form a radical. The radical then accepts one more electron from Na/liq.NH\(_3\) system to form an anion. This anion accepts a H\(^+\) from alcohol to form 1,4-cyclohexadiene. Obviously, when there is EDG, the carbanion cannot be formed at the ipso carbon and hence gives more substituted diene. Similarly when there is EWG, the carbanion is formed at the ipso carbon and hence the less substituted diene is formed.

Below you find the mechanism in presence of a EDG (–OMe).

**Bouveault Blanc Reduction:**
It is the reduction of ester by Na/EtOH to form two alcohols, one of which is bound to be primary (from acyl part).

**Claisen Condensation:**
* Ester containing \(\alpha\)-H atom undergoes self-condensation in presence of strong base like NaOEt/NaNH\(_2\)/NaH in EtOH to form \(\beta\)-keto ester. The famous acetoacetic ester is prepared by this method.
* An aq. acidic work-up is needed to get neutral product.

\[
\begin{align*}
\text{2} & \quad \text{O} \\
& \quad \text{O} \\
\text{1) NaOEt} & \quad \text{O} \\
\text{2) H}_3\text{O}^+ & \quad \text{O}
\end{align*}
\]
Mechanism:

α-H is abstracted by the strong base $\text{OEt}^-$ to form a stable enolate ion. The enolate reacts with another ester molecule in the r.d.s in a Ac-2 type of mechanism to form ethylacetoacetate(EAA) or acetoacetetic ester i.e the β-keto ester. But $\text{EtO}^-$ abstracts a $\text{H}^+$ ion from the active position of EAA and produces the enolate ion of the β-ketoester. So an aq. acidic work-up(not shown) is required to get neutral EAA.

General:

Cross Claisen condensation makes use of one containing α-H atom and the other not.

Ethyl acetate condenses with ethyl benzoate to form ethyl 3-oxo-3-phenylpropanoate.

* If ketone or alkanenitrile condenses as a doner with an ester, we get diketone and ketonenitrile respectively. Try for yourself. Note that ketone or nitrile has more acidic H atom than an ester. So the enolate ion will be formed from the former molecules.
Organic Name Reactions

**Claisen Rearrangement:**

*For Aromatics:*
- When allyl phenyl ether is heated (above 100°C) o-allyl phenol is formed. If ortho positions are blocked then p-allyl phenolic compound is formed.
- If it is ortho allyl, then the reaction is a [3,3] sigmatropic shift process under pericyclic mechanism which is thermally allowed (like Cope rearrangement shown elsewhere). Pericyclic reactions are concerted reactions occurring via cyclic TS. In [3,3] sigmatropic shift, there is shift of a sigma bond through 3 atoms on both the sides.

\[
\begin{align*}
\text{o-allyl phenol} & \\
\text{o-allyl phenyl ether} & \Delta
\end{align*}
\]

C–O bond at the 1-1’ position has undergone a shift through 3 atoms on either side during this cyclic TS. That is why it is called [3,3] sigmatropic shift. Note that the labelled carbon at 1’-position as a sp³ hybrid carbon in the reactant is located in the terminal position of allyl group as sp² hybrid carbon. This is the outcome of the bond breaking and making through cyclic TS.
- Claisen rearrangement can be considered as an oxa variant of Cope rearrangement (discussed elsewhere).
- If both the ortho positions are blocked then it allyl group makes two inversions to para position via the ortho position. One [3,3] shift (oxa equivalent of Cope) cannot bring about aromatisation. Hence the 2nd [3-3] shift (a real Cope rearrangement) occurs to para position, so as to aromatize by proton transfer. Note here that two continuous shifts occur without any intermediate formation. This is taken as concerted mechanism. Interestingly due to two times shifts, the labelled carbon (not shown below) comes to the sp³-carbon adjacent to -O- as in the original compound.

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For aliphatics:
* Allyl vinyl ether on heating rearranges to an unsaturated carbonyl compound due to similar [3,3] shift.

\[
\text{RC} = \text{O} \quad \Delta \quad \text{RC} = \text{CH}_2 + \text{H}_2\text{O}
\]

Allyl vinyl ether on heating gives pent-4-enal.

**Mechanism:**

**General:**

\[
\text{RC} = \text{O} \quad \Delta \quad \text{RC} = \text{CH}_2 + \text{H}_2\text{O}
\]

**Clemmensen Reduction:**

* Aldehydes and ketones are reduced by Zinc-amalgam(Zn-Hg) and conc. HCl to form their respective alkanes.
* It is suitable for those compounds which are stable under acidic conditions, but unstable in basic conditions. Aryl alkyl ketones, aldehydes/ketones not containing C-C multiple bonds are most suitable substrates for this reactions. A C-C multiple bond is always attacked by acids and hence should not be a part of the structure. The complimentary reaction which reduce a carbonyl compound to alkane in basic medium is “Wolff Kishner Reduction” to be discussed a bit later.

\[
\begin{align*}
\text{RC} = \text{O} & \quad \text{Zn(Hg)} \quad \text{HCl} \quad \text{RC} = \text{CH}_2 + \text{ZnCl}_2 + \text{H}_2\text{O} \\
\text{RC} = \text{O} & \quad \text{Zn} + \text{4HCl} \quad \text{RC} = \text{CH}_2 + \text{ZnCl}_2 + \text{H}_2\text{O}
\end{align*}
\]

In fact water and zinc chloride are formed are the co-products. Amalgamation of zinc is done to increases its reactivity towards the substrate.
Organic Name Reactions

Mechanism:
The mechanism of this reduction is not clearly understood. The most widely acceptable mechanism is ‘Carbenoid Mechanism’. You remember that carbenoids are organometallics which produce carbenes during the course of reaction. Ironically, carbone is not formed in the proposed mechanism. Just see to it casually.

Two Zn atoms react with the carbonyl group so as to fix the compound on the surface of the zinc metal. Then the unpaired electrons take part in the rearrangement involving breaking of C–O and formation of ZnO and carbenoid [Zn=C(R)(R’)]. Then the carbenoid undergoes the following changes.

I think, you understand what happened with carbenoid to produce alkane and ZnCl₂. Interestingly carbene is not produced in the mechanism, although a carbenoid has been proposed to have been formed.

ZnO reacts with 2HCl to form ZnCl₂ and H₂O.

Examples:
**Cope Rearrangement:**
* Thermal isomerisation of a 1,5-diene to another regiospecific 1,5-diene isomer due to [3,3]-sigmatropic shift in a concerted mechanism is called Cope Rearrangement. The mechanism is embedded in the following representation. (Please read Claisen rearrangement to know about what is [3,3] sigmatropic shift.

![Cope Rearrangement Diagram]

Example:

![Example Diagram]

**Oxy-Cope Rearrangement:**
* If -OH group is bonded to a sp³ carbon of the 1,5-diene on heating rearranges to first an enol, which tautomerises to the stable unsaturated carbonyl compound.

