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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, $NaIO_4$, an exciting reagent, has attracted an increasing attention enabling the development of these unprecedented oxidative transformations that are difficult to achieve otherwise. Thus, $NaIO_4$ 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 $NaIO_4$ 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 $NaIO_4$, have played an important role as one of the oxidizing agents. $NaIO_4$ is a colorless to white tetragonal, efflorescent crystalline compound with a molecular weight of 213.8918 g/mol, melting point of 300 ^oC 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).

$$HIO_3 + H_2O - 2\ e^- \rightarrow IO_4^- + 3\ H^+ \quad E° = 1.6V \qquad \text{.....eqn i}$$

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 H_2O, H_2SO_4, HNO_3, and CH_3CO_2H but insoluble in typical organic solvents.[1] In order to carry out periodic oxidation in non-aqueous media, heterogeneous reactions with $NaIO_4$-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 OsO_4 and RuO_4 are very expensive reagents. However, when periodates are employed in stoichiometric amounts as primary oxidants, it allows the use of

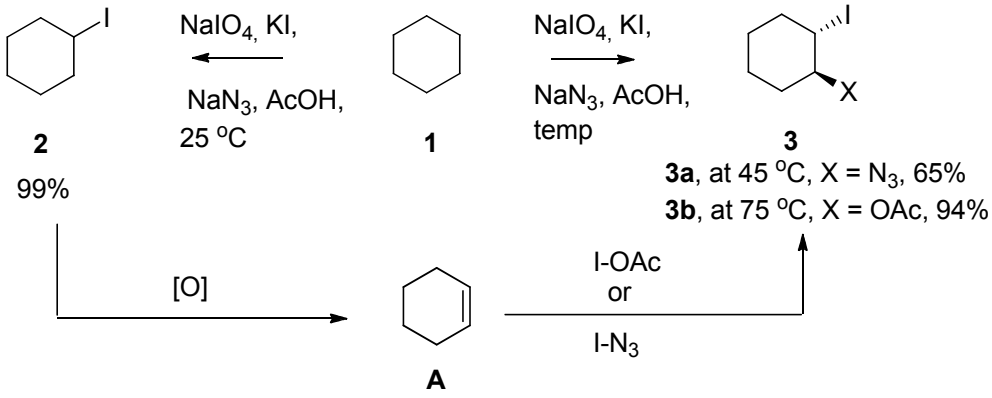
these expensive oxidants in catalytic amounts. Similarly, ruthenium tetroxide is generally prepared *in situ* by the reaction of the slightly less expensive ruthenium trichloride with sodium periodate, which initially oxidizes ruthenium trichloride to give active ruthenium tetraoxide.[4] Sodium periodate 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.[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.[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 $NaIO_4$

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 activationof C-H bonds in alkanes using enzymes, transition metal complexes and transformations involving halogenation reactions among others. In particular, $NaIO_4$ played a major role as an efficient, transition metal-free, mild reagent for C-H bond activation.

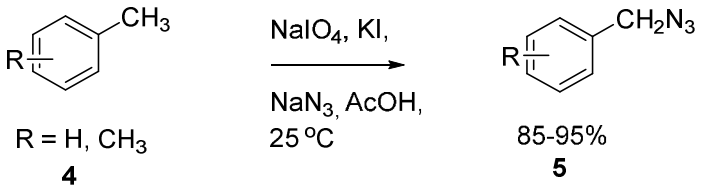
a. C–H bond functionalization in hydrocarbons

The 1, 2-functionalization of inactive C–H bonds in a single step represents a major challenge for organic chemists. The combination of $NaIO_4$–KI–NaN_3 in acetic acid at 25 ^oChas been found to be an efficient, reliable, and inexpensive reagent system for mono- and 1,2-difunctionalization of hydrocarbons **1***via* C–H bond activation to afford iodoalkanes**2**, 1-acetoxy- or 1-azido-2-iodocycloalkanes **3** (**Scheme 1**).[6]Mechanistically, $NaIO_4$ oxidizes KI as well as NaN_3 simultaneously, to liberate I_2 and an azide radical, the combination of which results in the formation of I–N_3. Azide radical formed by homolysis of I-N_3 abstracts proton from alkane to generate free radical which on combination with I_2 to give alkyl iodide **2** followed by oxidative elimination produces alkene**A** as an intermediate. Addition of either I–N_3 or I-OAc across the double bond in **A** formed during the course of reaction results in the formation of products **3a** and **3b** respectively.



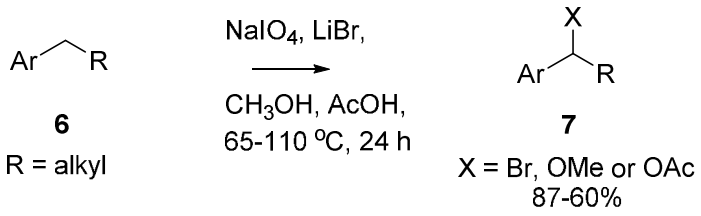
Scheme 1. C–H bond functionalization in aliphatic hydrocarbons with $NaIO_4$–KI–NaN_3

Also the direct addition of azide at benzylicC–H bonds has been achieved by using $NaIO_4$–KI–NaN_3. In this way toluene **4** can be functionalized smoothly to give benzylicazides**5** (**Scheme 2**).



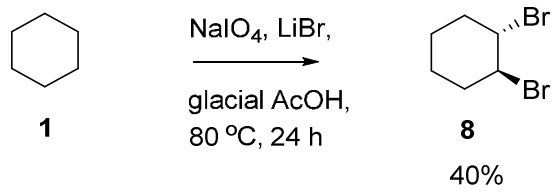
Scheme 2: Benzyliczides from toluene derivatives using $NaIO_4$–KI–NaN_3

Similarly, bromo and acetoxy derivatives of alkylbenzenes and alkanes **6** can be obtained in excellent yields using sodium periodate and LiBr as a halogen source under acidic reaction conditionsthrough C–H bond activation (**Scheme 3**).[7]A cyclic voltammogram study revealedthat Br_2 generated *in situ* from LiBr by oxidation with $NaIO_4$ 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.



Scheme 3: C-H bond activation ofalkylbenzenes and alkanes with LiBr - $NaIO_4$

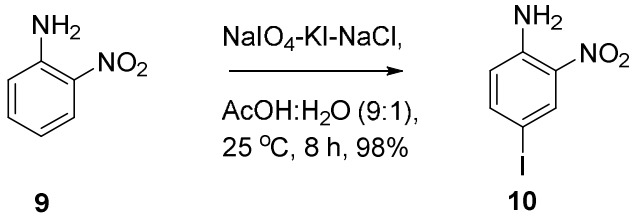
This protocol is also useful for the direct conversion of cyclohexane **1** to *trans*-1,2-dibromocyclohexane **8** (**Scheme 4**). In this case the formation of *trans*-1,2-dibromocyclohexane probably indicates the involvement of cyclohexene as the intermediate, followed by bromine addition to the double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



Scheme 4: Oxidative halogenation of cycloalkanes

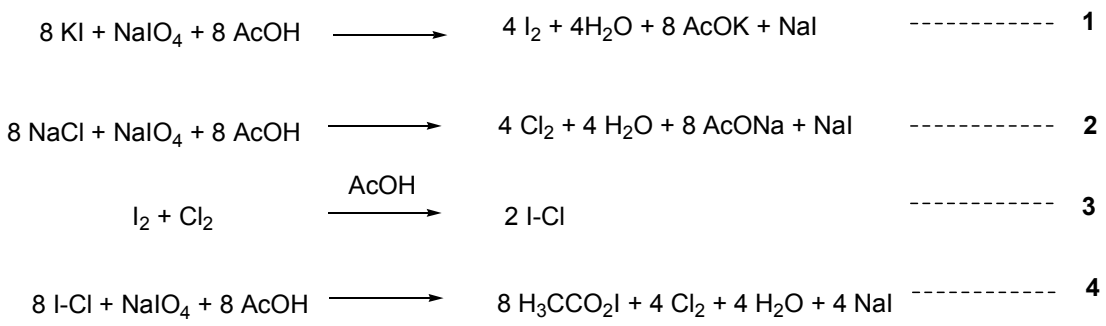
b. Oxidative iodination of arenes

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 $NaIO_4$/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**).[8] The reaction unfortunately fails for electron deficientarenes.



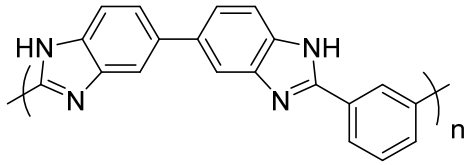
Scheme 5: Oxidative iodination ofelectron richarenes

The proposed reaction pathway for the iodination is shown in **Scheme 6**. $NaIO_4$ oxidizes alkali metal halides such as KI or NaCl in the presence of acid to liberate molecular halogens, I_2 and Cl_2(Eqns. 1–2). Iodine monochloride,thought to be formed from the liberated molecular halogens acts as the electrophile (Eqs. 3–4).



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

A remarkable feature of this system is that even easily oxidizableamino 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]

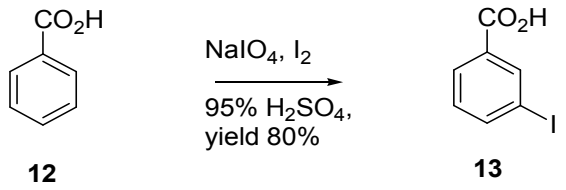


11

Fig. 1: Structure of polybenzimidazole (PBI)

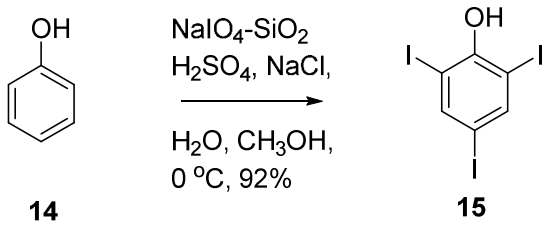
Oxidative iodination of deactivated arenes is also possible, yielding mono- or diiodinated derivatives by using $NaIO_4$/KI in a more acidic medium. Deactivated arenes**12** were mono- **13** or diiodinated with strong electrophilic I^+ reagents, which were prepared from $NaIO_4$ and either I_2 or KI in concentrated H_2SO_4 (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.



Scheme 7: Oxidative iodination of deactivated arenes

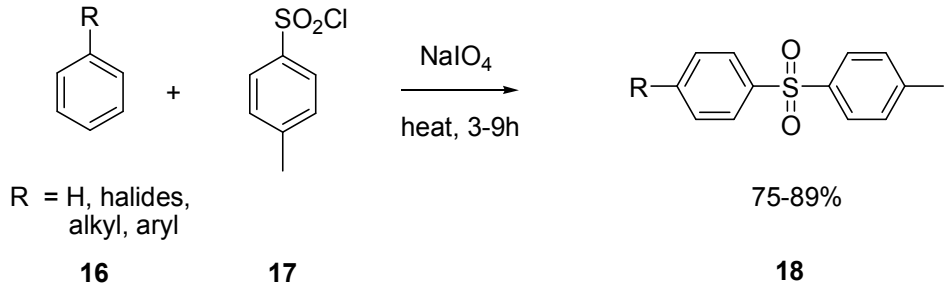
Oxidative iodination of reactive phenols **14** was possible using $NaIO_4$/NaCl in the presence of a combination of silica/sulfuric acid to provide triiodophenol**15** (**Scheme 8**).[10]The reaction proceeds through ICl as the electrophile.



