Section-I

A Novel Application of (Diacetoxyiodo) benzene for Carbon-Carbon Cleavage of Aryl Diamines.

2.1 INTRODUCTION:

2.2 LITERATURE SURVEY:

2.2.1 Synthesis of Muconitrile by Oxidative Cleavage of Aryldiamines:

2.2.2 Synthesis of Muconitrile from diazides:

2.3 OBJECTIVE OF THE WORK:

2.4 DESIGN AND DEVELOPMENT:

2.5 EXPERIMENTAL:

2.6 RESULT AND DISCUSSION:

2.6.1 Mechanism

2.7 APPLICATION:

2.8 SUMMERY AND CONCLUSION:

2.9 REFERENCES:

2.10 SPECTRA:
2.1 **INTRODUCTION**:

What is meant when we speak of oxidation and reduction. Inorganic chemists define oxidation in two ways: loss of electrons and increase in oxidation number. In organic chemistry, these definitions, while still technically correct, are not easy to apply. The practice in organic chemistry has been to set up a series of functional groups, in qualitative way, arranged in order of increasing oxidation state, and then to define oxidation as the conversion of a functional group in a molecule from one category to a higher one, and reduction is conversion to a lower one. Conversions within a category are neither oxidations nor reductions.

Depending on the type of bond change involved, the oxidation reactions are classified into different groups as follows.

A. Eliminations of Hydrogen

B. Oxidations Involving Cleavage of Carbon-Carbon Bonds

C. Reactions Involving Replacement of Hydrogen by Oxygen

D. Reactions in Which Oxygen is Added to the Substrate

E. Oxidative Coupling

   A. Elimination of Hydrogen:

   1) Aromatization of Six-Membered Rings:

   *Hexahydro-terelimination*

Six-membered alicyclic rings can be aromatized in a number of ways (Scheme 2.1). Aromatization is accomplished most easily if there are already one or two double bonds in the ring or if the ring is fused to an aromatic ring. The reaction can also be applied to heterocyclic five- and six-membered ring.¹

![Scheme 2.1](image-url)
1) **Dehydrogenations Yielding Carbon-Carbon Double bonds:**

*Dihydro-elimination*

Dehydrogenation of an aliphatic compound to give a double bond in a specific location is not usually a feasible process, though industrially mixtures of olefins are obtained in this way from mixtures alkanes (Scheme 2.2).

![Scheme 2.2](image)

2) **Oxidation or dehydrogenation of Alcohols to Aldehydes and Ketones:**

*C, O-Dihydro-elimination-

Here in this case primary alcohols can be converted to aldehydes and secondary alcohols to ketones (Scheme 2.3).

![Scheme 2.3](image)

3) **Oxidation of Phenols and Aromatic Amines to Quinones:**

*1/o,6/o-Dihydro-elimination*

Ortho and para diols are easily oxidised to *ortho-* and *para*-quinones, (Scheme 2.4) respectively.²
4) **Dehydrogenation of Amines**

**1/1/N,2/2C-Tetrahydro-bieliminination**

Primary amines at a primary carbon can be dehydrogenated to nitriles (Scheme 2.5). The reaction has been carried out with a variety of reagents, among others, IF₅, lead tetraacetate, nickel peroxide, NaOCl in micelles, K₂S₂O₈-NiSO₄ and CuCl-O₂-pyridine.³ᵃ-c

5) **Oxidation of Hydrazines, Hydrazones and Hydroxylamines**

**1/N,2/N-Dihydro-elimination**

N,N-Diarylhydrazines (hydrazo compounds) are oxidised to azo compounds by several oxidising agents (Scheme 2.6), including NaOBr, HgO, K₃Fe(CN)₆ under PTC condition, MnO₂ (for cis azobenzenes)⁴.
B. Oxidation Involving Cleavage of Carbon-Carbon Bonds:

1) Oxidative Cleavage of Glycols and Related Compounds:

2/O-De-hydrogen-uncoupling

1,2-Glycols are easily cleaved under mild conditions and in good yield with periodic acid or lead tetraacetate. The products are 2 equivalents of aldehyde, or 2 equivalents of ketone, or 1 equivalent of each, depending on the groups attached to the two carbons. The yields are so good that alkenes are often converted to glycols, and then cleaved with HIO₄ or Pb(OAc)₄ (Scheme 2.7) rather than being cleaved directly with ozone or dichromate or permanganate. The diol can be generated and cleaved in situ from an alkene to give the carbonyl compounds.

A number of other oxidizing agents also give the same products, among them activated MnO₂, and a ruthenium catalyst, PPh₃–DEAD, and pyridinium chlorochromate. Permanganate, dichromate, and several other oxidizing agents also cleave glycols, giving carboxylic acids rather than aldehydes, but these reagents are seldom used synthetically. Electrochemical oxidation is an efficient method, and is useful not only for diols, but also for their mono- and dimethoxy derivatives.

The two reagents (periodic acid and lead tetraacetate) are complementary, since periodic acid is best used in water and lead tetraacetate in organic solvents. Chiral lead carboxylates have been prepared for the oxidative cleavage of 1,2-diols. When three
or more OH groups are located on adjacent carbons, the middle one (or ones) is converted to formic acid.

Other compounds that contain oxygens or nitrogens on adjacent carbons undergo similar cleavage (Figure 1):

![Figure 1]

Cyclic 1,2-diamines are cleaved to diketones with dimethyl dioxirane. α-Diketones and α-hydroxy ketones are also cleaved by alkaline H₂O₂. The HIO₄ has been used to cleave epoxides to aldehydes (Scheme 2.8),⁶a for example, α-Hydroxy acids and α-keto acids are not cleaved by HIO₄, but are cleaved by NaIO₄ in methanol in the presence of a crown ether,⁶b Pb(OAc)₄, alkaline H₂O₂, and other reagents. These are oxidative decarboxylations. α-Hydroxy acids give aldehydes or ketones, and α-keto acids give carboxylic acids.

![Scheme 2.8]

The mechanism of glycol oxidation with Pb(OAc)₄ (Figure 2) was proposed by Criegee.⁶c-⁶d
2) Oxidative Cleavage of Ketones, Aldehydes, and Alcohols:

Cycloalkanone oxidative ring opening

Oxidative cleavage of open-chain ketones or alcohols is seldom a useful preparative procedure, not because these compounds do not undergo oxidation (they do, except for diaryl ketones), but because the result is generally a hopeless mixture. Despite problems with acyclic ketones, the reaction is quite useful for cyclic ketones and the corresponding secondary alcohols, the dicarboxylic acid being prepared in good yield. The formation of adipic acid from cyclohexanone (Scheme 2.9) is an important industrial procedure. Acid dichromate and permanganate are the most common oxidizing agents, although autoxidation (oxidation with atmospheric oxygen) in alkaline solution and potassium superoxide under phase transfer conditions have also been used.

Cyclic ketones can also be cleaved by treatment with NOCl and an alcohol in liquid SO₂ to give an o-oximinocarboxylic ester (Scheme 2.10).
Cyclic 1,3-diketones, which exist mainly in the mono-enolic form, can be cleaved with sodium periodate with loss of one carbon, for example (Figure 3).  

The species actually undergoing the cleavage is the triketone, so this is an example of *Oxidative Cleavage of Glycols and Related Compounds.*

3) **Ozonolysis-**

**Oxo-uncoupling**

Ozone, O₃, is an allotrope of oxygen that adds rapidly to carbon-carbon double bonds. Since the overall change in ozonolysis is more complex than a simple addition reaction, its mechanism has been extensively studied. Reactive intermediates called ozonides have been isolated from the interaction of ozone with alkenes, and these unstable compounds may be converted to stable products by either a reductive workup (Zn dust in water or alcohol) or an oxidative workup (hydrogen peroxide). The chief difference in these conditions is that reductive workup gives an aldehyde product when hydrogen is present on a double bond carbon atom, whereas oxidative workup gives a carboxylic acid or carbon dioxide in such cases. The following equations illustrate ozonide formation, a process that is believed to involve initial syn-addition of ozone, followed by rearrangement of the extremely unstable molozonide addition product. They also show the decomposition of the final ozonide to carbonyl products by either a reductive or oxidative workup.
When compounds containing double bonds are treated with ozone, usually at low temperatures, they are converted to compounds called ozonides (I) that can be isolated but, because some of them are explosive, are more often decomposed with zinc and acetic acid, or catalytic hydrogenation to give 2 equivalents of aldehyde, or 2 equivalents of ketone, or 1 equivalent of each, depending on the groups attached to the alkene (Scheme 2.11).\textsuperscript{8a} The decomposition of 16 has also been carried out with triethylamine \textsuperscript{8b} and with reducing agents, among them trimethyl phosphite,\textsuperscript{8c} thiourea,\textsuperscript{8d} and dimethyl sulfide.\textsuperscript{8e} However, ozonides can also be oxidized with oxygen, peroxyacids, or H\textsubscript{2}O\textsubscript{2} to give ketones and/or carboxylic acids or reduced with LiAlH\textsubscript{4}, NaBH\textsubscript{4}, BH\textsubscript{3}, or catalytic hydrogenation with excess H\textsubscript{2} to give 2 equivalents alcohol.\textsuperscript{8f} Ozonides can also be treated with ammonia, hydrogen, and a catalyst to give the corresponding amines,\textsuperscript{8g} or with an alcohol and anhydrous HCl to give the corresponding carboxylic esters.\textsuperscript{8h-j} Ozonolysis is therefore an important synthetic reaction.
4) Oxidative Cleavage of Double Bonds and Aromatic Rings:

*Oxo-de-alkylidene-bisubstitution and so on.*

Carbon-carbon double bonds can be cleaved by many oxidizing agents,\(^9a\) the most common of which are neutral or acid permanganate and acid dichromate. The products are generally 2 equivalents of ketone, 2 equivalents of carboxylic acid, or 1 equivalent of each, depending on what groups are attached to the alkene (Scheme 2.12). With ordinary solutions of permanganate or dichromate yields are generally low, and the reaction is seldom a useful synthetic method; but high yields can be obtained by oxidizing with KMnO\(_4\) dissolved in benzene containing the crown ether dicyclohexano-18-crown-6.\(^9b-c\) The crown ether coordinates with K\(^+\), permitting the KMnO\(_4\) to dissolve in benzene.

![Scheme 2.12](image)

Cleavage of alkynes is generally rather difficult, but treatment of internal alkynes with an excess of Oxone with a ruthenium catalyst leads to aliphatic carboxylic acids.\(^9d\) Aromatic rings can be cleaved with strong enough oxidizing agents. An important laboratory reagent for this purpose is ruthenium tetroxide along with a co-oxidant, such as NaIO\(_4\) or NaOCl (household bleach can be used).\(^10a\) Examples\(^10b-e\) are the oxidation of naphthalene to phthalic acid\(^10f\) and, even more remarkably, of cyclohexylbenzene to cyclohexanecarboxylic acid.\(^10g\) The latter conversion was also accomplished with ozone.\(^10h-k\) Another reagent that oxidizes aromatic rings is air catalyzed by V\(_2\)O\(_5\). The oxidations of naphthalene to phthalic anhydride and of benzene to maleic anhydride by this reagent are important industrial procedures.\(^10l\) *O-Diamines* have been oxidized with nickel peroxide, with lead tetraacetate,\(^10m\) and with O\(_2\) catalyzed by CuCl (Scheme 2.13).\(^10n\)
5) **Oxidation of Aromatic Side Chains:**

_Oxo,hydroxy-de-dihydro,methyl-ter substitution_

Alkyl chains on aromatic rings can be oxidized to COOH groups by many oxidizing agents, including permanganate, nitric acid, and acid dichromate (**Scheme 2.14**).\(^{11a}\) The method is most often applied to the methyl group, although longer side chains can also be cleaved. However, tertiary alkyl groups are resistant to oxidation, and when they are oxidized, ring cleavage usually occurs too.\(^{11b}\)

![Scheme 2.14](image)

6) **Oxidative Decarboxylation:**

_Acetoxy-de-carboxy-substitution_

Carboxylic acids can be decarboxylated\(^{12a-b}\) with lead tetraacetate to give a variety of products, among them the ester ROAc (formed by replacement of COOH by an acetoxy group), the alkane RH, and, if \(\alpha,\beta\) hydrogen is present, the alkene formed by elimination of H and COOH, as well as numerous other products arising from rearrangements, internal cyclizations (**Scheme 2.15**),\(^{12c-d}\) and reactions with solvent molecules. When R is tertiary, the chief product is usually the alkene, which is often obtained in good yield. High yields of alkenes can also be obtained when R is primary or secondary, in this case by the use of Cu(OAc)\(_2\) along with the Pb(OAc)\(_4\) (**Scheme 2.16**).\(^{12e-f}\)

![Scheme 2.15](image)
Hydro-carboxyl-elimination

The mechanism with lead tetraacetate is generally accepted to be of the free radical type (Scheme 2.17). First, there is an interchange of ester groups:

\[
Pb(OAc)_4 + ROO\rightarrow Pb(OAc)_3OCOR \text{ or } Pb(OAc)_2(OCOR)_2
\]

There follows a free-radical chain mechanism (shown for 28 although 29 and other lead esters can behave similarly)

\[
Pb(OAc)_3OCOR \rightarrow Pb(OAc)_2 + R'CO_2
\]

**Initiation**

\[
R' + Pb(OAc)_3OCOR \rightarrow R' + Pb(OAc)_2OCOR + OA^{-}
\]

\[
\cdot Pb(OAc)_2OCOR \rightarrow Pb(OAc)_2 + R' + CO_2
\]

**Propagation**

Products can then be formed either from R' or R+. Primary R' abstract H from solvent molecules to give RH. R' can lose H+ to give an alkene, react with HOAc to give the carboxylic ester, react with solvent molecules or with another functional group in the same molecule, or rearrange, thus accounting for the large number of possible products. The R’ group can also dimerize to give R R. The effect of Cu2+ ions is to oxidize the radicals to alkenes, thus producing good yields of alkenes from primary and secondary substrates. The Cu2+ ion has no effect on tertiary radicals, because these are efficiently oxidized to alkenes by lead tetraacetate.
In another type of oxidative decarboxylation, arylacetic acids can be oxidized to aldehydes with one less carbon (ArCH$_2$COOH $\rightarrow$ ArCHO) by tetrabutylammonium periodate. Simple aliphatic carboxylic acids were converted to nitriles with one less carbon (RCH$_2$COOH $\rightarrow$ RCN) by treatment with trifluoroacetic anhydride and NaNO$_2$ in F$_3$CCOOH.

7) **Bis-decarboxylation:**

*Dicarboxy-elimination*

Compounds containing carboxyl groups on adjacent carbons (succinic acid derivatives) can be bis-decarboxylated with lead tetraacetate in the presence of O$_2$ (Scheme 2.18).\textsuperscript{13a} The reaction has wide scope. The elimination is stereoselective, but not stereospecific (both meso- and dl-2,3-diphenylsuccinic acid gave trans-stilbene);\textsuperscript{13b} a concerted mechanism is thus unlikely.

![Scheme 2.18](image)

The following mechanism is not inconsistent with the data (Figure 5):
Compounds containing geminal carboxyl groups (disubstituted malonic acid derivatives) can also be bis-decarboxylated with lead tetraacetate\textsuperscript{13c}, gem-diacetates (acylals) being produced, which are easily hydrolysable to ketones (Scheme 2.19).\textsuperscript{13d}

![Scheme 2.19](image)

C. Reactions Involving Replacement of Hydrogen by Oxygen:

1) Hydroxylation at an Aliphatic Carbon:

*Hydroxylation or Hydroxy-de-hydrogenation*

Compounds containing susceptible C-H bonds can be oxidized to alcohols.\textsuperscript{14} Nearly always, the C-H bond involved is tertiary, and so the product is a tertiary alcohol. This is partly because tertiary C-H bonds are more susceptible to free-radical attack than primary and secondary bonds and partly because the reagents involved would oxidize primary and secondary alcohols further (Scheme 2.20).

![Scheme 2.20](image)

2) Oxidation of Methylene to OH, O\textsubscript{2}CR, or OR:

*Hydroxy (or alkoxy) -de-dihydro-bisubstitution*

Methyl or methylene groups α to a carbonyl can be oxidized to give α-hydroxy ketones, aldehydes, or carboxylic acid derivatives. Ketones can be a hydroxylated in good yields, without conversion to the enolates, by treatment with the hypervalent iodine reagents\textsuperscript{15a} α-iodosobenzoic acid\textsuperscript{15b-c} or phenyliodoso acetate, PhI(OAc)\textsubscript{2}, in ethanolic NaOH (Scheme 2.21).\textsuperscript{15d}
The latter reagent has also been used on carboxylic esters. Dioxygen (O₂) and a chiral phase-transfer catalyst gave enantioselective α-hydroxylation of ketones, if the α position was tertiary. Dimethyl dioxirane is quite effective for hydroxylation of 1,3-dicarbonyl compounds, and O₂ with a manganese catalyst, Oxygen with a cerium catalyst α-hydroxylates β-keto esters, Ceric ammonium nitrate has been used to hydroxylate C-2 of dibenzyl malonate, Methyl ketones (RCOMe) reacts with ammonium peroxydisulfate, (NH₄)₂S₂O₈, and a catalytic amount of diphenyl diselenide in MeOH to give α-keto acetics, RCOCH(OMe₂).

3) Oxidation of Methylene to Heteroatom Functional Groups Other Than Oxygen or Carbonyl:

Amino (or amido) -de-dihydro-bisubstitution
α-Amination or amidation of a CH unit is possible in some cases. Cyclic alkanes are converted to the N-alkyl N-tosylamine with PhI-NTs and a copper complex. Benzyl CH, such as in ethylbenzene, is oxidized with PhI(OAc)₂ in the presence of TsNH₂ and a fluorinated manganese porphyrin to give the corresponding N-tosylamine, PhCHMe(NHTs) (Scheme 2.22).

Sulfo-de-dihydro-bisubstitution
Similar reactions are possible, in some cases, to produce sulfur containing compounds. (Scheme 2.23)
Cyclic alkanes are converted to the corresponding alkylsulfonic acid with SO2/O2 and a vanadium catalyst.16c

4) Oxidation of Methylene to Carbonyl:

Oxo-de-dihydro-bisubstitution

Methyl or methylene groups α to a carbonyl can be oxidized with selenium dioxide to give, respectively, α-keto aldehydes and α-diketones (Scheme 2.24).17a-b The reaction can also be carried out α to an aromatic ring or to a double bond, although in the latter case, hydroxylation is the more common result. Selenium dioxide, SeO2, is the reagent most often used, but the reaction has also been carried out with N2O3 and other oxidizing agents,17c-d including hypervalent iodine compounds.17e

Mechanisms have been suggested for the reaction with SeO2. One of these involves a selenate ester of the enol. (Figure 6)

5) Oxidation of Arylmethanes to Aldehydes:

Oxo-de-dihydro-bisubstitution

Methyl groups on an aromatic ring can be oxidized to the aldehyde stage (Scheme 2.25) by several oxidizing agents. When the reagent is chromyl chloride (CrO2Cl2), the reaction is called the Etard reaction18a and the yields are high.18b Another oxidizing
agent is a mixture of CrO₃ and Ac₂O. In this case, the reaction stops at the aldehyde stage because the initial product is ArCH(OAc)₂ (an acylal), which is resistant to further oxidation. Hydrolysis of the acylal gives the aldehyde.

![Scheme 2.25](image)

**6) Oxidation of Aromatic Hydrocarbons to Quinones:**

*Arene-quinone transformation*

Condensed aromatic systems (including naphthalenes) can be directly oxidized to quinones by various oxidizing agents.¹⁹a–c Yields are generally not high, although good yields have been reported with ceric ammonium sulfate.¹⁹f Benzene cannot be so oxidized by strong oxidizing agents, but can be electrolytically oxidized to benzoquinone.¹⁹g Naphthalene derivatives, however, are oxidized to naphthoquinones (Scheme 2.26) with H₅IO₆ and CrO₃.¹⁹h 1,4-Dimethoxy aromatic compounds are oxidized to para-quinones with an excess of CoF₃ in water–dioxane.¹⁹i

![Scheme 2.26](image)

**7) Oxidation of Primary Halides and Esters of Primary Alcohols to Aldehydes:**

*Oxo-de-hydro, halo-bisubstitution*

Primary alkyl halides (chlorides, bromides, and iodides) can be oxidized to aldehydes (Scheme 2.27) easily and in good yields with dimethyl sulfoxide,²⁰a–b in what has been called the Kornblum reaction. In Kornblum’s original work, the reaction of a-halo ketones with DMSO at elevated temperatures gave good yields of the corresponding glyoxal (an a-keto-aldehyde).²⁰c If the glyoxal could be removed from the reaction medium by distillation as it was formed, the reaction was very efficient. In many cases, it was difficult to isolate high boiling glyoxals from DMSO.
8) Oxidation of Amines or Nitro Compounds to Aldehydes, Ketones, or Dihalides:

Oxo-de-hydro, amino-bisubstitution (overall transformation)

Primary aliphatic amines can be oxidized to aldehydes or ketones.\textsuperscript{21a} Other reagents used\textsuperscript{21b-c} have been N-bromoacetamide (for benzylic amines), 3,5-di-\textit{tert}-butyl-1,2-benzoquinone, and aqueous NaOCl with phase-transfer catalysts. Benzylic amine salts PhCHRNR\textsubscript{1}H\textsuperscript{+}Cl\textsuperscript{-} (R, R\textsubscript{1} \(\frac{1}{2}\) H or alkyl) give benzaldehydes or aryl ketones when heated in DMSO. Several indirect methods for achieving the conversion R R\textsubscript{1}CHNH\textsubscript{2} \(\rightarrow\) R R\textsubscript{1}CO (R\textsubscript{1} \(\frac{1}{2}\) alkyl, aryl, or H) have been reported (Scheme 2.28).