![Oxy-Cope Rearrangement Diagram]

* If -OH is first converted to alkoxide ion by treating with KH, then reaction is manyfold (10¹⁷ times) faster. Of course, aq. acidic work-up is necessary at the end to get neutral product. The reaction can be carried out at room temperature.

**Cope Reaction (Cope Elimination):**
* Pyrolysis of N-oxides of 3⁰-amine undergoes Ei(SYN) β-elimination to form alkene. (For details, please refer GOC-3(mechanism)
**Organic Name Reactions**

**Chugaev Reaction:**
* Pyrolysis of methyl xanthate undergoes Ei(SYN) β-elimination to form alkene.
(For details, please refer GOC-3(mechanism)

![Chemical structure](image)

**Curtius Rearrangement:**
Acyl azides on heating produces alkyl isocyanates. Isocyanates on acidic hydrolysis gives 1°-amine. On treatment with alcohol, it gives alkyl carbamate(ester of carbamic acid; R-NH-COOH) and with NH$_3$ or RNH$_2$ gives urea or its derivatie.

![Chemical structure](image)

**Mechanism:**
The reaction occurs in a concerted one-step mechanism involving migration of alkyl/aryl group from carbon to nitrogen atom with simultaneous expulsion of N$_2$ resulting alkyl/aryl isocyanate.
N.B: Earlier it was believed that the reaction goes via the formation of acyl nitrene intermediate. But recent research revealed that it is a concerted reaction. However, photochemical decomposition of acyl azide goes via nitrene formation. The is proved by the formation appreciable quantity of the unwanted nitrene insertion product with solvent molecule alongwith isocyanate.

**Photochemical Reaction:**

\[
\begin{align*}
\text{Ph-C} & \overset{hv}{\longrightarrow} \text{Ph-C} + \text{N} \equiv \text{N} \\
\text{1,2-shift} & \quad \text{Ar-N=C=O} \\
\text{alkyl isocyanate} & \\
\end{align*}
\]

(N-cyclohexylbenzamide (nitrene insertion product))

In the above photolysis reaction, nitrene is formed which is evidenced by the formation of the nitrene insertion product with cyclohexane solvent.

**Reactions for Isocyanates:**

(i) Isocyanate on hydrolysis gives primary amine.

(ii) Isocyanate reacts with an alcohol to form carbamate ester.

(N.B: ethyl carbamate i.e $\text{H}_2\text{N-COOC}_2\text{H}_5$ is called urethane. In polyurethane plastic, we have the urethane repeat unit in the $-\text{O-CO-NH}-$)

(iii) Isocyanate reacts with $\text{NH}_3$ or $\text{R-NH}_2$ to form substituted urea.
**Preparation of Acyl Azide:**

Acid chloride reacts with sodium azide or ester reacts with $\text{H}_2\text{N-NH}_2/\text{HNO}_2$ to form acyl azide.

\[
\begin{align*}
\text{RC} &\text{O} &\text{Cl} &\text{OR}' &\xrightarrow{\text{H}_2\text{N-NH}_2/\text{HNO}_2} &\text{RC} &\text{O} &\text{N}_3 &\text{R'} &\text{OH} &+ &\text{H}_2\text{O} \\
\end{align*}
\]

**Dakin Reaction (Oxidation):**

* Ortho or para hydroxy aryl aldehydes or ketones on treatment of $\text{H}_2\text{O}_2/\text{OH}^-$ forms benzene diol (catechol or quinol) along with salt of carboxylic acid from aldehyde/ketone part.

\[
\begin{align*}
\text{PhCH}_{2} &\text{CO} &\text{R} &\xrightarrow{\text{H}_2\text{O}_2/\text{NaOH}} &\text{PhOH} &+ &\text{R} &\text{CO} &\text{H} \\
\end{align*}
\]

This method can be used for the preparation of phenolic compound from aromatic aldehyde or ketone with other substituent at ortho/para position.

**Mechanism:**
**Demjanov Rearrangement:**

* It is the reaction of a 10-amine with nitrous acid to form rearranged alcohol. Most importantly a cyclic compound can undergo ring expansion to relieve its strain in this process.
* The goes via carbocation formation which is prone to rearrangement.

![Chemical Structure](image1)

Cyclobutymethanamine on treatment with nitrous acid gives cyclopentanol as the major product besides the minor cyclobutylmethano product. This is possible due to rearrangement of carbocations and in this case by ring expansion, as shown before.

* 5-membered ring also expands to form a six membered ring in this reaction.

![Chemical Structure](image2)

You can try the mechanism of your own, in the same way as shown for four membered ring. However in the last step, geminal diol will lose a molecule of water to form a ketone.

* Even the stability of carbocation can lead to ring contraction in this reaction. A four membered ring directly bonded to $-$NH$_2$ can contract to a three membered ring, as cyclopropyl methyl carbocation has unusually high stability due to bent bond stabilisation (so called dancing resonance).

![Chemical Structure](image3)

Cyclopropylmethanol is the major product when cyclobutyl amine is treated with nitrous acid. Try the mechanism for ring contraction yourself.

* Even a six membered ring can expand to seven membered ring, though the product may not be the major.
Organic Name Reactions

1-aminomethylcyclohexan-1-ol reacts with nitrous acid to form cycloheptanone as one of the products along with the diol. You can think of a parallel pinacol rearrangement for the vic. diol formed as the normal product. But pinacol does not take place here as the HNO₂ does not catalyse it, moreover, the stable carbocation woul be cyclohexyl and the shift of hydride ion from the other carbon would produce cyclohexane carboxaldehyde, which is not formed. But stability of a ketone in the Demjanov process, produces appreciable quantity of cycloheptanone.

**Dieckmann Condensation:**

* It is the intramolecular claisen condensation of diester to form cyclic β-keto ester. It works well to form 5-membered (from hexanediol) and 6-membered (from heptanediol).
* When dialkyl hexanediol or heptanediol reacts in presence of NaOEt in EtOH, we get 5-membered or 6-membered cyclic β-keto esters.

![Dieckmann Condensation Reaction Diagram](image)

**General:**

![General Reaction Diagram](image)

**Mechanism:**

![Mechanism Diagram](image)
Diels-Alder Reaction:

* It is a [4+2] cycloaddition reaction under Pericyclic Reactions, taking place in a concerted one step process via a TS. It is a thermally allowed reaction. The basis of this mechanism can be understood easily by FMO(Frontier Molecular Orbital) approach, not to be discussed here.

* When a mixture of a conjugated diene(DE) and alkene/alkyne(dienophile-DEP) is heated, a cyclohexene product is formed due to cyclization.

\[
\text{diene} + \text{dienophile} \xrightarrow{\text{heat}} \text{Cyclohexene}
\]

* **Regioselectivity:**

(a) If a EDG is bonded to either DE or DEP and a EWG is bonded to the other i.e either DEP or DE, then reaction is highly favourable.

