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Sodium Periodate Mediated Oxidative Transformations in Organic Synthesis

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Abstract:
Investigation of new oxidative transformation for the synthesis of carbon-heteroatom and heteroatom-heteroatom bonds is of fundamental importance in the synthesis of numerous bioactive molecules and fine chemicals. In this context, NaIO₄, an exciting reagent, has attracted an increasing attention enabling the development of these unprecedented oxidative transformations that are difficult to achieve otherwise. Thus, NaIO₄ has been successfully explored as a versatile oxidant for a variety of fundamental organic transformations such as C-H activation, oxidative functionalization of alkenes and other interesting oxidative transformations and its application in the synthesis of bioactive natural products. This review summarizes recent developments in this area with NaIO₄ as a versatile oxidant and brings out many challenges that still remain elusive for the future.

1. Introduction
Oxidation reactions constitute a number of important transformations in organic synthesis. They are a powerful tool to convert a functional group/position that is protected in a lower oxidation state to the desired functionality and for the activation of otherwise non-functionalized positions. Oxidation reactions are widely and abundantly used in academic
research and also in the production of variety of fine chemicals including pharmaceuticals, agrochemicals and their intermediates.

A main goal in this area is the design of more practical, economical, environmentally benign and safer reagents for cleaner processes. A wide variety of reagents have been developed over the years with varying reactivity, stability and ease of preparation for the oxidation of various functional groups. Periodates, such as NaIO₄, have played an important role as one of the oxidizing agents. NaIO₄ is a colorless to white tetragonal, efflorescent crystalline compound with a molecular weight of 213.8918 g/mol, melting point of 300 °C and specific gravity of 3.865. It is relatively cheap reagent, cost equal to $1000 for 1 kg. Modern industrial scale production involves the electrochemical oxidation of iodates (eqn i).

$$\text{HIO}_3 + \text{H}_2\text{O} - 2 \text{e}^- \rightarrow \text{IO}_4^- + 3 \text{H}^+ \quad E^o = 1.6V \quad ..........\text{eqn i}$$

It is being used extensively in oxidation reactions in organic synthetic applications. Sodium periodate can be used only in water or aqueous organic solvents. It is soluble in H₂O, H₂SO₄, HNO₃, and CH₃CO₂H but insoluble in typical organic solvents.¹ In order to carry out periodic oxidation in non-aqueous media, heterogeneous reactions with NaIO₄-supported silica, and homogeneous reactions with quaternary ammonium periodates and polymer-supported quaternary ammonium periodate have been developed.² Sodium periodate is reactive at neutral pH and under mild conditions which is compatible with a wide range of functionalities.³ Sodium periodate can be used alone or with transition-metals for oxidation reactions. For example, oxidizing agents such as OsO₄ and RuO₄ are very expensive reagents. However, when periodates are employed in stoichiometric amounts as primary oxidants, it allows the use of
these expensive oxidants in catalytic amounts. Similarly, ruthenium tetroxide is generally prepared \textit{in situ} by the reaction of the slightly less expensive ruthenium trichloride with sodium periodate, which initially oxidizes ruthenium trichloride to give active ruthenium tetraoxide.\textsuperscript{4} Sodium periodate was extensively used for the structural elucidation of carbohydrates before the advent of modern spectroscopic instrumentation. Considering its advantages over other oxidants, it is presently being widely used in organic synthesis.\textsuperscript{5a} Ever since the pioneering discovery of the cleavage of vicinal diol by periodate in 1928, sodium periodate has been actively used for oxidative transformations and to best of our knowledge no review has appeared since 1974 until today on sodium periodate and its applications in synthetic organic chemistry.\textsuperscript{5b} The aim of this review is to provide an overview on the synthetic applications of sodium metaperiodate classified by both the mode of oxidation (C–H bond activation and oxidative alkene functionalization) and type of substrates (functional group oxidations and other miscellaneous reactions).

2. C–H bond activation using NaIO\textsubscript{4}

Direct and selective replacement of unreactive C–H bonds in hydrocarbons that have also C–O, C–N, and C–X groups is an important, difficult and longstanding goal in synthetic organic chemistry. In recent years several catalytic methods have been developed for the activation of C–H bonds in alkanes using enzymes, transition metal complexes and transformations involving halogenation reactions among others. In particular, NaIO\textsubscript{4} played a major role as an efficient, transition metal-free, mild reagent for C–H bond activation.

a. C–H bond functionalization in hydrocarbons
The 1, 2-functionalization of inactive C–H bonds in a single step represents a major challenge for organic chemists. The combination of NaIO₄–KI–NaN₃ in acetic acid at 25 °C has been found to be an efficient, reliable, and inexpensive reagent system for mono- and 1,2-difunctionalization of hydrocarbons via C–H bond activation to afford iodoalkanes, 1-acetoxy- or 1-azido-2-iodocycloalkanes (Scheme 1). Mechanistically, NaIO₄ oxidizes KI as well as NaN₃ simultaneously, to liberate I₂ and an azide radical, the combination of which results in the formation of I–N₃. Azide radical formed by homolysis of I–N₃ abstracts proton from alkane to generate free radical which on combination with I₂ to give alkyl iodide followed by oxidative elimination produces alkene as an intermediate. Addition of either I–N₃ or I-OAc across the double bond in A formed during the course of reaction results in the formation of products and respectively.

Scheme 1. C–H bond functionalization in aliphatic hydrocarbons with NaIO₄–KI–NaN₃

Also the direct addition of azide at benzylic C–H bonds has been achieved by using NaIO₄–KI–NaN₃. In this way toluene can be functionalized smoothly to give benzylicazides (Scheme 2).
Similarly, bromo and acetoxy derivatives of alkyl benzenes and alkanes 6 can be obtained in excellent yields using sodium periodate and LiBr as a halogen source under acidic reaction condition through C–H bond activation (Scheme 3). A cyclic voltammogram study revealed that Br₂ generated in situ from LiBr by oxidation with NaIO₄ is probably responsible for the rapid bromination of the alkyl benzenes to produce bromo derivatives. Other halide sources such as NaBr, NaI, LiCl and KI failed to produce products.

This protocol is also useful for the direct conversion of cyclohexane 1 to trans-1,2-dibromocyclohexane 8 (Scheme 4). In this case the formation of trans-1,2-dibromocyclohexane probably indicates the involvement of cyclohexene as the intermediate, followed by bromine addition to the double bond.


Scheme 4: Oxidative halogenation of cycloalkanes

b. Oxidative iodination of arenes

Aromatic iodo compounds are versatile building blocks for the preparation of organometallic reagents and some are potential intermediates in the organic synthesis. They are especially important and useful in metal-catalyzed cross coupling reactions. Aromatic iodo compounds are typically prepared from their corresponding arenes. A NaIO₄/KI/NaCl reagent in aqueous AcOH provides an efficient and mild procedure for the synthesis of various aromatic iodo compounds at ambient conditions. The reaction is thought to occur through the iodination of activated aromatic compounds 9 with in situ generated iodine monochloride as the key reactive species to yield iodoaromatic compounds 10 in excellent yields with a high purity of 99.7% (Scheme 5). The reaction unfortunately fails for electron deficient arenes.