9) Oxidation of Primary Alcohols to Carboxylic Acids or Carboxylic Esters:

Oxo-de-dihydro-bisubstitution

Primary alcohols can be oxidized to carboxylic acids by many strong oxidizing agents including chromic acid (Scheme 2.29), permanganate,\textsuperscript{22a} and nitric acid.\textsuperscript{22b-c} Other reagents include H\textsubscript{5}IO\textsubscript{6}/CrO\textsubscript{3}.\textsuperscript{22d}
Hydroxylation or Hydroxy-de-hydrogenation

Oxidation of aldehydes-to-carboxylic acids is quite common\textsuperscript{23a-b} and has been carried out with many oxidizing agents (Scheme 2.30), the most popular of which is permanganate in acid, basic, or neutral solution. Chromic acid, bromine, and Oxone\textsuperscript{1}, are other reagents frequently employed. Bromate exchange resin in refluxing acetone oxidizes aryl aldehydes-to aryl-carboxylic acids. Silver oxide is a fairly specific oxidizing agent for aldehydes and does not readily attack other groups. Benedict’s and Fehling’s solutions oxidize aldehydes,\textsuperscript{23c} and there is a test for aldehydes that depends on this reaction, but the method is seldom used for preparative purposes.

\begin{center}
\begin{tikzpicture}
  \node (a) at (0,0) {R \hspace{0.5cm} \text{aldehyde}};
  \node (b) at (2,0) {R \hspace{0.5cm} \text{carboxylic acid}};
  \draw[->, bend left] (a) to node[midway, above] {oxidation} (b);
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.30}

11) Oxidation of Carboxylic Acids to Peroxy Acids:

Peroxy-de-hydroxy-substitution

The oxidation of carboxylic acids with H\textsubscript{2}O\textsubscript{2} and an acid catalyst is the best general method for the preparation of peroxy acids (Scheme 2.31).\textsuperscript{24a} A mixture of Me\textsubscript{2}C(OMe)OOH and DCC has also been used.\textsuperscript{24b} The most common catalyst for aliphatic R is concentrated sulfuric acid. The reaction is equilibrium and is driven to the right by removal of water or by the use of excess reagents. For aromatic R, the best catalyst is methanesulfonic acid, which is also used as the solvent.

\begin{center}
\begin{tikzpicture}
  \node (a) at (0,0) {R \hspace{0.5cm} \text{carboxylic acid}};
  \node (b) at (0,-1) {HO\textsuperscript{+}};
  \node (c) at (2,0) {R \hspace{0.5cm} \text{peroxy acid}};
  \node (d) at (2,-1) {H\textsuperscript{2}O};
  \draw[->, bend left] (a) to node[midway, above] {$H^+$} (c);
  \draw[<-, bend right] (b) to node[midway, below] {$H^+$} (a);
  \draw[<-, bend right] (b) to node[midway, above] {$H^+$} (c);
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.31}

D. Reactions in Which Oxygen is Added to the Substrate:

1) Oxidation of Alkenes to Aldehydes and Ketones:

1/1Oxo-(1/2/hydro)-migro-attachment

Monosubstituted and 1,2-disubstituted alkenes can be oxidized to aldehydes and ketones by palladium chloride and similar salts of noble metals (Scheme 2.32).\textsuperscript{25a-d}
1,1-Disubstituted alkenes generally give poor results. The reaction is used industrially to prepare acetaldehyde from ethylene (the Wacker process), but it is also suitable for laboratory preparations. The palladium chloride is reduced to palladium. Because the reagent is expensive, the reaction is usually carried out with a co-oxidant, most often CuCl₂, whose function is to reoxidize the Pd to Pd(II). The CuCl₂ is reduced to Cu(I), which itself is reoxidized to Cu(II) by air, so that atmospheric oxygen is the only oxidizing agent actually used up. Many other co-oxidants have been tried, among them O₃, Fe³⁺, and PbO₂. Terminal alkenes are oxidized to methyl ketones with O₂ and a palladium catalyst with 20% pyridine in Z-propanol.²⁵e

Scheme 2.32

The generally accepted mechanism involves p complexes of palladium (Figure 8).

Figure 8

This mechanism accounts for the fact, established by deuterium labeling, that the four hydrogens of the acetaldehyde all come from the original ethylene and none from the solvent.

2) The Oxidation of Alkynes to α-Diketones:

Dioxo-biaddition
Internal alkynes have been oxidized\textsuperscript{26a} to α-diketones by several oxidizing agents (Scheme 2.33),\textsuperscript{26b} including neutral KMnO\textsubscript{4}, bis(trifluoroacetoxy)iodobenzene, NaIO\textsubscript{4}-RuO\textsubscript{2}, I\textsubscript{2}-DMSO, MeReO\textsubscript{3}/H\textsubscript{2}O\textsubscript{2}, as well as by electro-oxidation. A ruthenium complex with a small amount of trifluoroacetic acid converts internal alkynes to the α-diketone. Ozone generally oxidizes triple-bond compounds to carboxylic acids, but α-diketones are sometimes obtained instead. Selenium dioxide (SeO\textsubscript{2}) with a small amount of H\textsubscript{2}SO\textsubscript{4} oxidizes alkynes to α-diketones as well as arylacetylenes to α-keto acids (ArCCH → ArCOCOOH).

\begin{center}
\begin{tikzpicture}
  \node (a) at (0,0) {R\equiv\equiv R\textsubscript{1}}; \\
  \node (b) at (2.5,0) {\text{ruthenium tetroxide}}; \\
  \node (c) at (2.5,1) {R\text{\footnotesize\textsuperscript{1}}\text{\footnotesize\textsuperscript{2}}}; \\
  \node (d) at (2.5,2) {R\text{\footnotesize\textsuperscript{1}}\text{\footnotesize\textsuperscript{2}}}; \\
  \draw[<->] (a) -- (b) -- (c) -- (d);
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.33}

3) Oxidation of Amines to Nitroso Compounds and Hydroxylamines and Related:

\textit{N-Oxo-de-dihydro-bisubstitution}

Primary aromatic amines can be oxidized\textsuperscript{27a} to nitroso compounds. Most often the conversion is accomplished by Caro’s acid (H\textsubscript{2}SO\textsubscript{5}) (Scheme 2.34) or with H\textsubscript{2}O\textsubscript{2} in HOAc.\textsuperscript{27b} Hydroxylamines, which are probably intermediates in most cases, can sometimes be isolated, but under the reaction conditions are generally oxidized to the nitroso compounds. Primary aliphatic amines can be oxidized in this manner, but the nitroso compound is stable only if there is no a hydrogen. If there is hydrogen, the compound tautomerizes to the oxime. Among the reagents used for this oxidation are sodium perborate H\textsubscript{2}O\textsubscript{2} with a titanium complex, HOF generated in situ, and Na\textsubscript{2}WO\textsubscript{4}/H\textsubscript{2}O\textsubscript{2}.

\begin{center}
\begin{tikzpicture}
  \node (a) at (0,0) {ArNH\textsubscript{2}}; \\
  \node (b) at (2.5,0) {H\textsubscript{2}SO\textsubscript{5}}; \\
  \node (c) at (2.5,1) {Ar-N=O}; \\
  \draw[<->] (a) -- (b) -- (c);
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.34}
The postulated mechanism with H₂SO₅ (Figure 9).

![Figure 9](image)

Secondary amines, R₂NH, are oxidized to hydroxylamines (R₂NHOH) which are resistant to further oxidation, by dimethyldioxirane and by benzoxy peroxide and Na₂HPO₄.²⁷c

4) Oxidation of Primary Amines, Oximes, Azides, Isocyanates, or Nitroso Compounds to Nitro Compounds:

Tertiary alkyl primary amines can be oxidized to nitro compounds in excellent yields with KMnO₄ (Scheme 2.35).²⁸a-c

![Scheme 2.35](image)

5) Oxidation of Tertiary Amines to Amine Oxides:

*N-Oxygen-attachment*

Tertiary amines can be converted to amine oxides by oxidation. Hydrogen peroxide is often used, but peroxyacids are also important reagents for this purpose (Scheme 2.36). Pyridine and its derivatives are oxidized by peroxyacids rather than hydrogen peroxide.²⁹

![Scheme 2.36](image)
6) Oxidation of Thiols and Other Sulfur Compounds to Sulfonic Acids:

*Thiol-sulfonic acid oxidation*

Thiols, sulfoxides, sulfones, disulfides,\(^{30a}\) and other sulfur compounds can be oxidized to sulfonic acids with many oxidizing agents, but for synthetic purposes the reaction is most important for thiols.\(^{30b}\) Among oxidizing agents used are boiling nitric acid, barium permanganate, and dimethyl dioxirane.\(^{30c}\) Autoxidation (oxidation by atmospheric oxygen) can be accomplished in basic solution (Scheme 2.37).

\[
\begin{array}{c}
\text{RSH} \\
\xrightarrow{\text{HNO}_3}
\end{array} \quad \begin{array}{c}
\text{RSO}_3\text{H}
\end{array}
\]

Scheme 2.37

7) Oxidation of Thioethers to Sulfoxides and Sulfones:

*S-Oxygen-attachment*

Thioethers can be oxidized to sulfoxides by 1 equivalent of 30% H\(_2\)O\(_2\) or by many other oxidizing agents (Scheme 2.38),\(^{31a-b}\) including H\(_2\)O\(_2\)–flavin catalyst, H\(_2\)O\(_2\) and a Sc(OTf)\(_3\) catalyst, NaIO\(_4\), dioxiranes, MeReO\(_3\)/H\(_2\)O\(_2\), O\(_2\) and a ceric ammonium nitrate catalyst, trichloroisocyanuric acid, BnPh\(_3\)P HSO\(_5\), KO\(_2\)/Me\(_3\)SiCl, Fe(NO\(_3\))\(_3\)/FeBr\(_3\)/air, singlet oxygen on MB–Bentonite composite, MnO\(_2\) with a H\(_2\)SO\(_4\)/SiO\(_2\) catalyst, hexamethylene triamine-Br\(_2\) with CHCl\(_3\)-H\(_2\)O, sodium perborate, H\(_3\)IO\(_6\)/FeCl\(_3\), hypervalent iodine compounds, and peroxyacids.

\[
\begin{array}{c}
\text{R-S-R} \\
\xrightarrow{\text{H}_2\text{O}_2}
\end{array} \quad \begin{array}{c}
\text{O} \\
\xrightarrow{\text{KMnO}_4}
\end{array} \quad \begin{array}{c}
\text{O-SO}_2\text{R}
\end{array}
\]

Scheme 2.38

E. Oxidative Coupling:

1) Coupling Involving Carbanions:

*De-hydro, chloro-coupling*
Alkyl halides with an electron-withdrawing group on the halogen-bearing carbon can be dimerized to alkenes by treatment with bases (Scheme 2.39). The Z group may be nitro, aryl, and so on. It is likely that in most cases the mechanism\textsuperscript{32a} involves nucleophilic substitution followed by elimination\textsuperscript{32b-d} (illustrated for benzyl chloride):

![Scheme 2.39](image)

**Figure 10**

2) Dimerization of Silyl Enol Ethers or of Lithium Enolates:

3/O-De-trimethylsilyl-1/C-coupling

Silyl enol ethers can be dimerized to symmetrical 1,4-diketones by treatment with Ag\textsubscript{2}O in DMSO or certain other polar aprotic solvents.\textsuperscript{33} The reaction has been performed with R\textsubscript{2}, R\textsubscript{3} ¼ hydrogen or alkyl, although best yields are obtained when R\textsubscript{2} ¼ R\textsubscript{3} ¼ H (Scheme 2.40).