(b) If the group is bonded to C-1 of DE then, then the ortho product is formed and if the group is bonded to C-2 of DE then the para product is formed.

\[
\begin{align*}
\text{penta-1,3-diene} + \text{acrylic acid} & \xrightarrow{\text{heat}} \text{2-methylcyclohex-3-en-1-carboxylic acid} \\
\text{2-methylbuta-1,3-diene} + \text{acrylic acid} & \xrightarrow{\text{heat}} \text{4-methylcyclohex-3-en-1-carboxylic acid}
\end{align*}
\]

Similar products would have obtained if EWG is bonded to DE and EDG is bonded to DEP.

* **Stereospecificity:** The reaction is stereospecific. If dienophile has Z or E configuration, then product retains the same i.e SYN and ANTI respectively.

\[
\begin{align*}
\text{maleic acid} & \xrightarrow{\text{heat}} \text{SYN-dicarboxylic acid} \\
\text{fumaric acid} & \xrightarrow{\text{heat}} \text{ANTI-dicarboxylic acid}
\end{align*}
\]

(The SYN exists as a mixture of Endo and Exo isomers. The endo isomer not shown above.)
Endoselectivity:
For unsymmetrical dieonophile (not showing E/Z isomersim) having a EWG when reacts with a cyclodiene to form a bicyclic product, then the endo isomer is the major product, though sterically looks less favourable. This is called Alder Rule. Neighbouring Group (C=O) participation with the orbitals of the diene is the cause for this (not to be discussed more about it now).

For cyclic dienophile with EWG groups like maleic anhydride, the exclusive product is the ENDO isomer.

Duff Reaction:
* Benzene ring with an EDG eg. phenol reacts with \((\text{CH}_2)_6\text{N}_4\) i.e hexamethylene tetraamine (HMTA) in presence of acetic acid followed by acidic hydrolysis to form ortho formyl derivative. If ortho positions are blocked then para formylation occurs.
* This is both analogous to Reimer Tiemann reaction (similarity of ortho formylation of phenol) and Vilsmer Haac reaction (similar to the presence of EDG).
**Organic Name Reactions**

**Mechanism:**

HMTA loses one ring in presence of H⁺ to form an iminium ion electrophile to react with phenol(ArOH) at the ortho position with the participation of the -OH group. After aromatisation, the other ring breaks to form another iminium ion. When this is saturated with a hydride transfer in space (most crucial step), a Me- group is formed. Again protonation produces another iminium ion adjacent to the ring. This on hydrolysis forms the –CHO group.

**Favorskii Rearrangement:**

* α-halo ketones on reaction with strong base such as OH⁻, RO⁻, produces rearranged c. acid or ester respectively.

* It is mostly studied in cyclic α-haloketone, which gives a ring contraction product. 2-chlorocyclohexanone on treatment with NaOH gives cyclopentanecarboxylic acid. With NaOEt it gives ethyl cyclopentanecarboxylate.
Abstraction of an $\alpha$-H from the other side produces a stable enolate ion, which attacks the other $\alpha$-carbon as a carbanion to form cyclopropanone intermediate.

This cyclopropanone intermediate is attacked by the base and the ring opens to form a carbanion first which abstracts a proton from $\text{H}_2\text{O}/\text{ROH}$ to form c.acid or ester as the case may be. If the cyclopropanone is symmetrical, a single product is obtained (as the case of 2-chlorocyclohexanone). However, if it is unsymmetrical, two products are obtained. The major product is determined from the relative stability of carbanion formed after the cyclopropane ring opens.

In this example, labelling of a-carbon suggests the occurrence of rearrangement.
In this case, the cyclopropanone opens in two ways to form a benzyl carbanion which is more stable than the other. Hence the corresponding product becomes the major product.

N.B: Using NH₃ as base, one can get rearranged amide in the similar manner.

**Favorskii Reaction:**
Cyclopropanone reacts with a base like OH⁻ or RO⁻ to form acyclic c.acid or ester.

**Mechanism:**

**Fries Rearrangement:**

* Phenolic esters (phenyl alkanoates) on treatment with Lewis acids like anhy. AlCl₃, TiCl₄, BF₃ or SnCl₄ rearranges to form a mixture of p-acyl phenol and o-acyl phenol. Lower temperature (25°C) favours the para-product while higher temperature (100°C or more) favours ortho product. Non-polar solvent also favours the ortho-product.
Organic Name Reactions

$\text{AlCl}_3$ forms a bond with $\text{=O}$ atom in the first step to form a complex. There is a migration of $\text{Ph-O}$ from carbon to $\text{Al}$, with simultaneous breaking of $\text{Al-Cl}$ bond (not shown). Thus a phenoxy complex (negative ion) of aluminium along with three other $\text{Cl}$-atoms is formed. Interestingly an acyl carbocation or acylium ion is formed, which makes $\text{ArSE}_1$ reaction at the o/p positions as it phenoxy complex is o/p selective.

**Temperature Effect:** At higher temperature, the reaction is kinetically controlled as the ortho product stabilises itself by forming a complex with $\text{Al}^{3+}$ as a bidentate ligand. But at lower temperature, it is thermodynamically controlled. Since the reaction is slow, a thermodynamically stable para (less steric crowding) is the major product.

**Solvent Effect:** More polar solvent makes an increase in para isomer as the dipole-dipole interaction will disfavour the complexation of bidentate ortho product.

* Variation: N-phenylalkanamides on

**Hunsdiecker’s Reaction:**

* Silver salt of carboxylic acid reacts with $\text{Br}_2$ or $\text{Cl}_2$ to form alkyl halide ($\text{RBr/RCI}$) with loss of one carbon atom as $\text{CO}_2$.
* Reactivity order
  1. $\text{Br}_2 > \text{Cl}_2$
  2. $1^0$-$\text{R} > 2^0$-$\text{R} > 3^0$-$\text{R}$

$$
\begin{align*}
\text{RC} & \text{-O} \text{O Ag}^+ + \text{Br}_2 \rightarrow \text{R}-\text{Br} + \text{CO}_2 + \text{AgBr} \\
\text{RC} & \text{-Br} \text{-AgBr} + \text{Br}_2 \rightarrow \text{R}-\text{Br}
\end{align*}
$$

**Mechanism:**

In literature, you may find mechanism, in which free-radical mechanism is presented in an usual way involving initiation and propagation steps. Most importantly alkyl free radical ($\text{R}^*$) is formed in the process. If this would be so, then why the reactivity order is primary $>$ sec $>$ tert- alkyl group? That is why i suggest the following radical pair mechanism.

