PART-B
CHAPTER-B.I
CHAPTER-B.I

QUATERNARY AMMONIUM SALTS IN 
OXIDATION OF ORGANIC SUBSTRATES

— A REVIEW

Quaternary ammonium salts are usually termed as the phase transfer catalysts (PTC). These phase transfer catalysts offer excellent opportunities for carrying out oxidations reactions using inexpensive primary oxidants such as oxygen, sodium hypochlorite, hydrogen peroxide, permanganate, periodic acids and others. Phase transfer catalyzed oxidation occurs by a variety of mechanism. One of the most popular aspects of PTC oxidations is the frequent use of transition metal co-catalysts, often in the form of easily transferable anions such as tungstate, molybdate, chromate and others. The combination of phase transfer catalysts plus metal co-catalysts allows the chemists to use the low cost basic oxidants as a source of oxidizing power.

PERMANGANATE OXIDATION

Permanganate anions or salts are among the easiest to transfer from aqueous to organic solutions. Quaternary ammonium, phosphonium and arsonium salts, crown ethers and some linear polyethers are all versatile transfer agents. Preformed quaternary ammonium permanganates can be prepared by simply mixing a quaternary ammonium chloride in organic solvent with
aqueous potassium permanganate. Removal of solvent from the organic layer leaves solid quaternary ammonium permanganate which is useful for the oxidation of several substrates. However, most quaternary ammonium permanganates are explosive and should be handled with utmost care. The PTC permanganate oxidation of olefins can be made to yield cis-diols, α-hydroxycarbonyls, carboxylic acids or aldehydes are the major products depending upon the reactions conditions and workup, as shown in Scheme B.I.1.

SCHEME B.I.1

Oxidation of olefins with $Q^+NMnO_4^-$

PTC–MnO₄ oxidation of alkynes in liquid-liquid systems where one phase is water, usually produces carboxylic acids in good yields, however, in solid-liquid conditions near anhydrous conditions with CH₂Cl₂ as the solvent, produces α-diketones as shown in Scheme B.I.2.
PTC permanganate oxidation of alcohols\textsuperscript{25}, phenols\textsuperscript{26}, aldehydes\textsuperscript{27} and ethers\textsuperscript{28} usually involves two liquid phase processes and produces carboxylic acids, quinones, and other oxidized products.

**OXIDATION WITH HYPOCHLORITE, HYPOBROMITE**

Lee and Freedman first recognized the value of hypochlorite as an inexpensive and readily available oxidant for use in PTC reactions\textsuperscript{29,30}. Hypochlorite anions in aqueous solutions exist in equilibrium with HOCl, chlorine and water, with the major species determined by pH (Scheme B.I.3).

**SCHEME B.I.3**

\[
\text{Cl}_2 + \text{H}_2\text{O} \xrightleftharpoons{\text{HCl}} \text{HOCl} \xrightarrow{\text{OH}^-} \text{H}_2\text{O} + \text{OCl}^- 
\]

The authors oxidized benzylic acid and secondary aliphatic alcohols to the corresponding carbonyl compounds using the hypochlorite in the presence of quaternary ammonium salts as shown in Scheme B.I.4.
Aliphatic primary alcohols were oxidized slowly to aldehydes and these are rapidly oxidized to the carboxylic acids which are stable under the reaction conditions.

Oxidation of 2,4-dimethyl-2-aminopentanitrile with aqueous sodium hypochlorite under phase transfer conditions, and at low temperatures, provide a low cost route to azoisohexanitrile (Scheme B.I.5).

The most interesting aspect of this oxidation is the use of two quaternary ammonium salts as catalysts. One catalyzes the organic phase reaction so that it takes place at low temperature and other speed up the transfer of the difficultly transferable hypochlorite ion to the organic phase. PTC-hypochlorite oxidation of primary amines, where the nitrogen is attached to
a terminal \(-\text{CH}_2-\) group yields nitriles which is a synthetically useful reaction (Scheme B.I.6, Reaction 1). Broda and Dehmlow\(^ {31} \) oxidized thioamides with hypochlorite under PTC conditions to produce synthetically useful materials. For example thioureas produces carbodiimides (Scheme B.I.6, Reaction 2). Further epoxidation of phenanthrene and other aromatics by hypochlorite with ordinary phase transfer catalysts gave the corresponding epoxides in good yield\(^ {32} \) (Scheme B.I.6, Reaction 3).

**SCHEME B.I.6**

**Reaction 1**

\[
R-\text{CH}_2-\text{NH}_2 + 2\text{NaOCl (aq.)} \xrightarrow{\text{Bu}_4\text{NCl}} R-\text{CN} + 2\text{NaCl} + \text{H}_2\text{O}
\]

**Reaction 2**

\[
\begin{align*}
R-\text{NH}-\text{C}-\text{NH-} & + \text{NaOCl (aq.)} \\
\bigg\| & \xrightarrow{\text{PhCH}_2\text{NET}_3\text{Cl}} \\
\bigg\| & \text{CH}_2\text{Cl}_2 \\
\text{S} & \xrightarrow{\text{PhCH}_2\text{NET}_3\text{Cl}} \\
\text{R-N=C=N-R} & \quad 55-80\% 
\end{align*}
\]

**Reaction 3**

![Diagram of reaction 3]
Phase transferred hypochlorite with ruthenium oxide as cocatalyst oxidizes methyl benzenes containing electron withdrawing substituents to the corresponding carboxylic acids in high yields. A mechanism of the oxidation was suggested as shown in Scheme B.I.7.

**SCHEME B.I.7**

\[
\begin{align*}
\text{CH}_3 + 4\text{NaOCl} & \xrightarrow{\text{Bu}_4\text{N}^+\text{Br}^- / \text{RuO}_4} \text{COONa} \\
X = \text{EWG}
\end{align*}
\]

Sodium hypochlorite in the presence of a phase transfer catalyst has also been used as a chlorinating agent. Alkyl aromatics are halogenated, a particular example is the oxidation of ethylbenzene with \( \text{NaOCl} \) in \( \text{CH}_2\text{Cl}_2 \) containing \( \text{Bu}_4\text{N}^+\text{Br}^- \) as the phase transfer catalyst which gave a mixture of products as shown in Scheme B.I.8.
Barak and Sasson \(^{37}\) suggested that \(\text{H}_2\text{O}_2\) is an attractive oxidizing agent because it is inexpensive, readily available and its byproducts cause no pollution problems. They noted that the performance of \(\text{H}_2\text{O}_2\) as an oxidant in two phase systems is remarkably improved by the addition of quaternary ammonium phase transfer agents \(^{38}\) during the oxidation of alkenes to epoxides \(^{39}\), oxidation of alcohols \(^{40}\), aldehydes \(^{41}\), sulfides \(^{42}\) and ketones \(^{43}\).

On shaking quaternary ammonium salt solutions in \(\text{CH}_2\text{Cl}_2\) with aqueous 35% \(\text{H}_2\text{O}_2\), various amounts of \(\text{H}_2\text{O}_2\) are transferred to the organic phase. Transfer of \(\text{H}_2\text{O}_2\) may occur by formation of complexes with anions similar to hydration by water. Hydrogen peroxide oxidation of cyclohexene using a quaternary ammonium salt and a co-catalyst multivalent metal tends to give different
products depending upon the nature of the metal co-catalyst as shown in Scheme B.1.9.

**SCHEME B.1.9**

Aqueous H$_2$O$_2$ oxidizes polynuclear aromatic hydrocarbons such as phenanthrene, pyrene, benzo(a)pyrene, chrysene, o-phenanthrene etc. in the presence of a phase transfer catalyst plus a tungstate cocatalyst and polyphosphoric acid to give aromatic dicarboxylic acid in high selectivity and conversion $^{44}$ (Scheme B.1.10).

**SCHEME B.1.10**
Barak and Sasson observed that when catalyzed by quaternary ammonium salts and ruthenium salts, $\text{H}_2\text{O}_2$ oxidizes cumene at 67% conversion to a mixture of 2-phenylpropane-2-ol and acetophenone (Scheme B.I.11).

**SCHEME B.I.11**

Further, $\text{H}_2\text{O}_2$ oxidation of aniline in the presence of quaternary ammoniumbromide gives a mixture of nitro and azoxybenzene. When ruthenium chloride and quaternary ammoniumbromide are used as catalysts, nitrobenzene becomes the main product (Scheme B.I.12).

**SCHEME B.I.12**
PHASE TRANSFER CATALYST-AIR OXIDATION

PTC has been used in a diverse range of air or oxygen oxidations. These include reactions involving carbanions, free radicals, "activated" oxygens, singlet oxygen and transition metal mediated oxidation systems. Oxidation of compounds with acidic C–H bonds proceed by formation of a carbanion using sodium hydroxide which when followed by addition of oxygen, rearrangement or decomposition of the intermediate peroxide anion occurs. These reactions are usually conducted with oxygen under pressure and at temperature of 40–50 °C. For example, the oxidation of phenylisopropyl ketone as shown in Scheme B.I.13.

SCHEME B.I.13

The role played by the PTC is to assist the formation of carbanion by transfer of hydroxide into the organic phase in a highly active form from where it can react with acidic C–H bond of the substrate. Halpern and Lysenko examined the PTC–NaOH catalyzed oxidation of dihalodiphenylmethanes to the corresponding dihalobenzoquinones with oxygen with findings similar to that of Sasson et. al. as shown in Scheme B.I.14.
Newmann and Sasson found that oxidation of p-nitrotoluene with oxygen in PTC system with NaOH, and with mechanical agitation, gave only dimeric products, whereas the use of ultrasonic agitation gave significant yields of p-nitrobenzoic acid \(^{52}\) (Scheme B.I.15).

The use of Rose Bengal [3,4,5,6-tetrachloro-2-(2,4,5,7-tetraido-6-hydroxy-3-oxo-3H-xanthen-9-yl)benzoic acid disodium salt] as a photosensitizer to convert triplet oxygen to singlet oxygen is not normally useful for oxidation,
but under PTC condition it can be used as an initiator of oxidation where photochemical generation of singlet oxygen can occur, producing selective oxidation of many organic compounds (Scheme B.1.16).

SCHEME B.1.16

\[
\text{Phenyl + O}_2 \xrightarrow{(+ \text{(R-N)}_2 \text{Rosebengal})} \text{Phenol}
\]

PHASE TRANSFER OXIDATION BY PERSULFATES

Persulfuric acid exists in two forms:

\[
\begin{align*}
\text{Peroxomonosulfuric acid} & \quad \text{Peroxydisulfuric acid} \\
\text{(Caro's acid)} & \quad \text{H-O-S-O-S-O} \\
\end{align*}
\]

These acids are unstable in aqueous solutions, hydrolysing to sulfuric acid and \(\text{H}_2\text{O}_2\). Some oxidation with persulfates do not require use of phase transfer catalysts but in some cases peroxyulfate anion can be used with phase transfer systems in several ways. They may be transferred directly to an organic phase for oxidation. Cocatalyst such as cerium, osmium, ruthenium in anionic form, may be used as transferred oxidants, while the persulfate acts as the primary oxidant to keep the cocatalyst anion in the oxidized form. Potassium persulfate, under PTC conditions, oxidizes sulfides to sulfoxides and sulfones (Scheme B.1.17).
Catalytic amount of ruthenium anion, generated by an aqueous phase reaction of RuCl$_2$, with potassium peroxydisulfate, are readily transferred into the organic solutions by quaternary ammonium salts for selective oxidation of benzylic and allylic alcohols to corresponding aldehydes and ketones (Scheme B.I.18).

**PHASE TRANSFER CATALYSIS WITH CHROMIUM COMPOUNDS**

Chromate ion is easily transferred from acidic aqueous solution into organic media, but not from basic or neutral aqueous medium$^{54}$. Chromate has been used as a mild and selective oxidant for reactions in a "stoichiometric PTC" technique wherein the chromate is first attached to an anion exchange resin, and then the organic material to be oxidized is passed through the insoluble solid, using a full molar quantity of oxidant$^{55}$. Dichromate dianions
is more difficult to transfer than chromate, although it has been used in a solid-liquid PTC technique with triacetylmethylammoniumchloride in organic solvent for oxidation of benzyl and secondary alcohols to the corresponding carbonyl compounds \(^{56}\). Dichromate can be extracted into organic solutions with Adogen-464 and these solutions oxidize allylic and benzylic alcohols to aldehydes or ketones in a rather slow reaction (15–18 hrs at 55 °C) \(^{57}\). If the aqueous dichromate phase is acidified with H\(_2\)SO\(_4\), a species can be extracted with tetrabutylammoniumhydrogensulfate into CH\(_2\)Cl\(_2\) which oxidizes primary alcohols to aldehydes within minutes \(^{58,59}\).

**PHASE TRANSFER CATALYST OXIDATION WITH HNO\(_3\), PERIODATE AND RELATED OXIDIZING AGENTS**

HNO\(_3\) oxidation of thioethers, mediated by gold salts, AuCl\(_4^-\), in combination with quaternary ammonium cations, gives sulfoxides \(^{60}\). Attack on the thiol group is selective even in the presence of other oxidizable functional groups (Scheme B.1.19, Reaction 1). PTC oxidation with periodate and related oxidizing agents involves the cleavage of 1,2-diols to the expected aldehydes and ketones in 85-90 % yield \(^{61}\). Sodiumperiodate under PTC conditions, oxidizes some unsaturated compounds to the allylic oxygenated products \(^{62}\). Tetraalkylammoniumperiodates in organic solvents may be prepared by mixing an organic solution of the quaternary salt with sodium periodate in water and this homogeneous ion pair extraction type oxidations have been used.
to oxidize sulfides, 2-hydroxyacids, 2-bromoketones and arylacetic acids \(63,64\) (Scheme B.I.19, Reaction 2).

**SCHEME B.I.19**

**Reaction 1**

\[
\begin{align*}
R - S - R' & \xrightarrow{\text{HNO}_3 \text{ (aq.)}} \text{Bu}_4\text{N} \text{AuCl}_4 \quad R - S - R' \\
\end{align*}
\]

**Reaction 2**

\[
\begin{align*}
\text{OH} & \quad \text{R-C-COOH} + \text{NaIO}_4 \quad \text{PTC} \quad \text{R-C-R'} \quad (80\text{–}90\%) \\
\text{OH} & \quad \text{Ph-CH-COOH} \quad \text{PTC} \quad \text{NaIO}_4 \quad \text{Ph-CHO} \quad (80\%) \\
\text{COOH} & \quad \text{COOH} \quad \text{PTC} \quad \text{NaIO}_4 \quad \text{R-CHO} + \text{R-COOH} \\
\text{Ph-S-Ph} & \quad \text{PTC} \quad \text{NaIO}_4 \quad \text{Ph-S-Ph} \\
\end{align*}
\]

In the presence of phase transfer catalyst, perborate is extracted from aqueous \(\text{NaBO}_3\) into \(\text{CH}_2\text{Cl}_2\) where \(\alpha,\beta\)-unsaturated ketones can be oxidized to
epoxides. The same reagent have been used for the oxidation of several aromatic amines to the nitro compounds (Scheme B.I.20, Reaction 1 & 2).

**SCHEME B.I.20**

**Reaction 1**

\[
\begin{align*}
\text{C=CH–C-CH}_3 \quad & \xrightarrow{\text{NaBO}_3, \ \text{(C}_6\text{H}_13)_4\text{NHSO}_4, \ \text{75 min.}} \\
\text{O} & \quad \text{C-CH}_3
\end{align*}
\]

**Reaction 2**

Potassium ferrate, under phase transfer conditions, has been found to be a highly selective oxidant for conversion of unsaturated alcohols to unsaturated aldehydes in yields ranging from 80–96%.

Potassium superoxide reacts very rapidly with water to produce oxygen and KOH. However, in the absence of water, potassium superoxides can be used in PTC systems, for example, in a solid–liquid system catalyzed by 18-crown-6, it acts as a powerful oxidizing agent. Thus K₂O oxidizes \(\alpha\)-disubstituted compounds to the corresponding carboxylic acids (Scheme B.I.21).
Potassium superoxide in benzene, with 18-crown-6 as catalyst, can also behave as a peroxidizing agent, via an $S_N2$ reaction to produce peroxides from alkyl halides $^{67}$. However, if DMSO is present, alcohols are produced instead of peroxides $^{68}$.

Sodium telluride with phase transfer catalyst has been used as a mild and highly selective oxidizing agent for conversion of thiols to unsymmetrical disulfides $^{69}$.

Literature is replete with such examples where the quaternary ammonium salts have been used as a catalyst for assisting the oxidation of organic substrate with a primary oxidant. Presently, synthetic organic chemists are engaged in modifying easily available quaternary ammonium salts so as to used them as the reagent (primary oxidant) itself. Some examples mentioned in this review falls into this category. Some additional examples of modification of the usual quaternary ammonium salts and their use as reagents are mentioned subsequently:

1. Tetrabutylammoniumhydrogensulfate was converted to the tetrabutylammoniumfluoride by the treatment of an aqueous solution
of TBAHSO$_4$ with KF.2H$_2$O. The resulting TBAF was used for
the esterification of several carboxylic acids to the esters
(Scheme B.1.22, Reaction 1).

2. Kim et al. 71 had reported the synthesis of chiral N-(3,5-di-t-
but-4-methoxy)benzylcinchoridiumbromide and performed the
enantioselective Michael reaction of malonates and chalcones.

3. White et al. 72 had prepared tetra-n-propylammoniumpermanganate
(TPAP) and used it as a mild room temperature oxidant of several
organic substrates.

4. Khan et al. prepared cetyltrimethylammoniumtribromide and
tetrabutylammoniumtribromide and used these tribromides for the
synthesis of α-bromoenones from the corresponding enones
(Scheme B.1.22, Reaction 2) 73. The authors have also used
these reagents for the cleavage of dithioacetals to the
corresponding carbonyl compounds 74 (Scheme B.1.22, Reaction 3).

5. In another study, benzyltrimethylammonium ICl$_4$ was prepared
from benzyltrimethylammoniumhydrogensulfate and used
for the conversion of several benzaldoximes to oxazolines
(Scheme B.1.22, Reaction 4) 75.

Similarly other quaternary ammonium salts were prepared and used for
the oxidative conversion of several oximes, phenylhydrazones and
semicarbazones to the parent carbonyl compounds. This property is discussed in
detail in subsequent chapters.
In our search for low costs, sensitive, easy to handle, environmentally benign and recyclable oxidizing agents, it was observed that the easily available tetra-n-alkylammoniumbromides could be converted by a mild and efficient
method to the corresponding tetra-n-alkylammoniumbromates and the experiments carried with these bromates indicate that they are excellent oxidizing agents for the oxidation of organic substrates. Bromates, in the form of their metal salts, have not been used as an oxidizing agent in synthetic organic chemistry, although thermochemical data in aqueous solutions indicate that bromates are strong oxidizing agents. The main reason why bromates have not been used extensively in organic chemistry is mainly because of their poor solubility in most organic solvents and consequently homogeneous phase oxidation of organic substrates is not possible.