Scheme 5: Oxidative iodination of electron rich arenes

The proposed reaction pathway for the iodination is shown in Scheme 6. NaIO₄ oxidizes alkali metal halides such as KI or NaCl in the presence of acid to liberate molecular halogens, I₂ and Cl₂ (Eqns. 1–2). Iodine monochloride, thought to be formed from the liberated molecular halogens acts as the electrophile (Eqns. 3–4).
8 KI + NaIO₄ + 8 AcOH → 4 I₂ + 4H₂O + 8 AcOK + NaI

8 NaCl + NaIO₄ + 8 AcOH → 4 Cl₂ + 4 H₂O + 8 AcONa + NaI

I₂ + Cl₂ → 2 I-Cl

8 I-Cl + NaIO₄ + 8 AcOH → 8 H₃CCO₂I + 4 Cl₂ + 4 H₂O + 4 NaI

Scheme 6: Proposed mechanistic pathway for the formation the active iodonation intermediate

A remarkable feature of this system is that even easily oxidizable amino substituted arenes can be iodinated quantitatively. This iodination procedure has been applied successfully for a cost-effective synthesis of 3,3'-diaminobenzidine, a key intermediate for preparing polybenzimidazole (PBI) 11, used as proton conducting membranes for fuel cell applications, (Fig. 1). High yields and a purity of 99.7% were reported.⁸

![Structure of polybenzimidazole (PBI)](image)

Oxidative iodination of deactivated arenes is also possible, yielding mono- or diiodinated derivatives by using NaIO₄/KI in a more acidic medium. Deactivated arenes 12 were mono- 13 or diiodinated with strong electrophilic I⁺ reagents, which were prepared from NaIO₄ and either I₂ or KI in concentrated H₂SO₄ (minimum 95% by weight)(Scheme 7).⁹ The iodinations were conducted at 25–30 °C with a reaction time of 1–2 h using either a ‘direct’ or an
‘inverse’ method of aromatic iodination to give mono- or diiodinated pure products in 31–91% optimized yields.

\[
\text{CO}_2\text{H} \quad \text{NaIO}_4, \text{I}_2 \quad \text{CO}_2\text{H}
\]

\[
\text{95\% H}_2\text{SO}_4, \text{yield 80\%}
\]

**Scheme 7:** Oxidative iodination of deactivated arenes

Oxidative iodination of reactive phenols 14 was possible using NaIO₄/NaCl in the presence of a combination of silica/sulfuric acid to provide triiodophenol 15 (**Scheme 8**).¹⁰ The reaction proceeds through ICl as the electrophile.

\[
\begin{align*}
\text{OH} & \quad \text{NaIO}_4\text{-SiO}_2 \\
\text{H}_2\text{SO}_4, \text{NaCl, H}_2\text{O, CH}_3\text{OH, 0 °C, 92\%}} & \quad 100
\end{align*}
\]

**Scheme 8:** Iodination of phenols

c. Sulfonylation of aromatic compounds

Sodium periodate was found to be efficient in catalyzing regioselective sulfonylation of aromatic compounds 15 with \( p\)-TsCl 17 (**Scheme 9**).¹¹ NaIO₄ gave exclusively para isomers of diarylsulfones 18 with good yields with no trace of other possible ortho/meta isomers.
R = H, halides, alkyl, aryl

\[
\begin{align*}
\text{16} + \text{17} \xrightarrow{\text{NaIO}_4, \text{heat, 3-9h}} \text{18} \\
75-89\%
\end{align*}
\]

**Scheme 9**: Regioselective sulfonylation of aromatic compounds

3. Oxidative functionalization of alkenes

a. Aziridination

Aziridines with a strained ring are of paramount importance in organic synthesis, since they are considered as valuable precursors of amino sugars, alkaloids, substituted α-amino acids and are often present in natural products.

\[
\begin{align*}
\text{19} \xrightarrow{\text{NaIO}_4, \text{LiBr, chloramine-T}} \text{20} \\
R_1 = \text{aryl, alkyl, H} \\
R_2 = \text{alkyl, aryl, CH}_2\text{Br} \\
\text{up to 81\% yield}
\end{align*}
\]

**Scheme 10**: NaIO\textsubscript{4}/LiBr-mediated aziridination of alkenes using chloramine-T

A mild protocol for aziridination of a variety of alkenes 19 by using a catalytic amount of sodium metaperiodate (NaIO\textsubscript{4}) has been developed.\textsuperscript{12} This one-pot procedure involves LiBr and chloramine-T as the bromine and nitrogen sources respectively for the preparation of \(N\)-tosyl-2-substituted aziridines 20 (Scheme 10).

b. Azidoiodination
The combination of NaIO₄, KI and NaN₃ has been found to be simple and inexpensive reagents for azidoioldination of alkenes 21. The 1,2-azidoioldination proceeds regiospecifically in an \textit{anti}-Markovnikov fashion to produce the corresponding β-iodoazides 22 (Scheme 11).²¹

\begin{equation}
\begin{array}{c}
\text{R}_1=\text{aryl, alkyl} \\
\text{R}_2=\text{H, alkyl,} \\
\text{CH}_2\text{OH, CH}_2\text{OAc}
\end{array}
\end{equation}

\textbf{Scheme 11:} Sodium periodate-mediated azidoioldination of alkenes

The proposed mechanistic pathway for the formation of β-iodoazides 22 is presented in Scheme 12.

\textbf{Scheme 12:} Proposed mechanistic pathway for azidoioldination of alkenes

NaIO₄ oxidizes both KI and NaN₃ simultaneously to liberate I₂ and an azide radical, respectively; the combination of which probably results in the formation of IN₃ (Scheme 12). Homolysis of
IN₃ provides an azide radical, which then adds onto alkenes 21 to produce a more stable alkyl radical species A, thus controlling the regiochemistry of the process. The reaction of the alkyl radical either with I₂ or with an iodide radical results in the formation of β-iodoazides 22.

c.Hydroxyhalogenation

NaIO₄ mediated oxidative bromohydroxylation of α, β-unsaturated carboxamides 23 using lithium bromide as the bromine source under acidic conditions at room temperature afforded the corresponding chiral α-bromo-β-hydroxycarboxamides 24 & 25 (Scheme 13). Excellent yields (77–90%) and diastereoselectivities of up to 10:1 along with high control over regioselectivity as well as selectivity to the anti-addition product are the main features of this method.¹⁴

![Scheme 13: NaIO₄-mediated asymmetric bromohydroxylation α,β-unsaturated carboxamides](image)

This methodology has been successfully applied in the enantioselective syntheses of two biologically important molecules namely (-)-cytoxzone (26) and L-threo-DOPS (droxidopa) (27) (Fig. 2).
In addition, NaIO$_4$ oxidizes alkali metal halides efficiently in aqueous medium to halogenate alkenes 28 and aromatic compounds to produce the corresponding halo derivatives in excellent regio and stereoselectivity.$^{15}$ This method was also used for enantioselective bromohydroxylation using $\beta$-cyclodextrin as a complexing agent, resulting in moderate enantiomeric excess. Furthermore, NaIO$_4$ together with NaCl was used for the chlorination of various aromatic compounds, although mixtures of regioisomers are sometimes obtained. The related NaIO$_4$ mediated bromination reaction, which used LiBr or NaBr as halogen source, affords the expected brominated products 29 in a regioselective fashion (Scheme 14).

**Scheme 14:** NaIO$_4$-mediated oxidative halogenation

---

d. Dihydroxylation

The oxidation of carbon-carbon double bonds to vicinal diols in a stereoselective fashion is a useful reaction which gives valuable synthetic intermediates in organic synthesis. NaIO$_4$ in...
combination with LiBr catalyzes the dihydroxylation of alkenes 30 to their corresponding cis or trans diols 31 with excellent diastereoselectivity (Scheme 15).\footnote{16}

\[
\text{Scheme 15: LiBr-catalyzed dihydroxylation of alkenes}
\]

This catalytic and transition metal free dihydroxylation of alkene to give stereoselective synthesis of vicinal diols is the most applicable method for the synthesis of valuable intermediate in organic synthesis. Thus, NaIO\(_4\) (30 mol\%) and LiBr (20 mol\%) in acetic acid catalyse mono- and diacetylation of alkenes which on subsequent basic hydrolysis furnish syn and anti diols with excellent diastereoselectivity ranging from 80:10 to 100:0. The catalytic and transition metal free version of Prevost-Woodward reaction makes this dihydroxylation reaction more prominent in organic synthesis.

Catalytic cycle for the dihydroxylation of olefins is presented in Scheme 16. A molecular halogen, for example Br\(_2\), generated \textit{in situ} from alkali metal bromide by oxidation with NaIO\(_4\) or PhI(OAc)\(_2\) rapidly undergoes bromoacetoxylation with alkenes \textit{via} the bromonium ion species A to produce a \textit{trans}-1,2-bromoacetate derivative B, which was isolated and characterized. The intermediate species C, formed from B in the presence of NaIO\(_4\), assisted anchimerically by the acetate group, is opened either by water to give cis hydroxy acetate 31b or
by acetic acid to give the trans diacetate\textit{31a} with concomitant liberation of Br$_2$.

![Scheme 16: Proposed catalytic cycle for dihydroxylation of alkenes](image)

e. Diazidation of styrene derivatives

Vicinal diazides\textit{33} are important precursors to 1,2-diamines, which are useful functional groups present in a variety of natural products, pharmaceuticals such as D-(+)-biotin and others. In addition, 1,2-diamines have been increasingly utilized in organic synthesis either as chiral auxiliaries or as ligands especially in the field of catalytic asymmetric synthesis. It was reported that NaIO$_4$ with NaN$_3$ can be used for the 1,2-diazidation of alkenes.$^{17}$ Several styrene derivatives as well as other aliphatic alkenes including linear and cyclic alkenes \textit{32} gave good yields of the corresponding vicinal 1,2-diazides \textit{33} (\textit{Scheme 17}).
In the case of internal alkenes, diazides were also obtained in high yields with moderate diastereoselectivity. However, it was found that α, β-unsaturated carbonyl compounds such as cinnamic esters and (R)-(−)-carvone as well as sterically hindered alkenes such as α-pinene were not oxidized under these reaction conditions. This may be a limitation of this method.

f. Epoxidation

Transition metal-based catalysts using periodate as oxidant is an useful method for the epoxidation of alkenes. The ultrasonic irradiation of a mixture containing styrene derivatives and sodium periodate in the presence of catalytic amounts of manganese porphyrins supported on polyvinylpyridine or an IRA-900 ion-exchange resin oxidizes styrene derivatives 34 to the corresponding styrene epoxide compounds 35 in high yields with excellent diastereoselectivity (Scheme 18).\(^{18}\) Moreover, Mn(III) salen,\(^{19}\) Ru(III)polyoxometallate and salophen,\(^{20}\) Mn(Br\(_8\)TPP)Cl and tetraphenylporphyrinatoMn(III) chloride\(^{21}\) were also used as catalysts for epoxidation of alkenes in presence of NaIO\(_4\).
4. Oxidation of basic functional groups

a. Oxidation of alcohols

Since 1928 NaIO₄ has been widely used for the oxidative cleavage of 1, 2-diols efficiently to yield carbonyl compounds (Scheme 19). Sodium periodate complements lead tetraacetate for oxidative cleavage of diols. The glycol cleavage reactions using NaIO₄ are usually very rapid, quantitative and substrate specific. For example, NaIO₄ cleaves 1,2-diols chemoselectively even in the presence of sulfide group. The carbonyl compounds generated are inert towards further oxidation under the reaction conditions. Sodium and potassium periodate can be used in water only or aqueous organic solvents as dictated by their solubility. In order to carry out periodic oxidation in nonaqueous media, NaIO₄-supported silica and quaternary ammonium periodates have been used. This method is convenient because isolation of products is possible by simple filtration of the reaction mixture and evaporation. Recently, a polymer-supported quaternary ammonium periodate, used for glycol cleavage reactions in CH₂Cl₂, has been reported as a practically useful alternative. This reaction was extensively used for the structural elucidation of carbohydrates before the advent of modern spectroscopic techniques.
The mechanism of carbon-carbon bond cleavage of diols by periodate is consistent with a cyclic, five-membered ring intermediate. Support for such a mechanism comes from the observations that the cis isomers of cyclic diols are more reactive than the trans isomers, threo-1,2-diols undergo oxidation faster than the erythro isomers, and the inert behavior of diaxialtrans-1,2-diols that cannot form a cyclic periodate ester intermediate.\(^{28}\)

A one-pot sequential oxidative cleavage/Wittig reaction of 40 was carried out by using an excess of NaIO\(_4\) supported on silica gel in the presence of stabilized ylides under anhydrous conditions to give unsaturated ester 41 (Scheme 20).\(^{29}\) NaIO\(_4\) is much a more efficient reagent than manganese dioxide for which only very low yields were obtained.
Not only 1,2-diols but also alcohols can be oxidized using sodium periodate in combination with other reagents, for example NH$_2$OH·HCl together with NaIO$_4$ serve as a mild reagent for the oxidation of alcohols 42 to carbonyl compounds 43 at room temperature (Scheme 21).\footnote{30}

\[
\begin{align*}
\text{OH} & \\
R_1 & \text{Alkyl, Aryl} \\
R_2 & \text{H, Alkyl, Aryl}
\end{align*}
\]

\[
\begin{align*}
\text{NH}_2\text{OH·HCl} & \text{(1.5 equiv.)} \\
\text{NaIO}_4 & \text{(1 equiv.), CH}_2\text{Cl}_2
\end{align*}
\]

\[
\begin{align*}
\text{R}_1 & \text{R}_2 \\
\text{O} & \\
\text{74-90\%}
\end{align*}
\]

**Scheme 21**: Oxidation of alcohols with hydroxylamine/periodate

NO generated from reaction of NH$_2$OH·HCl and NaIO$_4$ is responsible for oxidation of alcohols to aldehydes as shown its stoichiometry in eqn ii.

\[
6\text{NaIO}_4 + 14\text{NH}_2\text{OH·HCl} \rightarrow 3\text{I}_2 + 14\text{NO} + 24\text{H}_2\text{O} + 6\text{NaCl} + 8\text{HCl} \quad \text{eqn ii}
\]

Likewise TEMPO catalyzed the selective oxidation of alcohols 44 to the corresponding aldehydes and ketones 45 using NaIO$_4$ as the terminal oxidant (Scheme 22).\footnote{31}

\[
\begin{align*}
\text{OH} & \\
R_1 & \text{R}_2 \\
\text{O} & \\
\text{95-96\%}
\end{align*}
\]

**Scheme 22**: Oxidation of primary and secondary alcohols with TEMPO/bromide/periodate

The NaIO$_4$/TEMPO/NaBr system provides a mild and efficient and an alternative method for the oxidation of alcohols that are sensitive to basic reaction conditions. The reaction is biphasic at
room temperature. A biomimetic water-soluble metallocporphyrin (MnTEPyP) catalyst was also highly efficient for the oxidation of alcohols 46 to either aldehydes 47 or carboxylic acids 48 with NaIO₄ (Scheme 23) where selectivity was solvent dependent.³² The manganese porphyrin 49 showed an excellent activity for the product specific oxidation of various alcohols under mild conditions.

![Scheme 23](image)

**Scheme 23**: Product specific oxidation of alcohols

(Homo-)allylic and (homo-)propargylic alcohols 50 and 52 can be oxidized under slightly acidic conditions at ambient temperature with sodium periodate in the presence of sodium dichromate as the catalyst to yield the corresponding carboxylic acids 51 and 53, respectively (Scheme 24).³³ The method is particularly suitable for the oxidation of alcohols to carbonyl
compounds that are sensitive to elevated temperatures and alkaline or strongly acidic conditions. The mild conditions employed allow the oxidation of homopropargylic alcohols in high yields, notably preventing the rearrangement to the allenic isomers.

Scheme 24: Oxidation of alkenols and alkynols to carboxylic acids

Conventional methods for the synthesis of carboxylic acid esters involve the oxidation of aldehydes to carboxylic acids followed by esterification with alcohols catalyzed by either acid or base. The direct method for conversion of alcohols 46 or aldehydes 47 to carboxylic esters 54 holds promise in organic synthesis because it minimizes the number of steps. This was possible by treating alcohols 46 or aldehydes 47 with the combination of NaIO₄/LiBr in methanol or ethanol in an acidic medium in a single step (Scheme 25).34

Scheme 25: Direct oxidative esterification of benzylic alcohol and benzaldehydes

yield up to 95%

R = H, alkyl, OMe, Cl
Treatment of homoallylic alcohols 55 with NaIO₄:NaHSO₃ in aqueous tert-BuOH produced tetrahydrofuran derivatives 56 together with iodohydrins 57 in a stereospecific manner (Scheme 26).³⁵ Both the products formed are postulated to arise via an iodonium ion intermediate. The tetrahydrofuran derivative 56 is obtained by intramolecular stereoselective cyclization of the iodonium ion, whereas iodohydrins 57 are formed by nucleophilic addition of water to the iodonium ion intermediate. The products formed mainly depend on the nature of the olefin present in the starting material. cis-Disubstituted olefins and homoallylic alcohols with terminal olefins produce both the products as a mixture, because the iodonium ion intermediate also undergoes nucleophilic addition of water in addition to the intramolecular cyclization.

![Scheme 26: Reaction of homoallylic alcohols with NaIO₄:NaHSO₃](image)

**b. α-Oxidation of carbonyl compounds**

A silica-supported NaIO₄ act as a useful and green synthetic reagent for oxidative cleavage of α-hydroxyketones 58 under microwave irradiation (Scheme 27).³⁶ Sodium periodate provides a mild procedure to synthesize the corresponding carboxylic acid and aldehyde 59 in good yields, under solvent-free conditions. The same reaction with lead tetraacetate, gave mainly over-oxidized products, along with trace amounts of the desired oxoacid. The silica-supported sodium periodate protocol is very attractive for α-hydroxyketon esthats that are not soluble in polar media and for aldehydes and acids that are water soluble. It is worth mentioning that the
mildness of the method allows its use with sensitive substrates and produces selective oxidative cleavage even in the presence of sulfur functionalities.

\[
\begin{align*}
\begin{array}{c}
\text{Catalyst: NaIO}_4/\text{SiO}_2 \\
(3 \text{ equiv.}) \\
\end{array}
\end{align*}
\]

\[
\begin{array}{c}
\text{58} \\
\text{OHS} \\
\text{OH} \\
\text{C=O} \\
\rightarrow \\
\text{59} \\
\text{C=O} \\
\text{CHO} \\
\text{OHS} \\
\end{array}
\]

**Scheme 27**: Oxidation of α-hydroxyketones

Similarly, cleavage of unsaturated α-ketols 60 is best achieved using sodium periodate in THF to afford the hemiacetal 61 in good yield (**Scheme 28**).

\[
\begin{array}{c}
\text{60} \\
\text{OCH}_3 \\
\text{HO} \\
\text{C=O} \\
\rightarrow \\
\text{61} \\
\text{OCH}_3 \\
\text{HO} \\
\text{C=O} \\
\end{array}
\]

**Scheme 28**: Cleavage of unsaturated α-ketols

In order to facilitate the isolation of the carboxylic acid that emerged from the oxidation of unsaturated α-ketols, the crude product was typically treated with diazomethane in order to prepare the ω-oxo-α, ω-unsaturated methyl esters prior to separation. 37

The combination of NaIO4/LiBr in a refluxing acetonitrile-water solvent reacts at 90 °C with N-aryl γ-lactam-2-carboxylic acids 62 to give N-aryl maleimides 63 by decarboxylative oxidation and dehydrogenation in high yields (**Scheme 29**). 38 Mechanistic studies have proven that by decarboxylative hydroxylation the γ-lactam carboxylic acids 62 leads to formation of 5-hydroxy γ-lactam derivatives, which were then converted into the maleimides 63.
Geminal diazide compounds are potential candidates to be used as future generation high energy materials for defence applications. The combination of sodium periodate and sodium azide has been found to be an excellent reagent system suitable for the direct diazidation of benzylic alcohols 66, and aryl ketones 64 to produce the corresponding geminal diazides 65 in high yields under mild reaction conditions (Scheme 30)\(^\text{39}\).

**Scheme 29**: Synthesis of N-aryl maleimides

**Scheme 30**: NaIO\(_4\)-mediated α, α'-diazidation of aryl ketones and benzylic alcohols

Linear and cyclic aryl ketones 64 with α-methylene group (–CO–CH\(_2\)–) underwent selective oxidative diazidation with NaIO\(_4\) (1 equiv) and NaN\(_3\) (3 equiv) in AcOH–DMSO (1:4) as solvent at

\[
\text{Ar} = \text{phenyl}; R = \text{alkyl}
\]

\[
\text{Ar} = \text{phenyl}; R = \text{CH}_3; 75\%
\]

\[
\text{Ar} = \text{tetralol}; R = \text{H}; 70\%
\]
75 °C, to give α, α-diazido aryl ketones 65 in 91–96% yields. Benzylic alcohols 66, when treated under same reaction conditions gave the corresponding α,α-diazidoarylketones 65 in good yields. This diazidation reaction probably occurred via the initial oxidation of benzylic alcohols to form the corresponding aryl ketones, which then subsequently underwent diazidation at the α-position. Mechanistically, the reaction is believed to follow a radical pathway.

c. Halides

Iodylarenes (ArIO₂), the hypervalent aromatic oxidants have widely been used as mild and selective oxidants in organic transformations. They are generally prepared by oxidation of their corresponding iodoarenes. Examples include 2-iodosobenzoic acid (IBX) and its triacetylated derivative, the periodinane Dess-Martin reagent among the better known oxidants. Thus, NaIO₄ dissolved in boiling 30% aqueous AcOH solution is a versatile and efficient oxidant for the preparation of valuable iodosoarenes 68 from iodoarenes 67 (Scheme 31). Using NaIO₄, oxidation of iodoarenes proceeds in shorter reaction times and the products obtained are in good yields and very high purities. Under similar reaction conditions, 2-iodobenzoic acid (69) gave pure 2-iodosobenzoic acid (70) in 91-93% crude yields.
Scheme 31: Oxidation of iodoarenes to iodosoarenes

NaIO₄ in DMF oxidizes various primary 71 and secondary halides 73 to the corresponding aldehydes 72 and ketones 74 under reflux in high yields and short reaction times (Scheme 32). Interestingly, on treating α-halocarbonyl compounds with NaIO₄ a one carbon moiety is lost. For example, when phenacyl bromide was treated with sodium metaperiodate, the reaction results in the formation of benzaldehyde via decarboxylation of the initially formed phenylglyoxalic acid.

Scheme 32: Oxidation of primary and secondary halides
Although a variety of reagents are known to oxidize organic halides to aldehydes, no practical method exists other than oxidation with sodium periodate for the direct one-step conversion of benzylic bromide derivatives to the corresponding carboxylic acids. Thus, benzylic bromide derivatives \( \text{75} \) can be converted to their corresponding carboxylic acids \( \text{76} \), directly under transition metal-free conditions using \( \text{NaIO}_4/\text{H}_2\text{SO}_4 \) in high yields (71-89\%) (Scheme 33).\(^{42}\)

![Scheme 33: Oxidation of benzylic bromide derivatives](image)

Secondary benzylic bromides were also oxidized by \( \text{NaIO}_4/\text{H}_2\text{SO}_4 \) to give the corresponding ketones in 87\% yield. However, benzyl chloride was resistant to oxidation under these reaction conditions, probably because of the stronger C-Cl bond.

d. Oxidation of sulfides

Sulfoxides and sulfones are valuable intermediates in organic synthesis, and their preparation mainly relies on the selective oxidation of sulfides.

![Scheme 34. Oxidation of sulfides to sulfoxides and sulfones](image)

Wet silica-supported sodium metaperiodate plays a key role in this regard for the selective oxidation of both alkyl- and aryl sulfides \( \text{77} \) to the corresponding sulfoxides \( \text{78} \) and sulfones \( \text{79} \),
when, under microwave conditions, 1.7 and 3 equivalents of NaIO₄ are used, respectively. This environmentally benign solventless method provides the products in short reaction time of circa 3 min and excellent yields (Scheme 34).⁴³

Oxidation of sulfides with an equimolar amount of NaIO₄ was also conducted in organic solvents with a phase-transfer catalyst (PTC). For instance, refluxing a solution of sulfides in chloroform with an aqueous solution of sodium periodate in presence of PTC as catalyst gave the sulfoxides in 24-48 h.⁴⁴

Sodium periodate supported on acidic alumina was found to be a useful reagent for the oxidation of thiomorpholine (80) to sulfoxide 81 (91%) in ethanol. However, the oxidation of thiomorpholine in water by NaIO₄ alone afforded the sulfoxide 81 in only 30% yield (Scheme 35).⁴⁵

Scheme 35: Oxidation of thiomorpholine

Sodium periodate in combination with potassium permanganate oxidizes sulfides to the corresponding sulfones directly. Similarly a wide range of sulfides can be oxidized with sodium periodate catalyzed by the manganese (III) tetrapyridyloporphyrin supported on chloromethylated polystyrene. This catalyst shows high activity in the oxidation of various sulfides to their corresponding sulfoxides and sulfones at room temperature.
A practical, mild and efficient method for selective oxidation of albendazole, fenbendazole, and other benzimidazolesulfides was achieved with sodium periodate in an acidic reaction medium, affording the corresponding sulfoxides and sulfones respectively, depending upon the temperature (Scheme 36).

Scheme 36: Oxidation of benzimidazolesulfides

Oxidation of 3-sulfanyl-alcohols with NaIO₄ represents a novel synthetic route to disulfides and sultines depending upon the number of equivalents of NaIO₄ used. For example, the sultines can be obtained in a short time (4 h) with good yields using excess of NaIO₄ in CH₃CN at room temperature (Scheme 37).

Scheme 37: Oxidation of 3-sulfanyl alcohols
Oxidation of methylthioalkanoic acids with NaIO$_4$ (1 equiv) gave the corresponding methylsulfinylalkanoic acids in good yields, which are found to be potentially active, cardiac inotropic and antifungal agents. For example, the oxidation of 14-methylthiotetradecanoic acid (88) gives 14-methylsulfinyltetradecanoic acid (89), as illustrated in Scheme 38.$^{48}$

Scheme 38: Oxidation of methylthioalkanoic acids

α-Phosphorylsulfoxides$^{91}$ are useful reagents in the Horner-Wittig reaction for the synthesis of vinylicsulfoxides$^{93}$. In this way vinyl sulfides$^{91}$ can be prepared in quantitative yields using NaIO$_4$ from sulfides$^{90}$ (Scheme 39).$^{49}$ Further oxidation of the vinylsulfides$^{92}$ using NaIO$_4$ to yield vinylicsulfoxides$^{93}$ is then possible.$^{50}$

Scheme 39: Oxidation of α-phosphoryl and vinylic sulphides

NaIO$_4$ was found to oxidize unsymmetrical thiosulfinic S-esters 94 to thiosulfonic esters 95 effectively in quantitative yields, without cleavage of the S-S bond. NaIO$_4$ is also effective for
the selective oxidation of sulfide to sulfoxide in the presence of disulfide linkage. Other oxidants (CrO$_3$, H$_2$O$_2$ and mCPBA) when treated with sulfide result in decomposition via cleavage of the S-S bonds (Scheme 40).}

![Scheme 40: Oxidation of disulfides](image)

Sodium periodate mediated hydrolyses are used for deprotection of dimethyl dithioacetals of aldehydes and ketones to give the corresponding carbonyl compounds in moderate yields, as illustrated in Scheme 41.