The intermediate acyl hypohalite (in this case hypbromite) is formed (2). Then this goes homolytic cleavage to form radical pair (3), which loses a comolecule of $\text{CO}_2$ to form a radical pair (4). The radical pair (4) on recombines to form $\text{RBr}$. Thus no alkyl free radical is formed in the process to deny the order of reactivity. Intimate radical pair (like ion-pair) does not allow delocalisation stabilisation. Hence least sterically hindered hyphalite (1) reacts fastest. Since homolyis is most suitable in bonds containing $\text{Br}$, $\text{Br}_2$ reacts faster than $\text{Cl}_2$.

**Reaction with $\text{I}_2$ (Simonini Reaction):**

Silver salt reacts with iodine to form ester instead of alkyl iodide. Here two moles of silver salt reacts with one mole of $\text{I}_2$ to do the job.

$$
\begin{align*}
2 \text{R}-\text{C} & \text{-O} \text{ Ag}^+ + \text{I}_2 \rightarrow \text{R}-\text{C} & \text{-OR} + \text{CO}_2 + 2\text{AgI}
\end{align*}
$$

This is called Birnbaum-Simonini or Simonini Reaction.
**Hell Vohlard Zelinsky (HVZ) Reaction:** (α-halogenation of c. acid)

C.acid reacts with P₄/X₂ (Cl₂/Br₂) to give α-halo c. acid.

\[
\begin{align*}
R-\text{CH}_2-\text{COOH} & \xrightarrow{P_4/X_2} R-\text{CH}-\text{COOH} & R-\text{C}-\text{COOH} \\
\end{align*}
\]

Mechanism:
First PX₃ is formed which initiates the reaction with c.acid to form acid halide, which reacts with a molecule of X₂ followed by hydrolysis to form the α-halo c. acid.

**Hoffmann Bromamide Reaction (Hoffman Degradation of Amides):**
Primary amides react with Br₂/KOH to form a primary amine containing one carbon atom less. KOBBr can be used in place of Br₂/KOH. Intermediates formed are (a) N-bromoamide and (b) alkyl isocyanate. The reaction does not involve nitrene intermediate as it is sometimes wrongly believed. Alkyl isocyanate on hydrolysis gives 1⁰-amine and CO₂ (See its mechanism elsewhere).
Hofmann Martius Rearrangement:

* N–alkylaniline on heating forms a mixture of ortho and para alkyl aniline. This reaction is catalysed by HCl, so that the starting material is the conjugate acid (anilinium chloride).

The last step is the aq. NaOH work-up to convert the anilinium salt to neutral aniline. This step is not shown.

Mechanism:
**Libermann Nitroso Reaction:**

This a test for phenol. When Phenol is treated with excess NaNO2/conc.H2SO4, a red colouration is formed due to the formation of indophenol dye. This on treatment with base(KOH) forms a blue/green solution due to the formation of salt of the dye.

\[
\text{C}_9\text{H}_8\text{O}_2 \xrightarrow{\text{NaNO}_2, \text{in excess of H}_2\text{O}} \text{Red colouration} \xrightarrow{\text{NaOH, excess}} \text{Blue colouration}
\]

**Lossen Rearrangement:**

O-acyl or O-tosyl or O-sulfonyl hydroxamic acid on treatment with base(OH⁻), gives alkyl isocyanate, which can be converted to 10-amine on hydrolysis. This can also be converted to carbamate ester or substituted urea as happen in Curtius rearrangement.

Preparation of O-acyl or O-tosyl hydroxamic acid:
**Organic Name Reactions**

**Lossen Rearrangement:**
O-acyl or O-tosyl hydroxamic acid on treatment with base, forms alkyl isocyanate.

![Overall Mechanism Diagram]

The base deprotonates the O-acyl hydroxamic acid in the first step. Then second rate determining step, alkyl migration with simultaneous expulsion of alkanoate ion occurs to form alkyl isocyanate. Then after that you know its fate. Same thing happens when you take O-tosyl hydroxamic acid. Here TsO (tosylate) ion is expelled in the 2nd step in state of RCOO⁻.

**Malaprade Reaction**
*(Periodate degradation of vic. diols):*

* HIO₄/NaIO₄ breaks down the C–C bond of a vicinal diol to form two carbonyl compounds.
* If there is a H atom bonded to carbon, then aldehyde and if no H atom then ketone is formed. In other words, the carbony compounds formed depend on the structure of vic. diol.

![Malaprade Reaction Diagram]
Mechanism:
* The reaction involves the formation of 5-membered cyclic iodate ester with IO$_4^-$, which undergoes concerted ring opening like breaking of alkene ozonide to form two carbonyl compounds.

N.B: Pb(OAc)$_4$ can be used in place of periodate for the same reaction. But the mechanism is bit different (not shown).
* Cumulated polyols (triol, tetraol etc) cleave in the same fashion. The internal carbon atoms bonded to –OH forms carboxylic acid. Note that three –OH group added to a carbon atom produces a c.acid after dehydration.

Note that when you place two –OH groups each carbon atom on either side of the dividing line for a crude analysis (not mechanistic way), you will find that for terminal carbon atoms of polyol, there will be two –OH groups (one existing and the other added). The dehydration leads to carbonyl compound. But for internal carbon atoms there will be three –OH groups, whose dehdration produces c.acid.

* Number of IO$_4^-$ needed for polyol is one less than the total number of cumulated –OH groups. For glycerol, we need to have two HIO$_4$. For a tetraol, there will be requirement of 3 HIO$_4$ molecules.
* Presence of –CHO group or –CO– group in the structure is to be counted just like the presence of –OH group. But on HIO$_4$ oxidation, the aldehyde group will produce –COOH group and keto group (CO) will produce CO$_2$. 
Periodate oxidation of D-glucose and D-fructose.

The terminal –CHO and all the internal carbon atoms carrying –OH groups are oxidised to HCOOH, while the other terminal –CH$_2$OH group is oxidised to HCHO.

The two terminal –CH$_2$OH groups oxidised to two HCHO, the keto(CO) group is oxidised to CO$_2$ and the other three internal CHOH groups oxidised to three HCOOH.

* $\alpha$-aminoalcohols behave as vic. diols for oxidation by HIO$_4$. 2-aminoethanol gives two HCHO molecules exactly like ethylene glycol.
Meerwin-Pondorf-Varley Reduction (MPV Reduction):

- Aldehydes and ketones are reduced by an alcohol (ROH) in presence of catalyst (RO)_3Al to form the corresponding alcohols.
- (i-PrO)_3Al/i-PrOH is mostly commonly used.
- This is opposite of Oppenauer oxidation for 2° alcohols (see later). An alcohol in presence of a ketone and Al(OR)_3 catalyst gives the ketone or aldehyde in the Oppenauer oxidation. Same catalyst i.e Aluminium alkoxide is used.
- * C=C bond, if present in the compound, remains unaffected.

\[
\begin{align*}
\text{ROH} + \text{RC} = \text{H} & \rightarrow \text{RO} \cdot \text{C} \cdot \text{H} + \text{CH}_3 \cdot \text{C} \cdot \text{CH}_3 \\
\text{isopropyl alcohol} & \rightarrow \text{RCH}_2 + \text{CH}_3 \cdot \text{C} \cdot \text{CH}_3
\end{align*}
\]

Mechanism:

\[
\begin{align*}
\text{ROH} + \text{RC} = \text{H} & \rightarrow \text{RO} \cdot \text{Al} \cdot \text{C} \cdot \text{H} + \text{CH}_3 \cdot \text{C} \cdot \text{CH}_3 \\
\text{MPV} \rightarrow \text{RCH}_2 + \text{CH}_3 \cdot \text{C} \cdot \text{CH}_3
\end{align*}
\]

In the above scheme, both MPV reduction and Oppenauer oxidation have been shown together. If you take the help of alcohol (RA), then ketone is reduced to a 2° alcohol and alcohol is oxidised to ketone. This is MPV. If we take the help of ketone, then a 2° alcohol is oxidised to ketone and ketone (OA) reduced to a 2°-alcohol (Oppenauer oxidation).