It is deemed appropriate at this point to give a brief review of the chemical characteristics of halate ions with special reference to the bromates.

INTRODUCTION TO THE CHEMISTRY OF HALATE IONS

The preparative chemistry and technical applications of the halogen oxyacids and their salts have been actively pursued and developed for over centuries and can be summarized in terms of thermal decomposition of the halates and their complex redox chemistry reflects the interplay of both thermodynamic and kinetic factors. On the one hand, thermodynamically feasible reactions may be sluggish, whilst, on the other hand, traces of catalyst may radically alter the course of the reaction. In general, for a given cation, the thermal stability decreases in the sequence iodate > chlorate > bromate, but the mode and ease of decomposition can be substantially modified. For example, alkali metal chlorates decomposition when fused.
However, in the presence of a transition-metal catalyst such as MnO₂, decomposition of KClO₃ to KCl and oxygen begins at about 70° C and vigorously at 100° C.

\[
\text{2ClO}_3^- \rightarrow 2\text{Cl}^- + 3\text{O}_2
\]

For bromates and iodates, disproportionation to halides and perhalates is not thermodynamically feasible and decomposition occurs either with formation of halide and liberation of O₂ or by the formation of the oxide.

\[
\text{4XO}_3^- \rightarrow 2\text{O}^{2-} + 2X_2 + 5\text{O}_2
\]

\((X = I, Br)\)

The oxidizing power of the halate ions in aqueous solution, as measured by their standard reduction potentials, decreases according to the following sequence:

Bromate \(\geq\) Chlorate > Iodate
The oxidizing power of the bromate ions in aqueous solution is the highest among the halites though the reaction rates are moderate. Some oxidation reactions shown by bromate ions in aqueous solution are summarized as shown in Scheme B.I.23.

**SCHEME B.I.23**

![Scheme B.I.23](image)

In spite of the good oxidizing characteristics of the bromate ion, it has found limited use in organic synthesis. A few instances of the use of bromates as an oxidizing agent finds mention in the oxidation of gallic acid \(^79\), and in the Belousov–Zhabotinski oscillation reactions \(^80, 81\).
**PREPARATION OF TETRA-n-ALKYLAMMONIUMBROMATE**

In this study, three types of quaternary ammonium bromates were prepared namely the tetrathylammoniumbromate tetra-n-propylammoniumbromate, and tetra-n-butylammoniumbromate, the starting compounds being the respective bromides which are commercially available. It has been reported in literature that inorganic bromides can be converted to the bromates by passing chlorine gas through an alkaline solution of the bromide. Taking the clue from this reported procedure, chlorine gas was passed through an alkaline (aqueous NaOH) solution of the tetra-n-alkylammoniumbromide. On prolonged passage of chlorine gas, a yellow to orange oil separated which solidified on standing. The solid was separated by filtration and dried. A second crop of the yellow/orange precipitate was obtained by neutralizing the filtrate with dil. HCl. This second crop of the solid was also collected and observed to have similar characteristics with the first crop and therefore combined. The tetra-n-alkylammoniumbromates so prepared were soluble in the usual organic solvents as well as in water. There was however, a difference in the solubility of the three bromates in water. The tetraethylammoniumbromate and tetra-n-propylammoniumbromate were extensively soluble in water whereas the tetra-n-butylammoniumbromate was sparingly soluble in water. The three bromates responded positively to all the preliminary test for bromates. No precipitate was obtained on addition of AgNO₃ to an aqueous solution of the bromates,
however, addition of AgNO₃ after boiling an acidified aqueous solution gave a light yellow precipitate of the silver bromide essentially due to the decomposition of the bromate to the bromide in acid solution according to the Reaction 1, Scheme B.I.24.

On strong heating of an acidic solution of the bromate, oxygen evolution was observed which was detected by alkaline pyrogallol solution. The decomposition of the bromate to oxygen occur as per Reaction 2, Scheme B.I.24.

**SCHEME B.I.24**

*Reaction 1*

\[
2 \text{BrO}_3^- \rightarrow 2 \text{Br}^- + 3 \text{O}_2
\]

*Reaction 2*

\[
4 \text{BrO}_3^- \rightarrow 2 \text{O}^{2-} + 2 \text{Br}_2 + 5 \text{O}_2
\]

The fact that bromate give oxygen on heating or on acidification, suggested that it can be used as a primary oxidant for organic substrates. The composition and structure of the two bromates prepared were established by UV-visible, \(^1\)H-NMR spectroscopy and C,H,N analysis. Elemental analysis and \(^1\)H-NMR spectra gave conclusive evidence of the structure of all the three quaternary ammonium bromates prepared. Detail procedure of preparation and the
physical, chemical, and spectral characteristics of the bromates are given in the experimental section of this chapter. To establish that these bromates were oxidizing agents, a simple experiment was carried out in which several aromatic aldehydes were brought into reaction with these bromates, individually, in an appropriate solvent in inert nitrogen atmosphere, care was taken to expel the air from the reaction vessel. A small amount of dil. CH₃COOH was used to assist decomposition of the bromates during reflux. The results indicated that the bromates oxidized the aldehydes to the corresponding carboxylic acids. The fact that the quaternary ammoniumbromates are good oxidizing agent was established. Both the unspent bromates and the byproducts of the reaction were found to be water soluble and hence recovery of the product carboxylic acids were enormously simplified and involved addition of the reaction mixture to a large excess of water whence the product carboxylic acids precipitated out and recovered by simple filtration. The products were purified by repeated washing with water. Finally the products were dissolved in ethanol and reprecipitated by addition to a large excess of distilled water. The carboxylic acids were identified by comparing their melting points from literature and comparing their IR spectra with authentic samples of the products. The yield of the resultant carboxylic acids were as high as 85–90%. 
EXPERIMENTAL

The tetraethylammoniumbromide, tetra-n-propylammoniumbromide and tetra-n-butylammoniumbromide were produced from Loba Chimie (India) Ltd. Chlorine gas was prepared in the laboratory by the action of KMnO₄ on conc. HCl. All solvents were distilled under reduced pressure before use. IR spectra of the compounds reported were recorded in Perkin Elmer 1600 FT-IR spectrometer, in KBr discs. ¹H-NMR spectra recorded in EM 390, 90 MHz spectrometer in CDCl₃ and TFA with TMS as internal standard. Elemental analysis was done in a Hitachi 026 CHN analyzer. Chromatography was performed in prepared silica gel plates. Melting points were recorded in an apparatus from Scientific devices, India, Type MP-D in open capillaries.

Preparation of tetra-n-alkylammoniumbromate

(General procedure)

0.01 mol of the tetra-n-alkylammoniumbromide was dissolved in 50 ml of 5% aqueous NaOH, Cl₂ gas was passed through this solution continuously till a yellow oil separated. The reaction mixture was kept overnight whence the yellow oil solidified. The solid was filtered out, washed several times with water and dried. A second crop of the product was obtained on acidification of the filtrate with dil. CH₃COOH.

Using the general procedure, all the three alkylammoniumbromates namely tetraethyl, tetra-n-propyl, tetra-n-butylammoniumbromates were prepared.
Tetraethylammoniumbromate: Yield 84%; m.p. 79°C; colour orange, \(^1\)H-NMR \(\delta\) (CDCl\(_3\)) 2.6 (m, 12 H), 4.1 (m, 8H), C,H,N analysis found C, 37.3%; H, 7.72%; N, 5.39%; Calcd. C, 37.21%; H, 7.75%; N, 5.43%. Soluble in water and usual organic solvents.

Tetra-\(n\)-propylammoniumbromate: Yield 74%; m.p.114–116°C; colour yellow, \(^1\)H-NMR \(\delta\) (CDCl\(_3\)) 1.2 (t, 3 H), 2.3 (m, 2H), 4.5 (t, 2H); C,H,N analysis found C, 46.2%; H, 9.15%; N, 4.18%; calculated C, 45.86%; H, 8.92%; N, 4.46%. Soluble in water and usual organic solvents.

Tetra-\(n\)-butylammoniumbromate: Yield 70–75%; m.p. 61–63°C; colour yellow, \(^1\)H-NMR \(\delta\) (CDCl\(_3\)) 1.3 (t, 3H), 2.3 (m, 2H), 2.8 (m, 2H), 4.8 (t, 2H), C,H,N analysis found C, 50.86%; H, 9.92%; N, 3.93%; calculated C, 51.88%; H, 9.73%; N, 3.78%. Sparingly soluble in water but freely soluble in almost all organic solvents.

**OXIDATION OF AROMATIC ALDEHYDES TO THE CARBOXYLIC ACIDS**

**General procedure:**

0.01 mol of the aromatic aldehyde was dissolved in 50 ml of an appropriate solvent and the reaction vessel was flushed with nitrogen gas to expel all the air present. To this solution 0.01 mol of the quaternary ammoniumbromate dissolved in the same solvent was added and the reaction mixture refluxed till the yellow/orange colour of the reaction mixture faded to almost colourless. The reaction was monitored periodically by TLC using
prepared silicagel H plates using ethylacetate as the eluent. The reaction mixture was co-chromatographed with authentic samples of the starting aldehyde and the target carboxylic acid as references. The total disappearance of the aldehyde indicated completion of the reaction. The reaction mixture was brought to room temperature and quenched in large excess of water. The product carboxylic acids precipitated out, filtered, washed several times with water and dissolved in 2\% NaOH solution and reprecipitated by acidification with dil. HCl. When tetra-n-butylammoniumbromate was used as the oxidant, the product carboxylic acid was washed several times with water, dissolved in ethanol and reprecipitated by addition of the ethanol solution to a large excess of water. This operation had to be repeated several times to give pure samples of the product carboxylic acid. The products were identified by comparing their melting points from those obtained in literature and also by comparing their IR and \(^1\)H-NMR spectra. The reaction scheme is shown in Scheme B.I.25 and the results of the reactions carried out are summarized in Table B.I.1.

**SCHEME B.I.25**

\[ \text{R}_4\text{NBr} \xrightarrow{\text{ CHO}} \text{Cl}_2 \xrightarrow{\text{aq. NaOH (5\%)}\text{ }} \text{R}_4\text{NBO}_3 \]

\[ \text{CHO} \xrightarrow{\text{R}_4\text{NBrO}_3 \text{ solvent}} \text{COOH} \]

\( X = \text{substituents at the benzene ring} \)
TABLE B.I.1

(Ref. Scheme B.I.25)

Oxidation of aromatic aldehydes to carboxylic acid using tetra-n-alkylammoniumbromates

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Substrate</th>
<th>Product</th>
<th>Reflux Time (hrs)</th>
<th>Yield (%)</th>
<th>M. P. of products (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Obs.</td>
</tr>
<tr>
<td>1.</td>
<td>CHO</td>
<td>CHO COOH</td>
<td>4</td>
<td>88</td>
<td>120 122</td>
</tr>
<tr>
<td>2.</td>
<td>Cl-CHO</td>
<td>Cl-CHO COOH</td>
<td>3</td>
<td>93</td>
<td>240 243</td>
</tr>
<tr>
<td>3.</td>
<td>Br-CHO</td>
<td>Br-CHO COOH</td>
<td>4</td>
<td>90</td>
<td>156 155</td>
</tr>
<tr>
<td>4.</td>
<td>CHO CH3O</td>
<td>CHO COOH</td>
<td>3</td>
<td>96</td>
<td>182 183</td>
</tr>
<tr>
<td>5.</td>
<td>Cl-CHO Cl</td>
<td>Cl-CHO COOH</td>
<td>3</td>
<td>92</td>
<td>210 209</td>
</tr>
<tr>
<td>6.</td>
<td>Ph-CHO</td>
<td>Ph-CHO COOH</td>
<td>3</td>
<td>84</td>
<td>133 133</td>
</tr>
<tr>
<td>7.</td>
<td>CHO</td>
<td>CHO COOH</td>
<td>2.5</td>
<td>88</td>
<td>128 133</td>
</tr>
<tr>
<td>8.</td>
<td>CHO</td>
<td>CHO COOH</td>
<td>3</td>
<td>92</td>
<td>240 241</td>
</tr>
</tbody>
</table>
Conclusion:

The technique used in the preparation of the tetra-\textit{n}\textendash alkylammonium bromates from the bromide is simple. The quaternary ammonium bromates can be used as a primary oxidant for the easy oxidation of aldehydes to the carboxylic acids. The efficiency of these oxidants can be ascertained by the % conversion to products. Recovery of the products from the spent bromate is simple and involves only filtration of the precipitated products. Finally, the spent oxidizing agents can be recycled back to the bromate. Recycling was done by collecting the washings and reducing the volume to half. This solution was made alkaline with 5\% aqueous NaOH solution and chlorine gas passed till the yellow/orange precipitate reappeared. The yield obtained on recycling was to the extent of about 25-26\% which is not very encouraging.
References:


42. Bortolini, O.; diFuria, F.; Modena, G., 1985, 50, 2689.


CHAPTER-B.II
Oxidation of Alcohols — A Review

The oxidation of alcohols to the carbonyl compounds is a reaction which is extensively studied by the protagonists of synthetic organic chemistry. A variety of oxidizing agents have been developed for carrying out such oxidations. These oxidizing agents, vary in strength, efficiency and utility. Search for new selective and mild oxidizing agents have always remained the aim of many synthetic organic chemists.

It is deemed appropriate at this stage to give a brief review of the variety of oxidizing agents developed for the oxidation of alcohols to the carbonyl compounds. The first reagents of wide applicability are the chromium based oxidizing agents. The use of chromic acid in the oxidation of alcohols to the carbonyl compounds is usually effected with a solution of alcohols and aqueous acidic chromic acid in acetic acid. Oxidation of primary alcohols to the aldehydes with acidic solution of chromic acid is usually less satisfactory because of possible overoxidation to the carboxylic acid. Oxidation of alcohols to carbonyl compounds is believed to take place by the initial formation...
of chromate esters followed by breakdown of the ester as shown in the Scheme B.II.1.

**SCHEME B.II.1**

\[ \text{C}(-
\text{OH})_\text{H} \xrightarrow{\text{H}_2\text{CrO}_4} \text{C}(\text{O}-\text{Cr}(-\text{OH})_\text{H} \xrightarrow{\text{HN}} \text{C}(-\text{O}) + \text{HCrO}_3^- + \text{H}^+ \]

Oxidation with acid solution of chromic acid is also unsuitable for alcohols containing acid sensitive groups. A variation of chromium trioxide oxidation for compound containing acid sensitive groups are CrO$_3$-pyridine complex$^1$, an useful and mild reagent for the oxidation of primary and secondary alcohols to carbonyl compounds is MnO$_2$. The advantage of this reagent is that it is specific for allylic and benzylic hydroxyl groups and the reaction takes place at room temperature in neutral solvent like benzene, petroleum ether, water etc. Olefinic and acetylinic bonds are unaffected by this reagent$^2$. One of the earliest reagent used for such oxidation is the reaction of alcohols with DMSO and DCC in the presence of phosphoric acid or pyridiniumtrifluoroacetate as a proton source$^3$. This method has been used to oxidize a number of sensitive compounds in the steroids, alkaloids and carbohydrate series. The mechanism of the oxidation has been established by
tracer experiments and is thought to involve initial formation of a sulfoxide-carbodiimide adduct which reacts with alcohols to give an alkoxy sulphonium ion. This then undergoes proton abstraction to form an intermediate which collapses to the carbonyl compound and dimethyl sulphide by an intramolecular concerted process as shown in Scheme B.II.2.  

**SCHEME B.II.2**

\[
\begin{align*}
C_6H_{11}N=CH_2 & \xrightarrow{\text{DMSO}} C_6H_{11}N=CN-C_6H_{11} \\
\text{CH}_3-S-\text{CH}_3 & \\
\end{align*}
\]

Among the number of other useful methods for the selective oxidation of \( \text{1}^0 \) and \( \text{2}^0 \) alcohols to aldehydes and ketones under mild conditions are the Oppenauer oxidation, oxidation with \( \text{Pb}(\text{OAc})_4 \) and catalytic oxidation with oxygen and platinum.
Pb(OAc)₄ in refluxing benzene, hexane or CHCl₃ is a good reagent for oxidation of 1° and 2° alcohols to the corresponding aldehydes and ketones provided there is no γ-C-H group in the molecule. If γ-C-H is present, it gives high yield of the tetrahydrofuran derivative. Other useful reagents are the N-haloimides, N-bromosuccinimide, N-bromo- and N-chloroacetamide. In aqueous acetone or aqueous dioxane they readily oxidize 1° and 2° alcohols to aldehydes and ketones. Rees and Storr have shown that N-chlorobenzotriazole which is readily obtained from benzotriazole with NaOCl, is an excellent reagent for the oxidation of alcohols to carbonyl compounds under mild conditions. Oxidation of alcohols to aldehydes and ketones in neutral solution at room temperature has also been effected in good yield with 4-phenyl-1,2,4-triazoline-3,5-dione. Other recently developed oxidizing agents which are both selective and mild includes Silver carbonate precipitated on Celite as a good oxidizing agent for the oxidation of alcohols to carbonyl compounds as well as other oxidizable substrates (Scheme B.II.3).

**SCHEME B.II.3**

![Scheme B.II.3](image)

Some DMSO (Dimethylsulfoxide) based oxidizing agents that have been developed for similar oxidation are (i) DMSO-p-toluenesulphonyl

103
chloride and methane sulphonie anhydride\textsuperscript{10}, (ii) DMSO-acetic anhydride\textsuperscript{11}, (iii) DMSO-chloroformate\textsuperscript{12}, (iv) DMSO-Na\textsubscript{2}Cr\textsubscript{2}O\textsubscript{7}\textsuperscript{13} and they have all been used for the successful oxidation of alcohols to the carbonyl compounds. DMSO plays a very significant role in these oxidations. It not only acts as a good solvent for the reactants but also prevents the overoxidation of aldehydes to the carboxylic acids.

In this discussion, emphasis shall be given to those oxidizing agents which are derived from quaternary ammonium salts or related compounds which are capable of oxidizing primary and secondary alcohols to the carbonyl compounds so that the review is relevant to the study reported in this chapter.