![Scheme 41: Deprotection of dimethyl dithioacetals](image)

Oxidation of 2-methyl-, 2-phenyl-, and 2-tert-butyl-1,3-dithianes with NaIO$_4$ at low temperature gave the trans-1-sulfoxides exclusively. Stereoselective oxidation of naphtho[1,8-b,c]-1,5-dithiocin (100), using an excess of NaIO$_4$ at room temperature, results in the 95% yield of the cis-1,5-disulfoxide 101 (eqn 42a). Treatment of disulfide with NaIO$_4$ in EtOH at room temperature gave monosulfoxide 103 (95%), while at 50 °C, it gave trans-bis-sulfoxide 104 (84%, >99% de) (Scheme 42, eqn 42b).
Asymmetric oxidation of a number of aromatic sulfides in the presence of bovine serum albumin (BSA) using sodium metaperiodate resulted in the formation of chiral sulfoxides in reasonably high optical purities (Scheme 43).^57^  

\[
\text{Selenoxides are valuable co-oxidants for the osmium catalyzed cis-dihydroxylation of alkenes, where they are thought to function to reoxidize Os (VI) to Os (VIII) species.}^58^  
\]
Selenoxides are obtained from the oxidation of the corresponding selenides. For instance, diaryl, dialkyl and aryl alkyl selenides 107 are oxidized by an excess of NaIO₄ at 0°C to yield the corresponding selenoxides 108 in 88-92% yields (Scheme 44, eqn 44a). Vinyl selenide 109 undergoes oxidation smoothly with sodium periodate (1.1 equiv) in methanol at room temperature to give vinyl selenoxides 110 in high yields (eqn 44b). The reaction with mCPBA is much less selective.

\[
\begin{align*}
\text{Ar-S}e_{\text{Alkyl}} & \xrightarrow{\text{NaIO}_4, \text{MeOH}} \text{Ar-Se}_{\text{Alkyl}} & (44a) \\
\text{C}_2\text{H}_4\text{SePh} & \xrightarrow{\text{NaIO}_4, \text{MeOH}} \text{C}_2\text{H}_4\text{SePh} & (44b)
\end{align*}
\]

**Scheme 44:** Oxidation of selenides to selenoxides

It was also found that selenoxides readily undergo syn-elimination during the oxidation reaction to form alkenes, where both steps occur at below ambient temperatures. For example, the sodium metaperiodate mediated oxidation of phenyl selenide 111 in a MeOH-H₂O solvent results in the formation of the unstable organoselenoxide 112, which on subsequent syn-elimination gives the cyclohexenone derivative 113 in a 74% yield, an alkene that is unusually sensitive to polymerization and nucleophilic attack (Scheme 45, eqn 45a). Oxidation of selenides to selenoxides and its collapse at or below room temperature, makes a general method for alkene synthesis (eqn 45b).
f. Thioureas and selenoureas

Substituted thiourea compounds 117 are oxidized to the corresponding urea compounds 118 when treated with an aqueous solution of NaIO₄ in water/DMF (Scheme 46, eqn 46a).⁶² Yields are respectable and reaction times are short. NaIO₄ surpasses all other reagents used for this transformation, as the reaction proceeds under milder reaction conditions and has been shown to be sufficiently versatile for commercialization. When an amine nucleophile is also present in the reaction mixture, the initially formed urea derivatives react to yield guanidine derivatives 119 in one pot representing a good commercial route for the synthesis of guanidine compounds (Scheme 46, eqn 46b).
Different from the thiourea compounds, a facile oxidation of selenourea compounds 120 with NaIO₄ leads to removal of selenium and formation of carbodiimides 121 (Scheme 47).⁶⁴ The reaction is efficient for both symmetrical and unsymmetrical substrates. Neither the dimer of selenourea nor the trimer of the carbodiimide was observed in this oxidation. Carbodiimides are very important compounds for the construction of a wide variety of compounds. Sodium periodate is unique for this reaction and other oxidants, such as NaClO₄, KMnO₄, and Na₂CrO₄, did not yield the corresponding carbodiimide from selenourea.
Dimethylthiocarbamates (DMTCs) are good protecting groups for the corresponding alcohols because of their *inter alia*, low polarity, distinctive spectral signature, thermal stability and low reactivity. DMTCs 122 are orthogonal in chemical reactivity to most other alcohol protecting groups. For example, DMTCs are stable under the influence of a fluoride source, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) mildly acidic conditions, a Lewis acid such as TiCl₄, and base but readily reacts with NaIO₄ in MeOH/H₂O at 45 °C to give the unprotected alcohols 123 (Scheme 48).⁶⁵ The mechanistic pathway through which the deprotection takes place is that thionocarbamates undergo sulfur oxidation to give sulfenic acid followed by extrusion of SO₂ when oxidized with excess of NaIO₄ affording an immonium compound, which upon hydrolysis leads to the formate ester and finally to the parent alcohol.

\[
\begin{align*}
\text{RO} & \quad \text{NaIO}_4 \\
122 & \quad \text{CH}_3\text{OH}:\text{H}_2\text{O (20:1)} \\
& \quad 45 \degree \text{C}, 2 \text{ h}, 92-95\% \\
\rightarrow & \quad \text{RO} \quad \text{OM} \\
123 & \\
\text{R} &= \text{silyl, Bn, Ac, MOM, THP, etc}
\end{align*}
\]

*Scheme 48:* Deprotection of dimethylthiocarbamates to alcohols

**g. Phenols**

Quinone derivatives play an extremely important role in biological redox systems. Compared to other oxidants such as silver oxide, chromic and nitric acids, α-chloranil, N-chlorosuccinimide, and others, sodium periodiate has been found to be an efficient reagent for synthesizing α- and p-quinones 125 from dihydroxy aromatics 124 in high yields under very mild reaction conditions (Scheme 49, eqn 59a).⁶⁶

Only a limited number of reports describe the synthesis of quinone dimers because of their low stability. A synergistic effect is obtained by linking two quinones, resulting in unique physical
properties. Quinone dimers were prepared by treating the corresponding phenols with NaIO₄, for example oxidative treatment of compounds 126 with NaIO₄ resulted in the formation of quinone dimers 127 (Scheme 49, eqn49b). ⁶⁷

\[
\begin{align*}
\text{OH} & \quad \text{or} \quad \text{OH} \\
R & \quad \text{OH} \\
\text{OH} & \\
\text{NaIO}_4 & \quad \rightarrow \quad \text{O} \\
R & \quad \text{O} \\
\text{or} \quad \text{R} & \quad \text{O} \\
\end{align*}
\]