![Scheme 2.40](image)

3) Oxidation of Thiols to Disulfides:

*S-De-hydrogen-coupling*

Thiols are easily oxidized to disulfides (Scheme 2.41).\textsuperscript{34} Hydrogen peroxide is the most common reagent, but many oxidizing agents give the reaction, among them KMnO\textsubscript{4}/ CuSO\textsubscript{4}, Me\textsubscript{2}SO-I\textsubscript{2}, Br\textsubscript{2} under phase-transfer conditions, Br\textsubscript{2} on hydrated silica, sodium perborate, NaI/air, t-BuOOH/VO(acac)\textsubscript{2}, SmI\textsubscript{2}, PPh\textsubscript{3} with a rhodium catalyst, dibromohydantoin, cetyltrimethylammonium dichromate, and NO.
2.2 LITERATURE SURVEY:
From literature survey it was observed that, there are some limited methods available for oxidative cleavage of carbon-carbon bond of 1,2-diamino aryl compounds. In this section we only discuss 1,2 diaminobenzene and about quinone formation it has been discussed in section 2.

Characteristics of nucleus:

Figure 11-Muconitrile

<table>
<thead>
<tr>
<th>Structure</th>
<th>(2Z,4Z)-hexa-2,4-dienedinitrile</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUPAC Name</td>
<td>(2Z,4Z)-hexa-2,4-dienedinitrile</td>
</tr>
<tr>
<td>CAS No.</td>
<td>1557-59-1</td>
</tr>
<tr>
<td>Molecular Formula</td>
<td>C₇H₅NS</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>104.10</td>
</tr>
<tr>
<td>Melting Point</td>
<td>126°C</td>
</tr>
<tr>
<td>Density</td>
<td>1.024 gm/ml</td>
</tr>
<tr>
<td>Physical appearance</td>
<td>Colorless or white</td>
</tr>
</tbody>
</table>

2.2.1 Synthesis of Muconitrile By Oxidative Cleavage of Aryldiamines:

1) Copper-Catalyzed Oxidation of o-phenylenediamines to cis, cis-Mucononitriles\(^{35}\)
Here in this method oxidation of \( o \)-phenylenediamine (1) with molecular oxygen in the presence of CuCl in pyridine to give cis, cis mucononitrile [(Z,Z)-2,4-hexadienedinitrile] (Scheme 2.42) as achieved by selecting suitable reaction conditions. The molar ratio of opd to CuCl in the reaction medium should be maintained below 0.5 in order to prevent intermolecular coupling of opd.

Cuprous chloride is slightly soluble in pyridine under an inert atmosphere at room temperature, but a mixture of CuCl and pyridine absorbs oxygen with stirring under oxygen atmosphere to give a deep green solution. Exactly 1 mol of oxygen is absorbed per four atoms of copper. From this solution an oxygen complex was precipitated by addition of ethyl ether and its elemental analysis supported a composition of \((\text{CuCl})_4(C_6H_5N)_4O_2\) when a pyridine solution of 1 (0.5 molar equiv to CuCl) was added slowly to a pyridine solution of CuCl pretreated with oxygen, further absorption of oxygen was observed showing that the oxidation took place. The amount of oxygen absorbed during the oxidation was equimolar to 1 added, and after the usual work-up 2 was obtained nearly quantitatively. During the oxidation reaction the solution was purple, but it changed to deep green after the reaction suggesting the regeneration of the oxygen complex. The complex was isolated from the solution.

**Mechanism**: Mechanism is shown below
2) By using Pb(OAc)$_4^{36a}$

The lead tetra-acetate oxidation of o-phenylenediamine (I) and its derivatives also proceeds with the formation of the same product (IV) and presumably the same intermediates.

Mechanism: Mechanism is shown below.
3) By using Nickel peroxide\textsuperscript{36b}

To a solution of \(o\)-phenylenediamine in benzene or ether there was slowly added nickel peroxide with stirring at room temperature (Scheme 2.44). The oxidation was conducted by employing two times the theoretical amounts of nickel peroxide based on the available oxygen-content which was determined by iodometry. The reaction proceeded very rapidly and the colour of the solution was turned into red-brown.

After removal of nickel peroxide, the filtrate was concentrated and the mixture was chromatographed on alumina. Cis, cis-1,4-Dicyano-1,3-butadine obtained from the first elute was recrystallized from carbon tetrachloride to give white crystals, m.p. 128-129 °C, (Anal. Cal. for C\(_6\)H\(_4\)N\(_2\): C,69.21; H,3.88; N,26.91. Found: C, 69.12; H,3.97; N, 26.64). Catalytic reduction of the product over platin oxide afforded adiponitrile with absorption of two moles of hydrogen.

2.2.2 Synthesis of Muconitrile from diazides:

1) Muconitrile from \(o\)-diazides- Synthesis of 1,4-Dicyano-1,3-butadienes:\textsuperscript{37}
The thermal decomposition of \( o \)-diazidobenzene (I) was investigated as a possible source of benzyne. It was postulated that when I decomposed it might be expected to do so with the intermediate formation of the heterocycle II, which in turn might be expected to undergo further decomposition to give benzyne.

To check this possibility, \( o \)-diazidobenzene was allowed to decompose in hexadecane solution containing anthracene. If benzyne is formed in the decomposition, it should be trapped by its Diels-Alder reaction with anthracene to give tryptycene. However, when the reaction was worked up no tryptycene could be isolated. Instead, the formation of muconitrile was observed as characterized after analysis (Scheme 2.45).

\[
\text{Scheme 2.45}
\]

**2) From oxidation of 2-aminobenzotriazole:**

In this method 2-aminobenzotriazole in benzene is oxidised with lead tetra-acetate, nitrogen is rapidly evolved and cis, cis-mucononitrile (IV) (Scheme 2.46), is formed in 64% yield, presumably by way of the (possibly triplet) nitrenes (II) and (III). The same intermediates have been postulated in the thermal decomposition of \( o \)-diazidobenzene to mucononitrile by Hall, whose report prompts this preliminary communication.

\[
\text{Scheme 2.46}
\]
Despite the great variety of well known and tried methods, most of these protocols, however, suffer from drawbacks, namely long reaction times and use of corrosive acids or toxic metallic compounds that result in generation of waste streams, complicated workup procedures, by-products and consequently, low yields. Thus despite of the availability of variety of well known methods, the development of new general synthetic protocols for muconitrile is still an active field.

So from literature survey it was found that limited number of methods available for synthesis of muconitrile. Thus, in this connection we developed a novel application of hypervalent iodine reagent, (diacetoxyiodo)benzene for the oxidative cleavage of carbon-carbon bond of 1,2- diamino aryl compounds to corresponding nitriles and preparation of quinones from corresponding 1,4-diamino aryl compounds.

There are no reports in the literature for oxidative cleavage of aryl diamines or synthesis of quinone using hypervalent iodine reagents. It was noteworthy that, reaction with 1,3 diaminobenzene was unaffected.

2.3 OBJECTIVE OF WORK:

Hypervalent iodine reagents has attracted increasing interest during the last decade because of their selective, mild, and environmentally friendly properties as oxidizing agents in organic synthesis. So in this context we develop a first novel synthetic utility of hypervalent iodine reagent, (diacetoxyiodo)benzene for diamino aryl carbon-carbon cleavage is described. 1,2 diamino aryl compounds were successfully converted into corresponding nitriles, while the developed method also used for the preparation of quinone from corresponding 1,4 diamino aryl compounds.

Hypervalent iodine reagents have the great reputation in the field of organic synthesis for natural product synthesis, oxidative cyclization and process development.
2.4 DESIGN AND DEVELOPMENT:

(Diacetoxyiodo)benzene is a hypervalent iodine reagent which is readily available and frequently used in several oxidative transformation.\textsuperscript{40a-d} During the course of our studies, we found that treatment of (diacetoxyiodo)benzene to 1,2-diaminobenzene in acetone resulted into formation of \textit{cis}, \textit{cis}-mucononitrile by oxidative cleavage of carbon-carbon bond (\textbf{Scheme 2.47}).

\begin{center}
\begin{tabular}{c}
\textbf{Scheme 2.47} \\
\end{tabular}
\end{center}

It was interesting to come know that under these reaction conditions 1,3-diaminobenzene was unaffected while 1,4-diaminobenzene showed unexpected results by formation of benzoquinone rather than expected fumaronitrile and provided an interesting route for the synthesis of quinones (\textbf{Scheme 2.48}).

\begin{center}
\begin{tabular}{c}
\textbf{Scheme 2.48} \\
\end{tabular}
\end{center}

There are no prior reports found in the literature for oxidative cleavage of aryl diamines and synthesis of quinone using hypervalent iodine reagents especially from aryl diamines.
2.4 EXPERIMENTAL:

1. General Information

All $^1$H NMR and $^{13}$C NMR spectra were recorded on JEOL AL-300 FT-NMR at 300 MHz and 75 MHz respectively. IR spectra were recorded on a Perkin Elmer RX–100 spectrophotometer (KBr pellet); Mass spectra were taken on THERMO FINNINGAN LCQ advantage max (LCMS). Chemical shift values are expressed in $\delta$ units relative to tetramethylsilane (TMS) signal as internal reference in CDCl$_3$ and in DMSO. Data are reported as follows: chemical shift in ppm ($\delta$), multiplicity (s= singlet, d= doublet, t= triplet, br= broad singlet, m= multiplet), coupling constant $J$ (Hz). Infrared spectra (IR) were recorded neat as KBr pellet; absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were recorded on low resolution mass spectrometer (ESI-MS). All solvents were purchased from commercial sources and used without further purification. Wherever necessary the solvents were dried by standard procedures.

In $^1$H-NMR CDCl$_3$ peak occur at 7.2 ppm, DMSO peak observed at 2.4 ppm while peak at 3.4 is due to proton of water present in DMSO. In CMR peak at 77 ppm is due to CDCl$_3$ while DMSO peak at 40ppm.

2. General procedure for cleavage of 1,2 diaminobenzene:

**Table 5, entry 1: (2Z, 4Z)-hexa-2, 4-dienedinitrile (mucononitrile)**

To a stirred solution of (diacetoxyiodo)benzene (3 g, 2 equiv) in acetone (15 mL) was added 1,2 diaminobenzene (0.5 g, 1.0 equiv). The reaction mixture was stirred at room temperature. After completion of reaction (TLC), the reaction mixture was quenched in water (20 mL) and further diluted with ethyl acetate (30 mL). The organic layer was separated and washed successively with 10% sodium bisulfate solution (2 x 20 mL), 10% sodium bicarbonate (2 x 15 mL), and water (2 x 20 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give crude product. Pure mucononitrile as a colourless solid was obtained after silica gel column chromatography (10% EtOAc-hexane). **Yield was isolated 0.315g (65%)** White colour.
M.P. 127°C (lit. 44 m.p. 128-129°C); IR (KBr, cm⁻¹): 3019, 2220, 1622, 1215; \(^1\)H-NMR (300 MHz, CDCl₃): 5.71-5.72 (d, \(J=2.4\) Hz, 2H), 7.30-7.31 (d, \(J=2.4\) Hz, 2H); \(^{13}\)C-NMR (75 MHz, CDCl₃): 106.2, 114.6, 142.7; MS(ESI) m/z Calc. for C₆H₄N: 104.109, found: 104.00 (M⁺)

Table 5, entry 2: (2E, 4Z)-3-chlorohexa-2, 4-dienedinitrile

4-Chloro-o-phenylenediamine (0.5g, 1 equivalent) in 15 ml of acetone was treated by general procedure with DIB (2.25g, 2 equivalent) to gave the product with 60% yield (0.282 g) M.P. 90°C (lit. 44 m.p. 89-90°C); IR (KBr, cm⁻¹): 3050, 2220, 1640, 1111, 784; \(^1\)H-NMR (300 MHz, CDCl₃): 5.83-5.85 (d, \(J=6\) Hz, 1H), 5.89 (s, 1H), 7.32-7.31 (d, \(J=6\) Hz, 2H); \(^{13}\)C-NMR (75 MHz, CDCl₃): 105.6, 105.9, 135.7, 138.1, 147.9, 162.7; MS(ESI) m/z 137 (M⁺)

Table 5, entry 3: (2E, 4Z)-3-methylhexa-2, 4-dienedinitrile

4-Methyl-o-phenylenediamine (0.5g, 1 equivalent) in 15 ml of acetone was treated by general procedure with DIB (2.63g, 2 equivalent) to gave the product with 55% yield (0.265 g), M.P. 57°C (lit. 44 m.p. 56.5-57.5°C); IR (KBr, cm⁻¹): 3071, 2214, 1640, 1261, 1031, 797; \(^1\)H-NMR (300 MHz, CDCl₃): 2.41 (s, 3H), 5.51 (s, 1H), 5.68-5.70 (d, \(J=5.4\) Hz, 1H), 7.24-7.26(d, \(J=5.4\) Hz, 1H); \(^{13}\)C-NMR (75 MHz, CDCl₃): 20.6, 102.4, 105.2, 115.0, 115.7, 143.5, 153.1; MS(ESI) m/z 118 (M⁺)

Table 5, entry 4: (2E, 4Z)-3-methoxyhexa-2,4-dienedinitrile

4-Methoxy-o-phenylenediamine (0.5g, 1 equivalent) in 15 ml of acetone was treated by general procedure with DIB (2.33g, 2 equivalent) to gave the product with 60% yield (0.292g), M.P. 116°C (lit. 44 m.p. 116-117°C); IR (KBr, cm⁻¹): 3061, 2214, 1710, 1627, 1210, 803; \(^1\)H-NMR (300 MHz, CDCl₃): 3.86 (s, 3H), 4.80 (s, 1H), 5.67-5.71 (d, \(J=12\) Hz, 1H), 7.05-7.09(d, \(J=12\) Hz, 1H); \(^{13}\)C-NMR (75 MHz, CDCl₃): 29.6, 101.6, 105.9, 113.4, 113.9, 138.1, 148.0; MS(ESI) m/z 134 (M⁺)

Table 5, entry 5: Ethyl (2E, 3Z)-4-cyano-2-(cyanomethylene)but-3-enoate

ethyl 3,4-diaminobenzoate (0.5g, 1 equivalent) in 15 ml of acetone was treated by general procedure with DIB (1.78g, 2 equivalent) to gave the product with 60% yield (0.291g); IR (KBr, cm-1): 3061, 2214, 1745, 1627, 1210, 803; \(^1\)H-NMR (60 MHz,
Table 5, entry 6: (2E,4Z)-3-benzoylhexa-2,4-dienedinitrile

4-benzoylhexa-o-phenylenediamine (0.5g, 1equivalent) in 15 ml of acetone was treated by general procedure with DIB (1.54g, 2equivalent) to gave the product with 60% yield (0.296 g), M.P. 95°C; IR (KBr, cm⁻¹): 3019, 2214,1638, 1401, 1319; ¹H-NMR (300 MHz, CDCl₃): 5.75-5.78 (d, J= 10.8 Hz 1H), 5.82 (s, 1H), 7.27-7.30 (d, J= 10.8 Hz, 1H) 7.48-7.79(m, 5H); ¹³C-NMR (75 MHz, CDCl₃): 106.3, 108.4, 113.8, 114.0, 129.1, 130.0, 134.5, 135.0, 140.3, 153.1, 191.2; MS(ESI) m/z 208 (M⁺)

Table 5, entry 7: 2-[(Z)-2-cyanovinyl]benzonitrile

Naphthalene-1,2-diamine (0.5g, 1equivalent) in 15 ml of acetone was treated by general procedure with DIB (2.03g, 2equivalent) to gave the product with 60% yield (0.287 g),; M.P. 71°C; IR (KBr, cm⁻¹): 3061, 2220, 1627, 1210, 803; ¹H-NMR (60 MHz, CDCl₃): 5.62 (d, 1H) 7.42 (3, 1H).

2.5 RESULT AND DISCUSSION:

For our initial study we selected 1,2-diaminobenzene as a model substrate to explore the suitable reaction conditions with (diacetoxyiodo) benzene in acetone at room temperature (Scheme 2.1). In this case, the reaction afforded the corresponding cis, cis-mucononitrile I as the major product.⁴¹a-c The structure of I was indicated initially by its molecular formula of C₆H₄N₂, peak in its infrared spectrum at 2200 cm⁻¹ characteristic of cyano groups, and the cis, cis configuration of I was shown by the presence of an intense peak at 757 cm⁻¹ in its infrared spectrum and the absence of appreciable absorption in the vicinity of 990 cm⁻¹. Comparison of the infrared spectrum of I with that published by Hall H. J. et al⁴² of a compound, mp 124°C, prepared from 1,2-diazidobenzene, showed the spectra to be identical.

Afterward, the stereochemistry of the product confirmed by comparing the NMR coupling constant values which was reported earlier, whether it’s trans, trans or trans, cis or cis, cis. The coupling constant J value for trans proton normally its 16.5 Hz and
for cis proton it’s 11.9-12.1 Hz and we observed the value 11.2 Hz which matches with the reported value.

Further evidence for the presence of Cis-Cis hydrogen in I was obtained from their IR spectra. All the dinitriles absorbs infrared radiation in the range of 778-781 cm⁻¹ the region where olefins with cis hydrogen absorbs. So, the cis–cis configuration was again confirmed by using NMR, IR, Melting point and comparing with literature⁴³ as shown as follows (Table no.1).

**Table 1: Comparison of Observed values with reported**

<table>
<thead>
<tr>
<th>Reported Value</th>
<th>2Z,4Z (cis-cis)</th>
<th>2E,4E (trans-trans)</th>
<th>2Z,4E (trans-cis)</th>
<th>Observed 2Z,4Z (cis-cis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>J (Hz)</td>
<td>11.2 &amp; 2.45</td>
<td>16.5 &amp; 1.4</td>
<td>10.0 &amp; 0.5</td>
<td>11.2 &amp; 2.4</td>
</tr>
<tr>
<td>NMR (δ)</td>
<td>5.68 &amp; 7.31</td>
<td>5.54 &amp; 7.24</td>
<td>5.47, 5.54 &amp; 7.04,</td>
<td>5.71 &amp; 7.30</td>
</tr>
<tr>
<td>IR (cm⁻¹)</td>
<td>2220, 752</td>
<td>2210, 982</td>
<td>2212, 752, 982</td>
<td>2220, 751</td>
</tr>
<tr>
<td>M.P. (°C)</td>
<td>125</td>
<td>156</td>
<td>96</td>
<td>127</td>
</tr>
</tbody>
</table>

Hence, by doing comparison of results with that of literature as mention in the above table. Finally, we concluded that, the reaction product is muconitrile and its stereo chemical geometry is Cis-Cis.

So, next to, explore the possibility of other reagents (Table no. 2) for conversion of 1,2-diaminobenzene into cis, cis-mucononitrile, we also carried out the reaction with 1,2-diaminobenzene using various hypervalent iodine reagents including IBX, KIO₃, and 4,4'-bis-(dichloroiodo)-biphenyl. Unlike the situation with
(diacetoxyiodo)benzene, no formation of *cis, cis*-mucononitrile was observed even after long reaction times.

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Reagents</th>
<th>Time (h)</th>
<th>Reflux</th>
<th>Yielda (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>$t$-BuOCl + Pd(OAc)$_2$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>KMnO$_4$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>KMnO$_4$ + Silica</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>KMnO$_4$ + H$_2$SO$_4$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>K$_2$Cr$_2$O$_7$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>K$_2$Cr$_2$O$_7$ + H$_2$SO$_4$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>K$_2$Cr$_2$O$_7$ + Silica</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>Mo$_3$ + H$_2$SO$_4$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>9.</td>
<td>(Na$_2$)$_3$PO$_4$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>10.</td>
<td>NaNO$_2$ + KIO$_3$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>11.</td>
<td>NaNO$_2$ + KMnO$_4$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>12.</td>
<td>NiCl$_2$ + KIO$_3$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>13.</td>
<td>CAN + H$^+$</td>
<td>24</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>14.</td>
<td>DIB</td>
<td>5 min</td>
<td>RT</td>
<td>25</td>
</tr>
<tr>
<td>15.</td>
<td>IBX</td>
<td>12</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>16.</td>
<td>4,4'-bis-(dichloroiodo)-biphenyl</td>
<td>12</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>17.</td>
<td>DMP</td>
<td>12</td>
<td>NR</td>
<td>0</td>
</tr>
</tbody>
</table>

*isolated yield, *reaction was carried at room temperature, NR= no reaction.
To optimize the reaction condition using DIB, we studied the reaction at different equivalent (Table no. 3) and also in a variety of solvent. It was found that, as slightly increasing equivalent ratio of reagent to that of substrate, yield was increases drastically (Table 3 entries 1-3).

Next, from solvent study, it was noted that, this oxidative transformation takes place in chloroform and dichloromethane (Table 4 entry 1,2) solvent also, but lower yields were observed. Alongside acetone gave good yield (Table 4 entry 3) as compare to others. And finally from this study it was concluded that opd (1equiv.) and DIB (2 equiv) in acetone as a solvent is suitable for the reaction.

![Scheme 2.47](image)

Table 3: Reaction of OPD with DIB in DCE

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Substrate (equiv.)</th>
<th>Reagent (equiv.)</th>
<th>Time (min.)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1.5</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>55</td>
</tr>
</tbody>
</table>

Table 4: Effect of Solvent on Reaction yield

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Solvent</th>
<th>Time (min.)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Solvent</td>
<td>5</td>
<td>51</td>
</tr>
<tr>
<td>---</td>
<td>---------------</td>
<td>---</td>
<td>----</td>
</tr>
<tr>
<td>1</td>
<td>Dichloromethane</td>
<td>5</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>Dichloroethane</td>
<td>5</td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td>Acetone</td>
<td>5</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>Methanol</td>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td>Acetonitrile</td>
<td>5</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>5</td>
<td>55</td>
</tr>
</tbody>
</table>

In order to explore the reaction scope, a variety of substituted 1,2-diamino aryl compounds was prepared by standard reported procedures and converted into the corresponding nitriles by oxidative carbon–carbon cleavage in moderate to good yields, and the results are summarized in Table 5.