The reaction passes through a cyclic TS in which Al(i-Pr)_3 bonds partially with the ketone and then expels a molecule of acetone to form a bonded alkoxide from the ketone. Then one more molecule of alcohol (iPr-OH) ends the reaction by expelling the alcohol and itself entering into bondage to form (iPrO)_3Al.
**Organic Name Reactions**

**Oppenauer Oxidation:**

- 2\textsuperscript{nd} alcohol is oxidised to ketone by heating the alcohol with excess of acetone in presence of (i-PrO)\textsubscript{3}Al. The catalyst is the same as MPV reduction, which is the opposite of this oxidation. The OA is acetone here and there the RA was isopropyl alcohol. Here (t-BuO)\textsubscript{3}Al can be used in place of (i-PrO)\textsubscript{3}Al. Acetone is reduced to isopropyl alcohol and the 2\textsuperscript{nd}-alcohol is oxidised to the corresponding ketone.

\* C=C, if present in the compound, remains unaffected.

\* Oxidation of 1\textsuperscript{st}-alcohol can be achieved by this method, but it is seldom applied, as aldehyde product is prone to aldol condensation under the given conditions.
**Pinacol Rearrangement:**
* Vicinal diols on treatment with acidic catalysts rearrange to carbonyl compounds.
* Regioselectivity: The -OH group whose removal by as H₂O depends on the relative stability of carbocation.
* Migratory Aptitude:
  The migratory aptitude of the groups at the other carbon is as follows.
  \[ H > Ar > Alkyl(3^0 > 2^0 > 1^0 > Me) \]
  Aromatics: \( p-MeO-Ph > p-I-Ph > m/o EDG-Ph > Ph > p-I-M-Ph \)
  \( p-MeO-Ph > p-CH₃-Ph > m/o MeO-Ph = m/o Me-Ph > Ph > p-CI-Ph > p-O₂N-Ph \)
So more than one product is formed and major one is predicted from the above migratory aptitude.

![Mechanism](image)

**Examples:**
1. In this case, phenyl(Ph) has a greater preference of migration over alkyl group.

![Example 1](image)

2. \[ \text{CH}_3\text{CH}_2\text{C} \equiv \text{C} \equiv \text{CH}_3 + \text{H}_3\text{O}^+ \rightarrow \text{CH}_3\text{CH}_2\text{C} \equiv \text{C} \equiv \text{CH}_3 \quad (83\%) \]
   \[ \text{CH}_3\text{CH}_2\text{C} \equiv \text{C} \equiv \text{CH}_3 + \text{CH}_3\text{CH}_2\text{C} \equiv \text{C} \equiv \text{CH}_3 \quad (17\%) \]
Organic Name Reactions

In this case, the carbocation is formed in C-2 as it is more stable (Hyperconjugation more). Then the Et-migration gives the major product.

3.

\[
\text{OH} \quad \text{CH}_2 \text{OH}
\]

\[
\text{H}^+ \quad \text{OH} \quad \text{CH}_3
\]

\[
\text{CH}_2 \text{OH}
\]

\[
\text{H}^+ \quad \text{OH}
\]

\[
\text{CH}_3
\]

\[
\text{OH}
\]

\[
\text{OH}
\]

* Cis-1,2-dimethylcyclohexane-1,2-diol (ae/ea) gives rearranged cyclohexanone, as Me-group anti w.r.t to the H_2O^– migrates preferably. Though trans migration is not a major requirement in this reaction like Beckmann rearrangement, in ring systems, the group lying ANTI to the leaving group has a better chance of migration as the TS is energetically favourable. The trans isomer (ee/aa leads to ring contraction product, as the group trans to the leaving group (H_2O) is the ring residue which migrates resulting cyclopentane derivative i.e 1-acetyl-1-methylocyclopentane or 1(1-methylcyclopentyl)ethan-1-one.

* Note that in both the cases, we get a mixture of the two products, but the major product in each case has been shown.

4.

\[
\text{H}^+ \quad \text{(Hydride migration)}
\]

\[
\text{OH}
\]

\[
\text{CH}_2 \text{OH}
\]

\[
\text{H}^+ \quad \text{OCH}_3
\]

Since H- has greater migratory aptitude than aryl group in this reaction, the major product is due th hydride migration. Other minor products due phenyl migration and p-methoxyphenyl migration will also be formed.

**SAQ:**

1.

2.

3.
Ritter Reaction:
* Alkene and alchol react with an alkanenitrile in presence of acid to form 2°-amide.
* It is the nucleophilic addition of the nitrile to a carbocation generated from alkene/alcohol in acidic medium followed by aq. acid work-up.

\[
\text{R} + \text{R} = \text{N} \xrightarrow{\text{H}_2\text{SO}_4} \xrightarrow{\text{H}_2\text{O}} \text{R} - \text{N} = \text{O}
\]

\[
\text{R} - \text{OH} + \text{R} = \text{N} \xrightarrow{\text{H}_2\text{SO}_4} \xrightarrow{\text{H}_2\text{O}} \text{R} - \text{N} = \text{O}
\]

Mechanism:
Generation of carbocation:

\[
\text{O} \quad \xrightarrow{\text{H}^+} \quad \text{H} \quad \xrightarrow{\text{H}^+ + \text{H}_2\text{O}} \quad \text{CH}_2
\]

Nucleophilic addition:

\[
\xrightarrow{\text{H}^+} \xrightarrow{\text{H}^+ + \text{H}_2\text{O}}
\]

(N.B: Do not confuse the bar symbol with a negative charge. It is simply a lone pair. In the entire mechanistic pathways, there is no –ve charge in any specicies).