Scheme 8: Iodination of phenols

c. Sulfonylation of aromatic compounds

Sodium periodate was found to be efficient in catalyzingregioselectivesulfonylation of aromatic compounds **15** with *p*-TsCl**17** (**Scheme 9**).[11] $NaIO_4$ gave exclusively *para* isomers of diarylsulfones**18** with good yields with no trace of other possible *ortho/meta* isomers.

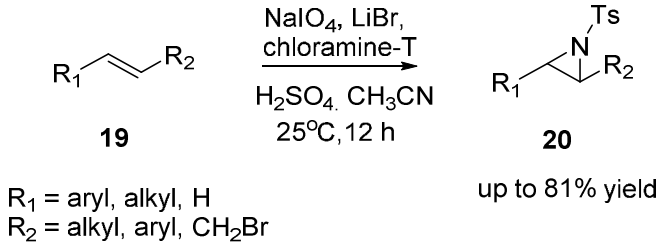


Scheme 9: Regioselectivesulfonylation of aromatic compounds

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.

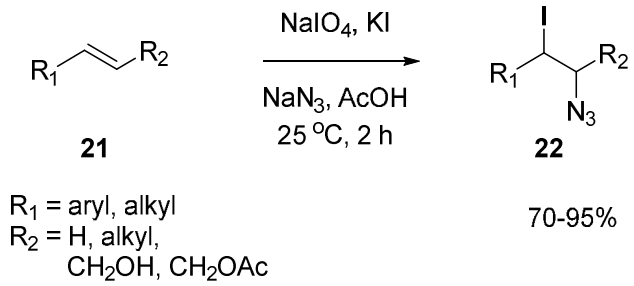


Scheme 10: $NaIO_4$/LiBr-mediated aziridination of alkenes using chloramine-T

A mild protocol for aziridination of a variety of alkenes **19** by using a catalytic amount of sodium metaperiodate ($NaIO_4$) has been developed.[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**).

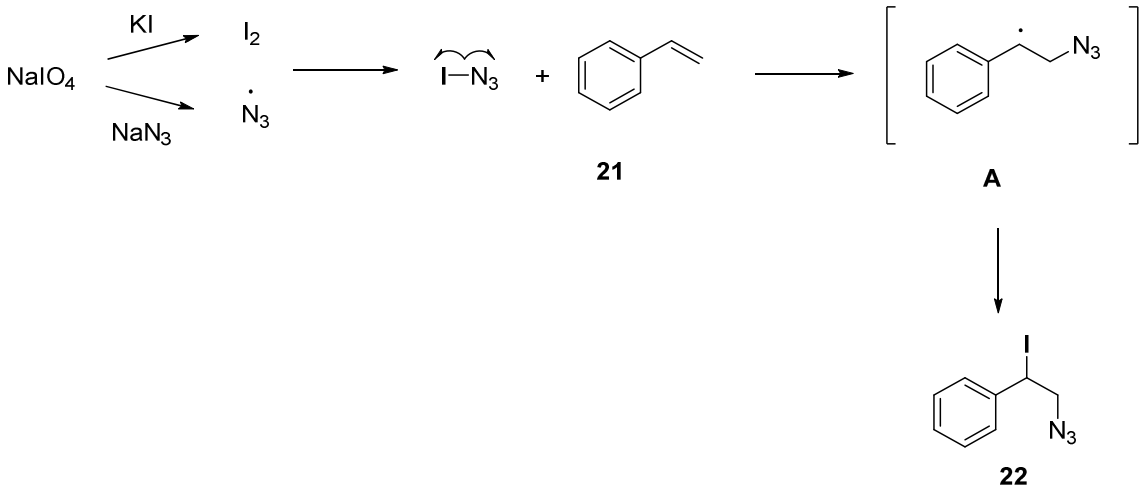
b. Azidoiodination

The combination of $NaIO_4$, KI and NaN_3 has been found to be simple and inexpensive reagents for azidoiodination of alkenes **21**. The 1,2-azidoiodination proceeds regiospecifically in an *anti*-Markovnikov fashion to produce the corresponding β-iodoazides**22** (**Scheme 11**).[13]



Scheme 11: Sodium periodate-mediated azidoiodination of alkenes

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



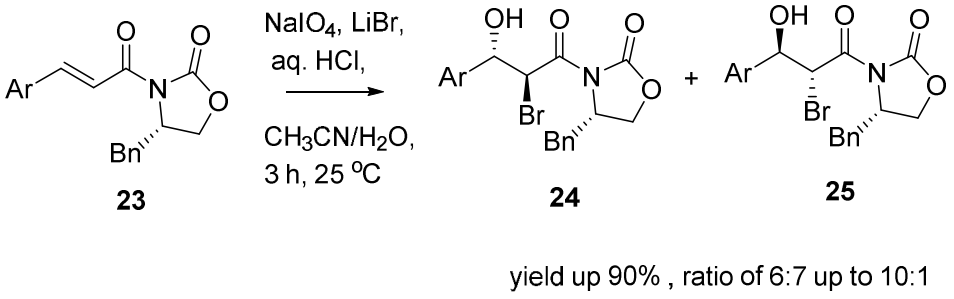
Scheme 12: Proposed mechanistic pathway for azidoiodination of alkenes

$NaIO_4$ oxidizes both KI and NaN_3 simultaneously to liberate I_2 and an azide radical, respectively; the combination of which probably results in the formation of IN_3 (**Scheme 12**). Homolysis of

IN_3 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 I_2 or with an iodide radical results in the formation of β-iodoazides**22**.

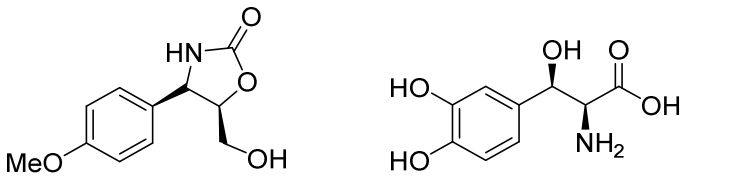
c.Hydroxyhalogenation

$NaIO_4$ 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: $NaIO_4$-mediated asymmetric bromohydroxylation α,β-unsaturated carboxamides

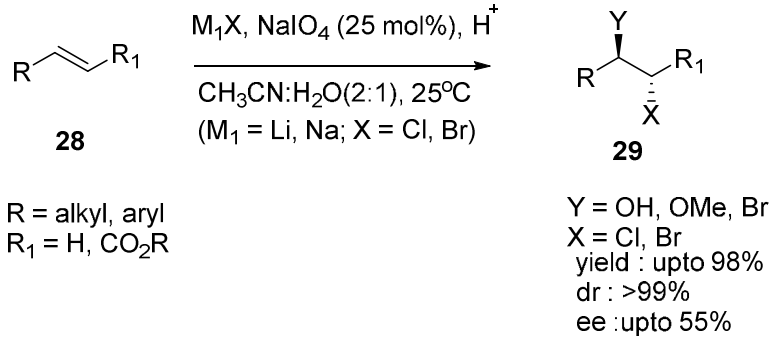
This methodology has been successfully applied in the enantioselective syntheses of two biologically important molecules namely (-)-cytoxazone (**26**)and L-threo-DOPS (droxidopa) (**27**) (**Fig. 2**).



26, (-)-cytoxazone **27**, L-threo-DOPS (droxidopa)

Fig. 2: Structure of bioactive molecules

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 enantioselectivebromo hydroxylation using β-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**).

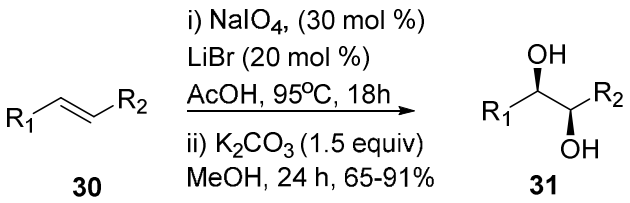


Scheme 14: $NaIO_4$-mediated oxidative halogenation

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 LiBrcatalyzesthe dihydroxylation of alkenes **30**to their corresponding *cis*or *trans*diols**31** with excellent diastereoselectivity (**Scheme 15**).[16]

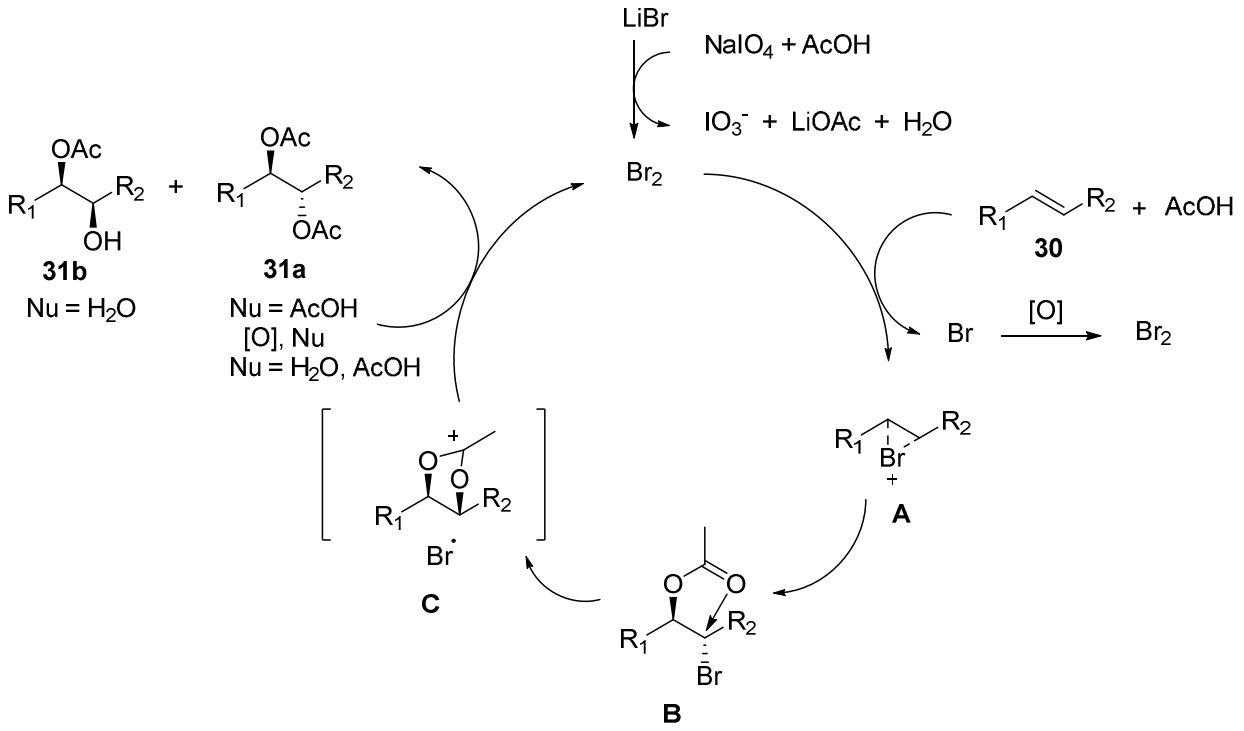


Scheme 15: LiBr-catalyzeddihydroxylation of alkenes

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 (20mol %) in acetic acid catalyse mono- and diacetylation of alkenes which on subsequent basic hydrolysis furnish *syn* and *anti*diols with excellent diastereoselectivityranging 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 *in situ* from alkali metal bromide by oxidation with $NaIO_4$ or $PhI(OAc)_2$ rapidly undergoes bromoacetoxylation with alkenes *via* the bromonium ion species **A** to produce a *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

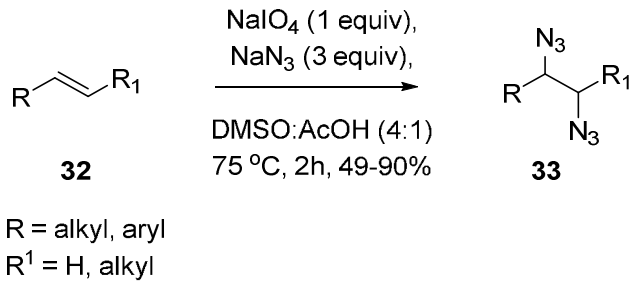
by acetic acid to give the *trans* diacetate**31a** with concomitant liberation of Br_2.