It was found that electron-rich 1,2-diaminobenzenes were suitable for this transformation, giving the dinitriles in moderate to good yields in short reaction times (Table 5, entries 2–4), while strongly electron-deficient 1,2-diaminobenzenes and heterocyclic diamines did not undergo this transformation (Table 5, entries 8 and 9).

It should be noted that, under these reaction conditions, methoxy and ester groups remain unaffected (Table 5, entries 4 and 5). The reaction system is also useful for 1,2-diaminonaphthalene (Table 5, entry 7).

Under the same reaction conditions, 1,4-diaminobenzene reacted with (diacetoxyiodo)benzene in acetone to give benzoquinone (Section-II).

2.6.1 MECHANISM:

Proposed mechanism for oxidative cleavage of o-aryldiamines (Figure 14).
In this mechanism, nucleophilic attack of amine on electrophilic hypervalent iodine took place and subsequently acetate ion will liberate. Again another free amine will attack on another molecule of reagent and liberated acetate ion from solution which pickup a proton from amine and by concerted way formation of imine bond and reduction of hypervalent iodine took place. This is a driving force of this reaction and key reactivity of hypervalent iodine species. In next step, an acetate ion again pickup a proton from imine and by concerted way oxidative cleavage of aromatic ring followed by reduction of hypervalent iodine took place.

Table 5. Reaction of (diacetoxyiodo)benzene with o-aryl diamino compounds

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
</table>
| 1     | \[
\begin{align*}
\text{NH}_2 \\
\text{NH}_2
\end{align*}
\] | \[
\begin{align*}
\text{CN} \\
\text{CN}
\end{align*}
\] | 15 | 65 |
<table>
<thead>
<tr>
<th></th>
<th>Structure 1</th>
<th>Structure 2</th>
<th>Reaction Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td><img src="image1" alt="Structure 1" /></td>
<td><img src="image2" alt="Structure 2" /></td>
<td>10</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td><img src="image3" alt="Structure 1" /></td>
<td><img src="image4" alt="Structure 2" /></td>
<td>10</td>
<td>55</td>
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<tr>
<td>4</td>
<td><img src="image5" alt="Structure 1" /></td>
<td><img src="image6" alt="Structure 2" /></td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td><img src="image7" alt="Structure 1" /></td>
<td><img src="image8" alt="Structure 2" /></td>
<td>20</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td><img src="image9" alt="Structure 1" /></td>
<td><img src="image10" alt="Structure 2" /></td>
<td>15</td>
<td>60</td>
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<tr>
<td>7</td>
<td><img src="image11" alt="Structure 1" /></td>
<td><img src="image12" alt="Structure 2" /></td>
<td>20</td>
<td>60</td>
</tr>
<tr>
<td>8</td>
<td><img src="image13" alt="Structure 1" /></td>
<td><img src="image14" alt="Structure 2" /></td>
<td>---</td>
<td>120</td>
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<tr>
<td>9</td>
<td><img src="image15" alt="Structure 1" /></td>
<td><img src="image16" alt="Structure 2" /></td>
<td>---</td>
<td>120</td>
</tr>
<tr>
<td>10</td>
<td><img src="image17" alt="Structure 1" /></td>
<td><img src="image18" alt="Structure 2" /></td>
<td>---</td>
<td>120</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reaction conditions: substrate (4.6 mmol), (diacetoxyiodo)benzene (2 equiv) in acetone (15 mL), rt.

<sup>b</sup>Isolated yields after column chromatography and structures were confirmed by comparison of IR and 

<sup>1</sup>H NMR with authentic materials. <sup>c</sup>NR: No reaction.

### 2.6 APPLICATION:

Based on literature survey, we found that this method can be successfully used for the synthesis of Adipic acid and Muconic acid. Adipic acid is important starting material
in the synthesis of nylon-66, and also a starting material for many drug molecules. Apart from these, muconic acid also has great importance, as it is important intermediate in the total synthesis of Deoxynijiromycien.

2.6.1 Synthesis of Muconic acid: \(^{37}\) (second step was reported)

![Diagram of Muconic acid synthesis]

Previously Muconic acid was synthesized in six steps from cyclohexanol. And from our method it can be synthesized in only two steps.

2.6.2 Synthesis of Adipic acid: (second and third step was reported)

Synthesis of adipic acid from adiponitrile was studied previously by Moreau. In that method they used a Brevibacterium. There were also reported on synthesis of adipic acid from muconitrile via adiponitrile route as shown below.

![Diagram of Adipic acid synthesis]

Reduction of muconitrile in NaBH\(_4\) and then oxidation of nitrile gave an adipic acid.
2.8 **SUMMARY AND CONCLUSION:**

A variety of substituted 1,2-diamino aryl compounds was prepared by standard reported procedures and converted into the corresponding nitriles by oxidative carbon–carbon cleavage.

All the dinitriles absorbs infrared radiation in the range of 778-781 cm$^{-1}$ the region where olefins with *cis* hydrogen absorbs. So, the cis–cis configuration was confirmed by using NMR, IR, Melting point and comparing with literature.

This methodology can be used in the synthesis of Adipic acid and Muconic acid. Adipic acid is important starting material in the synthesis of nylon-66, many drug molecules. The muconic acid also has great importance as it is important intermediate in the total synthesis of Deoxynijiromycien, which is natural product.

In conclusion, we exploited a novel application of (diacetoxyiodo)benzene for oxidative cleavage of carbon-carbon aryl diamines, to nitriles as well as a novel route for synthesis of quinones is describe in short reaction time. Both these applications are general, practical, economical, and efficient.
2.9 REFERENCES:

1. For reviews, see Haines-1985, Ref. 11, pp 16-22, 217-222; Fu; Harvey, Chem. Rev.; 1978, 78, 317-361
2. For reviews, see Haines-1988, Ref. 11, pp. 305-323


b) Rabjohn, N.; *Org. React.*, **1976**, 24, 261  

18. a) The name Etard reaction is often applied to any oxidation with chromyl chloride, for example, oxidation of glycols, alkenes, and so on.  

c) Hudlicky, M. Oxidations in Organic Chemistry, American Chemical Society, Washington, DC, 1990, pp. 94–96;  


45. Moreau, J. L.; Bigey, S. F.; Azza, A. A.; Galzy, P.; *Biocatalysis*, 1994, 10, 325
2.10 SPECTRA

Table 5, entry 1
Table 5, entry 1
Table 5, entry 1
Table 5, entry 1
Table 5, entry 2
Table 5, entry 2
Table 5, entry 2
Table 5, entry 3

<table>
<thead>
<tr>
<th>Frequency (cm⁻¹)</th>
<th>Relative Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>309.7</td>
<td>Medium</td>
</tr>
<tr>
<td>2955.0</td>
<td>Strong</td>
</tr>
<tr>
<td>2909.8</td>
<td>Medium</td>
</tr>
<tr>
<td>1569.8</td>
<td>Strong</td>
</tr>
<tr>
<td>1462.4</td>
<td>Weak</td>
</tr>
<tr>
<td>1395.0</td>
<td>Strong</td>
</tr>
<tr>
<td>1324.1</td>
<td>Medium</td>
</tr>
<tr>
<td>1356.8</td>
<td>Strong</td>
</tr>
<tr>
<td>1098.5</td>
<td>Medium</td>
</tr>
<tr>
<td>1072.1</td>
<td>Weak</td>
</tr>
<tr>
<td>1032.6</td>
<td>Strong</td>
</tr>
<tr>
<td>1018.1</td>
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</tr>
<tr>
<td>823.8</td>
<td>Medium</td>
</tr>
<tr>
<td>673.1</td>
<td>Weak</td>
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<tr>
<td>640.8</td>
<td>Medium</td>
</tr>
<tr>
<td>118.5</td>
<td>Strong</td>
</tr>
</tbody>
</table>

Note: The graph shows a spectrum with various peaks indicating different frequencies and relative intensities.
Table 5, entry 3
Table 5, entry 3
Table 5, entry 3
Table 5, entry 4
Table 5, entry 4
Table 5, entry 4
Table 5, entry 6
Table 5, entry 6
Table 5, entry 6
Section-II

A Novel Application of (Diacetoxyiodo)benzene for Synthesis of Quinones from 1,4 Aryl Diamines.

2.2.1 INTRODUCTION:

2.2.1.1 Importance of various API molecules in today’s life:

2.2.1.2 Classification of Quinones:

2.2.2 LITERATURE SURVEY:

2.2.2.1 Synthesis of quinone from 1,4 diamine.

2.2.2.2 From oxidation of amines.

2.2.3 DESIGN AND DEVELOPMENT:

2.2.4 EXPERIMENTAL:

2.2.5 RESULT AND DISCUSSION:

2.2.5.1 Mechanism:

2.2.6 APPLICATION:

2.2.7 SUMMERY AND CONCLUSION:

2.2.8 REFERENCES:

2.2.9 SPECTRA:
2.2.1 **INTRODUCTION:**

Quinones are an important class of heterocyclic compounds. Literature reports reveal that many synthetic quinones derivatives are used in pharmaceutical as anticancer, antibiotic, antitumor, in agrochemical as pesticide, and also found in many natural products.

The first benzoquinone (1) was the first synthesized quinone in the late 1830’s in Liebig’s laboratory as a result of the oxidation of quinic acid with manganese dioxide and sulfuric acid\(^{25}\); this reaction involves dehydration, decarboxylation and oxidation.

In general, quinones are being synthesized from phenols, 1,4-dihydroxybenzenes or hydroquinone’s and dimethoxybenzenes.

Quinones are highly reactive chemical entities and are widely distributed in nature. They exhibit a large variety of biological effects like toxicity to bacteria, fungi, and insects as well as specific biological activity exemplified by vitamin K\(_1\). Plants like *Plumbago rosea*, *Embelia ribes* and *Lawsonia alba*, from which quinones like Plumbagin, Embelin, and Lawsone respectively are obtained, have been used for medicinal purposes in India from ancient times. Quinones are the most extensively studied class of compounds. According to some reports, quinones are the second largest family of anticancer drugs clinically used in United States.\(^1\)

A vast majority of naphthalene and anthracene derivatives in nature are quinones. The quinonoid structural feature is widely spread in naturally occurring compounds isolated from moulds, lichens, plants, insects, which include not only substituted benzoquinones but also substituted polycyclic quinones i.e. for example anthraquinones and naphthoquinones.

These quinonoid systems which play a vital role in biosynthetic routes are found as structural units in antibiotics and pigments and are also found in compounds having anti-haemorrhagic activity (example the vitamin K group). In the laboratory, the substituted quinones are used as oxidizing agents and starting materials for the synthesis of polycyclic compounds by virtue of their dienophilic reactivity in the Diels-Alder reaction.\(^2\)
2.2.1.1 API molecules: Importance in today’s life.

Quinones in biological systems have a varied and significant role. Naphthoquinones of various degrees of structural complexity have antibiotic, antimicrobial, and anticancer activity, e.g., parvaquone,\textsuperscript{3a} atovaquone,\textsuperscript{3b} conocurvone.\textsuperscript{3c} Naphthoquinones may be found in natural dyes e.g., lawson, and fungicides, e.g., phygon\textsuperscript{3d} and are also useful for studying bioenergetic pathways.\textsuperscript{3e} The variety of applications of naphthoquinones has attracted the attention of researchers in preparative chemistry. Below is the schematic presentation (Scheme 2.1) for the importance of naphthoquinone moiety in the synthesis of various API molecules belonging to wide range of therapeutic category from antiprotozoal to anti-HIV.

![Scheme 2.1: Structure and therapeutic category of APIs containing naphthoquinone](image-url)
2.2.1.2 Classification and Nomenclature of Quinones:

*Quinone Background - Nomenclature*

![Figure-1](image)

Quinones are broadly classified into six categories.

1. Benzoquinones

![benzoquinone](image)

2. Naphthoquinones

![naphthoquinone](image)
3. Anthraquinones

![Anthraquinone](image)

4. Anthracyclinones

5. Extended Quinones

6. Miscellaneous Quinones

Benzoquinones are the simplest quinones which found in nature. Very simple benzoquinones are highly reactive species. They rarely occur in higher plants. Ubiquinones are the most widely distributed benzoquinones, found in liver, kidney and some other organs of man. They play a major role in respiratory electron transport chain (ETC). Polyporic acid and a number of its derivatives exhibit limited anti-tumor activity.

Recently it has been shown that some novel benzoquinones possess potential antitumor activity. 2,3,5-trimethyl-6-(3-pyridylmethyl)-1,4-benzoquinone (CV-6504)\(^{4}\) possess antitumor activity. 2,6-dimethoxy-1,4-benzoquinones is also an effective anticancer agents.\(^{5}\)

The distribution of naphthoquinones is sporadic and has been found in leaves, flowers, wood, bark, and fruits. Amongst the major families in which the compounds from this class have been distributed are Juglandaceae, Plumbaginaceae, boraginaceae and Lythraceae. Naphthoquinone normally do not occur as glycosides, but may exist in vivo in reduced form, which may be glycosidic. The Fusarium species elaborates a small representatives group of naphthoquinones, which have a fungal origin. The menaquinones occurs widely in bacteria.
Lapachol has been known to mankind since 1858. It possesses potential antitumor action and is also reported to have an analgesic activity.\textsuperscript{6} Lapachol has been reported to have some cytotoxic potential.\textsuperscript{7}

Lawsone and Plumbagin are also reported to show concentration dependent differential biphasic activity as immunomodulatory agents.\textsuperscript{8} Recent reports on group are potential inhibitors of Topoisomerase 1.\textsuperscript{9}

Anthraquinones form a large and compact group, nearly all of which are polyhydroxy (methoxy) derivatives with little variation in the skeletal structure. Anthraquinones are the largest group of natural quinones and, historically the most important. Many plants from rubiaceae family contain useful anthraquinones mordant dyes and these plants have been used for dyeing textile in many parts of the world since ancient times.\textsuperscript{10}

Doxorubicin probably the most important anticancer drug available because of its relatively broad spectrum of activity, and Daunorubicin is an important agent in treatment of acute lymphocytic and myelocytic leukemia. It contain a planar anthraquinone attached to an amino sugar.\textsuperscript{11}

The Anthracyclinones form a major group and occur as both free and as glycosides (anthracyclines) in combination with various sugars including amino sugars, not all have been isolated but rhodosamine is frequently present. The antibiotics daunomycin and adrimycin (FIG 1H) are from this class of quinones. The pigment collected together under the heading of extended quinones includes some of the most highly condensed aromatic compounds found in nature. Examples of extended quinones are the perylenequinones, the hypericins and the protoaphins in aphids.\textsuperscript{10} The miscellaneous quinones are collection of pigments that do not fit easily into any of above main groups. The examples are piloquinone, the only authentic natural phenanthraquinone, the royleanones and the tanshinones.\textsuperscript{11}
2.2.2 **LITERATURE SURVEY:**

On the basis of literature survey in the present era, there are a variety of methods reported by research scholars, scientists for the synthesis of quinones, by utilizing different substrates. But, in this section attention has been given basically only in quinone from 1,4-diaminobenzene compounds.

1. **Solid State Oxidation of Phenols to Quinones with Sodium Perborate on Wet Montmorillonite K10**

Phenols were oxidized to quinones using sodium perborate (SPB) on wet montmorillonite as oxidant. The reaction was carried out at ambient temperature on the solid phase under solvent free conditions.\(^\text{12}\)

![Scheme 2.2](image)

2. **From 4-bromo-phenol\(^\text{13}\)**

1,4-benzoquinones can also be prepared by using perchloric acid in presence of leadoxide at 20°OC.

![Scheme 2.3](image)

3. **From protected phenol\(^\text{14}\)**
Deprotection or desilylation of phenol gives 1,4–benzoquinone in presence of pyridiniumchlorochromate.

![Scheme 2.4](image)

**Scheme 2.4**

4. **From 4-aminophenol under microwave irradiation**

It can also be synthesized from 4-aminopenol using montomorillonate.

![Scheme 2.5](image)

**Scheme 2.5**

5. **By using hypervalent iodine**

Hypervalent iodine also be used previously for the synthesis of 4,4-benzoquinone starting from 2,2,2-trifluoro-N-(4-hydroxyphenyl)acetamide.
6. By using Sulfuric acid\textsuperscript{17}

1,4 diaminobenzene oxidised in presence of sulphuric acid.

\textbf{Scheme 2.6}

7. Synthesis of quinone from 1,4 diamine

In case of quinone formation from 1,4-diaminobenzene, there are only few methods reported, which includes metal oxides in combination of H\textsubscript{2}O\textsubscript{2}, where the lower yield and \textit{p}-nitro aniline as a major side product is observed (\textbf{Scheme 2.8}).\textsuperscript{18}

\textbf{Scheme 2.7}

8. From oxidation of naphthalene by using different oxidizing agents:

Various differently substituted naphthalene derivatives are oxidized to substituted 1,4 naphthoquinone compounds by using different oxidizing agents.\textsuperscript{19a-c}
9. Synthesis of naphthoquinone by oxidation of naphthol

Oxidation of functionalized phenols to naphthoquinone in presence of hydrogen peroxides and mesoporous titanium–silicate catalyst\textsuperscript{20}

10. Oxidation of 1,2 and 1,4 dihydroxy naphthalene by using hydrogen peroxide\textsuperscript{21}

Oxidation of dihydroxynaphthalene to 1,2 and 1,4 naphthoquinones, which is more convenient and less expensive method than the methods so far known. The procedure involves the oxidation of the dihydroxynaphthalene by $\text{H}_2\text{O}_2$ in methanolic or aqueous solution, depending on the solubility of the dihydroxynaphthalene at room temperature in the presence of catalytic amounts of I$_2$ or HI gives corresponding naphthoquinone compound (as shown in Scheme 1.25)
11. Photosensitized oxidation of 1-naphthol to naphthoquinone

The photosensitized oxidation of naphthol has been received a considerable attention in recent years. It involves the photo oxidation of 1-naphthols to 1,4-naphthoquinones, in which solution of the naphthol in methylene chloride-methanol (9:1) containing Methylene Blue were irradiated with visible light (W lamp) under oxygen (Scheme 1.27). Oxygen uptake was rapid at 15°C, and ceased abruptly after the absorption of 1 mol. equiv In this transformation only 1, 4 naphthoquinone has been formed and none of the 1, 2 isomer.

12. From oxidation of amines:

Naphthoquinone can also be formed by oxidation of naphthylamine by using Fremy’s salt. This mechanism also proceeded by radical pathway as shown in Scheme 2.13.
13. By Diels –alder reaction:

Diels-alder is well known cyclo-addition reaction has been extensively revised\textsuperscript{23} and attention will be focused towards its synthetic aspects\textsuperscript{24}. This reaction proceeded in three steps such as addition of conjugated dienes to starting quinone, aromatization of adducts, and then oxidation of resulting quinols. Diels alder is the most useful method for fusing benzene ring on to existing quinone ring. Yield of these reactions are usually good. In this case when anthroquinone (2,3-dimethyl-9,10-anthroquinone) can be synthesized\textsuperscript{25} by Diels-Alder reaction by using 1,4-naphthoquinones and 2,3-dimethylbuta-1,3-dine are used as a starting materials (Scheme 1.14).

Scheme 2.13 Fremy’s salt mediated oxidation of naphthylamine to naphthoquinone
14. From Synthesis of anhydried:

Synthesis of anthraquinone derivatives catalyzed by AlCl₃/H₂SO₄ under heterogeneous and mild conditions.²⁶

However, the different reagents show varying degree of success as well as limitations due to high reaction temperatures, the possibility of explosion, strongly basic or acidic conditions which may be incompatible with substituents on the aromatic rings and most of these reagents involve metal ions which are not environmentally friendly. So there is increasing emphasis on development of an efficient, clean method for the synthesis of quinone that employ environmentally friendly reagents and preferably without a metal ion thereby reducing the waste generation. From literature survey it is well known that synthesis of quinone from benzamide found fewer papers. So our attention to the synthesis of a quinones from benzamide using hypervalent iodine reagent (III).
2.2.2 **DESIGN AND DEVELOPMENT:**

Molecules with the quinoid structure constitute one of the most interesting classes of compounds in organic chemistry.

Our approach in this method was to increase the scope of a hypervalent iodine, i.e. DIB for the synthesis of quinones from 1,4 diaminoaromatic compounds.

Quinones classes have very important biological property and there are many routes available for its synthesis. Still there is scope to develop new routes starting from cheaply available raw materials.

A details literature survey showed that methods available for the synthesis of quinone have some limitations, like use of catalyst, use of corrosive acid etc.

To overcome these limitations there is scope for development of new route for synthesis of quinone from 1,4 diaminoaromatic compounds.

In fact, we are expected that cleavage of 1,4 diamine gives fumaronitrile, but unpredictably we got surprising quinone. And hence the route has been designed for the synthesis of quinone, which includes the reaction of 1,4-diaminobenzene in presences of hypervalent iodine reagent such as DIB. The synthetic scheme is shown above (Scheme 2.16).

![Scheme 2.16](image)
2.2.3 **EXPERIMENTAL:**

### 1. General Information:

All $^1$H NMR and $^{13}$C NMR spectra were recorded on JEOL AL-300 FT-NMR at 300 MHz and 75 MHz respectively. IR spectra were recorded on a Perkin Elmer RX–100 spectrophotometer (KBr pellet); Mass spectra were taken on THERMO FINNINGAN LCQ advantage max (LCMS). Chemical shift values are expressed in δ units relative to tetramethylsilane (TMS) signal as internal reference in CDCl$_3$ and in DMSO. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s= singlet, d= doublet, t= triplet, br= broad singlet, m= multiplet), coupling constant $J$ (Hz). Infrared spectra (IR) were recorded neat as KBr pellet; absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were recorded on low resolution mass spectrometer (ESI-MS). All solvents were purchased from commercial sources and used without further purification. Wherever necessary the solvents were dried by standard procedures.