The first among such oxidizing agents developed is the 4-(dimethylamino)pyridiniumchlorochromate\textsuperscript{14} which is reported to be a mild and selective reagent for the oxidation of complex allylic and benzylic alcohols to the carbonyl compounds. This reagent selectively oxidizes benzylic and allylic alcohols to the aldehyde in preference to other primary alcohols. This oxidizing agent was found to exhibit superior selectivity compared to other oxidizing agents such as 2,2′-bipyridiniumchlorochromate\textsuperscript{15,16}, and 2,2′-bipyridine-chromiumtrioxide\textsuperscript{17} complex reported earlier.

Ley et al\textsuperscript{18}, reported the development of tetra-n-propylammonium perruthenate (TPAP) as a mild, room temperature oxidant and used this reagent for the oxidation of both \textsuperscript{1}° and \textsuperscript{2}° alcohols to the carbonyl compounds (Scheme B. II.4).
Lee and Freedman oxidized benzylic and secondary aliphatic alcohols to the corresponding carbonyl compounds. Aliphatic primary alcohols are oxidized slowly to the aldehydes and these are rapidly oxidized to the carboxylic acid in high yield; in contrast to oxidation of benzylic alcohols which gives the aldehyde in good yield.

Similarly, the oxidation of alcohols to carbonyl products under PTC conditions can be achieved by a number of other reagents. Controlled oxidation of primary alcohols to the aldehyde stage is most often desirable. It has also been observed that for benzylic alcohols, the system consisting of solid KMnO₄ and N(CH₂–CH₂–OCH₂–CH₂–OCH₃)_3 and the liquid-liquid
reaction involving $Q^+Cl^-$ and aqueous hypochlorite$^{21}$ or $Q^+HSO_4^-$ and aqueous dichromate$^{22}$ give satisfactory results. The unusual oxidation of benzyl alcohol to benzaldehyde at room temperature involved stirring with iodobenzene in the presence of NaHCO$_3$ and catalytic amount of Pd(II) acetate and tetrabutylammoniumchloride$^{23}$. N-bromoquinuclidine in combination with pyridine can oxidize secondary alcohols at room temperature$^{24}$. Apparently, quinuclidine function as a phase transfer catalyst (Scheme B. II. 5).

**SCHEME B. II. 5**

In the present study, the quarternary ammoniumbromates, the preparation of which have been described in detail in the previous chapter, have been successfully used for the oxidation of a variety of primary and secondary alcohols to the carbonyl compounds. These reagents were found to be synthetically useful as the primary alcohols could be oxidized to the aldehydes and overoxidation was not observed. In addition to the above observations it was also possible to oxidize some benzyl halides to the corresponding aldehydes. This conversion is rarely observed with most oxidizing agents. The reaction conditions are simple and involves the
dissolution of the alcohols and the tetra-n-alkylammoniumbromate in equal proportion in an appropriate organic solvent and refluxing the solution for a particular duration till the yellow colour of the solution changed to almost colourless. The experimental details are discussed in detail in the experiments section of this chapter.

EXPERIMENTAL

All alcohols and benzyl halides were obtained from E. Merck Inc. and used without further purification. Benzhydrol and some alcohols were prepared from appropriate substrates by established procedure. The tetra-n-propylammoniumbromate and tetra-n-butylammoniumbromates were prepared by procedures described in Chapter-B.1. The product carbonyl compounds were identified by recording the m.p., IR, 'H-NMR spectra in spectrometers mentioned earlier and comparing the results with those reported in literature.

OXIDATION OF ALCOHOLS AND BENZYL HALIDES WITH TETRA-n-ALKYLAMMONIUMBROMATES

General procedure:

0.01 mol of the alcohol was dissolved in 50 ml of an organic solvent (Table B.II.1) and to this solution 0.01 mol of the quaternary ammoniumbromate was added and the solution refluxed. On refluxing the yellow colour of the solution turned to almost colourless. Further, the progress
of the reaction was followed by TLC in prepared silicagel plate. Aliquots of the reaction solution was withdrawn at different time interval and co-chromatographed with pure sample of the starting alcohol using ethylacetate : n-hexane ( 9:1 ) as eluent . The end of the conversion was indicated by the disappearance of the starting alcohol from the reaction mixture . In cases where the carbonyl compounds were liquids , they were converted to their 2,4-dinitrophenylhydrazones . Evaporation of the solvent gave the solid products which were washed several times with water to remove the spent tetra-n-alkylammoniumbromates . The solid was then washed with ethanol to remove the unreacted 2,4-dinitrophenylhydrazine and the phenylhydrazones in the pure form were crystallized out and characterized by observing their melting points , UV-visible , IR and $^1$H-NMR spectra . In those cases where the product carbonyl compound was a solid , the reaction mixture was cooled to ambient temperature and poured into crushed ice resulting in the precipitation of the product carbonyl compounds . The products were washed several times with water , dissolved in minimum quantity of ethanol and filtered directly into a large volume of water . The latter procedure of dissolution in ethanol and reprecipitation was performed several times so as to remove the last traces of by products . The target carbonyl compounds were recrystallized from appropriate solvent and characterized by recording their melting points , IR and $^1$H-NMR spectra and comparison with those obtained from authentic samples . The conversions were possible with both tetra-n-propylammoniumbromate as well as with tetra-n-butylammoniumbromate and the results obtained as shown in Table B . II . 1 . The conversion is shown in Scheme B . II . 6 .
SCHEME B.II.6

\[
\begin{align*}
\text{Rz}_1 + \text{R}_2 \xrightarrow{\text{R}_4N\text{BrO}_3/ \text{solvent/reflux}} \text{R}_2 \\
X = \text{HO}, \text{halogen}
\end{align*}
\]

**TABLE B.II.1**
Physical characteristics of oxidized product
(Ref. Scheme B.II.6)

<table>
<thead>
<tr>
<th>Sl.No. substrate</th>
<th>Product</th>
<th>Reflux time (hr)</th>
<th>Yield (%)</th>
<th>Solvent m.p./b.p. of Product (°C)</th>
<th>m.p. of 2,4-DNP derivatives (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>I</td>
<td>II</td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td>1</td>
<td><img src="#" alt="Chemical structure" /></td>
<td>2</td>
<td>2.5</td>
<td>94</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td><img src="#" alt="Chemical structure" /></td>
<td>2</td>
<td>1.5</td>
<td>76</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td><img src="#" alt="Chemical structure" /></td>
<td>1.5</td>
<td>1.5</td>
<td>91</td>
<td>77</td>
</tr>
<tr>
<td>4</td>
<td><img src="#" alt="Chemical structure" /></td>
<td>1.5</td>
<td>1.5</td>
<td>98</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td><img src="#" alt="Chemical structure" /></td>
<td>1</td>
<td>2.5</td>
<td>98</td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td><img src="#" alt="Chemical structure" /></td>
<td>1.5</td>
<td>1.5</td>
<td>92</td>
<td>88</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Sl.No.</th>
<th>Substrate</th>
<th>Product</th>
<th>Reflux time (hr)</th>
<th>Yield (%)</th>
<th>Solvent</th>
<th>m.p./b.p. of products (°C)</th>
<th>m.p. of 2,4-DNP derivatives (°C)</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
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<td>II</td>
<td>I</td>
<td>II</td>
<td>obs</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td>94</td>
<td>82</td>
<td>EtOH 41-43</td>
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<td>2</td>
<td>2</td>
<td>80</td>
<td>78</td>
<td>EtOH 56</td>
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<td>2</td>
<td>91</td>
<td>73</td>
<td>EtOH 245</td>
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<td>1.5</td>
<td>92</td>
<td>84</td>
<td>EtOH 177-78</td>
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<td></td>
<td>1.5</td>
<td>1.5</td>
<td>85</td>
<td>79</td>
<td>EtOH 178-79</td>
</tr>
</tbody>
</table>

X = Cl, Br

I indicates reaction with tetra-n-propy lammonium bromate, II with tetra-n-butylammonium bromate.
A FEW REPRESENTATIVE SPECTRAL DATA OF
OXIDIZED PRODUCT

➤ PRODUCT 2:

UV : $\lambda_{\text{max}}$ (EtOH) 295 nm;

IR : (KBr cm$^{-1}$) 1685 ($>\text{C}=\text{O}$);

$^1$H-NMR : (60 MHz, CDCl$_3$, $\delta$) 8.3 (1H, s), 7.9 (5H, m, broad),
4.7 (1H, s), 4.3 (1H, s), 4.1 (1H, s).

➤ PRODUCT 4:

UV : $\lambda_{\text{max}}$ (EtOH) 310 nm;

IR : (KBr cm$^{-1}$) 1660 ($>\text{C}=\text{O}$);

$^1$H-NMR : (60 MHz, CDCl$_3$, $\delta$) 8.1 (m, 10H,).

➤ PRODUCT 7:

UV : $\lambda_{\text{max}}$ (EtOH) 288 nm;

IR : (KBr cm$^{-1}$) 1690 ($>\text{C}=\text{O}$);

$^1$H-NMR : (60 MHz, CDCl$_3$, $\delta$) 8.3 (5H, m), 7.2 (5H, m,)
4.1 (1H, s), 3.2 (3H, s).

➤ PRODUCT 9:

UV : $\lambda_{\text{max}}$ (EtOH) 264 nm;

IR : (KBr cm$^{-1}$) 1665 ($>\text{C}=\text{O}$);

$^1$H-NMR : (60 MHz, CDCl$_3$, $\delta$) 7.6 (4H, m), 3.8 (3H, s),
3.2 (3H, s).
In conclusion, it can be said that the tetra-n-alkylammoniumbromates prepared and characterized are good oxidizing agents for the conversion of alcohols to the carbonyl compounds. They are synthetically useful because of the fact that primary alcohols could be converted to the aldehydes without their overoxidation to the carboxylic acid. Another interesting observation is the ease with which some benzyl halides could be oxidized to the corresponding aldehyde. This observation increases the importance of these oxidizing agents. Water solubility of the bromates as well as the byproducts makes it easy to separate out the product carbonyl compounds in the pure state. This was found to be particularly easy with tetra-n-propylammonium bromate as its solubility in water was higher compared to the tetra-n-butyl analog. Consequently, recovery and work up procedure were found to be simple and yield obtained are high.
References:


CHAPTER-B.III
Primary and secondary amines are very sensitive to oxidation and darkens quite rapidly on exposure to air. The susceptibility of such oxidation of solid amines is somewhat less than the liquids. On oxidation with a suitable oxidizing agent, anilines are converted to a variety of products such as azobenzene, azoxybenzene, benzoquinone and aniline black. Such oxidation are synthetically not important due to the varied nature of products and byproducts. Isolation of the individual products from the reaction mixture provides a tedious and time consuming process. It is reported that in the initial oxidative attack apparently involves extraction of a hydrogen attached to the nitrogen to give an unstable free radical which may dimerize or be further oxidized as shown in Scheme B. III. 1.
With most oxidizing agents, the azo compounds appears to be the usual product. Aniline treated with alkaline permanganate gives azobenzene. p-toluidine is oxidized in a similar manner to the azo compound \(^1\) (Scheme B. III. 2). Terent'ev and Mogilyanski\(^2\) found that aniline, p-toluidine, p-amino anisole could be readily oxidized at room temperatures to the corresponding azo compound in good yield. The oxidation is achieved with oxygen or air in pyridine containing cuprous chloride. The yield with the above three amines were 88, 95, 70 \%, respectively. Pyridine seems to be a specific solvent for the reaction although 2-picoline may be used. When sodium hypochlorite is used as the oxidizing agent p-aminophenol is obtained together with azobenzene and other products (Scheme B. III. 2). Further oxidation gives quinines. Lead tetraacetate also has been found to be an effective oxidizing agent for converting aromatic amines to sym-azo compounds \(^3\). Yields of the azo compounds amount to 25–40 \%. The reaction is postulated to proceed by a free radical mechanism. As an example, 4,4′-dibromoazobenzene has been prepared by adding finely powderd Pb(OAc)\(_4\) to a benzene solution of p-bromoaniline. Aniline is oxidized by permonophosphoric acid or a mixture of peracetic and phosphoric acid to give p-aminophenol and (p-NH-Ph)\(\text{H}_2\text{PO}_4\) \(^4\). Direct oxidation of aniline to give benzoquinone can be carried out with chromic acid or MnO\(_2\) and sulfuric acid (Scheme B. III. 2). Primary aromatic amines react with potassium nitrodisulfonate, (Fermy's salt), ON (SO\(_3\)K)\(_2\), to form red quinone imines. If the p-position of the amino group is occupied by an alkyl or alkoxy group, substituted quinone anils are formed \(^5\).
It is evident from the discussion that several oxidizing agents have been used for the oxidation of aromatic amines. The results have always been the formation of a variety of products. In some cases careful oxidation have yielded the azo compound in high quantities. Development of reagents for the direct oxidation of aromatic amines to nitro compounds without the formation of unwanted byproducts have always been a challenge to synthetic organic chemists. The direct oxidation of amines is very useful for the preparation of
nitro compounds. It is convenient procedure owing to the availability of the desired amines. Peracetic acid was one of the first oxidizing agent used for an effective oxidation of arylamines to the corresponding nitrobenzene. Anhydrous solutions of peracetic acid were prepared from acetic anhydride and 90% H$_2$O$_2$ at ice bath temperatures. After the exothermic formation of peracetic acid had occurred, the aromatic amines was oxidized in the boiling solution. The presence of small amounts of H$_2$O$_2$ and diacetyl peroxide does not interfere. Yield of the nitrobenzene was as high as 72–83%. In some cases, traces of highly coloured impurities, possibly of azoxybenzene, were found, which could be removed by adsorption on silicagel. Although this method was used for oxidation of aromatic amines to the nitro compounds, it was found to be applicable to several aliphatic amines also. Other oxidizing agents that have been employed with variable results were Caro's acid, peroxytrifluoroacetic acid, peroxymaleic acid, m-dichloroperbenzoic acid, and perbenzoic acid. Although the scope and limitations of these oxidants have not been completely established, some general observations may be noted.

1. The power of the oxidants is proportional to the acid strength of the deoxyperacid.

2. Peracetic acid and m-chloroperbenzoic acid are suitable for oxidation of aliphatic primary amines.

3. Peracetic acid, pertrifluoroacetic acid and peroxymaleic acids are best for oxidation of various ring substituted anilines, although certain
anilines with electron releasing groups such as alkoxy are destroyed
by peroxytrifluoroacetic acid.

4. Caro's acid has been employed for oxidation of amino pyridines \(15^{18}\).

5. With anilines one often obtains nitroso compounds \(18^{20,11}\). Other
oxidants of preparative value include \(\text{KMnO}_4\) \(^{21}\) and ozone \(^{22,23}\).

In the aliphatic series, saturated primary amines undergo oxidation
reactions by ozone. These reactions, thoroughly investigated by Bailey and
coworkers \(^{22,23}\), results in the corresponding nitroalkanes accompanied by several
other compounds depending on the reaction conditions. In an elegant method
reported by Keinon and coworkers \(^{22,25}\), ozonation was carried out in silicagel \(^{25}\)
and several aliphatic amines were converted to the nitro compounds in about
70% yield. In case of aromatic amines, the yield of the product nitro
compounds were found to be the corresponding ion. The low yields may be
explained by the reduced nucleophilicity of the \(-\text{NH}_2\) group and by the
competitive oxidation of the benzene ring. Thus substitution with the electron
withdrawing \(-\text{NO}_2\) group reduces the \(-\text{NH}_2\) nucleophilicity while substitution with
electron donating \(-\text{OCH}_3\) and \(-\text{CH}_3\) groups increases the ease of oxidation of
the benzene ring, both contributing to the low yields of the nitro compounds. It
has also been observed that the low yield of nitrobenzene is also dependent on
the water content of the silica gel and on the reaction temperature but
independent of the concentration of the starting materials. The mechanism of
aniline ozonation is shown in Scheme B. III. 3.
The particular advantages of the dry ozonation of amines are the simplicity of the experimental procedures and the purity of products isolated. Another convenient method was reported by Barnes et al. They have devised a convenient oxime to nitro conversion, a method more suited to the synthesis of secondary nitroparaffin. The method involves treatment of an oxime with chlorine to give chloronitroso compound, oxidation with ozone to the chloronitro compound and finally catalytic hydrogenation in the presence of 2 equivalent of sodium hydroxide to the nitro compound as shown in Scheme 4.

SCHEME 4

\[
\begin{align*}
R_1C(\text{Cl})(\text{NO})R_2 & \xrightarrow{\text{Cl}_2/\text{CH}_2\text{Cl}_2} R_1C(\text{Cl})(\text{NO})R_2 \\
& \xrightarrow{\text{O}_3/\text{CH}_2\text{Cl}_2} \\
& \xrightarrow{\text{NaOH}/\text{H}_2} \xrightarrow{\text{H}_2\text{O} - \text{Pd/C}} R_1\text{CH(NO}_2)R_2
\end{align*}
\]
The method is essentially a two pot operation. It is carried out without purification of the intermediates and the final product is easily isolated, usually in high purity. In another related study, Nielsen et al. 27 have successfully used peroxysulfuric acid as a reagent for the conversion of polynitroarylamines to polynitrobenzenes. In a typical procedure, peroxysulfuric acid was conveniently prepared by addition of 90–98% H\textsubscript{2}O\textsubscript{2} to oleum which successfully oxidized pentanitroaniline to hexanitrobenzene. The scope of the peroxysulfuric acid oxidation of amines to nitro compounds can be broadly outlined. Peroxysulfuric acid in sulfuric acid is the most powerful of all known peracid oxidants, with the possible exception of peroxytrifluoromethanesulfonic acid. It will oxidized the amines to a nitro group in trinitro, tetranitro and pentanitro anilines, all of which are not acted upon by peroxytrifluoroacetic acid. Crude products, isolated in excellent yields, are usually very pure. Impurities such as azo, azoxy or nitroso compounds, often contaminating the nitro products. When weaker peracids are employed, azo compounds were found to be absent\textsuperscript{28,29}.

From the above review of the different oxidative methods of the conversion of aromatic and aliphatic amines to the nitro compounds, it is evident that with the exception of a few methods reported most of the others suffer from serious drawbacks. The first drawback is the necessary use of a strong oxidizing which not only oxidizes the –NH\textsubscript{2} to –NO\textsubscript{2} but also attacks activated aromatic rings giving a multiplicity of products. Substrates, where easily oxidizable groups are also present, cannot be converted to the nitro compounds in high yield due to the susceptibility of the nonparticipating group towards oxidation by the strong oxidants used. Therefore, conversion of amino
to nitro compound is accompanied by several other compounds depending on the reaction conditions. The byproducts are derived mainly from the partially oxidized amines, which react with

i. the solvent.

ii. the solvent oxidized product.

iii. each other.