Scheme 16: Proposed catalytic cycle for dihydroxylation of alkenes

e. Diazidation of styrene derivatives

Vicinal diazides**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 **32** gave good yields of the corresponding vicinal 1,2-diazides **33** (**Scheme 17**).

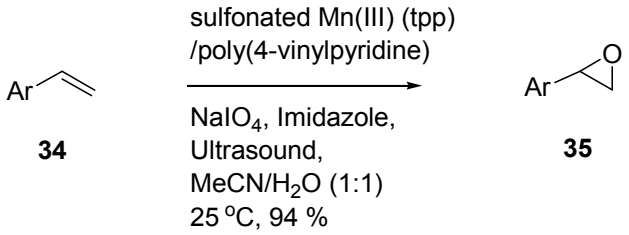


Scheme 17: $NaIO_4$-mediated 1,2-diazidation of styrene derivatives

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 diastereoslectivity (**Scheme 18**).[18] Moreover, Mn(III) salen,[19]Ru(III)polyoxometallate and salophen,[20]Mn(Br_8TPP)Cl and tetraphenylporphyrinatoMn(III) chloride[21] were also used as catalysts for epoxidation of alkenes in presence of $NaIO_4$.

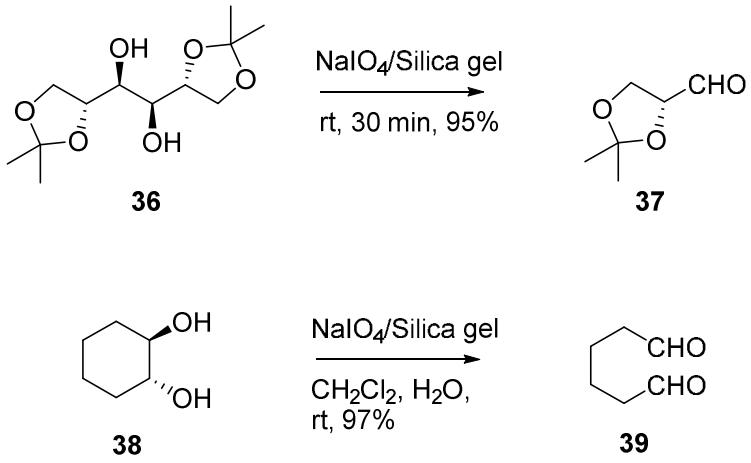


Scheme 18: Epoxidation of styrene derivatives

4. Oxidation of basic functional groups

a. Oxidation of alcohols

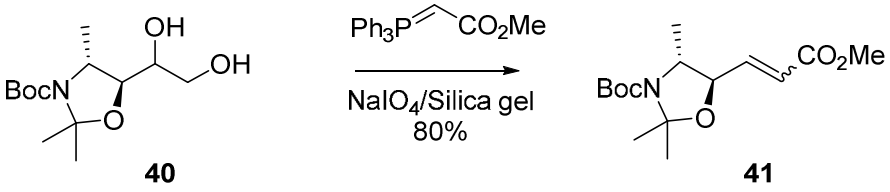
Since 1928 $NaIO_4$ has been widely used for the oxidative cleavage of 1, 2-diols efficiently to yield carbonyl compounds (**Scheme 19**).[22] Sodium periodate complements lead tetraacetate for oxidative cleavage of diols. The glycol cleavage reactions using $NaIO_4$ are usually very rapid, quantitative and substrate specific. For example, $NaIO_4$ cleaves 1,2-diols chemoselectively even in the presence of sulfide group.[23] 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.[24] In order to carry out periodic oxidation in nonaqueous media, $NaIO_4$-supported silica[25] and quaternary ammonium periodates[26] 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 CH_2Cl_2, has been reported as a practically useful alternative.[27] This reaction was extensively used for the structural elucidation of carbohydrates before the advent of modern spectroscopic techniques.



Scheme 19:Oxidative cleavage of 1,2-diols

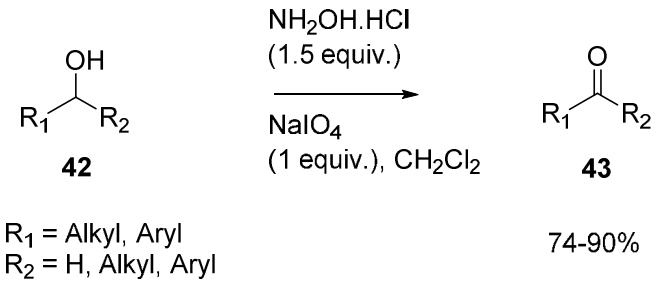
The mechanism of carbon-carbon bond cleavage of diols by periodate is consistent with a cyclic, five-membered ring intermediate. Support for such a mechanism comes from the observations that the *cis*isomers of cyclic diols are more reactive than the trans isomers, *threo*-1,2-diols undergo oxidation faster than the *erythro* isomers, and the inert behavior of diaxial*trans*-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.



Scheme 20:One-potoxidative cleavage and Wittig olefination

Not only 1,2-diols but also alcohols can be oxidized using sodium periodate in combination with other reagents, for example $NH_2OH.HCl$ together with $NaIO_4$ serve as a mild reagent for the oxidation of alcohols **42** to carbonyl compounds **43** at room temperature (**Scheme 21**).[30]

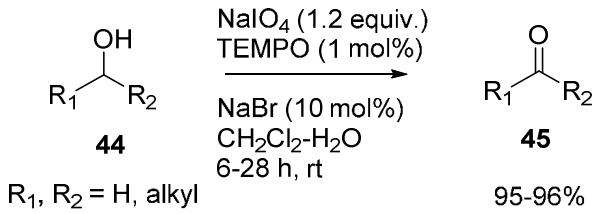


Scheme 21: Oxidation of alcohols with hydroxylamine/periodate

NO generated from reaction of $NH_2OH.HCl$ and $NaIO_4$ is responsible for oxidation of alcohols to aldehydes as shown its stoichiometry in eqn ii.

$$6NaIO_4 + 14NH_2OH.HCl \text{ --------> } 3I_2 + 14NO + 24H_2O + 6NaCl + 8HCl \quad \ldots\ldots \quad \text{eqn ii}$$

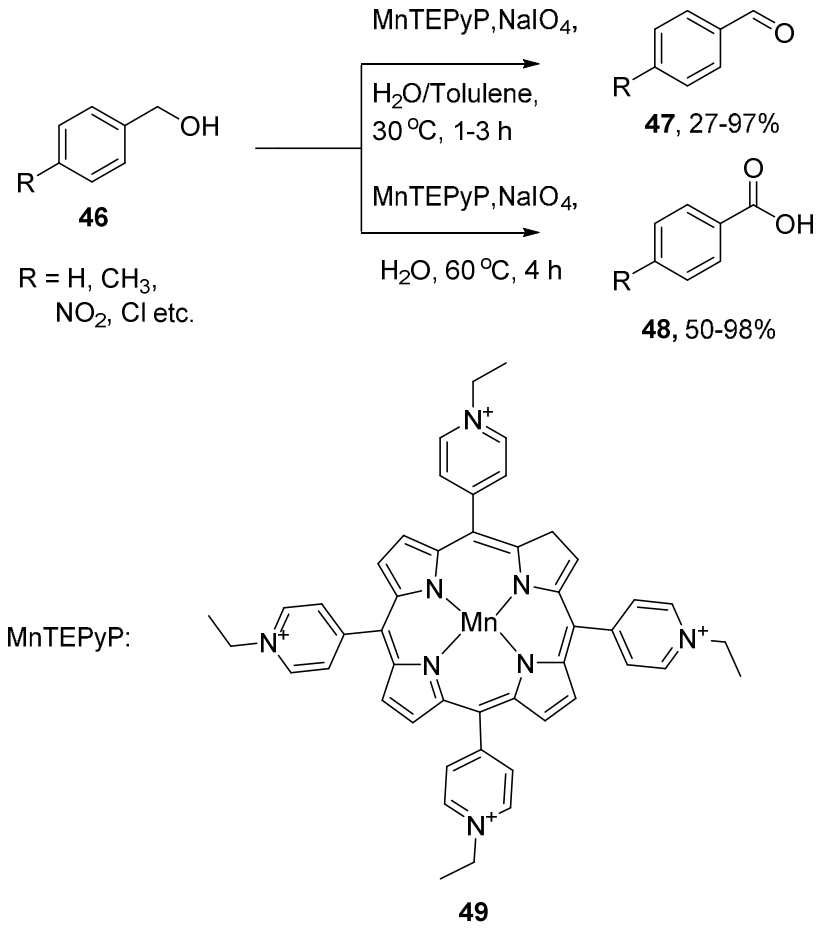
Likewise TEMPO catalyzed the selective oxidation of alcohols **44** to the corresponding aldehydes and ketones **45** using $NaIO_4$ as the terminal oxidant (**Scheme 22**).[31]



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

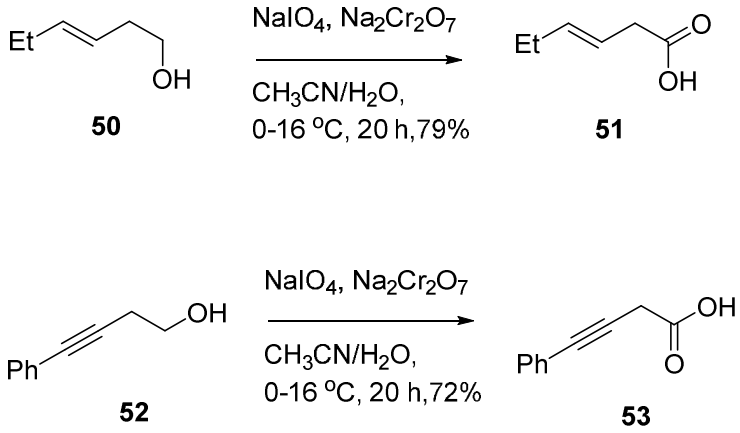
room temperature. A biomimetic water-soluble metalloporphyrin**49** (MnTEPyP) catalyst was also highly efficient for the oxidation of alcohols **46** to either aldehydes **47** or carboxylic acids **48** with $NaIO_4$ (**Scheme 23**) where selectivity was solvent dependent.[32] The manganese porphyrin**49** showed an excellent activity for the product specific oxidation of various alcohols under mild conditions.