\( \text{124} \quad \text{125} \)

\( R = \text{OMe, Me, Cl, etc.} \)

\[
\begin{align*}
\text{OH} & \quad \text{or} \quad \text{OH} \\
\text{RS} & \quad \text{OH} \\
\text{OH} & \quad \text{OH} \\
\text{SR} & \quad \text{OH} \\
\text{NaIO}_4 & \quad \rightarrow \quad \text{O} \\
\text{RS} & \quad \text{O} \\
\text{O} & \quad \text{SR} \\
\end{align*}
\]

\( \text{126} \quad \text{127} \)

\( R = \text{Alkyl} \)

\[\text{Scheme 49: Oxidation of phenols to quinones}\]

Oxidation of o-hydroxymethylphenols 128 having at least one bulky substituent using NaIO₄ leads to the formation of monomeric spiro-epoxy-2,4-cyclohexadienones 129 in good yields. Once formed thespiro-epoxy compound readily isomerizes photochemically to give the corresponding salicylaldehyde derivative 130 (Scheme 50, eqn50a). ⁶⁸ This strategy was successfully applied for the oxidation of 2-hydroxymethyl-6-(3-hydroxy-hex-5-enyl)-phenol 131 to give spiroepoxycyclohexa-2,4-dienone 132, which is a key intermediate in the synthesis of platencin 133 (eqn50b). ⁶⁹
Similarly, in an attempt at the oxidation of o-hydroxy substituted diarylcarbinols with periodate, a novel oxidative rearrangement was observed which led to the formation of the corresponding benzo-1,3-dioxols under mild conditions. For instance, oxidation of o-hydroxynaphthyl phenyl carbinol 134 with NaIO₄ gives the benzo-1,3-dioxol derivative 135 (Scheme 51).

**Scheme 51:** Oxidative rearrangement of o-hydroxynaphthylphenylcarbinol

**h. Oxidation of indoles and tetrahydro-β-carbolines**
Action of sodium periodates on indoles gives different products based on the pattern of substitution in indole derivative. For example, 3-alkylindoles (136) result in formation of the corresponding o-amidoacetophenone137 in good yields by the oxidative cleavage of the indolic double bonds (Scheme 52, eqn 52a). Even though oxidation of indoles using ozonolysis, peracids and autoxidation also results in cleavage of indole double bonds, sodium periodate oxidation is easy to carry out and gives very high yields. Under the same reaction conditions, 2,3-diphenyldinoloes result in lower yields of the corresponding oxidative cleavage product, while the oxidation of 2-alkylindoles 138 using NaIO₄ gives a mixture of dimerized products (Scheme 52, eqn 52b).

Scheme 52: Oxidation of indoles

Tetrahydrocarbazoles and tetrahydro-β-carbolines are also oxidized effectively using NaIO₄ at room temperature in methanol/water. Tetrahydrocarbazoles139 gave benzocyclononene-2,7-dione derivatives 140 upon reaction with NaIO₄. However, the type of products formed in the oxidation of tetrahydro-β-carbolines141 depends upon the degree of substitution at C-1 position of the carbolines (Scheme 53).
5. Miscellaneous Reactions:

a. Oxidation of aromatic amines:

Sodium periodate is a useful synthetic reagent for carbon–carbon cleavage in 1,2-diamino arenes to yield the corresponding nitriles in nearly quantitative yields. On the other hand, this same method yields 1,4-benzoquinone derivatives from the corresponding aryl 1,4-diamine compounds. The advantages of this protocol are shorter reaction times and milder reaction conditions to obtain moderate to good yields (Scheme 54). Other oxidants such as KMnO₄, CAN, NaCl₂, and K₂Cr₂O₇ were also examined for the oxidative carbon–carbon cleavage of 1,2-diaminobenzene, but the reaction failed even at higher temperature and at a longer reaction time.
b. Oxidation of epoxides:

Sodium periodate was found to be a useful reagent for the oxidative cleavage of the C–C bond in epoxides 147 to the corresponding carbonyl compounds 148 in up to 91% yields (Scheme 55). The reaction proceeds in two-steps: First the epoxide ring is oxidatively opened to form a vicinal diol. Then in situ cleavage of diol to the corresponding carbonyl compound occurs. Apparently, the trans-diols formed from cyclic epoxides isomerize under the acidic reaction conditions before undergoing C–C bond cleavage. Highly substituted epoxides appear to be more reactive, which may be due to the ease of initial oxidative formation of the vicinal diols from the epoxide ring opening reaction. This aqueous one-step procedure provides access to a variety of carbonyl compounds, which are important intermediates in organic synthesis. This method also can be considered a chemoselective alternative to ozonolysis of an alkene.
c. Oxidative rearrangements:

α-Keto esters and amides undergo oxidative rearrangement when treated with periodate at pH 7-9 to give malonic acid derivatives. When the amide is cyclic, from example, α-ketolactams, ring contraction occurs. Thus, 1-methyl-2,3-piperidinedione 149 is converted into 3-carboxy-1-methyl-2-pyrrolidinone 150 in 80% yield (Scheme 56).\(^{75}\) Another example is the oxidation of N,N-dimethyl-2-oxobutanamide 151 to give N,N-dimethylmethylmalonamic acid 152 in a 69% yield.

\[ \text{Scheme 55: Epoxide C–C bond cleavage} \]

\[ \text{α-Keto esters and amides undergo oxidative rearrangement when treated with periodate at pH 7-9 to give malonic acid derivatives.} \]

\[ \text{When the amide is cyclic, from example, α-ketolactams,} \]

\[ \text{ring contraction occurs. Thus, 1-methyl-2,3-piperidinedione 149 is converted into 3-carboxy-1-methyl-2-pyrrolidinone 150 in 80% yield (Scheme 56).}^{75} \]

\[ \text{Another example is the oxidation of N,N-dimethyl-2-oxobutanamide 151 to give N,N-dimethylmethylmalonamic acid 152 in a 69% yield.} \]

\[ \text{Scheme 56: Oxidative rearrangement of α-keto amides} \]

\[ \text{d. Oxidation of oximes:} \]

\[ \text{NaIO}_4 \text{ supported on wet silica gel can be used for the conversion of ketoximes 153 to the} \]

\[ \text{corresponding ketones 154 in microwave reactions within 2 min (Scheme 57).}^{76} \]

\[ \text{On the other hand, the alternative “regular” heating protocol affords the products after 36 h at 110 °C.} \]
**Scheme 57**: Microwave-assisted deoximation

\[
\begin{align*}
\text{R}_1, \text{R}_2 &\equiv \text{aryl, alkyl} & \text{yield up to 93\%}
\end{align*}
\]

**e. Oxidation of dihydrazones:**

Sodium periodate serves as a mild and efficient oxidant for the conversion of dihydrazones of \(\alpha\)-diketones and then to acetylenes in excellent yields (Scheme 58). Sodium periodate is also found to be an economical and practical oxidant, suitable for deprotection of monohydrazones of aldehydes and ketones to the corresponding aldehydes and ketones in excellent yields (Scheme 58).