### 2. General Procedure for the Oxidation of 1,4-Diaminobenzene:

**Table1, entry 1: Synthesis of 1,4-benzoquinone**

To a stirred solution of (diacetoxyiodo)benzene (2.98 g, 2 equiv) in acetone (15 mL) was added 1,4 diaminobenzene (0.5 g, 1.0 equiv). The reaction mixture was stirred at room temperature. After completion of reaction (TLC), the reaction mixture was quenched in water (20 mL) and further diluted with ethyl acetate (30 mL). The organic layer was separated and washed successively with 10% sodium bisulfate solution (2 x 20 mL), 10% sodium bicarbonate (2 x 15 mL), and water (2 x 20 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give crude product. Pure mucononitrile as a colourless solid was obtained after silica gel column chromatography (10% EtOAc-hexane). *Yield was isolated 0.349g. (70%)*
M.P. 114°C; IR (KBr, cm⁻¹): 3264, 3072, 2946, 1669, 1592, 1313, 1264, 896; ¹H-NMR (60 MHz, CDCl₃): 7.65-7.66 (s, 4H); ¹³C-NMR (75 MHz, CDCl₃): 140.5, 187.2

Table 1, entry 2: Synthesis of 2-chloro-1,4-benzoquinone
2-chlorobenzene-1,4-diamine (0.5g, 1equiv) in 15 ml of acetone was treated by general procedure with DIB (2.25g, 2 equiv) to gave the product with 65% yield (0.328g), M.P. 58°C; IR (KBr, cm⁻¹): 3055, 1670, 1115, 788; ¹H-NMR (60 MHz, CDCl₃): 7.60-7.63 (s, 3H); ¹³C-NMR (75 MHz, CDCl₃): 140.5, 187.2

Table 1, entry 3: Synthesis of 2-methyl-1,4-benzoquinone
2-methylbenzene-1,4-diamine (0.5g, 1equiv) in 15 ml of acetone was treated by general procedure with DIB (2.63g, 2 equiv) to gave the product with 67% yield (0.335 g), M.P. 69°C; IR (KBr, cm⁻¹): 3057, 2926, 2671, 1668, 1600, 1111, 826, 761; ¹H-NMR (60 MHz, CDCl₃): 2.45 (s, 3H), 6.89 (s, 1H), 7.10-7.12 (d, 2H); ¹³C-NMR (75 MHz, CDCl₃): 14.9, 133.9, 136.7, 145.1, 187.2, 187.8

Table 1, entry 4: Synthesis of 1,4-naphthoquinone
Naphthalene-1,4-diamine (0.5g, 1equiv) in 15 ml of acetone was treated by general procedure with DIB (2.03g, 2 equiv) to gave the product with 70% yield (0.348 g) M.P. 121°C; IR (KBr, cm⁻¹): 3050, 1675, 1111, 784; ¹H-NMR (60 MHz, CDCl₃): 7.62-7.94 (m, 6H); ¹³C-NMR (75 MHz, CDCl₃): 126.8, 132.4, 135.5, 138.3, 185.7

Table 1, entry 5: Synthesis of 9, 10-anthraquinone
9,10-dihydroanthracene-9,10-diamine (0.5g, 1equiv) in 15 ml of acetone was treated by general procedure with DIB (1.54g, 2 equiv) to gave the product with 70% yield (0.350 g) M.P. 285°C; IR (KBr, cm⁻¹): 3437, 3070, 1705, 1678, 1624, 1333, 1117, 721; ¹H-NMR (60 MHz, CDCl₃): 7.85-7.86 (d, 4H), 8.27-8.28 (d, 4H); ¹³C-NMR (75 MHz, CDCl₃): 125.6, 132.9, 134.4, 138.1, 182.3, 162.7

Table 1, entry 6: 1-chloroanthracene-9, 10-dione
1-chloro-9,10-dihydroanthracene-9,10-diamine (0.5g, 1equiv) in 15 ml of acetone was treated by general procedure with DIB (1.33g, 2 equiv) to gave the product with 70% yield (0.351 g) M.P. 162°C; IR (KBr, cm⁻¹): 3082, 1673,1574, 1318, 1264, 702; ¹H-NMR (300 MHz, CDCl₃): 7.69-8.30 (m, 7H); ¹³C-NMR (75 MHz, CDCl₃): 127.54,
128.3, 130.3, 133.1, 134.4, 134.7, 135.3, 135.8, 138.5, 182.6, 183.0; MS(ESI) m/z 242 (M⁺)

**Table 1, entry 7: 9, 10-dioxo-9, 10-dihydroanthracene-1-sulfonic acid**

9,10-diamino-9,10-dihydroanthracene-1-sulfonic acid (0.5g, 1equiv) in 15 ml of acetone was treated by general procedure with DIB (1.11g, 2 equiv) to gave the product with 65% yield (0.324 g), (lit.44d mp 218°C); IR (KBr, cm⁻¹): 3455, 1682,1581, 1316, 1228, 1044; ¹H-NMR (300 MHz, DMSO): 7.87-8.45 (m, 7H); ¹³C-NMR (75 MHz, DMSO): 126.9, 127.6, 128.8, 132.5, 132.6, 134.5, 135.5, 136.1, 138.1, 178.8; MS(ESI) m/z 287 (M⁺)

**Table 1, entry 9: 2-aminoanthracene-9, 10-dione**

9,10-dihydroanthracene-2,9,10-triamine (0.5g, 1equiv) in 15 ml of acetone was treated by general procedure with DIB (1.44g, 2 equiv) to gave the product with 66% yield (0.330 g), M.P. 303-306°C; IR (KBr, cm⁻¹): 3434, 3331, 1673, 1625, 1588, 1337, 714m; ¹H-NMR (300 MHz, DMSO): 6.68 (s, 2H) 6.92-8.10 (m, 7H); ¹³C-NMR (75 MHz, DMSO): 109.8, 118.2, 126.5, 129.7, 133.4, 133.5, 134.4, 135.0, 154.8, 180.2; MS(ESI) m/z 224 (M⁺)

1) **Application- Synthesis of Lawson** *(See IR Spectra-Lawson)*

1,4-diamino-1,4-dihyronaphthalen-2-ol (0.5g, 1equiv) in 15 ml of acetone was treated by general procedure with DIB (1.82g, 2 equiv) to gave the product with 55% yield (0.271 g); M.P. 192°C; IR (KBr, cm⁻¹): 3156, 2893, 1676, 1577, 1381, 1213, 872, 720; ¹H-NMR (60 MHz, DMSO): 3.5 (bs, 1H), 6.18 (s, 1H), 7.80-8.10 (m, 4H)
2.2.4 **RESULT AND DISCUSSION:**

In this section we used same optimized reaction condition for 1,4-diaminobenzene as discussed earlier in previous section-I that for 1,2-diaminobenzene. Considering this fact, we studied various substituted 1,4-diaminobenzenes in acetone and obtained the corresponding quinones in short reaction times (Table 1).

In order to explore the reaction scope, a variety of substituted 1,4-diamino aryl compounds was prepared by standard reported procedures and converted into the corresponding quinones by oxidation in moderate to good yields, and the results are summarized in Table 1.

During the course of substrate study, it was observed that substituted 1,4-diaminobenzenes were also suitable for this transformation, giving the quinones in moderate to good yields in short reaction times (Table 1, entries 2, 3). The method was also successfully applied to the synthesis of napthaquinone and anthraquinone from the corresponding diamino compounds (Table 1, entries 4–7). While the reaction with 1,3-diaminobenzene was unaffected (Table 1, entry 8).

Table 1. Reaction of (diacetoxyiodo)benzene with o-aryl diamino compoundsa

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield b (%)</th>
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<td>3</td>
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<td><img src="image6" alt="Product 3" /></td>
<td>15</td>
<td>67</td>
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</tbody>
</table>
4 | ![Image](image1.png) | ![Image](image2.png) | 10 | 70  
5 | ![Image](image3.png) | ![Image](image4.png) | 15 | 70  
6 | ![Image](image5.png) | ![Image](image6.png) | 10 | 70  
7 | ![Image](image7.png) | ![Image](image8.png) | 25 | 65  
8 | ![Image](image9.png) | ![Image](image10.png) | 10 | 66  

*aReaction conditions: substrate (4.6 mmol), (diacetoxyiodo)benzene (2 equiv) in acetone (15 mL), rt.
*bIsolated yields after column chromatography and structures were confirmed by comparison of IR and 1H NMR with authentic materials.

### 2.2.5.1 MECHANISM: Proposed Mechanism for Quinone formation

![Mechanism Diagram](image11.png)

*Figure 2*
In this mechanism, nucleophilic attack of amine on electrophilic hypervalent iodine took place and subsequently acetate ion will liberate. Again liberated acetate ions absorb a proton from amine and by concerted way formation of imine, which was in situ hydrolysis to give quinone. Here hydrolysis took place because of moisture present in solvent.

### 2.2.5 APPLICATION:

This method of quinone synthesis from a 1,4-diaminocompounds has great importance. Variety of quinones can also be synthesized, and they are successfully used in the synthesis of natural products, as drug intermediates etc.

2) **Synthesis of Lawson:**

We used here our methodology for the synthesis of Lawson a natural product (Scheme 2.17). This compound can use in a verity of reactions, or intermediate in the synthesis. It is an also important starting material for the synthesis of Sterekunthal A.

![Scheme 2.17](image-url)
2.2.6 **SUMMARY AND CONCLUSION:**

Quinones are highly reactive chemical entities and are widely distributed in nature. They exhibit a large variety of biological effects like toxicity to bacteria, fungi, and insects as well as specific biological activity exemplified by vitamin K1. Quinones are the most extensively studied class of compounds. According to some reports, quinones are the second largest family of anticancer drugs clinically used in United States.

In summary the new route has been developed for the synthesis of quinone. This new route started from the oxidation of 1,4-diaminocompounds which is a cheap starting material with DIB in acetone as a solvent. This reaction was carried out in room temperature for 10 min. to obtained a quinones in a good yield.

Quinones in biological systems have a varied and significant role. Naphthoquinones of various degrees of structural complexity have antibiotic, antimicrobial, and anticancer activity, e.g., parvaquone, atovaquone, conocurvone. Naphthoquinones may be found in natural dyes e.g., lawsone, and fungicides, e.g., phygon and are also useful for studying bioenergetic pathways.

In conclusion, we exploited a novel application of (diacetoxyiodo)benzene for oxidative cleavage of carbon-carbon aryl diamines, to nitriles as well as a novel route for synthesis of quinones is describe in short reaction time. Both these applications are general, practical, economical, and efficient.
2.2.7 REFERENCES:

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23) Butz, L. W.; Rytina, A. W.; Org. Reactions 1949, 5, 136
2.2.8 **SPECTRA:**

*Table 1, entry 6*
Table 1, entry 6

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**Table 1**

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Table 1, entry 6
Table 1, entry 7
Table 1, entry 7
Table 1, entry 7
Table 1, entry 8

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[Chemical structure image]

*Development and Application of New Methodologies for Synthesis of Bioactive Molecules* 172
Table 1, entry 8
Table 1, entry 8