Reformatsky Reaction:
* α-haloester reacts with carbonyl compound(aldehyde/ketone) in presence of Zn to form β-hydroxy ester.
* An organo zinc compound is formed first, which undertakes nucleophilic addition to the carbonyl compound, of course in a different style, involving a six membered cyclic TS.

\[
\text{X} = \text{Cl}, \text{Br}, \text{I}
\]

\[
\xrightarrow{1. \text{Zn}(0)} \xrightarrow{2. \text{acid work-up}}
\]

(\text{e.g. HX})

β-hydroxyester
Organic Name Reactions

Mechanism:

It can simply put as follows.

$$\text{Br}_2\text{CO} \cdot \text{OR} + \text{Zn} \rightarrow \left[\begin{array}{c}
\text{H}_2\text{C} \cdot \text{O} \cdot \text{OR} \\
\text{H}_2\text{C} \cdot \text{CO} \cdot \text{OR}
\end{array}\right] + \text{ZnBr}$$

Zn forms a zinc elolate (shown inside square bracket), which reacts with the carbonyl compound to form alcohol after aq. work-up step. It is not same as GR reaction with a carbonyl compound.

Examples:

1.

$$\text{Br}_2\text{CO} \cdot \text{OR} + \text{Zn} + \text{C}_6\text{H}_5\text{O} \rightarrow \text{H}_2\text{O} \rightarrow \text{OH} \cdot \text{CO} \cdot \text{OR}$$
Organic Name Reactions

2.

Schimdt Reaction:

(1) Carboxylic acid reacts with hydrazoic acid in presence of acid catalyst to form primary amine via a protonated isocyanate.

\[ \text{RCOOH} \xrightarrow{\text{H}_2\text{SO}_4, \text{HN}_3} \text{R}-\text{NH}_2 \]

(2) Ketone reacts with hydrazoic acid in presence of acid catalyst to form sec-amide.

\[ \text{R-C-R'} \xrightarrow{\text{H}_2\text{SO}_4, \text{HN}_3} \text{R-C-NH-R'} \]

Mechanism (1): Protonated carboxylic acid on dehydration gives acyl carbonation which reacts with HN₃ in the second step to form protonated acyl azide. In the third step, which is rate determining, alkyl group migrates over C–N bond with simultaneous expulsion of N₂ to form protonated alkyl isocyanate. This on hydrolysis followed by loss of H⁺ and CO₂ forms primary amine (RNH₂). Unlike Curtius rearrangement in which a stable alkyl isocyanate was formed as intermediate, here in Schimdt reaction, protonated isocyanate is formed instead which gives primary amine under the same acidic conditions. So no scope to isolate isocyanate to get desired product as we found in Curtius rearrangement.

Hydrazoic acid has the following RSs.
Organic Name Reactions

[H N= N= N] ↔ [H N= N≡ N]

Example:

\[
\text{COOH} \xrightarrow{\text{H}_2\text{SO}_4, \text{HN}_3} \text{NH}_2
\]

Mechanism(2):

1. \(R-C\) → 2. \(R-C\) → 3. \(R-C\) → 4. \(R-C\) → 5. \(R-C\) → 6. \(R-C\) → 7. \(R-C\) → 8. \(R-C\)

\(\text{HN}_3\) makes nucleophilic attack onto protonated ketone for form intermediate (3), which on dehydration(\(\beta\)-elimination of \(\text{H}_2\text{O}\)) form \(\text{C}≡\text{N}\) containing intermediate (4). Then follows the rate determining step of alkyl group migration over \(\text{C}–\text{N}\) bond with simultaneous expulsion of \(\text{N}_2\) to form imminium ion (5). This is attacked by water followed by deprotonation to give the imidol (7), which quickly tautomerizes to stable \(2^\alpha\)-amide.

Note that in the step of alkyl group migration, we have two choices. The migratory aptitude that we followed in Baeyer Villiger reaction will approximately be valid here.

* This analogous to Baeyer Villiger oxidation of ketones to ester. Here -NH- group is inserted on the side of more substituted alkyl group.

N.B: In respect of ketone, Schmidt reaction has an advantage over Curtius rearrangement as it has no ketone counterpart.

Example:

1.

\[
\text{H}_2\text{SO}_4, \text{HN}_3 \xrightarrow{\text{caprolactam}} \text{NH}
\]
**Swern Oxidation:**

1\textsuperscript{st} and 2\textsuperscript{nd} alcohols are oxidised to aldehyde and ketone respectively by treating the alcohol with oxalyl chloride in DMSO followed by reacting with excess of organic base such as (CH\textsubscript{3})\textsubscript{3}N.

\[ 	ext{RC(OH)CH}_2 \xrightarrow{\text{(i) oxalyl chloride/DMSO}} \text{RC(OH)} \xrightarrow{\text{(ii) Me}_3\text{N}} \text{RC} \]

\[ \text{RCHCH-R'} \xrightarrow{\text{(i) oxalyl chloride/DMSO}} \text{RC-R'} \xrightarrow{\text{(ii) Me}_3\text{N}} \]

**Mechanism:**

The polar RS of DMSO reacts with oxalyl chloride at sub-zero temperature to form an intermediate (3) which decomposes losing CO\textsubscript{2} and CO to form chloro(dimethyl)sulfonium chloride(4). (4) then reacts with alcohol to form alkoxy sulfonium chloride(6). This reacts with the base Me\textsubscript{3}N to form the sulfur ylide (7) by losing a H\textsuperscript{+}. This ylide loses Me\textsubscript{2}S to give the desired carbonyl compound(8).
**Ullmann Reaction:**

* The original Ullmann reaction is the preparation of symmetrical biaryls via copper-catalysed coupling of halobenzene.

* Ullmann reaction also includes the reaction of phenol and anilides with halobenzene to form diaryl ether and diaryl amine respectively. These are called “Ullmann type reactions”.

\[
2 \text{R-I} + 2 \text{Cu} \xrightarrow{\Delta} \text{biaryl} + 2 \text{CuI}
\]

\[
2 \text{R-Cl} \xrightarrow{\text{Copper}} \text{biaryl} + \text{CuCl}_2
\]

\[
\text{C}_6\text{H}_5\text{NHCOC}_2\text{H}_5 + \text{C}_6\text{H}_5\text{Br} + \text{K}_2\text{CO}_3 \xrightarrow{\text{Cu}_{\text{refl}}} \text{C}_6\text{H}_5\text{NHCH}_2\text{H}_2 + \text{CH}_3\text{COOK} + \text{KBr}
\]

acetanilide  bromobenzene  diphenylamine

\[
\text{C}_6\text{H}_5\text{OH} + \text{C}_6\text{H}_5\text{Br} + \text{KOH} \xrightarrow{\text{Cu}_{\text{refl}}} (\text{C}_6\text{H}_5)_2\text{O} + \text{KBr} + \text{H}_2\text{O}
\]

phenol  bromobenzene  diphenyl ether

\[
2\text{C}_6\text{H}_5\text{I} + \text{Cu} \xrightarrow{\Delta} \text{C}_6\text{H}_5\text{C}_6\text{H}_5 + \text{CuI}_2
\]

iodobenzene

\[
\text{O}_2\text{N}-\text{O} \quad \text{Cu, KOH} \quad 160 \degree \text{C}, 30 \text{ min.}
\]

\[
\text{O}_2\text{N}-\text{O} \quad 80\%
\]

Mechanism: (Original Ullmann)

The mechanism is explained in two different schools of thought, as it is not yet convincingly proved.

Thought-1: **Radical Mechanism:**

In this approach, two aryl radicals are formed independently by the help of two moles of Cu with two moles of aryl halide. Then the combination of the two aryl radicals make the job.

Dr S. S. Tripathy
Thought-II: **Mechanism involving Aryl Copper Intermediate:**

![Mechanism Diagram]

In this approach, Cu(0) converts to Cu(I) in the first step (oxidative addition) by forming aryl copper(I) halide. This reacts with second mole of Cu(0) to form an aryl copper(I) intermediate. This intermediate reacts with 2nd mole of aryl halide to form Cu(III) compound i.e diaryl copper(III) halide by another oxidation addition process. Finally this Cu(III) complex undergoes reductive elimination losing a molecule of Cu(I)X to form the diaryl.

This approach looks more acceptable by many authors.

* The Ullmann type of reactions with phenol and anilides in presence of base is a mere extention of ArSN. Phenoxide ion in case of phenol and anilide, as such makes nucleophilic attack on to aryl halide and forms ether and amine respectively. These are catalysed by copper. The case of anilide is a mystery, as –COR group has also to leave. Since mechanism is not readily available to me for these types of Ullmann reaction, i do not venture to propose from my side.

**Vilsmeier Haack Reaction:**

* It is an example of para-formylation of benzene ring w.r.t a EDG like -OME, -NR₂ etc. When such compound reacts with DMF or N-methyl-N-phenyl formamide in presence of POCl₃, a para formyl product is formed.
Organic Name Reactions

Mechanism:

DMF reacts with POCl₃ to form an iminium ion with removal of \([PO₂Cl₂]^-\). This ion, as an electrophile, is attacked by benzene(ArS₂). This is followed by deprotonation for aromatization. Then hydrolysis of the intermediate and subsequent removal of Me₂NH produces the –CHO group. EDG group is not shown in the structure for simplicity. The para attack is because EDG is o/p orienting. Why not ortho is obvious on steric grounds.

N.B: In contrast to ortho formulation of phenol in Reimer Tiemann reaction, it is para formylation in Vilsmeir Haac reaction.

**Von Richter Reaction:**

* Halonitrobenzene on treatment with ethanolic KCN, gives product in which the –NO₂ group is substituted by -COOH group at the position ortho to the nitro group and closer to the halo group.
Mechanism:
It is an aromatic nucleophilic substitution occurring in an interesting manner. CN⁻ attacks at the ortho carbon w.r.t to the -NO₂ (leaving group) and then a five-membered ring is formed in which here is a –N-O-C linkage in the ring and the other N is outside the ring. Then rearrangement occurs to form a ring with N–N–C linked ring which breaks down with elimination of N₂ to place -COOH in the ortho position w.r.t the expelled -NO₂ group. The actual leaving groups are N₂ and H₂O, while H⁺ from alcohol helps in this magical outcome. Interestingly -halo group(-Br) does not take part in the mechanism. But without its presence the reaction does not occur. Moreover -Cl group gives poor yield(20%), hence -Br is the preferred halo group in this reaction.
Organic Name Reactions

**Wacker’s Oxidation of Terminal Alkenes:**

* Alkene transforms to carbonyl compound when oxidised by of PdCl₂/CuCl₂ catalyst/cocatalyst mixture in H₂O/DMF to which O₂ gas is constantly bubbled. Ethene gives ethanal and all other alkenes give ketones. Especially terminal alkenes (alk-1-ene) are suitable for this process resulting methyl ketones. In this reaction, H₂O plays an important role in the mechanism (the first nucleophile attack made by H₂O onto the alkene bonded to PdCl₂) while O₂ plays secondary role for converting Cu⁺ formed back to Cu²⁺ in the last step. So never consider this as the addition of alkene with O₂ molecule. Here the OA is Pd²⁺ which is reduced to Pd(0), which is converted back to Pd²⁺ by Cu²⁺ which is reduced to Cu⁺. O₂ ultimately converts Cu⁺ to Cu²⁺. Thus Cu²⁺ acts as a co-catalyst with Pd²⁺.

\[
\begin{align*}
H₂C=CH₂ & \xrightarrow{PdCl₂ (cat) \text{ CuCl₂ (cat), O₂, H₂O}} CH₃CHO + Pd + 2HCl \\
CH₂=CH₂ + PdCl₂ + H₂O & \rightarrow CH₃CHO + Pd + 2HCl \\
Pd + 2CuCl₂ & \rightarrow PdCl₂ + Cu₂Cl₂ \\
Cu₂Cl₂ + \frac{1}{2} O₂ + 2HCl & \rightarrow CuCl₂ + H₂O \\
& \text{(note that the solution contains ample free HCl formed in the reaction steps.)}
\end{align*}
\]

* It is an industrial process of manufacturing ethanal and acetone from ethene and propene respectively. It is a homogenous catalysis.

N.B: If alcohol (R’OH) is used instead of H₂O, then we get alkoxy alkene (CH₂=C(OR’)R in stead of carbonyl compound)

\[
\begin{align*}
R-CH=CH₂ & \xrightarrow{\text{PdCl₂/CuCl₂, O₂ (H₂O/DMF), 60-70°C}} R-C=CH₃ \\
R-CH=CH₂ & \xrightarrow{\text{PdCl₂/CuCl₂, O₂ (MeOH/DMF), 60-70°C}} R-C=CH₂
\end{align*}
\]
Mechanism:

The aqua complex $[\text{Pd}(\text{H}_2\text{O})_2\text{Cl}_2]$ (1) forms a pi-complex (2) with alkene. Then $\text{H}_2\text{O}$ makes uncleophilic attack onto alkene with the formation of $\sigma$-complex (3). Elimination of $\text{HCl}$ gives (4). Then $\beta$-elimination from (4) gives alkenol which forms another $\pi$-complex with Pd(5). (5) turns to a $\sigma$-complex (6), which undergoes $\beta$-elimination to form carbonyl compound with Pd reduced to zero(0) state. Then $\text{Cu}^{2+}$ converts it back to the original aqua Pd(II) complex and itself reduced to $\text{Cu}^{+1}$. Now oxygen gas bubbled converts $\text{Cu}^{+1}$ ro $\text{Cu}^{2+}$. That's it.

Wagner Meerwin Rearrangement:

* Any reaction in which the carbon skeleton undergoes change due to carbocation rearrangement.
* Many alcohols dehydrate with changed carbon skeleton. You know plenty of examples.

1. The following example needs no explanation. Do the mechanism yourself.

2. 3-methylbutan-2-ol and neopentyl alcohol gives the same product i.e di-tert-pentyl derivative. It means the former alcohol reacts via carboncations rearrangement.
The bicyclic compound reacts with acid via nonclassical carbocation leading to ring opening.

**Willgerodt Reaction:**
* Aryl ketones reacts with ammonium polysulfide i.e \((\text{NH}_4)_2\text{S}_x\) or Sulfur to form primary amide with reversal of carbon chain. Ammonium salt of c.acid is the minor byeproduct.

Example
Acetophenone reacts with NH₂OH in excess of Sulfur in pyridine/H₂O mixed solvent (in situ formation of ammonium polysulphide) to form 2-phenylethanamide as the major product. The acid (minor product) is obtained after aq. acid work-up.

**Wittig Reaction:**

* Organophosphorous ylides (Wittig reagent) reacts with an aldehyde or a ketone to form a higher alkene. In this method, the position of C=C remains the same as the C=O in carbonyl compound and hence is one of the best methods of preparation of alkene. In other methods like dehydration of alcohols or dehydrohalogenation of alkyl halides we get a mixture of isomeric alkenes, which is not the case here.

* Ylides are compounds having opposite charges on adjacent atoms each of which is a completely filled octet. In P-ylides, phosphours atom will carry +ve charge and the adjacent C-atom will carry −ve charge.

Alkylidenetriphenylphosphorane is a P- ylide, in which P atom carries +ve charge and the adjacent C-atom carries −ve charge. This has another resonance structure in which there is a P=C due to lateral overlapping of a filled C-orbital with a vacant d-orbital of P- atom. The dipolar ion (Zwitterion) is more stable and more contributing to the hybrid. However, while showing the reaction, sometimes we shall take the P=C structure. The suffix ‘idene’ is given for indicating the divalency of the carbon bearing group. P- ylides can be very easily prepared from alkyl halides and triphenylphosphine (Ph₃P) (just wait for amoment).

* Wittig reaction is the reaction of the phosphorous ylide with aldehyde or ketone to form alkene (both trans and cis) and triphenylphosphine oxide.

**Example:**

1. \[ \begin{align*} \text{Ph₃PC=CH₂} + \text{CH₃COCH₃} &\rightarrow \text{Ph₃P} \quad \text{acetylidenetriphenylphosphorane} \\ \text{Ph₃PO} &\quad \text{triphenylphosphine oxide} \end{align*} \]

2. \[ \begin{align*} \text{Ph₃PC=CH₂} + \text{Ph₃P=CH₂} &\rightarrow \text{Ph₃P} \quad \text{isoproylidenetriphenylphosphorane} \\ \text{Ph₃PO} &\quad \text{2-methyl-1-phenylprop-1-ene} \end{align*} \]
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N.B: Cyclic or aromatic aldehydes and ketones can also undergo Wittig reaction with P-Ylides.

Preparation of P-Ylides:
* First the corresponding alkyl halide is allowed to react with Ph₃P(triphenyl phosphine), a wonderful nucleophile(soft base). Sₙ₂ reaction leads to an phosphonium salt.
* This salt is then allowed to react with a strong base like alkyl or aryl lithium(BuLi, or PhLi) to carry out deprotonation from the carbon atom to form a –ve charge, thus forming the stable P – ylide.

\[
\text{Ph}_3\text{P} + \text{RCH}_2\text{X} \rightarrow \text{phosphonium salt}\]

Mechanism:

Wittig reaction involves three steps. First the P - Ylide makes a nucleophilic attack using its carbanioninc centre onto the electrophilic carbonyl carbon of the aldehyde or ketone to form a bipolar intermediate. In the second step the negative charge(lone pair) of O– atom forms a bond with the electron deficient P– atom to produce a four membered cyclic intermediate(oxaphosphetane). This cyclic intermediate, in the third state undergoes intramolecular ring opening to form the alkene and triphenylphosphine oxide.

Example:
**Wolff Kishner Reduction:**

* Carbonyl compound (Aldehyde and ketones) which are not otherwise affected by base are reduced to alkanes by heating (180 - 200°C) the compound in a mixture of hydrazine (H₂N-NH₂) in alkali (NaOH). Simple aldehydes and ketones also are reduced to alkanes by this method like Clemmensen’s method.

\[
R-C-R'(H) \xrightarrow{H_2NNH_2, OH/heat} R-CH_2-R'(H) + N_2 + H_2O
\]

**Mechanism:**

The carbonyl compound first forms hydrazone by reacting with hydrazine. This is a case of Ad₅, followed by dehydration. The hydrazone is then transferred to a carbanion by losing a molecule of N₂ in multip-step mechanisms. See below.

N.B: The mechanism is self-explanatory. (Like hydrazones, semicarbazones of aldehydes and ketones also on heating give alkanes).

* In case of α,β-unsaturated carbonyl compounds, this reduction may lead to migration of C=C.

**Wurtz Reaction:**

Alkyl halide couple with itself in presence of Na in dry ether to form higher alkane. Wurtz coupling is Sₙ₂ reaction and as you know for 3° halide, E2 elimination completely takes over Sₙ₂. So 3° halides are not used for Wurtz reaction. In fact 1° halides are best candidates for Wurtz coupling, as 2° halides behave closer to 3° halides in reactions.

Step-I:

\[
R-X + Na \rightarrow R + Na^+Cl^{-}
\]
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Step-II :
\[ \cdot R + Na \rightarrow R^- + Na^- \]
\[ \text{carbanion} \]

Step-III (S_N2):
\[ \cdot R + R^- + X \rightarrow R-R^- + X \]

In the first step, alkyl free radical is formed, and in the second step alkyl carbanion is formed. That is why 2 moles of sodium are needed. In the final step, the carbanion acts as a nucleophile to bring about S_N2 reaction with another alkyl halide molecule.

Side Reaction (Elimination)
You know that elimination and substitution go hand in hand. For 1° halide, the elimination is the minor product. Hence some unwanted side products are always formed in Wurtz reaction along with alkane (R–R) in small quantities. For 3° halide, the elimination is the exclusive product, hence not used. For 2° halide, we get both S_N2 and E2 products with appreciable quantities.

\[ 2CH_3CH_2Br \rightarrow 2Na_2 \rightarrow \text{butane (major product)} + \text{elimination products (minor)} \]

When ethyl bromide is subjected to Wurtz coupling, we get butane as the major product (>90%), and also we get a mixture of ethane and ethene as byproducts. The latter mixture is due to the elimination reaction which always go together with substitution reaction.

\[ CH_3CH_2^\cdot + CH_2CH_2^\cdot \rightarrow CH_3CH_3 + CH_2=CH_2 \]

For 2° halide, the elimination products will be quite appreciable and for 3° halide, there is only the elimination product. Moreover, the carbanion formation in a 3° halide is very less probable as it is the least stable carbanion.
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E-CONCEPT IN CHEMISTRY

For Class XI/XII (+2 Science)

Organic Name Reactions

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