In addition to this competitive oxidation of carbon atoms in the substrate is often observed.

OXIDATION OF AROMATIC AMINES TO NITRO COMPOUNDS USING QUATERNARY AMMONIUMBROMATES

In the study reported in this chapter of the thesis, a simple and convenient procedure of oxidative transformation of some aromatic amines to the corresponding nitro compound is reported. The oxidizing agents used for this transformation are the tetra-n-propylammoniumbromate and the tetra-n-butylammoniumbromates. The preparation of these two quaternary ammonium bromates and their physical characteristics are reported in detail in Chapter B.1. As many as fourteen aromatic amino compounds have been oxidized to the nitro compound by a simple method and elaborate purification and recovery procedures were not involved. The method is also of the general type and a common procedure can be used for the conversion. The general procedure involves refluxing the aromatic amine, the quaternary ammoniumbromate in acetic acid for a varied period of time to give the products. The separation of
the products from the reaction mixture was also simple and involved addition of the reaction mixture to the cold water. The unreacted quaternary ammonium bromate, the byproducts of oxidation are all soluble in water whereas the product nitro compound was insoluble and precipitated out. A simple filtration was enough to recover the products in yields as high as 90% in some cases. The details of the experiments carried out are given in the experimental section of this chapter.

The transformation is shown in the Scheme B. III . 5.

**SCHEME B. III . 5**

**Oxidation of aromatic amines to nitro compounds**

\[
\begin{align*}
R_4 \text{NBr}^+ & \quad \xrightarrow{\text{Cl}_2} \quad R_4 \text{NBrO}_3^- \\
\text{aq. NaOH (5%)} & \\
\end{align*}
\]

As it has already been mentioned, the usual disadvantages of oxidative conversion of amino to nitro compounds such as,

1. use of costly reagents.
2. vigorous reaction conditions.
3. possibility of formation of other oxidized by product because most of the oxidizing agents used were particularly strong oxidizing agents.

4. formation of highly coloured by products such as azo, azoxy and other products obtained by the reaction of partially oxidized amino compounds with itself, with the solvent and with oxidized solvents.

5. low yield.

6. difficult and cumbersome recovery procedures were not observed in this procedure and therefore the quaternary ammoniumbromates are much superior to all the reagents reported as yet including the perborate oxidation of amino compounds to nitro compounds reported by McKillop et al.³⁰.

The transformations were carried out with both tetra−n−propylammonium bromate and tetra−n−butylammoniumbromate (Scheme B. III. 5). The general observation is that reflux time required in case of tetra−n−propylammonium bromate was less than that required for tetra−n−butylammoniumbromate. Further, when the quaternary propyl bromate was used the conversion was better and yield were found to be high. Another reason why the tetra−n−propylammoniumbromate is a superior reagent is because of its higher solubility in water compared to tetra−n−butylammoniumbromate. This made recovery of products in the former case, easier.
EXPERIMENTAL

All aromatic amines used were procured from Merck Inc. Ltd. and were purified by procedures reported in literature before use. The tetra-n-propyl ammoniumbromate and tetra-n-butylammoniumbromates were prepared by procedures described in Chapter B.I. The product nitro compounds were identified by recording the m. p., IR and \(^1\)H-NMR spectra in spectrometers mentioned earlier and comparing the results with those reported in literature.

**General Procedure:**

0.001 mol of the aromatic amine was dissolved in 20 ml of glacial acetic acid followed by addition of 0.002 mol of the tetra-n-alkylammonium bromate, 5 ml of 6N \( \text{H}_2\text{SO}_4 \) was added to the solution dropwise. On refluxing, the yellow colour of the solution became almost colourless. The progress of the reaction was monitored by TLC in silica gel plates using authentic samples of the target nitro compounds. Ethanol was used as the eluent. The end of the reaction was determined by observing the disappearance of the starting amino compound. The reaction solution was brought to room temperature and poured into crushed ice. The solid obtained on standing was filtered, dissolved in ethanol and filtered directly into a large volume of distilled water. In some cases, this procedure of dissolution in ethanol and reprecipitation had to be repeated several times to obtain the nitro compound in pure form. As it has already been mentioned, the product nitro compound was identified by recording
their melting points, UV, IR and $^1$H-NMR spectra authentic samples.
The results of the experiments carried out are summarized as shown in
Table B. III. 1.

**TABLE B. III. 1**
(Ref. Scheme B. III. 5)

Physical characteristics of nitro compounds

<table>
<thead>
<tr>
<th>Sl.No.</th>
<th>Aromatic amine</th>
<th>Nitro compound$^a$</th>
<th>Reflux time (min)</th>
<th>Yield (%)</th>
<th>M.P. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>I</td>
<td>II</td>
<td>I</td>
</tr>
<tr>
<td>1.</td>
<td>Br—NH$_2$</td>
<td>Br—NO$_2$</td>
<td>60</td>
<td>110</td>
<td>84</td>
</tr>
<tr>
<td>2.</td>
<td>NH$_2$</td>
<td>NO$_2$</td>
<td>75</td>
<td>110</td>
<td>88</td>
</tr>
<tr>
<td>3.</td>
<td>NH$_2$</td>
<td>NO$_2$</td>
<td>90</td>
<td>125</td>
<td>92</td>
</tr>
<tr>
<td>4.</td>
<td>CH$_3$—NH$_2$</td>
<td>CH$_3$—NO$_2$</td>
<td>80</td>
<td>95</td>
<td>90</td>
</tr>
<tr>
<td>5.</td>
<td>MeO—NH$_2$</td>
<td>MeO—NO$_2$</td>
<td>90</td>
<td>145</td>
<td>88</td>
</tr>
<tr>
<td>6.</td>
<td>Cl—NH$_2$</td>
<td>Cl—NO$_2$</td>
<td>90</td>
<td>105</td>
<td>81</td>
</tr>
<tr>
<td>7.</td>
<td>Cl—NH$_2$</td>
<td>Cl—NO$_2$</td>
<td>90</td>
<td>110</td>
<td>86</td>
</tr>
</tbody>
</table>

(continued)
Products were characterized by IR, $^1$H-NMR and mass spectra and by comparing the observed melting points to those found in literature.

For 2-aminopyridine, a slow stream of air was passed through the reaction solution during reflux reaction carried out in ethanol solution without sulfuric acid and acetic acid.

Solvent used was glacial acetic acid.

<table>
<thead>
<tr>
<th>Sl.No.</th>
<th>Aromatic amine</th>
<th>Nitro compound $^a$</th>
<th>Reflux time (min)</th>
<th>yield (%)</th>
<th>M.P. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.</td>
<td>CH$_2$-NH$_2$</td>
<td>CH$_3$-NO$_2$</td>
<td>75 90</td>
<td>84 82</td>
<td>85 83</td>
</tr>
<tr>
<td>9.</td>
<td>Br$_3$-NH$_2$</td>
<td>Br$_3$-NO$_2$</td>
<td>60 95</td>
<td>79 65</td>
<td>97</td>
</tr>
<tr>
<td>10.</td>
<td>H$_2$N- COOH</td>
<td>O$_2$N- COOH</td>
<td>90 80</td>
<td>74 55</td>
<td>246 241</td>
</tr>
<tr>
<td>11.</td>
<td>NH$_2$</td>
<td>NO$_2$</td>
<td>90 125</td>
<td>78 70</td>
<td>73–74 79</td>
</tr>
<tr>
<td>12.</td>
<td>NH$_2$</td>
<td>NO$_2$</td>
<td>600 720</td>
<td>40 55</td>
<td>82 75</td>
</tr>
</tbody>
</table>

$^a$ I indicates oxidation with tetra-n-propylammoniumbromate and II with tetra-n-butylammoniumbromate.

$^b$ Products were characterized by IR, $^1$H-NMR and mass spectra and by comparing the observed melting points to those found in literature.

$^b$ For 2-aminopyridine, a slow stream of air was passed through the reaction solution during reflux reaction carried out in ethanol solution without sulfuric acid and acetic acid.

Solvent used was glacial acetic acid.
Some spectral characteristics of the nitro compounds

➤ PRODUCT 1:

UV : $\lambda_{\text{max}}$ (EtOH) 279 nm;

IR : (KBr cm$^{-1}$) 1475, 1300 (–NO$_2$);

$^1$H-NMR : (CDCl$_3$,δ) 7.3 (d,4H).

➤ PRODUCT 2:

UV : $\lambda_{\text{max}}$ (EtOH) 317 nm;

IR : (KBr cm$^{-1}$) 1458, 1305 (–NO$_2$);

$^1$H-NMR : (CDCl$_3$,δ) 7.2 (m,4H).

➤ PRODUCT 4:

UV : $\lambda_{\text{max}}$ (EtOH) 261 nm;

IR : (KBr cm$^{-1}$) 1510, 1345 (–NO$_2$);

$^1$H-NMR : (CDCl$_3$,δ) 7.2–7.9 (d,4H), 1.4 (3H, s).

➤ PRODUCT 5:

UV : $\lambda_{\text{max}}$ (EtOH) 285 nm;

IR : (KBr cm$^{-1}$) 1480, 1286 (–NO$_2$);

$^1$H-NMR : (CDCl$_3$,δ) 7.2 (4H), 1.4 (3H, s).

➤ PRODUCT 8:

UV : $\lambda_{\text{max}}$ (EtOH) 305 nm;

IR : (KBr cm$^{-1}$) 1475, 1285 (–NO$_2$);

$^1$H-NMR : (CDCl$_3$,δ) 7.7 (d,4H).
In conclusion it may be mentioned that the quaternary ammonium bromates reported herein can be referred to as superior reagents for the conversion of the aromatic amines to the nitro compounds in terms of easy of its preparation, simple reaction conditions necessary for the conversion and the simple techniques that are used for recovery of products. Yields are also higher than most of the results reported in literature.
References:

1. Green, A.G.; Ber, 1893, 26, 2772.


CHAPTER-B.IV
CHAPTER-B. IV
DEOXIMATION USING TETRA-\(n\)-ALKYLAMMONIUMBROMATE
—A REVIEW

Oximes are prepared by the reaction of carbonyl compounds with hydroxylamine in the form of their hydrochloride or other Bronsted acid salts. The reaction is a typical nucleophilic addition reaction to a carbon–heteroatom double bond. Oxime formation is usually catalyzed by acids. The mechanism of oxime formation is shown in Scheme B.IV.1.

SCHEME B.IV.1
Formation of oximes

Two isomeric oximes are possible when unsymmetrical carbonyl compounds are used as the substrate. Oximes are extensively used as preferred...
derivative for purification and characterization of carbonyl compounds. These derivatives assumed added importance after the discovery of Barton reaction in which oximes were produced at activated hydrocarbon sites. Their synthesis from non carbonyl compounds by nitrosation of active methylene groups, nitrosation of α-halocarbonyl compounds, condensation of nitroalkenes with an aldehyde, followed by deoximation of the product oximes provided a very important and unique method of converting compounds of the type $Z_1-CH_2-Z_2$ to $Z_1-CO-Z_2$ where $Z_1$ and $Z_2$ are electron withdrawing groups as shown in Scheme B.IV.2.

**SCHEME B.IV.2**

$$
\begin{align*}
Z_1 & \xrightarrow{HNO_2 \text{ or isoamyl nitrite}} Z_1 & C=\text{N-OH} & \xrightarrow{} Z_1 \xrightarrow{Z_2} C=O\\
Z_2 & & & \text{oximes} & \text{carbonyl compounds}
\end{align*}
$$

It was also recently reported that allylic nitro compounds react with carbondisulfide in the presence of a solid base and quaternary ammonium salts to give the aldoximes. Deoximation of these oximes, may therefore, offer opportunities for the conversion of allylic nitro compounds to $\alpha\beta$-unsaturated aldehydes as shown in Scheme B.IV.3.
Furthermore, oximation plays an important role in the protection of carbonyl group\(^7\) in a multistep synthetic protocol and also in the selective activation of the carbon atom \(\alpha\) to the carbonyl\(^8\) considering that the \(>\text{C} = \text{N}\)-bond is a good electron withdrawing group. Oximes are also intermediates in the preparation of amides by Beckmann rearrangement\(^9\), synthesis of nitriles by dehydration with \(\text{P}_2\text{O}_5\). Lawn et al. has also reported the use of oximes in the generation of iminoxylradicals as transient intermediates by oxidation with ceric ammoniumnitrate and leadtetraacetate\(^10\).

There has been continued research in the generation of the parent carbonyl compounds from stable and readily prepared oximes under mild conditions. Regeneration of the carbonyl from the oxime is popularly known as deoximation. The importance of deoximation is exemplified by the voluminous amount of research efforts directed towards developing new reagents and new methods for the regeneration of the carbonyls from their oximes. At present there are numerous procedures and reagents developed for the purpose and hence a wide range of techniques and conditions for deoximation are available. Some of these techniques are discussed subsequently.
HYDROLYTIC METHODS OF DEOXIMATION

Hydrolysis of the oximes to the parent carbonyl can be accomplished under acidic, basic and neutral conditions. The oldest and classical methods for the recovery of aldehydes and ketones from the corresponding oximes is hydrolysis under acidic conditions which removes the resultant hydroxylamine from the equilibrium. Under neutral condition hydrolytic methods involved an equilibrium of hydroxylamine with the liberated carbonyl compound which may take several hours to reach completion. Acid hydrolysis had been carried out with various acids such as HCl, HBr, H$_2$SO$_4$, 4-toluenesulphonic acid, phthalicanhydride-water, oxalic acid and acetic acid. With HCl the best results are obtained particularly for the regeneration of aromatic aldehydes and ketones. Hydrolysis has also been employed in neutral or alkaline medium but results are unfavourable in comparision to the acidic conditions. To achieve a complete conversion of the oxime to the carbonyl compounds, other procedures such as addition of catalytic salts to the acidic medium are also used. Some of the salt catalysts used are FeCl$_3$, CuSO$_4$.5H$_2$O, clay supported ammoniumnitrate. The use of NaHSO$_3$ to drive the equilibrium in favour of the carbonyl was introduced a long time back, it interacts with the oximic compound in acidic medium to give a sulfine, which produces a carbonyl compound on exposition to cold acid (Scheme B.IV.4).

SCHEME B.IV.4

\[
\begin{align*}
R_1\text{CONH} &\xrightarrow{\text{NaHSO}_3, \text{H}_2\text{O}} R_1\text{C} \overset{\text{OH}}{-} \overset{\text{+}}{\text{SO}_3\text{Na}} \\
\text{H}_2\text{O} &\xrightarrow{\text{H}^+} R_1\text{C} \overset{\text{R}_2}{\text{O}}
\end{align*}
\]
EXCHANGE REACTION WITH OTHER CARBONYL COMPOUNDS

The exchange reaction with other carbonyl compounds have been extensively applied, formaldehyde being the most often used carbonyl compound as it is economic and gives best yield with aldoximes, for example, the regeneration of 1,3-dimethyluramazine–6-carbaldehyde could be accomplished by boiling the corresponding oxime in dilute aqueous HCl or H₂SO₄ in the presence of large excess of formaldehyde. By this method various oximes were converted to the carbonyl compounds mostly in quantitative yields by simply allowing them to react with excess of acetone at temperature ranging between 20°C–80°C (Scheme B.IV.5).

SCHEME B.IV.5

The acetone and formaldehyde oximes being water soluble makes recovery of the target carbonyl compound easy. The exchange reaction with acetone offers additional advantage as the exchange procedure involves non acidic medium. Cyclohexanone was regenerated in 72% yield by the use of acetone and acetone with Amberlyst-15²². The treatment of purified
5'-aldoximes of protected adenine nucleotides with acetone and aqueous CF₃COOH gave clean samples of 5'-carboxaldehyde in good yield.

**REDUCTIVE METHODS OF DEOXIMATION**

Many of the hydrolysis reagents used for the conversion of oximes to the corresponding carbonyl compounds are quite nonselective. These are very few reductive reagents reported. Some reagents used were hydrogen gas in heterogeneous catalyst, metals and acids, sulferated reagents, metal carbonyls etc. and transition metals were used because of their favourable redox potentials. The selection of these reductive reagents is based on premise that the reduction would cause the fission of the oxime N-O linkage to give an imine which then would suffer rapid hydrolysis to the carbonyl compound (Scheme B.IV.6).

**SCHEME B.IV.6**

![Scheme B.IV.6](image)

Platinum oxide (PtO₂) and Raney nickel were widely applied as heterogeneous catalysts. The procedure of using hydrogen gas over PtO₂ has been shown to be effective in the hydrolysis of erythromycin oxime only when an uneconomically high ratio of catalyst to substrate was used. A simple method of deoximation of steroidal ketoximes involve the reductive hydrolysis of
the ketoxime with Zn/CH₃COOH/H₂O system. Hexamethylphosphoramidate (HMPA) is reported to be able to divert the Lithiumaluminiumhydride reduction of oximes from its normal oxime products. LAH reduction in HMPA yields the ketones from the ketoximes of acetophenone, 4-methylacetophenone, 3,4-dihydro-1(2H)naphthylene and 2,4-dibutylcyclohexane. The mechanism of LAH/HMPA reductive deoximation is given in Scheme B.IV.7.

Among the methods which use sulfurred reagents such as Na₂S₂O₃ and NaHSO₃ is the treatment of oximes with aqueous sodiumdithionite (Na₂S₂O₄) at room temperature either alone or in the presence of NaHSO₃ or NaOAc to afford the parent carbonyl after acid addition. Two possible mechanisms are suggested. Firstly, the solution of the dithionite anion is unstable and decompose in a complex manner to hydrogensulfide and then the process can occur via hydrolytic pathway in analogy to the reaction of the oxime with NaHSO₃. Alternatively, the cleavage might occur via a reductive pathway. The oxime is
first reduced to the imine which is immediately hydrolyzed to the carbonyl compound (Scheme B.IV.8).

**Scheme B.IV.8**

Particularly Na$_2$S$_2$O$_4$ was used for the deoximation of triazene ketoxime namely oxime of 3–methyl–5–formyl, 3–methyl–5–acetyl triazenes etc. Aqueous sodiumhydrogensulfite, Na$_2$S$_2$O$_3$ was found to convert 2–oxopropionaldehyde oxime into the corresponding aldehyde in good yield. Further, tributylphosphine–diphenyldisulfide which is a self drying reagent is capable of reducing ketoximes to the imines and finally to the carbonyl compound after hydrolysis (Scheme B.IV.9).