Scheme 23: Product specific oxidation of alcohols

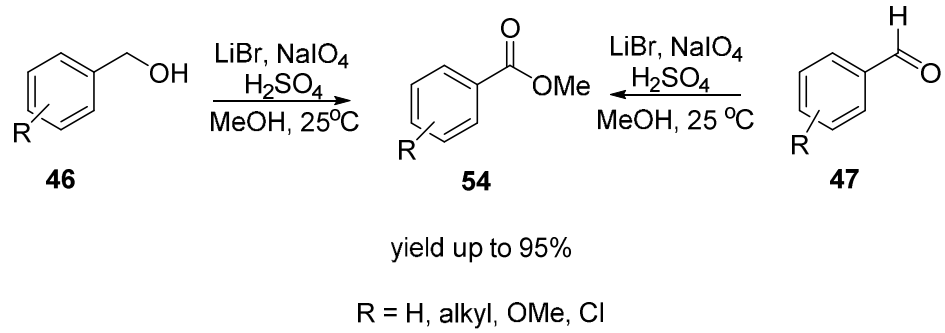
(Homo-)allylic and (homo-)propargylic alcohols **50** and **52** can be oxidized under slightly acidic conditions at ambient temperature with sodium periodate in the presence of sodium dichromate as the catalyst to yield the corresponding carboxylic acids **51** and **53**, respectively (**Scheme 24**).[33]The 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.



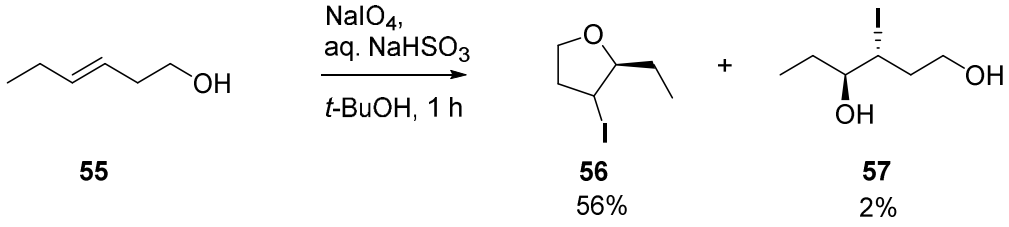
Scheme 24: Oxidation of alkenols and alkynols to carboxylic acids

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 $NaIO_4$/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

Treatment of homoallylic alcohols **55** with $NaIO_4$:$NaHSO_3$ 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* aniodonium ion intermediate. The tetrahydrofuran derivative **56** is obtained by intramolecularstereoselective cyclization of the iodonium ion, whereas iodohydrins**57** are formedby 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 undergoesnucleophilic addition of water in addtion to the intramolecular cyclization.

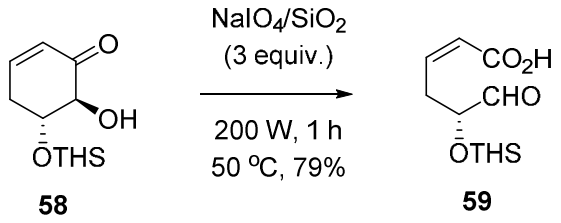


Scheme 26: Reaction of homoallylic alcohols with $NaIO_4$:$NaHSO_3$

b. α-Oxidation of carbonyl compounds

A silica-supported $NaIO_4$ 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-hydroxyketonesthat are not soluble in polar media and for aldehydes and acids that are water soluble.It is worth mentioning that the

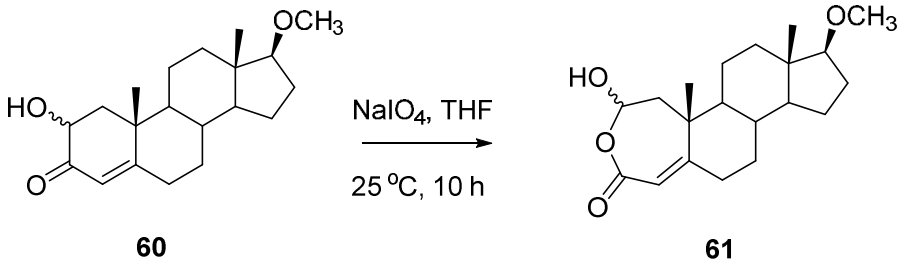
mildness of the method allows its use with sensitive substrates and produces selective oxidative cleavage even in the presence of sulfur functionalities.



58 59

Scheme 27: Oxidation of α-hydroxyketones

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

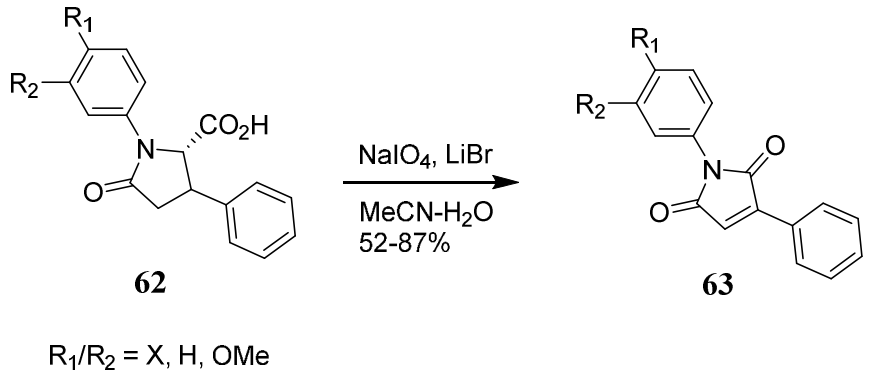


60 61

Scheme 28: Cleavage of unsaturated α-ketols

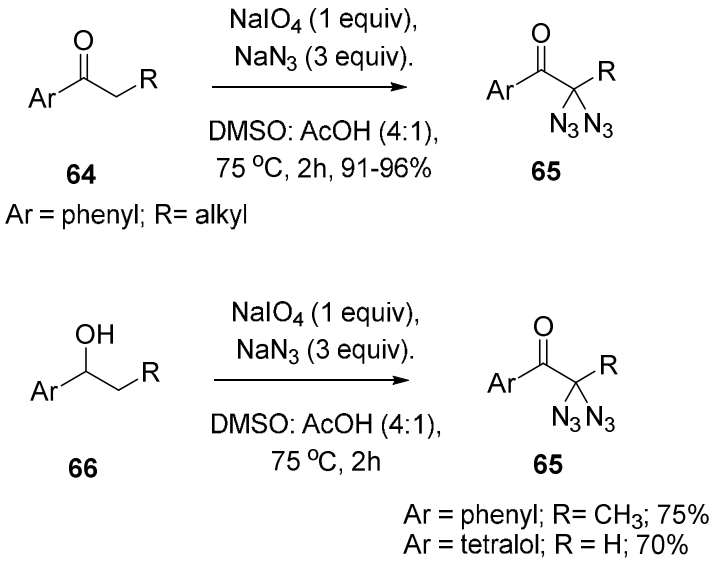
In order to facilitate the isolation of the carboxylic acid that emerged from the oxidation of unsaturated α-ketols, the crude product was typically treated with diazomethane in order to prepare the ω-oxo-α, ω-unsaturated methyl esters prior to separation.[37]

The combination of $NaIO_4$/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**.



Scheme 29: Synthesis of *N*-aryl maleimides

Geminaldiazide 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 geminaldiazides**65** in high yields under mild reaction conditions (**Scheme 30**).[39]



Scheme 30: $NaIO_4$-mediated α, α -diazidation of aryl ketones and benzylic alcohols

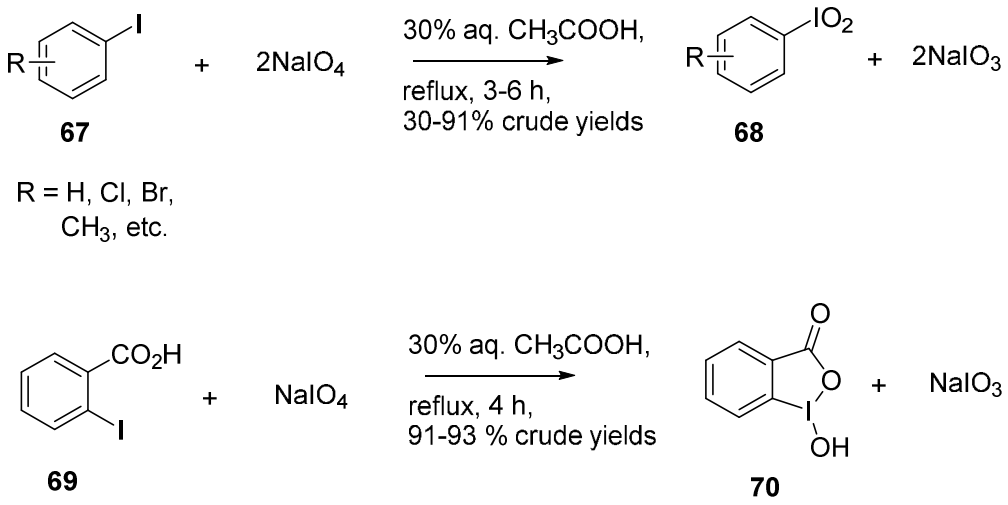
Linear and cyclic aryl ketones **64** withα-methylene group (–CO–CH_2–) underwent selective oxidative diazidation with $NaIO_4$ (1 equiv) and NaN_3 (3 equiv) in AcOH–DMSO (1:4) as solvent at

75 ^{o}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 reactionprobably 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

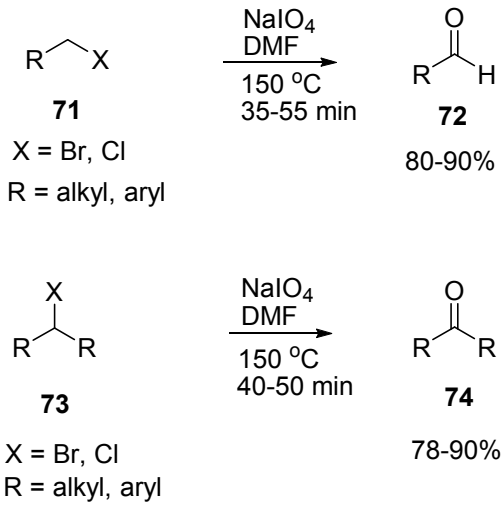
Iodylarenes ($ArIO_2$), the hypervalent aromatic oxidants have widely been used as mild and selective oxidants in organic transformations. They are generally prepared by oxidation of their corresponding iodoarenes. Examples include 2-iodosobenzoic acid(IBX) and its triacetylated derivative, the periodinaneDess-Martin reagent among the better known oxidants.

Thus, $NaIO_4$ 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)**.[40]Using $NaIO_4$,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.



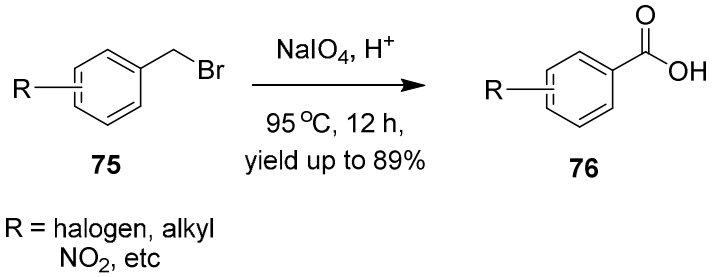
Scheme 31: Oxidation of iodoarenes to iodosoarenes

$NaIO_4$ 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**).[41]Interestingly, on treating α-halocarbonyl compounds with $NaIO_4$ 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 formedphenylglyoxalic 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 **75** can be converted to their corresponding carboxylic acids **76**, directly under transition metal-free conditions using$NaIO_4/H_2SO_4$ in high yields (71-89%) (**Scheme 33**).[42]

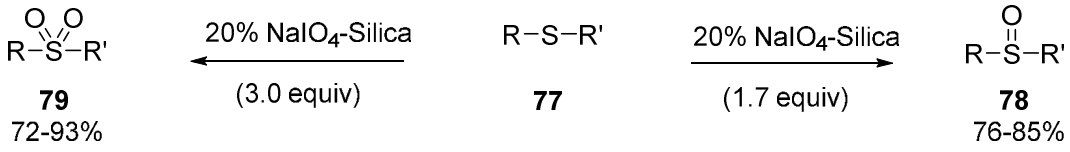


Scheme 33: Oxidation of benzylic bromide derivatives

Secondary benzylic bromides were also oxidized by $NaIO_4/H_2SO_4$ to give thecorresponding 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.