**Scheme 58**: Oxidation of benzildihydrazone

\[
\begin{align*}
\text{R}_1, \text{R}_2 &\equiv \text{Aryl} & 87-90\% \\
\text{R}_1, \text{R}_2 &\equiv \text{H, Aryl, alkyl} & 70-90\%
\end{align*}
\]

**f. Oxidative carbonylation of amines:**

Carbonylation of amines can be achieved in methanol without a transition metal catalyst in the presence of \(\text{NaIO}_4\) to produce formamide derivatives in good to excellent yields (Scheme 59). Secondary aliphatic amines including cyclic amines were found to produce the...
formamides in moderate yields. Labeling experiments have confirmed that CO is the source of formyl group while its hydrogen is derived from the protic solvent.

\[
\begin{align*}
\text{NH}_2 \quad \text{X} \quad \text{X} \\
\text{NaIO}_4, \text{NaI, K}_2\text{CO}_3 \quad 24 \text{ h, CO (45 atm)} \\
90^\circ\text{C, CH}_3\text{OH} \quad 36-92\%
\end{align*}
\]

**Scheme 59:** Oxidative carbonylation of amines

**g. Carbonylation of amines to urea derivatives:**

Transition metal catalyst free oxidative carbonylation of amines can be achieved using NaIO\(_4\) as the oxidant and NaI as a promoter that affords good to excellent yields of urea derivatives from primary amines (**Scheme 60**).\(^{79}\) Conversion of amines 161 to urea derivatives 162 using NaIO\(_4\) is a mild and atom economical protocol taking place at room temperature under CO pressures as low as 20 atm. High yields of urea have been obtained for unhindered primary alkyl amines and benzylationines. The reaction is sensitive to steric hindrance as evidenced by low yields obtained for tert-butylamines substrate (20% yield).

\[
\begin{align*}
\text{X} = \text{H, OCH}_3, \\
\text{Cl, NO}_2 \text{ etc} \\
10-81\%
\end{align*}
\]

**Scheme 60:** Oxidized carbonylation of amines to urea derivatives

**h. Synthesis of nitriles**
Sodium periodate and potassium iodide in aqueous ammonia provides a simple, efficient and interesting methodology for the one-pot conversion of aldehydes 163 and alcohols 164 into nitriles 165 in moderate to good yields (Scheme 61). This transformation proceeds via an in situ oxidation-amination-aldimine oxidation sequence. The significant features of the reagent system are: (i) good to excellent yields are obtained with both aldehydes and alcohols; (ii) no need for special equipment, and the work up is simple; (iii) the reagents and chemicals needed are commercially available, with no need for toxic and/or expensive metals and (iv) purification of products is not time consuming.

\[
\begin{array}{ccc}
R-CHO \text{ or } R-CH_2OH & \xrightarrow{\text{NaIO}_4/\text{KI}} & R-CN \\
\text{aq. NH}_3, 60 ^\circ \text{C} & & 1.5-3 \text{~h,} \\
R = \text{aryl} & & 12-89\% \\
163 & 164 & 165
\end{array}
\]

Scheme 61: Conversion of aldehydes and alcohols into nitriles

i. Oxidative acetylation

Acetylation of bisphenol 166 is possible in high yields using sodium periodate in acetic anhydride (Scheme 62). Acetylation of the two hydroxyl moieties in bisphenol may be synchronous or stepwise. It is believed that periodate first attacks the carbonyl carbon of the anhydride to generate sodium acetate and ethanoylperiodate. Sodium acetate thus formed initiates the nucleophilic reaction of bis-phenol 166 with ethanoylperiodate to give the acetylated product 167.
j. Deprotection of silyl ethers

NaIO₄ can be used for the mild and efficient deprotection of silyl ethers (Scheme 63). Silyl groups such as TBS, TIPS, TMS, TES, TIBS and TPs are effectively removed in the reaction with an excess of NaIO₄ in THF at room temperature affording alcohols in high yields. However, the TBDPS group provides only low yields even at high temperature or after long reaction times. It was found that NaIO₄ is the actual cleaving reagent rather than the residual periodic acid that can be found in the commercial source of NaIO₄, because even at neutral or slightly basic conditions the reaction still takes place.

![Scheme 63: Deprotection of silyl ethers](image)

k. Oxidative cleavage of boronic esters

Oxidative cleavage or oxidative hydrolysis of the boronic esters 170 with NaIO₄ in a 4:1 mixture of THF/H₂O gives aryl boronic acids 171 in moderate to good yields (Scheme 64). The major
limitation of this protocol is the incompatibility of the oxidative hydrolysis to electron-rich heteroarylboronate esters.

\[
\begin{align*}
\text{R} = \text{CH}_3, \text{Cl}, \\
\text{CF}_3, \text{OCH}_3 \text{ etc}
\end{align*}
\]

\begin{align*}
\text{170} & \xrightarrow{\text{NaIO}_4, \text{THF/H}_2\text{O}} \text{171} \\
\text{66-93\%}
\end{align*}

**Scheme 64:** Cleavage of boronic esters

### I. Formation of stable radicals

Sodium periodate has been shown to be a useful oxidant for the synthesis of stable radicals from the corresponding alcohols or amines. For example N,N'-di-hydroxyimidazolidine\textsuperscript{172} reacts with sodium periodate to afford the stable nitroxidebiradical\textsuperscript{173} in moderate to good yield (Scheme 65).\textsuperscript{84a} Similarly, NaIO\textsubscript{4} is efficient for the synthesis of the 1,5-dimethyl-6-oxoverdazyl radical (175) in a high yield, while other oxidizing agents such as ferricyanide and silver oxide were found to be unsuccessful for these transformations.\textsuperscript{84b}
Scheme 65: Synthesis of stable radicals

6. Conclusions and Outlook

Sodium periodate has been proven to be a more practical, economical and selective reagent for various oxidation reactions at ambient conditions with a broad substrate scope. It is extensively used for the oxidation of alcohols, alkenes, halogens, aromatics, sulfides, selenides and others. Based on the broad reaction scope, it is clear that sodium periodate will find extensive application in synthetic organic chemistry and it is believed that NaIO₄ will be a suitable oxidant and make a significant impact in many other organic oxidative transformations as well. Though exciting progress has been made in the area of oxidative transformation using sodium periodate, from a fundamental perspective some areas still remain to be explored further such as (i) asymmetric oxidation using NaIO₄; (ii) remote oxygenations of unfunctionalized C-H bonds; (iii) use of periodates in catalytic amounts for oxidations; (iii) recyclability of periodate
by using two-phase reactions or by supported periodates and (iv) oxidative reactions to mimic transition metals or bioenzymes. From an applications perspective future research in this direction will be instrumental in greatly expanding the scope and application of periodates as useful oxidant.

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8. References


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