**Scheme B.IV.9**
Among the metal carbonyls, those of iron have been used extensively, but cobalt and magnesium carbonyls have demonstrated efficiency. The treatment of an aldehyde and ketone oxime of widely differing character with an equimolar quantity of ironpentacarbonyl and catalytic amount of BF₃ in refluxing dibutylether results in the formation of the carbonyl compound in moderate to good yield. The reaction is shown in Scheme B.IV.10.

**SCHEME B.IV.10**

\[
\begin{align*}
R_1\text{NOH} & \xrightarrow{\text{Fe(CO)}_5} R_1\text{N}^+\text{OH} \xrightarrow{\text{Fe(CO)}_5} R_1\text{N}^+\text{Fe(CO)}_4 \\
\xrightarrow{\text{H}_2\text{O}} & R_1\text{NH} \xrightarrow{\text{H}_2\text{O}} R_1\text{CO}
\end{align*}
\]

Dicobaltoctacarbonyl [Co₂(CO)₈] was found to serve as an alternative tool for the easy regeneration of carbonyl functionality from their oxime derivatives. The use of molybdenumhexacarbonyl in the presence of water induced the conversion of oximes to their corresponding aldehydes and ketones.

Titanium ion Ti³⁺ are represented more extensively within transition metal ions. The cleavage of oximes was achieved in excellent yield at room temperature using one molar equivalent of TiCl₃. The titanium tetrachloride/sodium iodide (TiCl₄/NaI) system generating low valent titanium (LVT), is a mild, efficient and selective reagent which carries out the
The reductive cleavage of oximes to afford the corresponding carbonyl compounds.
The reaction is very rapid when CH$_3$CN is used as the solvent with a 1:2:2 ratio of oxime/NaI/TiCl$_4$. The reaction proceeds by the following mechanism$^{35}$ (Scheme B.IV.11).

**SCHEME B.IV.11**

\[
\text{TiCl}_4 + \text{NaI} \stackrel{\text{CH}_3\text{CN}}{\text{RT}} \rightarrow [\text{LV}T] + \text{I}_2
\]

\[
\begin{align*}
\text{R}_1\text{NOH} + [\text{LV}T] & \stackrel{\text{CH}_3\text{CN}}{\text{RT}} \rightarrow \left[ \begin{array}{c}
\text{R}_1 \\
\text{R}_2
\end{array} \right] \\
\left[ \begin{array}{c}
\text{R}_1 \\
\text{R}_2
\end{array} \right] & \stackrel{\text{H}_2\text{O}}{\text{OH}^-} \rightarrow \left[ \begin{array}{c}
\text{R}_1 \\
\text{R}_2
\end{array} \right]
\end{align*}
\]

**REGENERATION OF THE CARBONYL UNDER MICROWAVE IRRADIATION**

Recently, the growing interest in the application of microwave irradiation in chemical reaction enhancement is due to the high reaction rates and the formation of cleaner products$^{36}$. The solvent free reactions under these conditions are especially appealing for providing an environmentally benign system. The inexpensive reagents and solvent free conditions makes the procedure using clay supported ammonium nitrate "Clayan"$^{37}$, ammonium chlorochromate absorbed on Montmorillonite$^{38}$ and bis(trimethylsilyl)chromate$^{39}$, simple and economic. It has also been reported that microwave irradiation with
pyridiniumchlorochromate (PCC) resulted in enormous reduction in reaction time. Furthermore, excellent yields were obtained using either a solution of an oxime in anhydrous Et₂O or without using any solvent. It was observed that the reaction tolerates many sensitive functional groups even hindered oximes, αβ-unsaturated oximes were successfully deoximated with ease. High yields of aldehydes and ketones were obtained by oxidation with Zn(NO₃)₂·6H₂O and Cu(II)nitrate supported on silica gel under solvent free conditions.

The conversion of ketone oximes with sodium periodate supported on wet silica takes place in the range of two minutes in good yield. Some deoximation reactions using microwave irradiation is summarized in the Scheme B.IV.12.
OXIDATIVE METHODS OF DEOXIMATION

There are numerous oxidizing agents for the regeneration of the carbonyl compounds from oximes. Although some of these are readily available and inexpensive, only a limited number of methods are efficient because of the very low solubility of oxidative reagents in most organic solvents and the required mildness of the reaction condition cannot be achieved. Further, although these methods are generally useful, they have limited applicability when extended to complex molecules having functional groups, which are also susceptible to oxidation under the reaction conditions used. These oxidative procedures were carried out with varying degree of success depending on the nature of the oxime and the oxidizing agent used.

Among the chromium based oxidizing agents, the best known are the pyridinedichromate (PDC) and poly(vinylpyridine–N–oxide)–supported dichromate. Halochromates have also found extensive use as oxidizing agents. Among these are the pyridinium and quinoliniumfluorochromates which are reported to have afforded maximum yield of the product carbonyl compounds. 3-carboxypyridiniumchlorochromate, an inexpensive and easily prepared oxidizing agent and trimethylsilylchlorochromate (TMSCC) can carry out the oxidative deoximation quicker than observed in all other cases. The superiority and wide utility of these oxidizing agents are exemplified by the fast and mild cleavage of ketoximes and aldoximes to carbonyl compounds with no further oxidation. Another chlorochromate used is the triethylammoniumchlorochromate.
(TEACC) which proved to have some advantage over PCC as it is completely soluble in CH₂Cl₂. A combination of pyridinium dichromate and t-butylhydroperoxide have been found to provide an excellent reagent for highly selective deblocking of ketoximes. The coordination polymer of pyrazine and oxodiperoxochromium (VI) compound as a new and stable form of CrO₅(Pyz-CrO₅)n, was introduced for the oxidation of a wide variety of organic compounds including the oximes. Some methods of deoximation using chromium based oxidizing agents are summarized as in the following Scheme (Scheme B.IV.13).

SCHEME B.IV.13
The direct conversion of oximes to aldehydes and ketones by treatment with Thallium(III)nitrate $^{52}$ (TNT) was found to be rapid and non exothermic reaction. From an examination of the conversion of a wide range of oximes with TNT under a variety of conditions the following advantages and limitations appear.

(a) the reaction occurs on a free oxime and prior conversion into a derivative is unnecessary.

(b) the reaction proceeds virtually instantaneously at room temperature and yields of pure products are uniformly high.

(c) considerable variations in experimental conditions were possible depending on the solubility characteristics of the starting oxime.

(d) the procedure is unsuccessful when applied to arylaldehydes or ketones which contain 2- and 4- substituted phenolic hydroxyl or aromatic amino group.

(e) deoximation of $\alpha\beta$-unsaturated aldoximes and ketoximes proceed smoothly. The deoximation process may be explained in terms of the reaction given below (Scheme B.IV.14).

**SCHEME B.IV.14**

\[\begin{align*}
R_1\text{NOH} & \xrightleftharpoons{\text{Tl(NO}_3\text{)}_3} \overset{\text{HNO}_3}{\text{\text{\rightarrow R}_1\text{NO}_2\text{O-Tl(NO}_3\text{)}_3}} \\
R_1\text{NO}_2\text{O-Tl(NO}_3\text{)}_3 & \xrightarrow{\text{H}_2\text{O}^+} \text{R}_1\text{CO}
\end{align*}\]
Several oximes were oxidized with success by cerium(IV)ammonium nitrate \(^{53}\) to the parent carbonyl compounds. Good yields were obtained from rapid reaction at 0\(^o\)C or below where transient blue colours were often observed together with vigorous gas evolution.

Because of their low price and versatility, halogens and halogenated compounds such as Cl\(_2\), Br\(_2\), HOCl, N-bromoamides, perchloric acids, perchlorates, periodic acids, periodates and hypervalent iodines have been successfully used. In particular, deoximation using the Dess–Martin periodinane (DMP) and o-iodobenzoic acid (IBX) \(^{54}\) has been particularly interesting because, it overcomes many of the disadvantages associated with other methods. Sodiumhydrogencarbonate buffered solution of aqueous bromine in CH\(_2\)Cl\(_2\) \(^{55}\) or along with hexamethylenetetramide (HMTA) \(^{56}\) in CHCl\(_3\) has been used under mild conditions at room temperature for an efficient and selective oxidative cleavage of oximes to yield their corresponding carbonyl compounds in good to excellent yield. Besides, iron(III) perchlorate absorbed on silicagel \(^{57}\) 1-benzyl-4-aza-1-azoniabicyclo[2,2,2]octaneperiodate \(^{57}\) readily prepared from commercially available 1,4-diazabicyclo[2,2,2]octaneperiodate are able to convert a wide array of oximes into the corresponding carbonyl compounds (Scheme B.IV.15).

**SCHEME B.IV.15**

\[
\begin{align*}
\text{R}_1 & \quad \text{NOH} & \quad \text{BAABCP} & \quad \text{in reflux CH}_3\text{CN} & \quad \text{R}_1 \\
\text{R}_2 & \quad \text{O} & & & \quad \text{R}_2
\end{align*}
\]
The salient feature of Dess–Martin periodinane (DMP) and IBX method is that the reaction occurs (1) in water saturated ether or DMSO–THF (2) at room temperature and at rapid rate (3) mild nature of DMP and IBX (4) easy workup condition and (5) high yield. In the field of oxidation of organic substrates with \( \text{H}_2\text{O}_2 \), a new catalytic method employing titaniumsilicate (TS-1) and dil.\( \text{H}_2\text{O}_2 \) in acetone solution \(^5\) was found to be applicable to selective oxidative cleavage of oximes. The efficiency of this catalyst was demonstrated in the case of acetophenone oxime where 5% by weight of TS-1 is sufficient to bring about deoximation in excellent yield.

Similarly alkaline \( \text{H}_2\text{O}_2 \), obtained from \( \text{H}_2\text{O}_2 \) and NaOH \(^5\) \( \text{t-butylhydroperoxide (TBHP)} \) was also found to be an efficient and selective reagent \(^6\). Deoximation was also observed along with dehydration when oximes were treated with a mixture of Cu(II)acetatedihydrate and benzoylperoxide \(^6\). Finally, deoximation of ketoximes to ketones with dimethyldioxirane \(^6\) and peroxobis( triphenyl phosphate )–palladium \(^6\) takes place readily and smoothly under extremely mild conditions especially for \( \alpha\beta \)- and \( \gamma\delta \)-unsaturated oximes. The mechanism of the last mentioned reaction is as shown in Scheme B.IV.16.
Reaction of oximes with nitrosating agents to produce the parent carbonyl compounds is well known and has been observed also in the absence of donor solvents such as water and alcohol. Deoximation has been carried out by nitric oxide in the presence of oxygen and good results were obtained with a variety of oximes (Scheme B.IV.17).

**SCHEME B.IV.16**

**SCHEME B.IV.17**
Benzeneselenicanhydride (BSA) proved to be an effective reagent for ketoximes in THF at 40 °C-50 °C and also for aldoximes. The mechanism is shown in Scheme B.IV.18.

**SCHEME B.IV.18**

\[
\begin{align*}
\text{R}_1\text{N}=\text{O} \quad &\rightarrow \quad \text{PhSeO}^+ \quad + \quad \text{R}_1\text{N}=\text{OSePh}^+ \\
\text{PhSeO} \quad &\rightarrow \quad \text{PhSeO}^+ \quad + \quad \text{PhSeO}^-
\end{align*}
\]

Finally, an elegant method of oxidative deoximation is reported by Demir et al. wherein it is reported that manganetriacetate in benzene can be conveniently and efficiently used as a reagent for the deoximation of oximes according to the following Scheme (Scheme B.IV.19).

**SCHEME 19**

\[
\begin{align*}
\text{R}_1\text{N}=\text{NOH} + \text{Mn(OAc)}_3 &\rightarrow \quad \text{CO} + \text{N}_2 + \text{Mn(OAc)}_2 + \text{AcOH}
\end{align*}
\]
DEOXIMATION USING TETRA-n-ALKYLAMMONIUMBROMATES

In this chapter, the experimental details of the use of tetra-n-alkylammoniumbromates as a convenient deoximation reagent is reported. It has already been mentioned in earlier chapters is that, quaternary ammonium salts are not only being used as versatile phase transfer catalyst for accelerating a variety of transformations including oxidation reactions, a modern day synthetic organic chemist is constantly exploring possibilities of preparing new quaternary ammonium salts which may act as the reagent itself. The usual and cheaply available quaternary ammonium salts can be easily converted to another form and the best advantage of these salts is that they are freely soluble in both organic solvents as well as in water and hence capable of carrying out reactions in a variety of solvents including water depending upon the demand of the substrate.

In this study, two quaternary ammoniumbromates namely the tetra-n-propylammoniumbromate and tetra-n-butylammoniumbromates were prepared. The preparation procedure of these two bromates and their physical and chemical characteristics are mentioned in the previous Chapter B.1. The fact that these bromates are efficient and clean oxidizing agents have also been demonstrated and reported earlier. In this study, the bromates have been used as reagents for the oxidative deoximation of a variety of oximes derived from a wide variety of carbonyl compounds. A review of literature on deoximation

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reagents and methods, indicate that bromates have never been used earlier. As such, the tetra-n-alkylammoniumbromates mentioned here are new reagents developed for the deoximation. It has already been mentioned in the review that most reagents used for deoximation suffer from the disadvantage of being insoluble in organic solvents, they are also incapable of restricting the reaction to the carbonyl function. In case of aldehydes, overoxidation is the general rule rather than the exception. The tetra-n-alkylammoniumbromates used here overcomes first of the two disadvantages being soluble in all organic solvents as well as in water.

Experimental results have shown that deoximation of aldoximes leaves the aldehyde without further oxidation to the carboxylic acids. The conditions under which deoximation done is mild, recovery and workup procedures are simple and the yield of the product carbonyl is high. All these results indicates that the tetra-n-alkylammoniumbromates are excellent reagent for oxidative deoximation of oximes. The transformation is shown in the Scheme B.IV.20.

**SCHEME B.IV.20**

\[
\begin{align*}
\text{R}_1 \text{NOH} & \quad + \quad \text{R}_4 \text{NBrO}_3 \\
\text{solvent, reflux} & \quad \rightarrow \\
\text{R}_1 \text{O} & \quad \text{R}_2
\end{align*}
\]

The general procedure of oxidation involved dissolving the oxime and the quaternary ammoniumbromate in a suitable solvent and refluxing the solution for different period of time. The progress of the reaction was monitored by
TLC on prepared silica gel plates using ethylacetate : hexane (1:9) as the eluent. The reaction mixture was run in the chromatogram along with authentic samples of the substrate oxime and the target carbonyl compound and the end point of the reactions were indicated by a complete disappearance of the substrate oxime in the chromatogram. Several oximes were deoximated and the results are summarized in the Table B.IV.2. From the results, it can be concluded that a comparison of the efficiency of both the quaternary ammonium bromates used can be made. Results indicated that tetra-n-propylammonium bromate is a better reagent than tetra-n-butylammonium bromate in terms of yield and reaction time. More than 70% yield of the parent carbonyls were observed.

EXPERIMENTAL

All starting compounds were purified before use by methods reported in literature 67. The preparation of tetra-n-alkylammoniumbromates and their spectral, physical and chemical characteristics have already been mentioned in Chapter B.I. The starting oximes were prepared from their carbonyl compounds by standard methods reported in literature. Some of the carbonyl compounds from which the oximes were prepared namely benzaldehyde, 4-chlorobenzaldehyde, 4-nitrobenzaldehyde, 2-nitrobenzaldehyde, 2,6-dichlorobenzaldehyde, 4,4'-dimethylaminobenzaldehyde, anisaldehyde, 4-hydroxybenzaldehyde, cyclohexanone, naphthylmethylketone, benzil, camphore
were prepared and recrystallized or distilled under reduced pressure (for liquids) before use. Other carbonyl compounds such as chalcone, benzalacetone, were prepared from appropriate reagents. M.p./b.p. were recorded in an apparatus from Scientific Devices, India, Type MP-D in open capillaries; UV was recorded in Hitachi U 3210 spectrophotometer, IR recorded in KBr pallets in a Perkin Elmer 1600 FT-IR spectrometer; $^1$H-NMR in EM 390, 90 MHz spectrometer in CDCl$_3$ with TMS as internal standard.

**Preparation of chalcone (mp, 58° C) $^{68}$:**

2.2 g of NaOH is placed in a mixture of 20 ml of water and 12 ml of EtOH. The flask is immersed in an ice bath and to it 5.2 g (5.5 ml) of acetophenone is added and the mixture stirred vigorously. To this mixture 4.4 ml of pure benzaldehyde is added carefully so that the temperature of the mixture does not exceed 25° C. The reaction mixture is stirred for 30 minutes and kept overnight and the solid product is recover by filtration. The crude chalcone is purified by recrystallization from rectified spirit. Pure chalcone, i.e., benzylidene acetophenone, m.p. 58° C.

**Preparation of benzylidene acetone (m.p. 42° C) $^{69}$:**

4 ml of pure benzaldehyde and 6.3 ml of pure acetone was taken in a 100 ml flask equipped with a mechanical stirrer. The reaction flask was immersed in an ice bath and 5 ml of a 10% aqueous solution of NaOH was added dropwise so that the reaction temperature does not exceed 25° C. The
mixture was stirred at room temperature for 2 hours. The mixture was then made slightly acidic by careful addition of HCl. The product benzylidene acetone was extracted with toluene. Toluene was then removed by distillation under reduced pressure. The residue on standing gave benzylideneacetone m.p. 42 °C.