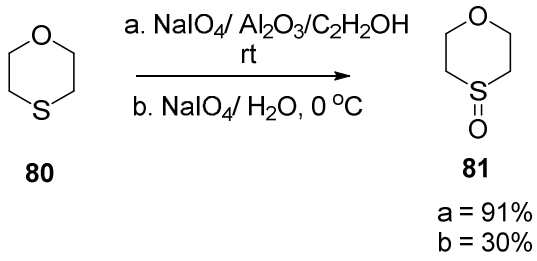
Scheme 34. Oxidation of sulfides to sulfoxides and sulfones

Wet silica-supported sodium metaperiodate plays a key role in this regard for the selective oxidation of both alkyl- and aryl sulfides**77** to the corresponding sulfoxides**78** and sulfones**79**,

when, under microwave conditions, 1.7 and 3 equivalents of $NaIO_4$ 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 $NaIO_4$ 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 ascatalyst gave the sulfoxides in 24-48 h.[44]

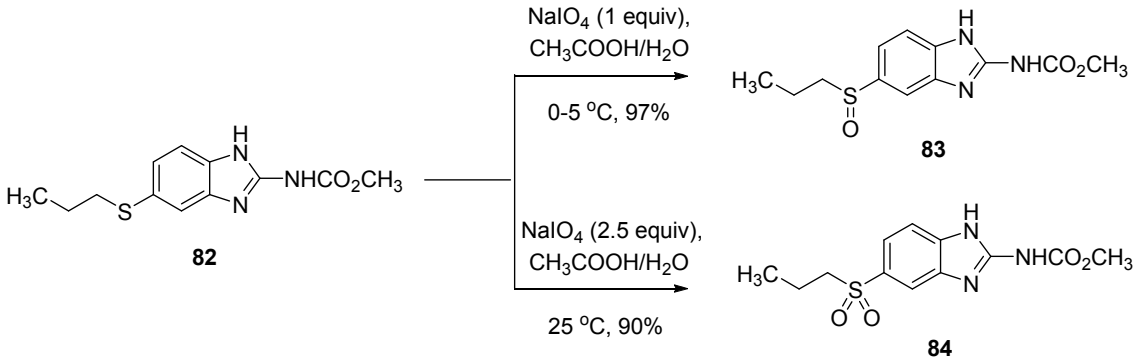
Sodium periodate supported on acidic alumina was found to be a useful reagent for the oxidation of thiomorpholine (**80**) to sulfoxide**81** (91%) in ethanol.However, the oxidation of thiomorpholine in water by $NaIO_4$ alone afforded the sulfoxide**81** in only 30% yield (**Scheme 35**).[45]



Scheme 35: Oxidation of thiomorpholine

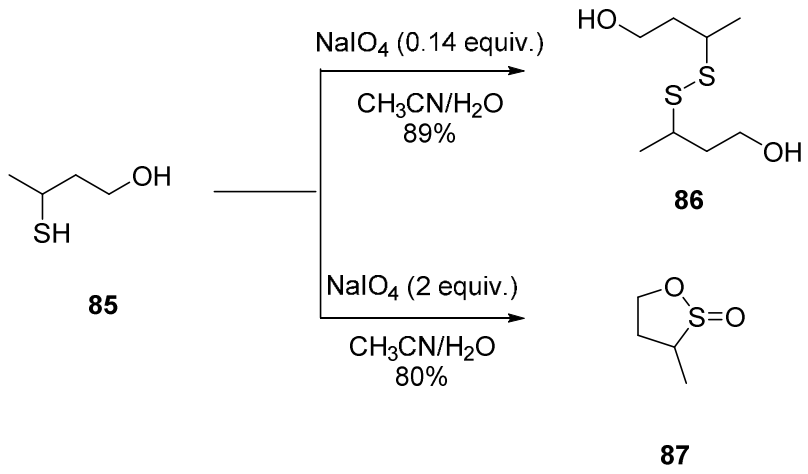
Sodium periodate in combination with potassium permanaganate oxidizes sulfides to the corresponding sulfones directly. Similarly a wide range of sulfides can be oxidized with sodium periodatecatalyzed by the manganese (III) tetrapyridylporphyrin supported on chloromethylatedpolystyrene. This catalyst 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**82**, fenbendazole, and other benzimidazolesulfides was achieved with sodium periodate in an acidic reaction medium, affording the corresponding sulfoxides**83**and sulfones**84** respectively, depending upon the temperature (**Scheme 36**).[46]



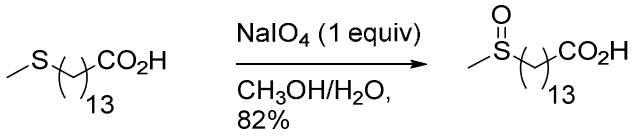
Scheme 36: Oxidation of benzimidazolesulfides

Oxidation of 3-sulfanyl-alcohols **85** with $NaIO_4$ represents a novel synthetic route to disulfides**86** and sultines**87** depending upon the number of equivalents of $NaIO_4$ used. For example, the sultines can be obtained in a short time (4 h) with good yields using excess of $NaIO_4$ in CH_3CN at room temperature (**Scheme 37**).[47]



Scheme 37: Oxidation of 3-sulfanyl alcohols

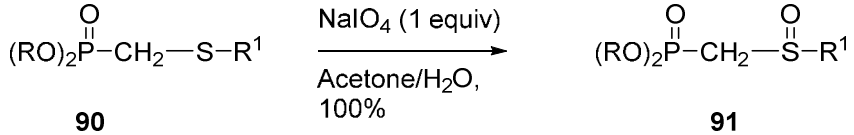
Oxidation of methylthioalkanoic acids with $NaIO_4$ (1 equiv) gave the corresponding methylsulfinylalkanoic acids in good yields, which are found to be potentially active, cardiac inotropic and antifungal agents.For example, the oxidation of 14-methylthiotetradecanoic acid (**88**) gives 14-methylsulfinyltetradecanoic acid (**89**), as illustrated in **Scheme 38**.[48]



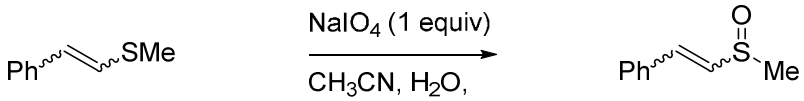
88 **89**

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]



90 **91**

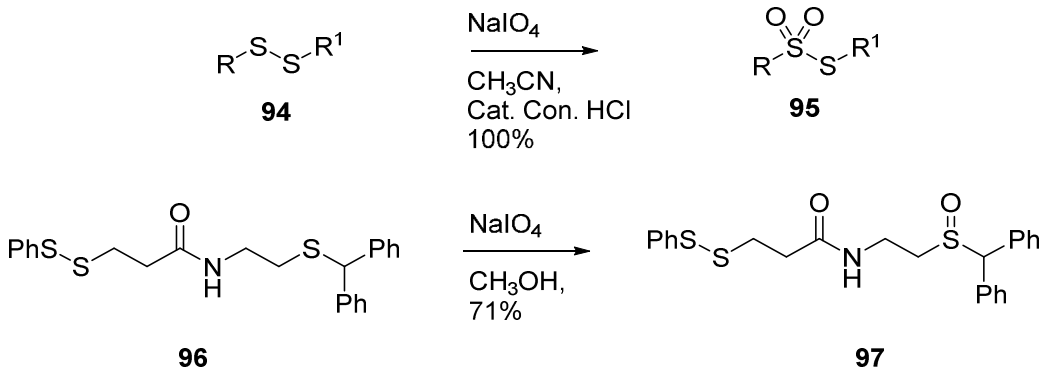


92 **93**

Scheme 39: Oxidation of α-phosphoryl and vinylic sulphides

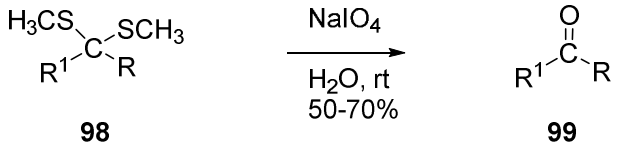
$NaIO_4$ was found to oxidize unsymmetricalthiosulfinic S-esters **94** to thiosulfonic esters **95**effectiviely in quantitative yields, without cleavage of the S-S bond. $NaIO_4$ is also effective for

the selective oxidation of sulfide**96** tosulfoxide**97** in the presence of disulfide linkage.[51]Other oxidants (CrO_3, H_2O_2 and *m*CPBA) when treated with sulfide**96** result in decomposition *via*cleavage of the S-S bonds (**Scheme 40**).[52]



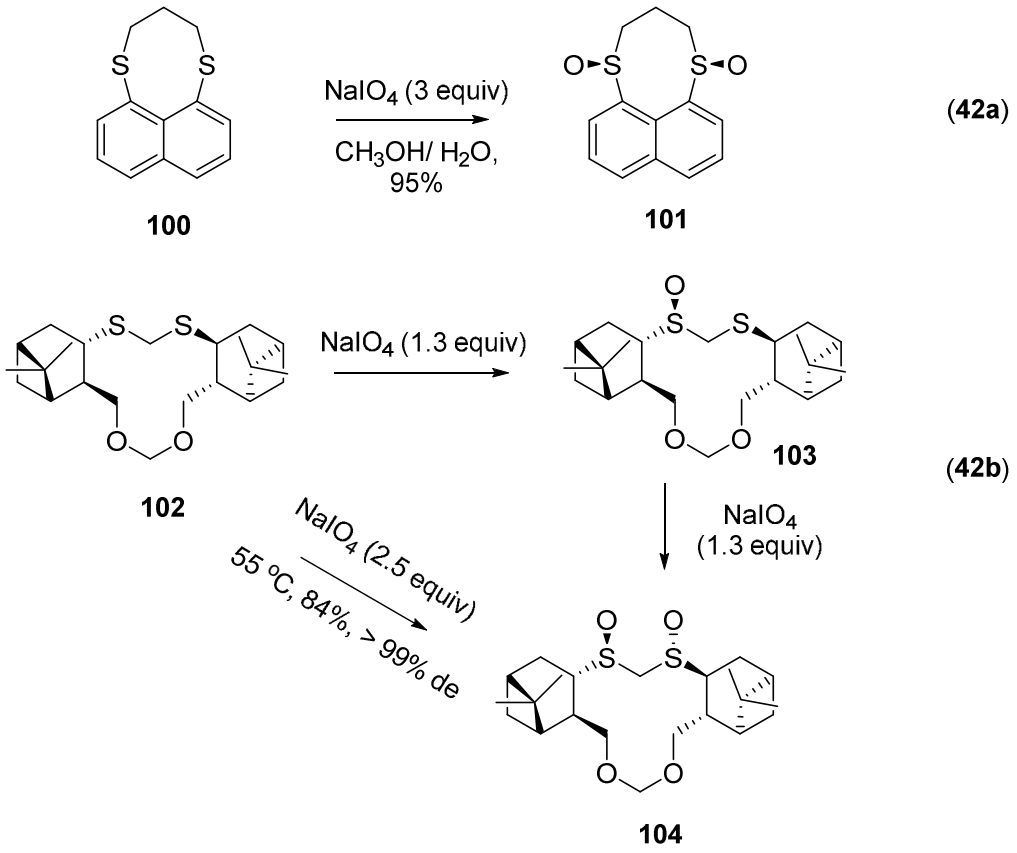
Scheme 40: Oxidation of disulfides

Sodium periodate mediated hydrolyses are used for deprotection of dimethyl dithioacetals**98** of aldehydes and ketones to give the corresponding carbonyl compounds **99** in moderate yields, as illustrated in **Scheme 41**.[53]