**Preparation of oximes**

1 g of hydroxylaminehydrochloride and 2 g of sodium acetate is dissolved in 5–10 ml of water. To this solution 0.5 g of aldehydes or ketone is added and shaken. To obtain a clear solution it was necessary sometimes to add a small amount of alcohol or water. For water insoluble aldehyde or ketone, 0.5 ml of pyridine is added. The mixture is refluxed on a water bath for 15–60 minutes. Ethanol is removed either by distillation (water bath) or by evaporation of the hot solution in a stream of air (water pump). Then 5 ml of cold water is added to the residue and stirred in an ice bath till the oxime recrystallized. The solid is filtered off, washed with a little water and dried. Finally, it is recrystallized from EtOH, benzene or benzene–light petroleum (b.p. 60°–80°C).
### TABLE B.IV.1

**Physical characteristics of oximes prepared**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Carbonyl Compound</th>
<th>Oxime</th>
<th>M.P. (°C)</th>
</tr>
</thead>
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<td></td>
<td></td>
<td>obs.</td>
</tr>
<tr>
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<td><img src="image1" alt="Phenylacetyl" /></td>
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</tr>
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<td>2.</td>
<td><img src="image3" alt="Chloroacetyl" /></td>
<td><img src="image4" alt="Chloro" /></td>
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</tr>
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<td>3.</td>
<td><img src="image5" alt="N,N-Dimethylethylacetyl" /></td>
<td><img src="image6" alt="N,N-Dimethylethyl" /></td>
<td>147</td>
</tr>
<tr>
<td>4.</td>
<td><img src="image7" alt="Nitroacetyl" /></td>
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<td>132</td>
</tr>
<tr>
<td>5.</td>
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<td>70</td>
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(continued)
<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Carbonyl Compound</th>
<th>Oxime</th>
<th>M.P. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
<tr>
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<td><img src="image8" alt="Chemical Structure" /></td>
<td>145-46</td>
</tr>
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<tr>
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DEOXIMATION OF OXIMES TO THE CARBONYL COMPOUNDS

(General procedure)

0.001 mol of the oxime and 0.001 mol of the tetra-n-propylammonium bromate were dissolved in 25 ml toluene and refluxed. The progress of the reaction was monitored by TLC in prepared silicagel plates using ethylacetate: hexane (1:9) as the eluent. The test solution was run along with authentic samples of the starting oxime and the expected target carbonyl compound. Disappearance of the oxime indicated completion of the reaction. The progress of the reaction was also followed by colour change of the reaction mixture. The initial yellow to orange colour of the solution changed to an almost colourless solution. After the completion of the reaction, toluene was removed by reduced pressure distillation in a rotavapour and water was added to the semisolid obtained. The solid was washed several times with distilled water. The solid product was then dissolved in minimum volume of ethanol and the solution filtered on to a beaker containing large volume of water. This process of dissolution, filtration and reprecipitation was repeated several times till pure product of the carbonyl compound was obtained.

In case where liquid carbonyl compounds were the end product, the reaction mixture was distilled under reduced pressure to separate out the solvent and the product from the spent quaternary ammoniumbromate. Careful fractional distillation of the mixture of solvent and product gave the product carbonyl
compounds in the pure form. The final identification of the liquid carbonyl compounds were done by measuring their boiling points and also by converting them to the 2,4-dinitrophenylhydrazones using Brady's reagent. The physical characteristics of the product carbonyl compounds, reaction time and percentage yield is given in Table B.IV.2.

**TABLE B.IV.2**
(Ref. Scheme B.IV.20)

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Oxime</th>
<th>Carbonyl Compounds</th>
<th>Reflux time (hrs)</th>
<th>Yield (%)</th>
<th>M.P. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td></td>
<td>I</td>
<td>II</td>
<td>I</td>
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<tr>
<td>1.</td>
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<td><img src="image" alt="PhCO" /></td>
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<td><img src="image" alt="ClNOH" /></td>
<td><img src="image" alt="ClCO" /></td>
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<td>3</td>
<td>89</td>
</tr>
<tr>
<td>3.</td>
<td><img src="image" alt="CH₃NNOH" /></td>
<td><img src="image" alt="CH₃NCO" /></td>
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<td>79</td>
</tr>
<tr>
<td>4.</td>
<td><img src="image" alt="NO₂NOH" /></td>
<td><img src="image" alt="NO₂CO" /></td>
<td>2.5</td>
<td>3</td>
<td>84</td>
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<tr>
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<td><img src="image" alt="NO₂CO" /></td>
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<td><img src="image" alt="HO-CO" /></td>
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<td>92</td>
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</table>

(continued)
<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Oxime</th>
<th>Carbonyl Compounds</th>
<th>Reflux time (hrs)</th>
<th>Yield (%)</th>
<th>M.P. (°C)</th>
</tr>
</thead>
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<tr>
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<td>II</td>
<td>I</td>
</tr>
<tr>
<td>8.</td>
<td><img src="image1.png" alt="image" /></td>
<td><img src="image2.png" alt="image" /></td>
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<td>2</td>
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<td>2.5</td>
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<td>1.5</td>
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<td>2</td>
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<td>1.5</td>
<td>89</td>
</tr>
<tr>
<td>14.</td>
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<td><img src="image14.png" alt="image" /></td>
<td>1.5</td>
<td>2</td>
<td>88</td>
</tr>
<tr>
<td>15.</td>
<td><img src="image15.png" alt="image" /></td>
<td><img src="image16.png" alt="image" /></td>
<td>1.5</td>
<td>2</td>
<td>71</td>
</tr>
</tbody>
</table>

I indicates reaction with tetra-n-propylammoniumbromate and II indicate reaction with tetra-n-butyrammoniumbromate.
Some spectral characteristics of the regenerate carbonyl compounds

➤ **PRODUCT 3:**

UV : \( \lambda_{\text{max}} \) (EtOH) 260 nm;

IR : (KBr cm\(^{-1}\)) 2215 [N(CH\(_3\)\(_2\)], 1610 (> C=O);

\(^1\)H-NMR : (60 MHz, CDCl\(_3\), d) 8.1 (1H, s), 7.8 (4H, d), 1.3 (6H, s).

➤ **PRODUCT 4:**

UV : \( \lambda_{\text{max}} \) (EtOH) 265 nm;

IR : (KBr cm\(^{-1}\)) 1660 (> C=O), 1510, 1325 (NO\(_2\));

\(^1\)H-NMR : (60 MHz, CDCl\(_3\), d) 8.2 (1H, s), 7.7-7.9 (4H, d).

➤ **PRODUCT 6:**

UV : \( \lambda_{\text{max}} \) (EtOH) 235 nm;

IR : (KBr cm\(^{-1}\)) 1625 (> C=O);

\(^1\)H-NMR : (60 MHz, CDCl\(_3\), d) 8.2 (1H, s), 7.6 (3H, d).

➤ **PRODUCT 11:**

UV : \( \lambda_{\text{max}} \) (EtOH) 272 nm;

IR : (KBr cm\(^{-1}\)) 1666 (> C=O);

\(^1\)H-NMR : (60 MHz, CDCl\(_3\), d) 8.2 (5H, s), 7.6-8.1 (7H, m)

2.6 (3H, s).
It may be concluded from the above study that the prepared tetra-n-alkylammoniumbromates are excellent reagents for deoximation of oximes to the parent carbonyl compounds. Yields are found to be high and the reaction conditions are mild. The procedure for product recovery is also found to be simple and requires only washing with water as the byproducts of the reactions are water soluble and hence can be removed easily. The “soft” reaction techniques, easy recovery of products, high yield combined with the fact that quaternary ammoniumbromates do not oxidize other oxidizable groups present in the substrates such as olefinic bond, phenolic–OH, makes this reagent superior to other deoximation reactions used. Even sterically hindered camphor oximes have been successfully deoximated with ease and in high yield.
References:


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CHAPTER-B.V

OXIDATIVE CLEAVAGE OF >C=\text{N}- OF PHENYLHYDRAZONES AND SEMICARBAZONES

REGENERATION OF CARBONYL COMPOUNDS FROM THEIR HYDRAZONES, PHENYLHYDRAZONES, AND 2,4-DINITROPHENYLHYDRAZONES USING TETRA-n-ALKYLAMMONIUMBROMATES

Similar to the oximes, the hydrazones, phenylhydrazones and the 2,4-dinitrophenylhydrazones are also prepared in high yields and by a simple procedure from the carbonyl compounds. They are well defined and highly crystalline coloured compounds. The formation of various hydrazones derivatives of aldehydes and ketones is a common and popular methods for the isolation, purification and quantitative estimation of the carbonyl compounds. Purification of these derivatives followed by regeneration of the parent carbonyl is a good procedure for the isolation of the desired carbonyl compound from a complex mixture\(^1\). The hydrazones are often used to protect the carbonyl group in a multistep synthesis. They are also found to be of considerable synthetic importance\(^2\). They are the appropriate starting material for the preparation of nitriles\(^4,5\), thioketones\(^6,7\) and others. An indirect method of carrying out the conversion \(\text{R}_1\text{CO-R}_2 \rightarrow \text{R}_1\text{CH}($CN$)$\text{R}_2\) has also been reported recently via the hydrazones specifically by the addition of KCN to triisopropylbenzene sulphonylhydrazones of several carbonyl compounds\(^8\).
Hydrazones can be prepared by the condensation reaction of hydrazine and an aldehyde or a ketone. Hydrazine itself gives hydrazones only with arylketones but with other aldehydes and ketones, no useful product can be isolated because the second amino (\(-\text{NH}_2\)) group of the hydrazine can further react with a second molecule of the carbonyl to give the azine so that a mixture of two products is usually obtained as shown in Scheme B.V.1.

SCHEME B.V.1

Formation of hydrazones and azines

\[
\begin{align*}
\text{R}_1\text{R}_2\text{C}=\text{O} + \text{NH}_2\text{NH}_2 & \rightarrow \left[ \begin{array}{c}
\text{R}_1 \\
\text{R}_2 \\
\text{OH}
\end{array} \right] \\
\text{R}_1\text{N}\text{N}\text{R}_2 & \rightarrow \text{N} \equiv \text{N} \\
\text{R}_1\text{R}_2\text{C}=\text{O} & \rightarrow \text{N} \equiv \text{N}
\end{align*}
\]

A convenient method for preparation of hydrazones from hydrazines involves a process of exchange reaction. In this technique, the carbonyl compound is first converted to the N,N-dimethylhydrazone which is subsequently treated with excess hydrazine to give the hydrazone by an exchange reaction.
This method precludes the formation of the undesired azine product as shown in Scheme B.V.2.

**SCHEME B.V.2**

Synthesis of hydrazone by exchange reaction

\[ R_1R_2C\equiv R_2 + \text{NH}_2N<Me\text{Me} \rightarrow R_1R_2\text{Me}N-N<Me\text{Me} \]

\[ \text{NH}_2\text{NH}_2 \rightarrow R_1R_2\text{N-NH}_2 \]

The hydrazones that are generally used for characterization, purification and protection of the carbonyl group are the phenylhydrazones and the 2,4-dinitrophenylhydrazones. These substituted hydrazines give the corresponding hydrazones with most aldehydes and ketones and in quantitative yield. A convenient small scale method is to add hydrochloric acid dropwise to a mixture of the carbonyl compound and the phenylhydrazine in diglyme, the desired derivatives precipitate out from solution.

The development of mild and efficient methods for the selective cleavage of the >C=N– bond of hydrazones to regenerate the parent carbonyl compound continues to be a significant aspect of organic functional group transformation. Several reagents have been reported in literature which involves
hydrolytic, reductive as well as oxidative reactions. The reagents developed vary in their characteristics, reaction conditions, yield and the reaction environment. Some of the important methods of regeneration of carbonyl compounds from their hydrazones are reviewed below:

**HYDROLYTIC METHODS**

Hydrazones can be hydrolyzed to the corresponding aldehydes and ketones. Hydrolysis is easy and often a very reactive aldehyde is added to trap the hydrazine liberated, formaldehyde being the most useful aldehyde for the purpose. Hydrolysis in acidic medium is catalyzed efficiently by levulinic acid. The hydrolysis of carbon nitrogen double bonds involves initial addition of water and elimination of a nitrogen moiety as shown in Scheme B.V.3.

**SCHEME B.V.3**

*Mechanism of hydrolytic cleavage of >C=N– bond*

\[
\begin{align*}
\text{Hydrolysis:} & \quad \text{Y} \quad \text{H}_2\text{O} \quad (\text{+)OH}_2 \quad (\text{-)N-W} \quad \text{OH} \quad H^+ \\
\text{Hydrolysis:} & \quad \text{OH} \quad -\text{NH}_2\text{W} \quad \text{OH} \quad (\text{+)NH}_2\text{W} \quad \text{OH} \quad -\text{H}^+ \\
\end{align*}
\]
Some of the other reagents used for the hydrolytic cleavage of the $\text{C}=\text{N}$ bond are (i) aqueous TiCl$_3$ and CH$_3$COOH $^{11}$ (ii) aqueous NaHSO$_3$ $^{12}$ (iii) NaOCl $^{13}$. Acidic hydrolytic methods of cleavage is not suitable in the presence of acid sensitive groups when present in the substrate hydrazone.

OXIDATIVE METHODS

An alternative but destructive method of regeneration of the carbonyl group from the hydrazones is the oxidative method of cleavage of the $\text{C}=\text{N}$-group of hydrazones. The development of such reagents have been receiving continued attention from synthetic organic chemists. The main thrust of research effort have always been to develop reagents which offer mild experimental conditions, which are cost effective, efficient, selective and environmentally benign.

Among the known oxidizing agents potassium peroxymonosulfate (2 KHSO$_5$, KHSO$_4$, K$_2$SO$_4$) commercially available as “oxone” is reported to be a convenient, inexpensive and an efficient oxidizing agent often used as a powerful oxidant. This reagent has been successfully used for the oxidative cleavage of the $\text{C}=\text{N}$- bond of phenylhydrazones, tosylhydrazones and semicarbazones $^{14}$ (Scheme B.V.A, Reaction 1).

Kim et al. $^{15}$ in their studies involving the use of dinitrogentetroxides as an oxidizing agent in organic synthesis reported that this reagent can also be
used not only for the deoximation of oximes but also for the oxidative cleavage of hydrazones to the carbonyl compounds (Scheme B.V.4, Reaction 2).

**SCHEME B.V.4**

\[ \text{HSO}_3^- / \text{CH}_3\text{COOH} \]

**Reaction I**

- \[ R_1\text{C}=\text{O} \]
- \[ R_2 \]
- \[ X = \text{NHCONH}_2,\text{NTs},\text{-NHPh} \]

**Reaction II**

- \[ -40^\circ\text{C}, 10\text{ min.} \]
- \[ R_1\text{C}=\text{O} \]
- \[ R_2 \]
- \[ X = \text{NPh},\text{NH}_2\text{ etc.} \]

It has also been reported by Edwards et al. that oxidation of organic substrates employing dioxiranes have been found to have the advantage of high selectivity, mild reaction conditions and ease of product isolation. The most common dioxiranes employed are dimethyldioxirane (I) and methyl-(trifluoromethyl)dioxirane (II).

\[
\begin{array}{c}
\text{(I)} \\
\begin{array}{c}
\text{CH}_3 \\
\text{O} \\
\text{CH}_3 \\
\text{O}
\end{array}
\end{array}
\begin{array}{c}
\text{(II)} \\
\begin{array}{c}
\text{CF}_3 \\
\text{O} \\
\text{CF}_3 \\
\text{O}
\end{array}
\end{array}
\]

The authors have reported that the carbonyl group can be regenerated from its phenylhydrazones using dimethyloxirane generated in situ from the reaction of acetone with potassiumperoxymonosulfate. The oxidative cleavage of
>C=N– simply entailed addition of aliquots of the dioxirane solution to the hydrazone substrate. Further experiments have shown that dioxiranes unmask the carbonyl moiety from steroidal hydrazones keeping ester group, if present in the substrate, untouched. The authors have also given a possible mechanism of the oxidation as shown in Scheme B.V.5.

**SCHEME B.V.5**

**Mechanism of oxidative cleavage of >C=N– with dioxiranes**

There are also several metal based oxidizing agents which can be utilized for the oxidative cleavage of the >C=N– resulting in the regeneration of the carbonyl precursor. Molybdenum salts, in their different valency states (+2 to +6) can be expected to be versatile redox reagents. Unlike the numerous application of manganese and chromium based compounds, the use of
molybdenum reagents in organic synthesis has been surprisingly limited. Olah et al. has reported the use of molybdenum fluoride (MoF₆) and molybdenyl chloride (MoOCl₃) in the oxidative cleavage of hydrazones in nonpolar organic solvents such as chlorofluorocarbon (Freon) under mild conditions. The mechanism of the regeneration of the parent carbonyl from the hydrazones as described by Olah et al. is shown in Scheme B.V.6.

**SCHEME B.V.6**

*Oxidative cleavage of >C=N− with Molybdenum based oxidizing agents*

**Cleavage with MoOCl₃**

\[
\begin{align*}
R_1\underbrace{-N-N-}_{\text{R_2}}\underbrace{R_3}_+ + \text{MoOCl}_3 & \rightarrow R_1\underbrace{-N-N-}_{\text{R_2}}\underbrace{R_3}_+ \text{(+) OMoCl}_3 \\
\left[ R_1\underbrace{\bigg\lceil C-N-}_{\text{R_2}}\underbrace{\bigg\rfloor}_{\text{OMoCl}} \right] \text{Cl}^- & \rightarrow R_1\underbrace{\bigg\lceil C-N-}_{\text{R_2}}\underbrace{\bigg\rfloor}_{\text{OMoCl}} + \text{MoCl}_3 + R_3^+ N=N^- \\
\end{align*}
\]

**Cleavage with MoF₆**

\[
\begin{align*}
R_1\underbrace{-N-N-}_{\text{R_2}}\underbrace{R_3}_+ + \text{MoF}_6 & \rightarrow \left[ R_1\underbrace{\bigg\lceil N-}_{\text{R_2}}\underbrace{\bigg\rfloor}_{\text{MoF}_5} \right] ^- F^- \\
\text{H}_2\text{O} & \rightarrow R_1\underbrace{-O}_{\text{R_2}} + \text{MoF}_4 + 2\text{HF} + R_3^+ N=N^- \\
\end{align*}
\]
A solid phase method of oxidative cleavage was reported by Laszlo et al.\textsuperscript{19} wherein the authors have used inexpensive clay supported ferricnitrate (clayfen) as the oxidizing agent. The method is simple and the carbonyl compound is isolated in high yield. The workup procedure for isolation of the products is also found to be simple. It has also been observed by Olah et al.\textsuperscript{20} that Cobalt(III)trifluorides can also be conveniently used for the regeneration of the carbonyl compounds from both the N,N-dimethylhydrazones and the tosylhydrazones. The conversion is shown in Scheme B.V.7.

**SCHEME B.V.7**

Conversion of hydrazones to carbonyl using CoF$_3$

\[
\begin{align*}
R_1-N-N^+X_1 &+ \text{Co (III)F}_3 \rightarrow \left[ R_1-N-N^+X_1 \right]^{\text{F}^-} \\
& \quad \downarrow \text{H}_2\text{O} \\
R_1=O &+ \text{NH}X_1^+X_2^+ + \text{Co(II)O} + 2\text{HF}
\end{align*}
\]

Barton\textsuperscript{21} has reported that hypervalent organoiodine reagent can be used for the regeneration of several $\alpha$-ketoesters from their phenylhydrazones. In the experiment carried out, the authors used the [bis(trifluoroacetoxy)iodo]-benzene (BTIB) or [hydroxy(tosyloxy)iodo]benzene (HTIB) as the hypervalent iodine reagent for the oxidative cleavage. It has further been observed that both $E$ and $Z$ phenylhydrazones were transformed with equal ease. A solid state
cleavage of phenylhydrazone with clay supported ammoniumpersulphate using microwave irradiation or exposure to ultrasonic was reported by Varma et al. 22. In some examples cited in the report, conversion was completed in less than a minute exposure of the reaction mixture to ultrasonic irradiation but yields were moderate.

Finally, some quaternary "Onium" based reagents have also been used to regenerate the carbonyl from the phenylhydrazones, hydrazones and tosylhydrazones. All these reagents have been very conveniently derived from easily available quaternary "onium" salts. As for example, the cetyltrimethylammoniumpermanganate 23 obtained by mixing the cetyltrimethylammoniumbromide or chloride with an aqueous solution of KMnO₄, was found to be a mild and selective reagent for such a transformation. It has also been observed that 2,4-dinitrophenylhydrazones could be cleaved without effecting a hydroxyl group present in the substrate further, olefinic bonds were also not effected. This established the selective nature and versatility of the oxidizing agent. Among the best known chromium based oxidizing agents is the benzyltriphenylphosphoniumchlorochromate 22. Using this reagent, phenylhydrazones, 2,4-dinitrophenylhydrazones have been successfully deprotected to afford the corresponding aldehydes and ketones in moderate to excellent yield. A notable feature of this transformation is that aldehydes do not undergo further oxidation to the carboxylic acid. Another feature of the reagent is that it could be stored over a long period of time without loss in its

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oxidative potential. Lewis acid in the form of AlCl₃ was necessary as a co-reagent, although the role played by AlCl₃ not certain.

It may be mentioned that most of the methods discussed above require strongly oxidative or hydrolytic conditions (both basic and acidic) and involves tedious reaction and workup conditions besides expensive starting materials. Most of the procedures suffer from severe limitations such as use of hazardous reagents, high temperature, long reaction periods etc. Consequently, there is a need for the development of synthetic protocols and reagents which are easy, readily available, low cost and safe to handle besides being environmentally benign.

In the present study, the tetra-n-alkylammoniumbromates were used for the oxidative cleavage of the >C=N- bond of phenylhydrazones for the regeneration of the parent carbonyl compound. Two different quaternary “Onium” bromates were used for this regeneration of the carbonyl group. One of the reagent namely the tetra-n-propylammoniumbromate and the other is tetraethylammoniumbromate. The preparation of these two bromates is already mentioned in Chapter B.1. Several hydrazones, phenylhydrazones and 2,4-dinitrophenylhydrazones were synthesized by established procedure from the corresponding carbonyl compounds.

These hydrazones were refluxed with equimolar proportion of the appropriate quaternary ammoniumbromate in an organic solvent for a varying period of time. It was observed that ordinarily the yield of parent carbonyl
compounds was not found satisfactory. However, in the presence of trace amounts of mineral acid or acetic acid, the oxidative cleavage proceeded smoothly and the yield of the parent carbonyl was excellent and almost quantitative. It is probable that the presence of mineral acid or acetic acid accelerated the decomposition of the bromate with concomitant release of oxygen which is responsible for the oxidative cleavage. In a typical reaction procedure, equimolar quantities of the hydrazone and the 'onium bromate' was dissolved in an appropriate organic solvent and to this mixture trace of dil. HCl or acetic acid was added and refluxed. The progress of the reaction could be easily followed by observing the colour change of the reaction solution. The progress of the reaction was also monitored by drawing aliquots of the reaction mixture and performing cochromatography of the reaction mixture with authentic samples of the substrate hydrazone and the target carbonyl compound. Disappearance of the coloured hydrazone from the reaction mixture indicated the end of the reaction. TLC was performed in prepared silicagel G plates using ethanol:ethylacetate (9:1) mixture as the eluent.

At the end of the reaction, the reaction mixture was added to a large volume of distilled water, the product carbonyl compound separated out as a solid whereas the byproducts, if any, and the spent bromates remained dissolved in the aqueous solution. Recovery was done by filtration and decolourized using activated charcoal. The products were identified by comparing the melting points, IR and $^1$H-NMR spectra with authentic samples. Yield of the product carbonyl compound was obtained to the extent of about 95% in
some cases. The details are given in the table and the reaction carried out is summarized in Scheme B.V.8.

**SCHEME B.V.8**

Oxidative cleavage of >C=N–bond using tetra-n–alkylammoniumbromates

![Chemical Reaction Diagram]

Where $Q'\text{NBrO}_3^-$ = Tetra-n–propylammoniumbromate

= Tetraethylammoniumbromate

**EXPERIMENTAL**

All starting materials were purified by establish procedures available in text $^{24}$. Melting points and boiling points were recorded in an apparatus from Scientific Devices, India, Type MP-D in open capillaries; IR spectra were recorded in KBr pallets in a Perkin Elmer 1600 FT-IR spectrophotometer; UV was recorded in Hitachi U 3210 spectrophotometer; $^1$H-NMR in EM 390, 90 MHz spectrometer in CDCl$_3$ with TMS as internal standard. C,H,N, analysis of the product was recorded in Hitachi 026 CHN analyzer. Chromatography was done on prepared silicagel G plates.

The quaternary ammoniumbromates namely tetraethylammoniumbromate and tetra-n–propylammoniumbromate were prepared by procedures mentioned in Chapter B.I.
PREPARATION OF HYDRAZONES
FROM CARBONYL COMPOUNDS

1) Preparation of hydrazone:

A solution of 0.8gm of NaOAc in 5 ml of water were prepared and 0.5 gm of hydrazine hydrochloride were dissolved in it. To this solution 0.4 gm of aldehyde or ketone dissolved in a little ethanol were added. The resulting mixture was shaken and a little more ethanol was added to remove the resulting turbidity. The solution was warmed on a water bath for 10 -15 minutes and cooled. The crystalline derivative obtained was filtered off and dried. The products were recrystallized from dil. ethanol.

2) Preparation of phenylhydrazone:

A solution of 0.8gm of NaOAc in 5 ml of water were prepared and 0.5 gm of the colourless phenylhydrazinehydrochloride was dissolved in it. To this solution 0.4 gm of aldehyde or ketone dissolved in a little ethanol were added. The resulting mixture was shaken and a little more ethanol was added to remove turbidity that appeared. The solution was warmed on a water bath for 10-15 minutes and cooled. The crystalline derivative obtained was filtered off and dried. The products were recrystallized from dil. ethanol.

3) Preparation of 2,4-dinitrophenylhydrazones:

0.25 gm of 2,4-dinitrophenylhydrazine was suspended in 8 ml of CH₃OH and 0.5 ml of conc. H₂SO₄ was cautiously added to it. The warm solution was filtered and 0.2 gm of carbonyl compound dissolved in a small volume of methanol was added to it and the resulting mixture was warmed in a water bath for about 5 minutes. The mixture was allowed to cool to room
temperature. The crystalline solid which separated out within few minutes was filtered by suction and was washed with a little amount of methanol. The product was recrystallized methanol. The physical characteristics of the product obtained was reported in Table B.V.1.

TABLE B.V.1

Physical characteristics of hydrazones prepared

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Substrate</th>
<th>Product</th>
<th>M. P. / B. P. of products (°C)</th>
</tr>
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<td>Obs</td>
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<tr>
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<td><img src="image1" alt="Substrate 1" /></td>
<td><img src="image2" alt="Product 1" /></td>
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<tr>
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<td><img src="image4" alt="Product 2" /></td>
<td>102</td>
</tr>
<tr>
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<td><img src="image5" alt="Substrate 3" /></td>
<td><img src="image6" alt="Product 3" /></td>
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</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="Substrate 4" /></td>
<td><img src="image8" alt="Product 4" /></td>
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<td><img src="image9" alt="Substrate 5" /></td>
<td><img src="image10" alt="Product 5" /></td>
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<tr>
<td>6</td>
<td><img src="image11" alt="Substrate 6" /></td>
<td><img src="image12" alt="Product 6" /></td>
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<tr>
<td>7</td>
<td><img src="image13" alt="Substrate 7" /></td>
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</tr>
<tr>
<td>8</td>
<td><img src="image15" alt="Substrate 8" /></td>
<td><img src="image16" alt="Product 8" /></td>
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<table>
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<tr>
<th>Sl. No.</th>
<th>Substrate</th>
<th>Product</th>
<th>M. P./B. P. of products (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.</td>
<td>![Substrate Image]</td>
<td>![Product Image]</td>
<td>257 (d)/253 (d)</td>
</tr>
</tbody>
</table>

a) \(Z_1 = \text{N-NH}_2\), \(Z_2 = \text{N-NH-Ph}\), \(Z_3 = \text{N-NH-Ph}^+\)

b) Melting points are recorded in an apparatus from Scientific Devices, India, Type MP-D in open capillaries.
OXIDATIVE CLEAVAGE OF HYDRAZONES USING TETRA-n-ALKYLAMMONIUMBROMATES

*General procedure*:

A mixture of 0.001 mole of the hydrazone and and 0.001 mole of the tetra-n-alkylammoniumbromates were dissolved in 25 ml of ethanol or acetic acid and the mixture was refluxed for varying amount of time. The progress of the reaction was periodically monitored by TLC in prepared silicagel plates using authentic samples of the starting and the target compounds as references. The end of the conversion was indicated by the disappearance of the starting compound. After the completion of the reaction, the solution was poured in a large excess of water. The solid was filtered and washed several times with water. The solid products obtained were recrystallized from the appropriate solvent. With different products, minor variations were made in the work up procedure. The results of the experiments carried out are summarized as shown in Table B.V.2. The product carbonyl compounds were identified by recording their m.p./ b.p. and comparing the IR, UV and $^1$H-NMR spectra with authentic samples.
### TABLE B.V. 2
(Ref. Scheme B.V.8)

Physical characteristics of the regenerated carbonyl compounds

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Substrate</th>
<th>Product</th>
<th>Reagent / Solvent</th>
<th>Reflux Time</th>
<th>Yield</th>
<th>M. P. / B. P. of products (°C)</th>
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<tbody>
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<td></td>
<td></td>
<td></td>
<td>(h r s )</td>
<td></td>
<td>Obs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(%)</td>
<td></td>
<td>Lit</td>
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<tr>
<td>1.</td>
<td><img src="substrate1.png" alt="Image" /></td>
<td><img src="product1.png" alt="Image" /></td>
<td>EtOH</td>
<td>2 hrs (1*)</td>
<td>80</td>
<td>48 (m.p.)</td>
</tr>
<tr>
<td>2.</td>
<td><img src="substrate2.png" alt="Image" /></td>
<td><img src="product2.png" alt="Image" /></td>
<td>EtOH</td>
<td>3 hrs 15 mins (1*)</td>
<td>71</td>
<td>108 (m.p.) 95 (m.p.)</td>
</tr>
<tr>
<td>3.</td>
<td><img src="substrate3.png" alt="Image" /></td>
<td><img src="product3.png" alt="Image" /></td>
<td>Dioxan</td>
<td>9 hrs (II*)</td>
<td>95</td>
<td>95 (m.p.)</td>
</tr>
<tr>
<td>4.</td>
<td><img src="substrate4.png" alt="Image" /></td>
<td><img src="product4.png" alt="Image" /></td>
<td>EtOH</td>
<td>2 hrs (1*)</td>
<td>83</td>
<td>80 (m.p.)</td>
</tr>
<tr>
<td>5.</td>
<td><img src="substrate5.png" alt="Image" /></td>
<td><img src="product5.png" alt="Image" /></td>
<td>Dioxan</td>
<td>2 hrs 45 mins (II)</td>
<td>75</td>
<td>51 (m.p.)</td>
</tr>
<tr>
<td>6.</td>
<td><img src="substrate6.png" alt="Image" /></td>
<td><img src="product6.png" alt="Image" /></td>
<td>EtOH</td>
<td>1 hrs 45 mins (1*)</td>
<td>78</td>
<td>243 247 (b.p.)</td>
</tr>
<tr>
<td>7.</td>
<td><img src="substrate7.png" alt="Image" /></td>
<td><img src="product7.png" alt="Image" /></td>
<td>Toluene</td>
<td>3 hrs 50 mins (1*)</td>
<td>66</td>
<td>110 112-114 (b.p.)</td>
</tr>
<tr>
<td>8.</td>
<td><img src="substrate8.png" alt="Image" /></td>
<td><img src="product8.png" alt="Image" /></td>
<td>EtOH</td>
<td>6 hrs 45 mins (1*)</td>
<td>69</td>
<td>125 127 (b.p.)</td>
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</table>

(continued)
<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Substrate</th>
<th>Product</th>
<th>Reagent / Solvent</th>
<th>Reflux Time (hrs)</th>
<th>Yield (%)</th>
<th>M. P. / B. P. of products (°C)</th>
</tr>
</thead>
<tbody>
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<td></td>
<td></td>
<td>Obs</td>
</tr>
<tr>
<td>9.</td>
<td></td>
<td></td>
<td>EtOH</td>
<td>11 hrs 45 mins (1**)</td>
<td>75</td>
<td>155</td>
</tr>
<tr>
<td>10.</td>
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<td>CH$_3$COOH</td>
<td>40 mins (II)</td>
<td>68</td>
<td>248</td>
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<tr>
<td>11.</td>
<td></td>
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<td>CH$_3$COOH : EtOH (3:2)</td>
<td>1 hr (II**)</td>
<td>75</td>
<td>243</td>
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<td>EtOH</td>
<td>2 hrs (I*)</td>
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<td>14.</td>
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<td></td>
<td>CH$_3$COOH</td>
<td>2 hrs (II**)</td>
<td>65</td>
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<tr>
<td>15.</td>
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<td></td>
<td>CH$_3$COOH</td>
<td>1 hr 20 mins (II)</td>
<td>73</td>
<td>173</td>
</tr>
</tbody>
</table>

a) I indicates yield with tetraethylammoniumbromate and II with tetra-n-propylammoniumbromate

b) Z$_1$ = N-NH$_2$, Z$_2$ = N-NH-Ph, Z$_3$ = N-NH-Ph$_2$

c) * indicates 3-4 drops conc HCl ** indicates 2-3 drops conc H$_2$SO$_4$

d) 2-3 drops of conc. HCl was added to the reaction mixture in all cases except Sl. 10, 11, and 12.

e) In case of liquid products % yield was obtained by conversion to the corresponding oximes.

f) M.p. / B. p. recorded in open capillaries.
References:


The reaction of semicarbazides with carbonyl compounds to give the semicarbazones is yet another examples of nucleophilic addition reaction to the carbonyl group. The general reaction is as follows:

\[
\text{R}_1\text{C}=\text{O} + \text{NH}_2\text{NH}^-\text{C}^-\text{NH}_2 \rightarrow \text{R}_1\text{N}^+\text{NH}^-\text{C}^-\text{NH}_2
\]

The semicarbazones are also well defined crystalline compounds with sharp melting points and other physical properties. The reaction of the carbonyl compounds with semicarbazide give almost quantitative yield of the semicarbazone, therefore these compounds are more often used to isolate and purify the carbonyl compounds from a mixture. Conversion to the semicarbazone is yet another method of protection of the carbonyl group. It has been reported that semicarbazones are preferred over the oximes and the hydrazones as a protecting group. Therefore, regeneration of the parent carbonyl compound from semicarbazones is an important step in a multistep synthesis where the carbonyl group needs to be protected. As it has already been highlighted in the previous chapters, there are innumerable methods for the regeneration of the carbonyl compounds from oximes and hydrazones, but not
many methods are known for the regeneration of carbonyl compounds from their semicarbazones under mild conditions \textsuperscript{5,6}. Most of the reported procedures involve hydrolysis under stringent conditions \textsuperscript{7,8,9} or strong oxidation \textsuperscript{10} and therefore are not attractive specially when sensitive groups are present elsewhere in the molecule. Some of the procedures used for the regeneration of the carbonyl compound from semicarbazones are, the use of phthalicanhydride \textsuperscript{11}, pyruvic acid as an acceptor in a transfer reaction \textsuperscript{12} nitrous acid in acetic acid \textsuperscript{13} thallium(III)nitrate \textsuperscript{14}, benzeneseleninicanhydride \textsuperscript{15} cericammoniumnitrate \textsuperscript{16}, clay supported ferricnitrate \textsuperscript{10} and cation exchange resins \textsuperscript{17,18}.

Although some reactions are carried out under mild conditions, most of those used for the regeneration of the carbonyl compounds from semicarbazones require drastic conditions, rare reagents, toxic reagents and sometimes long reaction time. Thus there is still a need for improved methods for regeneration of the carbonyl compounds from the semicarbazones. A mild method of deprotection using cheap and readily available reagents would be highly attractive.

In this study, semicarbazones of several aldehydes and ketones were prepared by established procedures and characterized by comparing their melting points, IR and \textsuperscript{1}H-NMR spectra with those found in literature. These semicarbazones were then reacted with the tetra-n-alkylammoniumbromate and under reflux conditions, the parent carbonyl compound could be generated. In other words, the tetraethylammoniumbromate obtained from the easily available and cheap tetraethylammoniumbromide could be conveniently used in a simple oxidative method for the cleavage of the \textsuperscript{1}C=N bond of semicarbazones to

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give the carbonyl compounds. The conversion involved, mere heating the semicarbazone with the bromate in an appropriate solvent in the presence of trace amount of mineral acid. The parent carbonyl was regenerated in high yield. The workup procedure for isolation and separation of the carbonyl compounds was also simple and required filtration and washing with water only. The target products were obtained in more than 70% average yield. The results obtained is given in a tabular form in Table B.V.3 and the reaction is shown in Scheme B.V.9.

**SCHEME B.V.9**

![Scheme B.V.9](image)

The regenerated carbonyl was identified by recording their m.p/b.p. and also by conversion to their 2,4-DNP derivatives which are reported in literature. The target products were also identified by recording their IR and $^1$H-NMR spectra and comparing the results with those obtained from authentic sample. A general procedure for oxidative regeneration of the carbonyl from their semicarbazones is given in the experimental section.
EXPERIMENTAL

All starting compounds were obtained from E Merck Inc. and used without further purification. Melting points and boiling points were recorded in an apparatus from Scientific Devices, India, Type MP-D in open capillaries; IR spectra were recorded in KBr pallets in a Perkin Elmer 1600 FT-IR spectrophotometer; UV was recorded in Hitachi U 3210 spectrophotometer; $^1$H-NMR in EM 390, 90 MHz spectrometer in CDCl$_3$ with TMS as internal standard. Chromatography was done on prepared silica gel G plates.