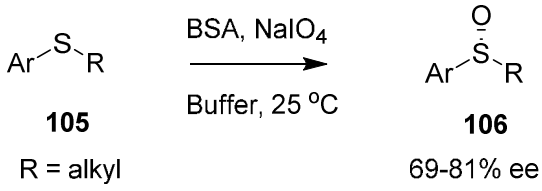
Scheme 41: Deprotection of dimethyl dithioacetals

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.[54]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**).[55]Treatment of disulfide**102** with $NaIO_4$ in EtOH at room temperature gave monosulfoxide**103** (95%), while at 50 ^{o}C, it gave *trans*-bis-sulfoxide**104** (84%, >99% de) (**Scheme 42,** eqn**42b**).[56]



Scheme 42: Stereoselectiveoxidation of dithianes

Asymmetric oxidation of a number of aromatic sulfides**105** in the presence of bovine serum albumin (BSA) using sodium metaperiodate resulted in the formation of chiral sulfoxides**106** in reasonably high optical purities (**Scheme 43**).[57]

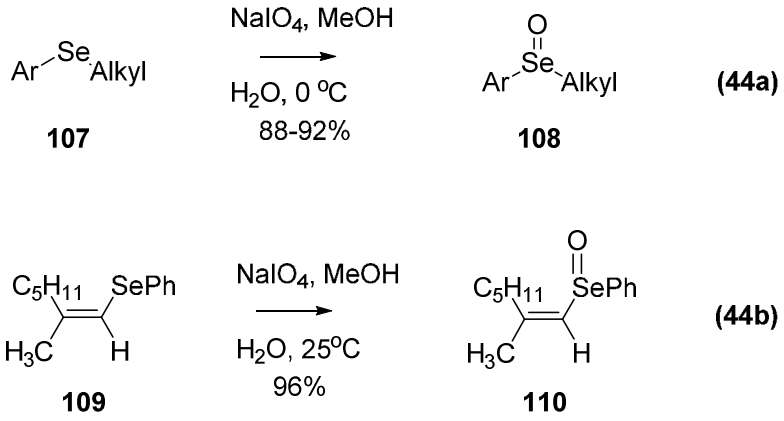


Scheme 43: Asymmetric oxidation of sulfides

e. Oxidation of selenides

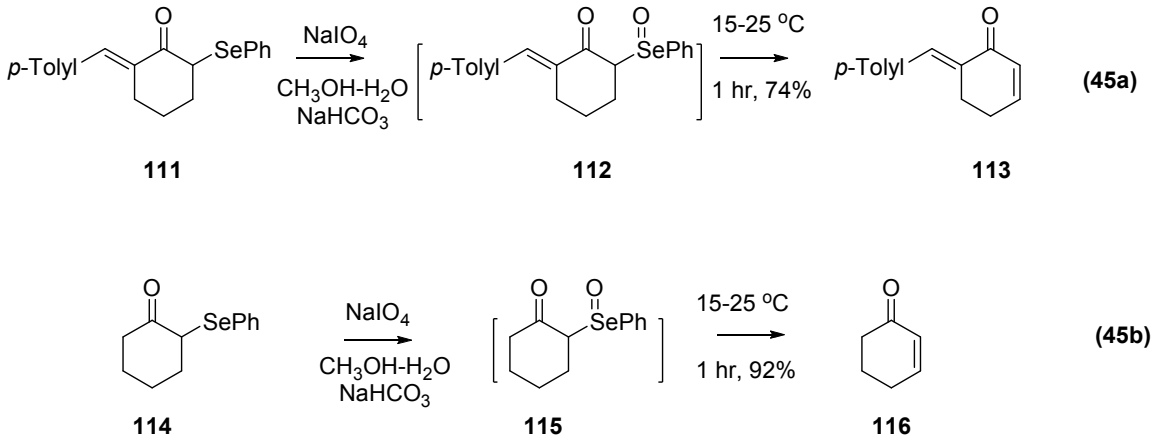
Selenoxides are valuable co-oxidants for the osmium catalyzed*cis*dihydroxylation of alkenes, where they are thought to function to reoxidizeOs (VI) to Os (VIII) species.[58] In general

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 $NaIO_4$ at 0°C to yield the corresponding selenoxides**108** in 88-92 % yields (**Scheme 44**, eqn**44a**).[59] 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**).[60] The reaction with mCPBA is much less selective.



Scheme 44: Oxidation of selenides to selenoxides

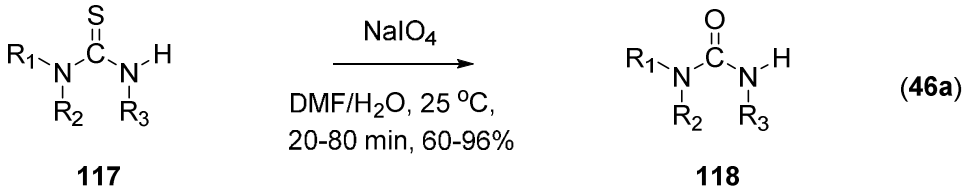
It was also found that selenoxides readily undergoes *syn*-elimination during the oxidation reaction to form alkenes, where both steps occur at below ambient temperatures. For example, the sodium metaperiodate mediated oxidation of phenyl selenide**111** in a MeOH-H_2O solvent results in the formation 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 (**Scheme45**, eqn**45a**).[61] Oxidation of selenides to selenoxides and its collapse at or below room temperature, makes a general method for alkene synthesis (eqn**45b**).



Scheme 45: *syn*-Elimination for alkene synthesis

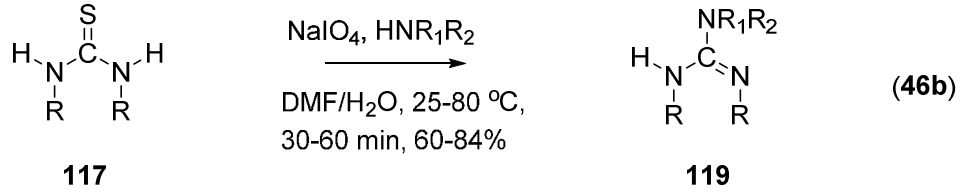
f. Thioureas and selenoureas

Substituted thiourea compounds **117** are oxidized to the corresponding urea compounds **118** when treated with an aqueous solution of $NaIO_4$ in water/DMF (**Scheme 46,** eqn**46a**).[62] Yields are respectable and reaction times are short. $NaIO_4$ 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[63] (**Scheme 46,** eqn**46b**).



117 **118** (**46a**)

R_1, R_2, R_3 = alkyl and aryl

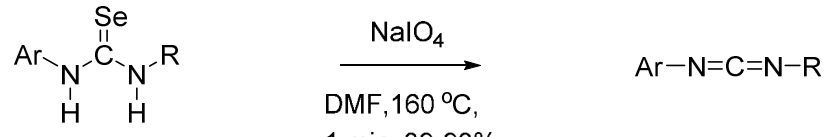


117 **119** (**46b**)

R_1, R_2, R_3 = alkyl and aryl

Scheme 46: Oxidation of thiourea derivatives

Different from the thiourea compounds, a facile oxidation of selenourea compounds **120** with $NaIO_4$ 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 $NaClO_4$, $KMnO_4$, and Na_2CrO_4, did not yield the corresponding carbodiimide from selenourea.

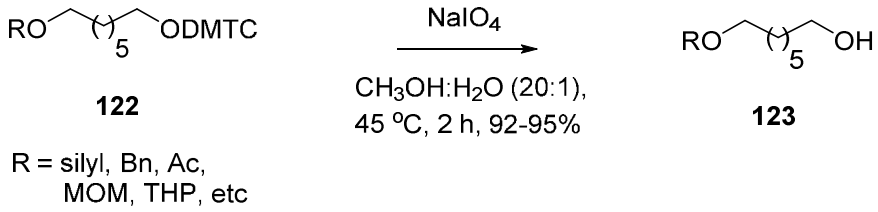


120 **121**

R = alkyl and aryl

Scheme 47: Oxidation of selenourea compounds

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 $TiCl_4$, and base but readily reacts with $NaIO_4$ in $MeOH/H_2O$ 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 SO_2 when oxidized with excess of $NaIO_4$ affording an immonium compound, which upon hydrolysis leads to the formate ester and finally to the parent alcohol.



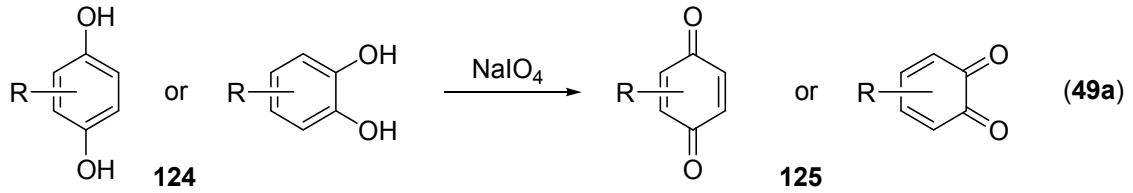
Scheme 48: Deprotection of dimethylthiocarbamates to alcohols

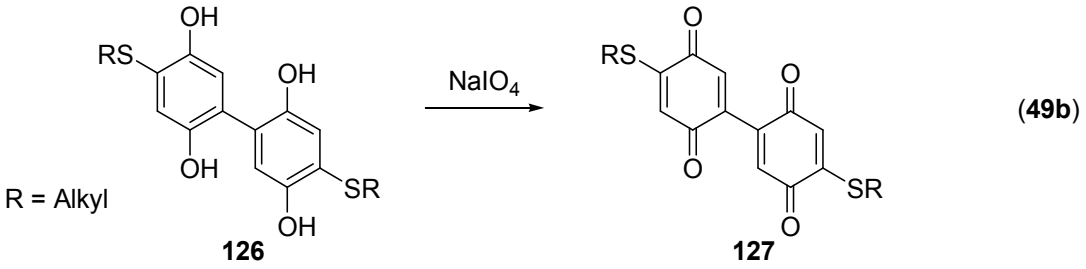
g. Phenols

Quinone derivatives play an extremely important role in biological redox systems. Compared to other oxidants such as silver oxide, chromic and nitric acids, *o*-chloranil, *N*-chlorosuccinimide, and others, sodium periodiate has been found to be an efficient reagent for synthesizing *o*- 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

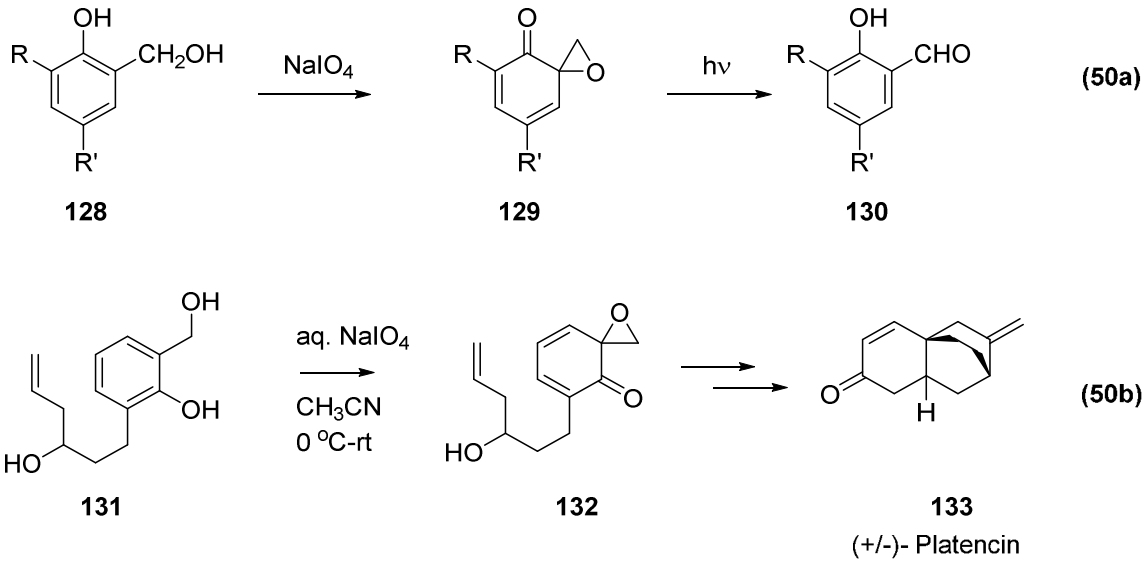
properties. Quinone dimers were prepared by treating the corresponding phenols with $NaIO_4$, for example oxidative treatment of compounds **126** with $NaIO_4$ resulted in the formation of quinone dimers **127** (**Scheme 49,** eqn**49b**).[67]





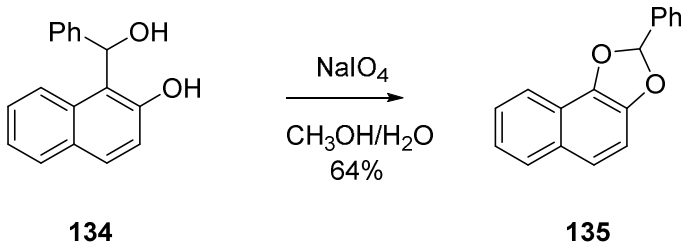
Scheme 49: Oxidation of phenols to quinones

Oxidation of *o*-hydroxymethylphenols**128** having at least one bulky substituent using $NaIO_4$ 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** (**Scheme50**, eqn**50a**).[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** (eqn**50b**).[69]



Scheme 50: Oxidation of *o*-hydroxymethylphenols

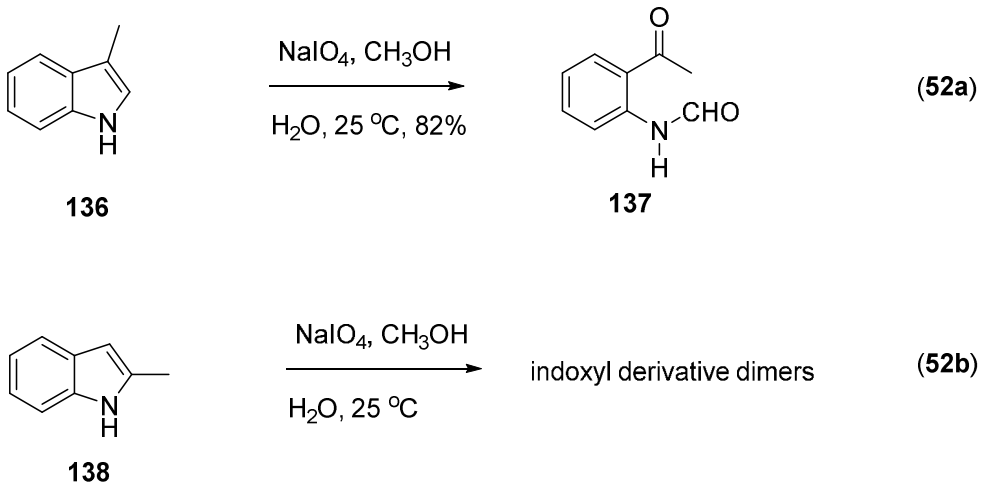
Similarly, in an attempt at the oxidation of *o*-hydroxy substituted diarylcarbinols with periodate, a novel oxidative rearrangement was observed which led to the formation of the corresponding benzo-1,3-dioxols under mild conditions. For instance, oxidation of *o*-hydroxynaphthyl phenyl carbinol**134** with $NaIO_4$ gives the benzo-1,3-dioxol derivative **135** (**Scheme51**).[68]



Scheme 51: Oxidative rearrangement of *o*-hydroxynaphthylphenylcarbinol

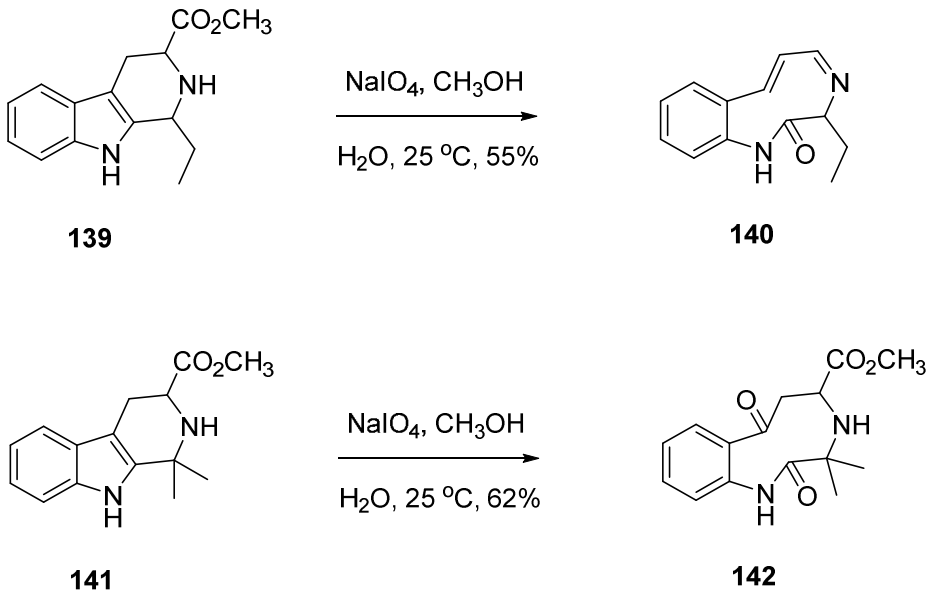
h. Oxidation of indoles and tetrahydro-β-carbolines

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*-amidoacetophenone**137**ingood yields by the oxidative cleavage of the indolic double bonds (**Scheme 52**, eqn**52a**).[70] 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-diphenylindoles resultsin lower yields of the corresponding oxidative cleavage product, while the oxidation of 2-alkylindoles **138**using $NaIO_4$ gives a mixture of dimerized products (**Scheme 52**, eqn**52b**).[71]



Scheme 52: Oxidation of indoles

Tetrahydrocarbazoles and tetrahydro-β-carbolines are also oxidized effectively using $NaIO_4$ at room temperature in methanol/water.[70,72]Tetrahydrocarbazoles**139** gave benzocyclononene-2,7-dione derivatives **140**upon reaction with $NaIO_4$. However, the type of products formed in the oxidation of tetrahydro-β-carbolines**141** depends upon the degree of substitution at C-1 position of the carbolines(**Scheme 53**).[72a]

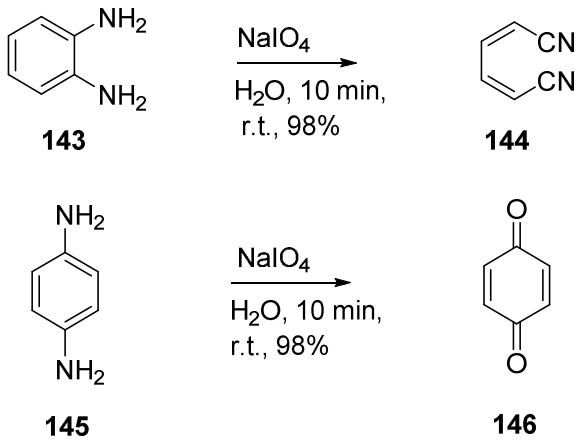


Scheme 53: Oxidation of tetrahydro-β-carbolines

5. Miscellaneous Reactions:

a. Oxidation of aromatic amines:

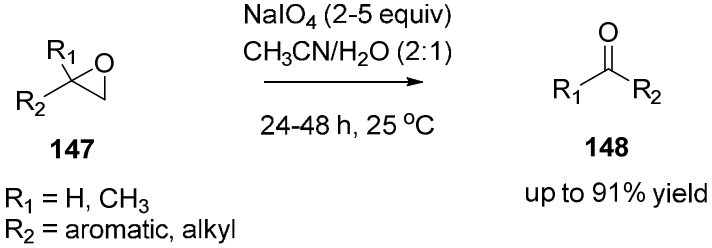
Sodium periodate is a useful synthetic reagent for carbon–carbon cleavagein 1,2-diamino arenes**143**to yield the corresponding nitriles **144** in nearly quantitiative yields.[73]On the other hand this samemethod yields 1,4-benzoquinone derivatives**146** from the corresponding aryl 1,4-diamine compounds**145**. 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 $KMnO_4$, CAN, $NaICl_2$, and $K_2Cr_2O_7$ 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.



Scheme 54: Oxidation of diaminobenzenes

b. Oxidation of epoxides:

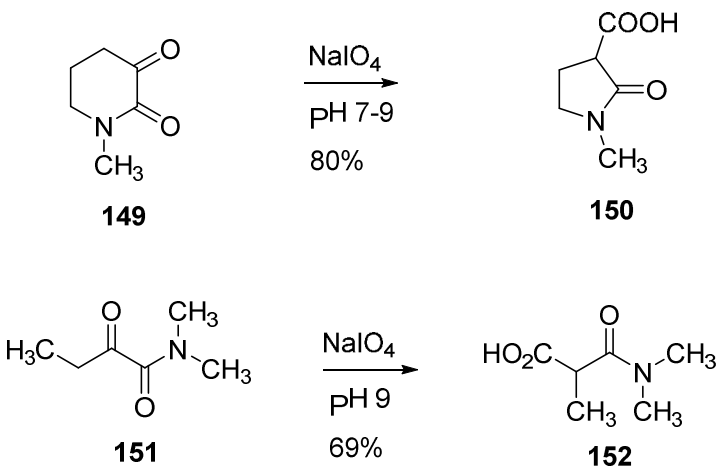
Sodium periodatewas found to be a useful reagent for the oxidative cleavage of the C–C bond in epoxides **147** to the corresponding carbonyl compounds **148** in up to 91% yields (**Scheme 55**).[74] The reaction proceeds in two-steps: First the epoxide ring is oxidativelyopened to form a vicinal diol. 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.



Scheme 55: Epoxide C–C bond cleavage

c. Oxidative rearrangements:

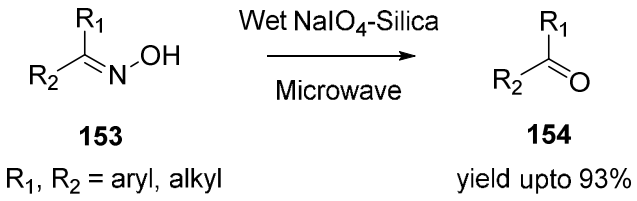
α-Keto esters and amides undergo oxidative rearrangement when treated with periodate at pH 7-9 to give malonic acid derivatives. When the amide is cyclic, from example, α -ketolactams, ring contraction occurs. Thus, 1-methyl-2,3-piperidinedione **149** is converted into 3-carboxy-1-methyl-2-pyrrolidinone **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.



Scheme 56:Oxidative rearrangement of α-keto amides

d. Oxidation of oximes:

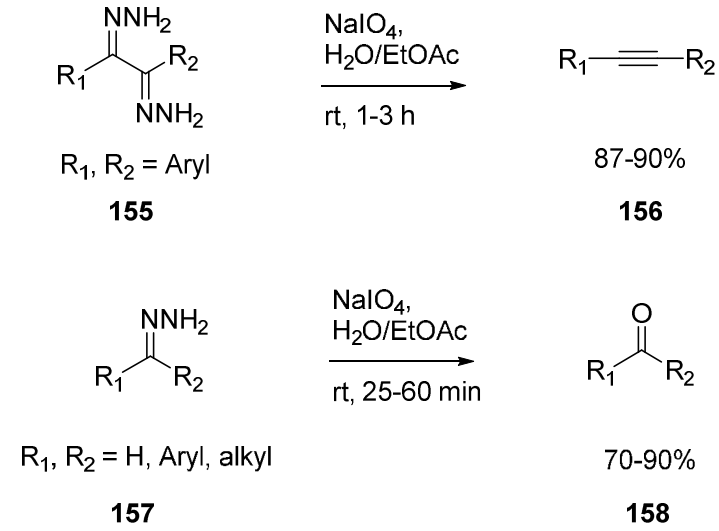
$NaIO_4$ supported on wet silica gel can be used for the conversion of ketoximes **153** to the corresponding ketones **154** in microwave reactions within 2 min (**Scheme 57**).[76] On the other hand, the alternative "regular" heating protocol affords the products after 36 h at 110 ^{o}C.



Scheme 57: Microwave-assisted deoximation

e. Oxidation of dihydrazones:

Sodium periodate serves as a mild and efficient oxidant for the conversion of dihydrazones of α-diketones**155**and then to acetylenes **156** in excellent yields (**Scheme 58**).[77] Sodium periodate is also found to be an economical and practical oxidant, suitable for deprotection of monohydrazones**157** of aldehydes and ketones to the corresponding aldehydes and ketones **158** in excellent yields(**Scheme 58**).

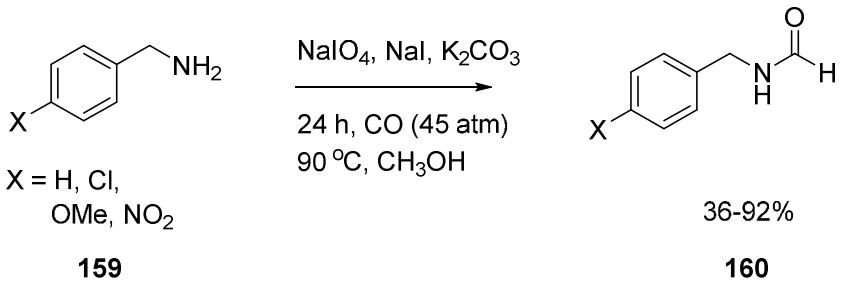


Scheme 58: Oxidation of benzildihydrazone

f. Oxidative carbonylation of amines:

Carbonylation of amines **159** can be achieved in methanol without a transition metal catalyst in the presence of $NaIO_4$ to produce formamide derivatives **160** in good to excellent yields (**Scheme 59**).[78] 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.

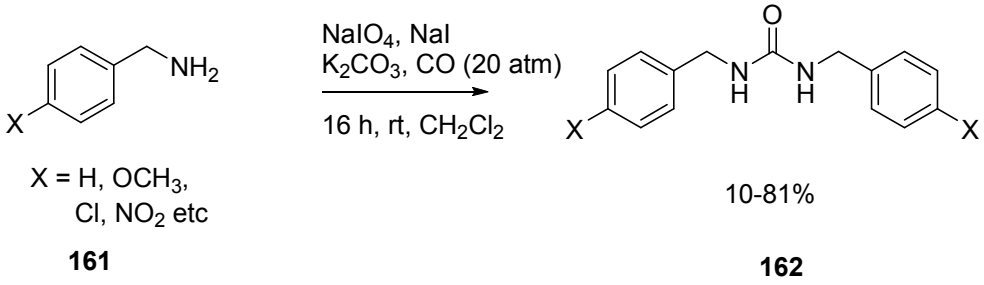


159 **160**

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 benzylamines. The reaction is sensitive to steric hindrance as evidenced by low yields obtained for *tert*-butylamineas substrate (20% yield).

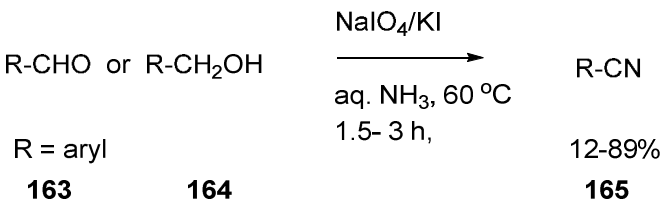


161 **162**

Scheme 60: Oxidized carbonylation of amines to urea derivatives

h. Synthesis of nitriles

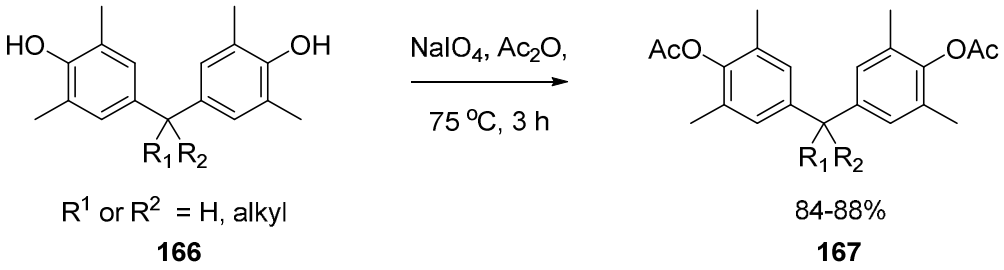
Sodium periodate and potassium iodide in aqueous ammonia provides a simple, efficient and interesting methodology for the one-pot conversion of aldehydes **163** and alcohols **164** into nitriles **165** in moderate to good yields (**Scheme 61**).[80] This transformation proceeds *via* an *in situ* oxidation-imination-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.



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**).[81] Acetylation of the two hydroxyl moieties in bisphenol may be synchronous or stepwise. It is believed that periodatefirst 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**.



R^1 or R^2 = H, alkyl

166

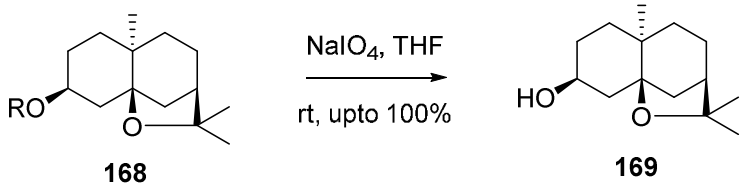
84-88%

167

Scheme 62: Acetylation of bisphenol derivatives

j. Deprotection of silyl ethers

$NaIO_4$ can be usedfor the mild and efficient deprotection of silyl ethers (**Scheme 63**).[82] Silyl groups such as TBS, TIPS, TMS, TES, TIBS and TPs are effectively removed inthe reaction with an excess of $NaIO_4$ 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 $NaIO_4$ is the actual cleaving reagent rather than the residual periodic acid that can be found in the commercial source of $NaIO_4$, because even at neutral or slightly basic conditions the reaction still takes place.



168

R = silyl protection

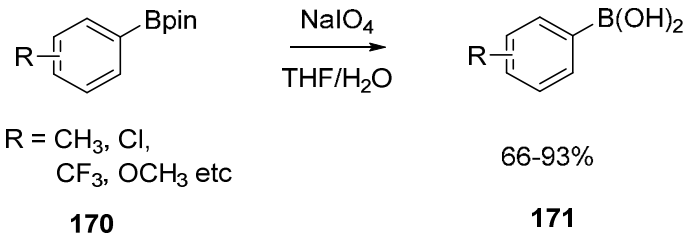
169

Scheme 63: Deprotection of silyl ethers

k. Oxidative cleavage of boronic esters

Oxidative cleavage or oxidative hydrolysis of the boronic esters **170** with $NaIO_4$ in a 4:1 mixture of THF/H_2O gives aryl boronic acids **171** in moderate to good yields (**Scheme 64**).[83]The major

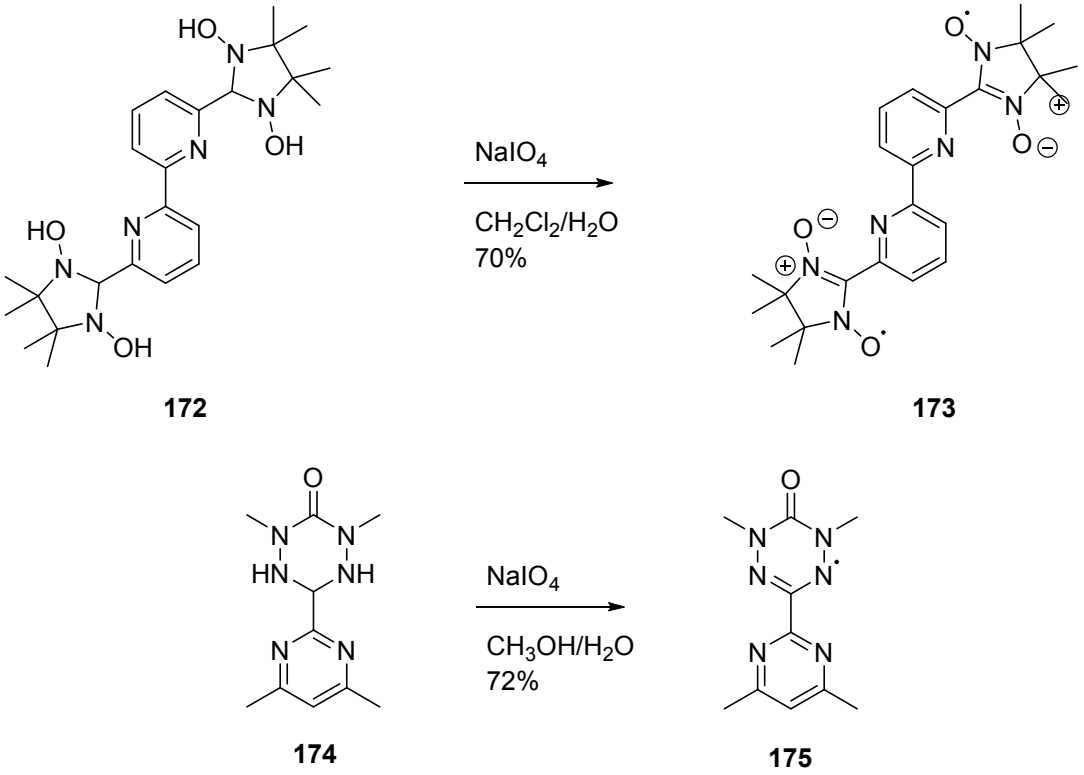
limitation of this protocol is the incompatibility of the oxidative hydrolysis to electron-rich heteroarylboronate esters.



Scheme 64: Cleavage of boronic esters

l. 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**172** reacts with sodium periodate to afford the stable nitroxidebiradical**173** in moderate to good yield (**Scheme 65**).[84a] Similarly, $NaIO_4$ 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.[84b]



Scheme 65: Synthesis of stable radicals

6. Conclusions and Outlook

Sodium periodatehas 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, selenidesand 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 $NaIO_4$ 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 $NaIO_4$; (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.

7. Acknowledgement

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