Preparation of the semicarbazones

General procedure:

A solution of 0.8gm of NaOAc in 5 ml of water were prepared and 0.5 gm of Semicarbazide hydrochloride were dissolved in it. To this clear solution 0.5gm of aldehyde or ketone dissolved in a little ethanol were added. The resulting mixture was then heated gently on a water bath for upto 10 minutes and cooled in ice-water. The product obtained was filtered off and washed with a little cold water and recrystallized from from aqueous ethanol. The physical characteristics of the products are given in Table B.V.3.
TABLE B.V.3

Physical properties of semicarbazones prepared

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Substrate</th>
<th>Product</th>
<th>M.P. (°C)</th>
</tr>
</thead>
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<th>Product</th>
<th>M.P. (°C)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Obs.</td>
</tr>
<tr>
<td>11</td>
<td><img src="image" alt="Substrate" /></td>
<td><img src="image" alt="Product" /></td>
<td>235</td>
</tr>
<tr>
<td>12</td>
<td><img src="image" alt="Substrate" /></td>
<td><img src="image" alt="Product" /></td>
<td>123</td>
</tr>
<tr>
<td>13</td>
<td><img src="image" alt="Substrate" /></td>
<td><img src="image" alt="Product" /></td>
<td>223</td>
</tr>
<tr>
<td>14</td>
<td><img src="image" alt="Substrate" /></td>
<td><img src="image" alt="Product" /></td>
<td>128</td>
</tr>
<tr>
<td>15</td>
<td><img src="image" alt="Substrate" /></td>
<td><img src="image" alt="Product" /></td>
<td>206</td>
</tr>
<tr>
<td>16</td>
<td><img src="image" alt="Substrate" /></td>
<td><img src="image" alt="Product" /></td>
<td>215</td>
</tr>
<tr>
<td>17</td>
<td><img src="image" alt="Substrate" /></td>
<td><img src="image" alt="Product" /></td>
<td>111</td>
</tr>
<tr>
<td>18</td>
<td><img src="image" alt="Substrate" /></td>
<td><img src="image" alt="Product" /></td>
<td>195</td>
</tr>
</tbody>
</table>

(1) where $Z = \text{-NH-}C-\text{-NH}_2$

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GENERAL PROCEDURE FOR OXIDATIVE CLEAVAGE OF \( \text{C} = \text{N} \)- OF SEMICARBAZONES

---Regeneration of the carbonyl---

0.01 mol of the substrate semicarbazone and 0.01 mole of the tetra-n-alkylammoniumbromate were dissolved in an appropriate solvent, 2–3 drops of dil. HCl was added and the solution refluxed for varying amount of time. The progress of the reaction was followed by drawing aliquots from the reaction mixture at time intervals of 10 minutes and chromatography performed on prepared TLC plates using silica gel as absorbent and ethanol as eluent. Chromatography was performed along with the authentic samples of semicarbazone and the carbonyl compounds. The disappearance of the semicarbazone was taken as time of completion of the conversion. The reaction mixture was cooled and added to large excess of distilled water and kept overnight to obtain the white solid carbonyl compound. In some cases, precipitation did not occur, in which case the aqueous solution was extracted with ether and the solid obtained on room temperature removal of ether. The products were finally purified by column chromatography in silica gel using toluene as the eluent. For benzoin and benzil two equivalents of the oxidants were used. The results are summarized in Table B.V.4.
TABLE B.V.4
(Ref. Scheme B.V.9)

Physical characteristics of oxidized products of semicarbazone

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Substrate Product</th>
<th>Oxidant</th>
<th>M.P.(°C)</th>
<th>% Yield</th>
<th>Reflux time (mins)</th>
<th>2,4-DNP of the carbonyl Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Structure" /></td>
<td>I</td>
<td>112</td>
<td>109</td>
<td>64</td>
<td>120 not prepared EtOH</td>
</tr>
<tr>
<td>2</td>
<td><img src="image2" alt="Structure" /></td>
<td>II</td>
<td>105</td>
<td>106</td>
<td>72</td>
<td>120 - do - Dioxane</td>
</tr>
<tr>
<td>3</td>
<td><img src="image3" alt="Structure" /></td>
<td>II</td>
<td>44</td>
<td>44</td>
<td>70</td>
<td>120 - do - Toluene</td>
</tr>
<tr>
<td>4</td>
<td><img src="image4" alt="Structure" /></td>
<td>II</td>
<td>80</td>
<td>81</td>
<td>65</td>
<td>300 - do - Toluene</td>
</tr>
<tr>
<td>5</td>
<td><img src="image5" alt="Structure" /></td>
<td>(1) l</td>
<td>112</td>
<td>114</td>
<td>(1) 70</td>
<td>120 - do - (1) Dioxane</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2) II</td>
<td></td>
<td></td>
<td>(2) 64</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td><img src="image6" alt="Structure" /></td>
<td>I</td>
<td>46</td>
<td>47</td>
<td>71</td>
<td>75 - do - Dioxane</td>
</tr>
<tr>
<td>7</td>
<td><img src="image7" alt="Structure" /></td>
<td>II</td>
<td>51</td>
<td>53</td>
<td>80</td>
<td>75 - do - EtOH</td>
</tr>
<tr>
<td>8</td>
<td><img src="image8" alt="Structure" /></td>
<td>II</td>
<td>136</td>
<td>137</td>
<td>85</td>
<td>120 - do - EtOH</td>
</tr>
<tr>
<td>9</td>
<td><img src="image9" alt="Structure" /></td>
<td>(1) I</td>
<td>95</td>
<td>95</td>
<td>(1) 80</td>
<td>13 hrs b - do - (1) Dioxane</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2) II</td>
<td></td>
<td></td>
<td>(2) 84</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td><img src="image10" alt="Structure" /></td>
<td>I</td>
<td>47</td>
<td>48</td>
<td>90</td>
<td>180 - do - MeOH</td>
</tr>
<tr>
<td>Sl. No.</td>
<td>Substrate</td>
<td>Product</td>
<td>Oxidant (M.P/B.P. °C)</td>
<td>% Yield</td>
<td>Reflux time (mins)</td>
<td>2,4-DNP of the carbonyl</td>
</tr>
<tr>
<td>--------</td>
<td>-----------</td>
<td>---------</td>
<td>-----------------------</td>
<td>---------</td>
<td>-------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Obs. Lit.</td>
<td></td>
<td></td>
<td>Obs. Lit.</td>
</tr>
<tr>
<td>11.</td>
<td><img src="image1" alt="Substrate" /></td>
<td><img src="image2" alt="Product" /></td>
<td>I 177 179 (m.p.)</td>
<td>82</td>
<td>150</td>
<td>not prepared</td>
</tr>
<tr>
<td>12.</td>
<td><img src="image3" alt="Substrate" /></td>
<td><img src="image4" alt="Product" /></td>
<td>I 127 127 (b.p.)</td>
<td>65</td>
<td>120</td>
<td>105 106</td>
</tr>
<tr>
<td>13.</td>
<td><img src="image5" alt="Substrate" /></td>
<td><img src="image6" alt="Product" /></td>
<td>I 177 179 (b.p.)</td>
<td>82</td>
<td>90</td>
<td>237 237</td>
</tr>
<tr>
<td>14.</td>
<td><img src="image7" alt="Substrate" /></td>
<td><img src="image8" alt="Product" /></td>
<td>I 158 156 (b.p.)</td>
<td>84</td>
<td>180</td>
<td>160 160</td>
</tr>
<tr>
<td>15.</td>
<td><img src="image9" alt="Substrate" /></td>
<td><img src="image10" alt="Product" /></td>
<td>I 244 247 (b.p.)</td>
<td>77</td>
<td>470</td>
<td>253 253</td>
</tr>
<tr>
<td>16.</td>
<td><img src="image11" alt="Substrate" /></td>
<td><img src="image12" alt="Product" /></td>
<td>I 250 252 (b.p.)</td>
<td>72</td>
<td>600</td>
<td>255 255</td>
</tr>
<tr>
<td>17.</td>
<td><img src="image13" alt="Substrate" /></td>
<td><img src="image14" alt="Product" /></td>
<td>I 102 102 (b.p.)</td>
<td>66</td>
<td>300</td>
<td>144 142</td>
</tr>
<tr>
<td>18.</td>
<td><img src="image15" alt="Substrate" /></td>
<td><img src="image16" alt="Product" /></td>
<td>I 150 151 (b.p.)</td>
<td>68</td>
<td>300</td>
<td>88 89</td>
</tr>
</tbody>
</table>

(1) Where oxidant I = tetraethylammoniumbromate, II = tetra-n-propylammoniumbromate.

(2) $Z = \text{NH-C-NH}_2$

(3) % yield of liquid carbonyl compounds were obtained by conversion to their 2,4-DNP derivatives.

(4) 'a' and 'b' indicates the time of reflux was 13 hrs and 18 hrs respectively.
Recovery procedures for individual products:

1. For 4-hydroxyacetophenone: Reaction mixture added to a large volume of water. Precipitate obtained on standing. The product was purified by column chromatography using silica gel as absorbent and toluene as eluent.

   Using this procedure the other carbonyl compounds recovered were benzoin, benzil, benzophenone, 4-nitrobenzaldehyde, vaniline, 2-nitrobenzaldehyde, 4-hydroxybenzaldehyde, and 4-chlorobenzaldehyde.

2. For methyl-2-naphthyl ketone: The reaction mixture was added to large excess of water. The aqueous solution extracted with ether and ether removed by evaporation at room temperature. Using the same procedure camphor was also recovered.

   In case of liquid carbonyl compounds, the reaction mixture was subjected to column chromatography with toluene as the eluent and the extracted product separated by fractional distillation in a rotary evaporator. The yields were calculated on the basis of the amount of 2,4-DNP derivatives obtained.

   The experiments carried out indicates that both the phenyl hydrazones as well as the semicarbazones can be cleaved to regenerate corresponding carbonyl compounds in good to excellent yield using the tetra-n-alkylammoniumbromates.
References:

4. Eisenbraun, E. J.; Wesley, R. P.; Budhram, R. S.; Dewprasad, B.
5. Vakatkar, V. V.; Tatake, J. G.; Sunthankar, S. V.; Chem. Ind (London),
   1977, 742.
   1557.


CHAPTER-B.VI
CHAPTER-B. VI

OXIDATIVE CYLIZATION IN THE SYNTHESIS OF 1,2,3-TRIAZOLE

There are two classes of simple triazoles, the vicinal triazoles and the symmetrical triazoles depicted by structure I and structure II respectively. The former is the 1,2,3-triazoles and 1,2,4-triazoles.

\[
\begin{align*}
\text{vicinal triazoles} & \quad \text{symmetrical triazoles} \\
1,2,3\text{-triazoles} & \quad 1,2,4\text{-triazoles} \\
(\text{structure I}) & \quad (\text{structure II})
\end{align*}
\]

The initial name of "osotriazone" and "osotriazoles" have since been discontinued. The biological function of the 1,2,3-triazoles have not been elaborately investigated but the formation of the vic-triazoles have given enough informations regarding the structure of monosaccharides and the study of their mutarotations.

1,2,3-triazoles have been prepared by a great number of distinct routes. The most important of these involves cyclization of the fragments shown Scheme B.VI.1.
In addition 1,2,3-triazoles have been obtained also by (i) ring contraction of dihydro-1,2,3,4-tetrazenes and (ii) oxidative rupture of benzene ring of benzotriazoles and related compounds. The most popular routes for the synthesis of triazoles involve the use of oxidative cyclization of bisphenylhydrazones using CuSO₄ and sodium periodate. These two methods have been extensively used for the synthesis of the triazoles derived from monosaccharides³⁴⁵.

In continuation of the use of quaternary ammoniumbromate for the oxidation of variety of functional groups, it was found possible that these bromates could also be used to convert the bisphenylhydrazones of 1,2-dicarbonyl compounds and monosaccharides to the triazoles. With these aim in view several 1,2-bisphenylhydrazones were prepared from the corresponding dicarbonyl compounds and monosaccharides and refluxed in acetic acid solution with the quaternary ammoniumbromates prepared earlier. It was observed that
oxidative cyclization did occur to give the triazole as shown in the following Scheme B.VI.2.

\[ \text{Scheme B.VI.2} \]

\[ \begin{align*}
\text{(I)} & \quad \text{+ } 2\text{NH}_2\text{N=Ph} \quad \text{---} \quad \text{(II)} \\
\text{(III)} \quad \text{+ Q BrO}_3^{-} & \quad \text{CH}_3\text{COOH, reflux} \quad \text{---} \\
\end{align*} \]

**EXPERIMENTAL**

*Preparation of the bisphenyl hydrazones:

2 gm of the dicarbonyl compound was dissolved in 40 ml of acetic acid. The solution was refluxed and to this solution was added 5 gm of the phenylhydrazone and the mixture heated on a water bath for one hour. The bisphenylhydrazone separated out on cooling which were recrystallized from the appropriate solvent. In an alternative procedure 2 gm of sodium acetate was added to the reaction mixture in addition to the above. In a similar procedure, the osazones of the monosaccharides were also prepared. The physical properties of the 1,2-bisphenylhydrazones are given in Table B.VI.1.*
TABLE B.VI.1
Bisphenylhydrazones prepared from 1,2-dicarbonyl compounds and monosaccharides

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>dicarbonyl compound used</th>
<th>M.P. (°C)</th>
<th>Recrystallized from</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Obs.</td>
<td>Lit.</td>
<td>Recrystallized from</td>
</tr>
<tr>
<td>1.</td>
<td>Diacetyl</td>
<td>247</td>
<td>243</td>
<td>EtOH</td>
</tr>
<tr>
<td>2.</td>
<td>Benzil</td>
<td>234</td>
<td>235</td>
<td>EtOAc</td>
</tr>
<tr>
<td>3.</td>
<td>D-Glucose</td>
<td>203</td>
<td>205</td>
<td>hot H₂O</td>
</tr>
<tr>
<td>4.</td>
<td>D-Galactose</td>
<td>200</td>
<td>201</td>
<td>hot H₂O</td>
</tr>
<tr>
<td>5.</td>
<td>D-Arabinose</td>
<td>161</td>
<td>166</td>
<td>hot H₂O</td>
</tr>
<tr>
<td>6.</td>
<td>D-Mannose</td>
<td>200</td>
<td>205</td>
<td>hot H₂O</td>
</tr>
</tbody>
</table>

General methods of preparation of 1,2,3-triazole:

0.2 gm of the bisphenylhydrazones or osazone and 1.5 gm of the tetra-n-butylammoniumbromate were dissolved in 20 ml of acetic acid and the solution was refluxed for 15 – 20 minutes. The solution was poured into 200 ml of ice cold water. A white solid precipitated on standing. The precipitate was recovered and recrystallized from ethanol. The products were identified as the 1,2,3-triazoles. The physical data of the products are given in Table B.VI.2.
### TABLE B.VI.2

Physical data of 1,2,3-triazoles

(Ref. Scheme B.VI.2)

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Substrate bisphenylhydrazone</th>
<th>( N_2 ) phenyltriazole</th>
<th>M.P. (°C)</th>
<th>( R_f ) value (CH(_2)Cl(_2))</th>
<th>Colour</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Diacetyl</td>
<td></td>
<td>166</td>
<td>0.52</td>
<td>white</td>
<td>90</td>
</tr>
<tr>
<td>2.</td>
<td>Benzil</td>
<td></td>
<td>85–86</td>
<td>0.84</td>
<td>yellow</td>
<td>60</td>
</tr>
<tr>
<td>3.</td>
<td>D-Glucose</td>
<td></td>
<td>196–97</td>
<td>0.41</td>
<td>yellow</td>
<td>70</td>
</tr>
<tr>
<td>4.</td>
<td>D-Galactose</td>
<td></td>
<td>98</td>
<td>0.68</td>
<td>yellow</td>
<td>92</td>
</tr>
<tr>
<td>5.</td>
<td>D-Arabinose</td>
<td></td>
<td>94</td>
<td>0.75</td>
<td>brown</td>
<td>65</td>
</tr>
<tr>
<td>6.</td>
<td>D-Mannose</td>
<td></td>
<td>196</td>
<td>0.71</td>
<td>yellow</td>
<td>68</td>
</tr>
</tbody>
</table>
A few spectroscopic data of triazoles prepared

- **Triazole from Diacetyl bisphenylhydrazone**:
  
  - **UV**: $\lambda_{\text{max}}$ (CH$_2$Cl$_2$, nm) 367;
  
  - **IR**: KBr (cm$^{-1}$) 1599 ($\text{C=N}$);
  
  - $^1$H-NMR: (δ) 7.3–7.8 (5H, Ar), 3.8 (6H, CH$_3$).

- **Triazole from Benzil bisphenylhydrazone**:
  
  - **UV**: $\lambda_{\text{max}}$ (EtOH, nm) 363, 245;
  
  - **IR**: KBr (cm$^{-1}$) 1635 ($\text{C=N}$);
  
  - $^1$H-NMR: (δ) 7.6–7.9 (broad, m, Ar–H).

- **Triazole from D–Glucosazone**:
  
  - **UV**: $\lambda_{\text{max}}$ (CH$_2$Cl$_2$, nm) 336;
  
  - **IR**: KBr (cm$^{-1}$) 3221 (–OH), 1642 ($\text{C=N}$);
  
  - $^1$H-NMR: (δ) 7.2–7.5 (broad, m, Ar–H), 4.2–4.6 (m, broad, –OH).

- **Triazole from D–Galactosazone**:
  
  - **UV**: $\lambda_{\text{max}}$ (CH$_2$Cl$_2$, nm) 369;
  
  - **IR**: KBr (cm$^{-1}$) 3300 (–OH), 1590 ($\text{C=N}$);
  
  - $^1$H-NMR: (δ) 6.8–7.3 (broad, m, Ar–H), 2.3–3.6 (m, broad).
Triazole from D–Arabinosazone:

**UV:** $\lambda_{\text{max}}$ (CH$_2$Cl$_2$, nm) 372;

**IR:** KBr (cm$^{-1}$), 3235 (-OH), 1610 (>C=N-);

$^1$H-NMR: (δ) 7.2–7.8 (broad, m, Ar–H), 3.3–3.6 (m, broad).

Triazole from D–Mannosazone:

**UV:** $\lambda_{\text{max}}$ (CH$_2$Cl$_2$, nm) 336;

**IR:** KBr (cm$^{-1}$), 3222 (-OH), 1642 (>C=N-);

$^1$H-NMR: (δ) 7.2–7.5 (broad, m, Ar–H), 4.2–4.6 (m, broad).

From the above study it can be concluded that the quaternary ammonium bromates are versatile oxidizing agents and could also be used for oxidative cyclization to synthesize the 1,2,3-triazole derivatives from the corresponding 1,2-bisphenylhydrazones or the osazones derived from some monosaccharides.
References:


