MANGANESE(III) ACETATE MEDIATED REGENERATION OF CARBONYL COMPOUNDS FROM OXIMES

A THESIS SUBMITED TO
THE GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES
OF
MIDDLE EAST TECHNICAL UNIVERSITY

BY

ERTAN ALTINEL

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR
THE DEGREE OF MASTER OF SCIENCE
IN
CHEMISTRY

MAY 2006

Approval of the Graduate School of Natural and Applied Sciences

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ABSTRACT

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May 2006, 53 pages

A facile method for the direct conversion of oximes into carbonyl compounds by treatment with manganese triacetate is described. Manganese triacetate can be used for an effective and mild oxidizing agent for the regeneration of carbonyl compounds in good yield. Many functional groups are tolerated under reaction conditions.

Keywords: Manganese(III) acetate, Aldehyde, Ketone, Oxime, Regeneration of carbonyl compounds, mild oxidizing agent.

ÖZ

MANGAN(III) ASETAT KULLANILARAK OKZİMLERDEN KARBONİL BİLEŞİKLERİ REGENERASYONU

Ertan Altınel

Yüksek Lisans, Kimya Bölümü

Tez Yöneticisi: Prof. Dr. Ayhan S. Demir

Mayıs 2006, 53 sayfa

Oksimlerin karbonil bileşiklerine doğrudan dönüştürülmesi için yeni bir metod Mangan(III) asetat kullanılarak tanımlanmıştır. Mangan(III) asetat ılımlı bir yükseltgen madde olarak oksimlerden karbanil bileşiklerinin yüksek verimli regenerasyonu için etkin bir şekilde kullanılmıştır. Tepkime şartlarında birçok fonksiyonlu grup özelliğini kaybetmeden korunmuştur.

Anahtar Kelimeler: Mangan(III) asetat, Aldehit, Keton, Oksim, Karbonil regenerasyonu, ılımlı yükseltgen madde.

To my Family

ACKNOWLEDGEMENT

I would like to thank and express my deep gratitude to my supervisor Prof. Dr Ayhan S. Demir for his encouragement, patience and guidance throughout this study.

I would like to thank to Prof. Dr. Simeon Arseniyadis for endless support, encouragement and patience throughout this study.

I am also thankfull to all my friends in Organic Chemistry Research Group whose support and friendship were extremely helpful.

I would like to thank Mustafa Emrullahoğlu for his cooperation and friendship whenever I need.

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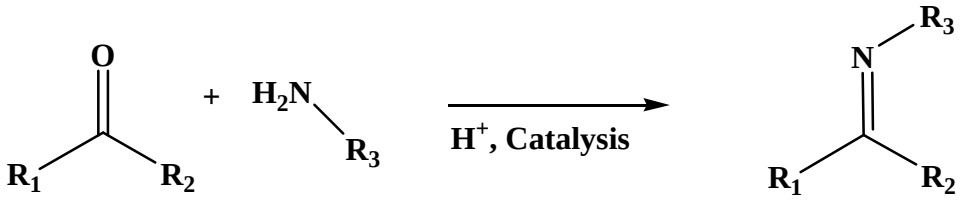
CHAPTER 1

INTRODUCTION

Oximes are one of the important compounds in organic chemistry. Their general formula is $R_1R_2C=NOH$, where R_1 is an organic side chain and R_2 is hydrogen, forming an aldoxime, or another organic group, forming a ketoxime. Oximes exist as two stereoisomers, a Z isomer and an E isomer which can be separated almost completely and obtained as pure isomers.

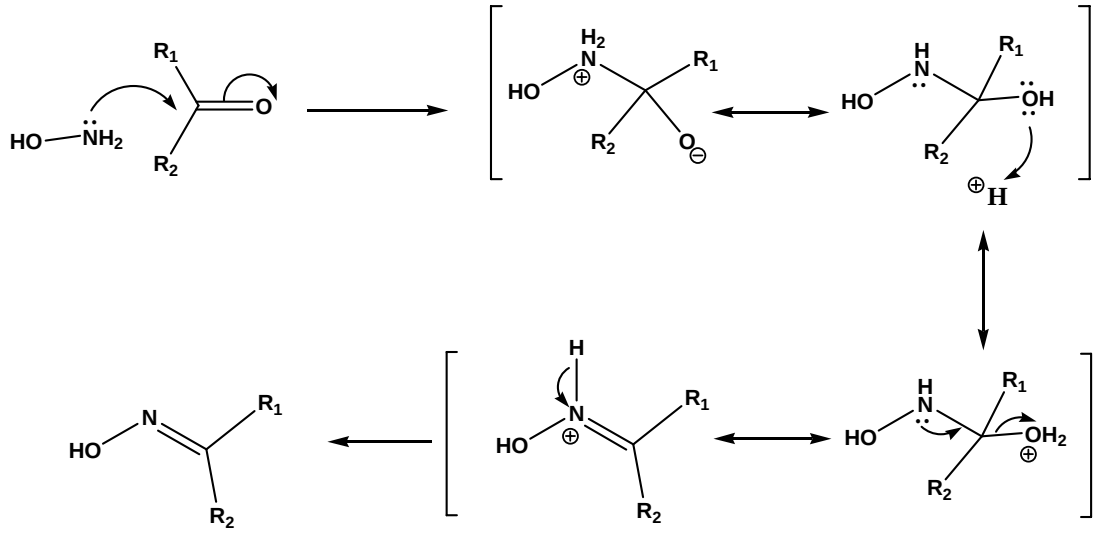
They can be defined as special form of imines. Imines are formed when any primary amine reacts with aldehyde or ketone under appropriate conditions. First, amine attacks the aldehyde or the ketone and the intermediate is formed. Then, dehydration gives the imine. Acid catalyst is added for amine formation. It's important to notice that acid is not needed for addition part of the mechanism[1]. Indeed, protonation of amine means that this step is very slow in strong acid, but is needed for the elimination of water later on the reaction. Imine formation is in fact fastest at about pH 4-5; at lower pH too much amine is protonated and that lowers the rate of addition, above pH 5 proton concentration is too low to allow protonation of OH leaving group in the dehydration step[2].



Ketone or R_2= H Aldehyde **Primary Amine** **Imine**

Scheme 1

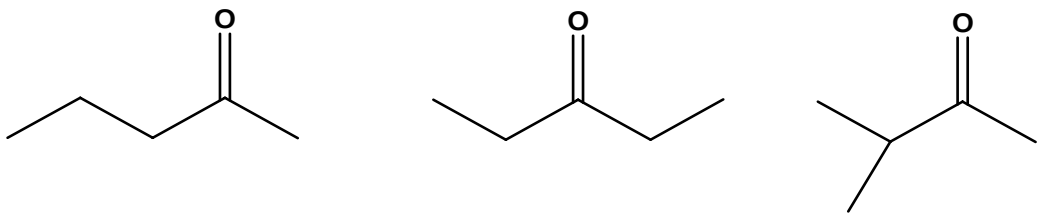
Imines (R_3=H or R_3=alkyl) are the least stable form of C=N type functional group. Schiff bases (R_3=Aryl), hydrazones (R_3=NHR), semicarbazones (R_3=$HNCONH_2$) and oximes (R_3=OH) are more stable than imines. Oxime can be formed without acid catalysis but it is much faster with acid and final product is often in crystal form.



Scheme 2 acid catalyzed oxime formation

Oximes are used for purification of carbonyl compounds. Impure carbonyl mixture is converted to oxime and produced crystalline structure which can be isolated from media. Regeneration of oxime to related carbonyl compound gives desired aldehyde or ketone in pure form.

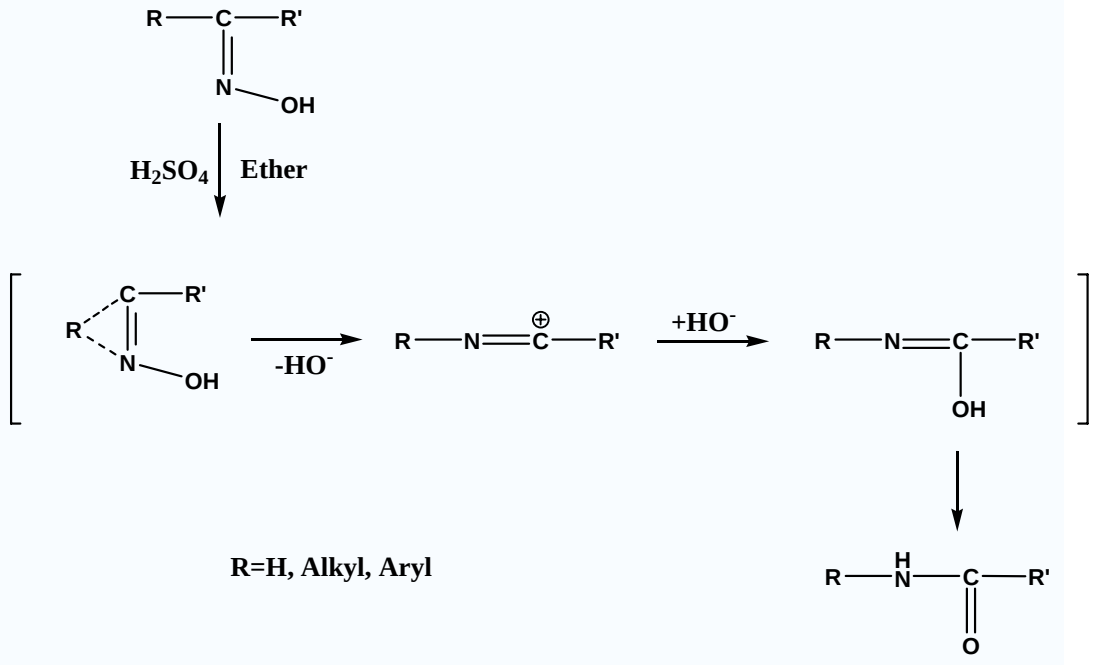
Oximes are very important in characterization of aldehydes and ketones. Since, many methods are known with high yields, conversion of aldehydes and ketones to oximes are a part of characterization works. Aldoxime and ketoxime solid structures are good for X-Ray studies. Before NMR, isomeric ketones were transferred to oxime and in this form it was possible to analyses their structure. Physical properties of isomeric ketones are very close to each other (*scheme 3*), when they transferred to oximes these values become differentiable[3].



b.p.: 102^0C b.p.:102^0 C b.p.:106^0C

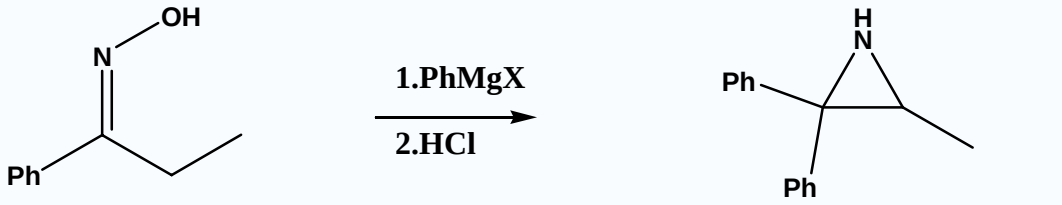
Scheme 3 boiling points of three isomeric five-carbon ketone

Oximes can be converted to the corresponding amide derivatives by treatment with various acids. This reaction is called Beckmann rearrangement[4]. In this reaction, a hydroxyl group is replaced with the group that is in the anti position of the hydroxyl group. The amide derivatives that are obtained by Beckmann rearrangement can be transformed into a carboxylic acid and an amine by hydrolysis. Beckmann rearrangement is used for the industrial synthesis of caprolactam, which is the material used to make nylon-6.



Scheme 4 Beckmann rearrangement

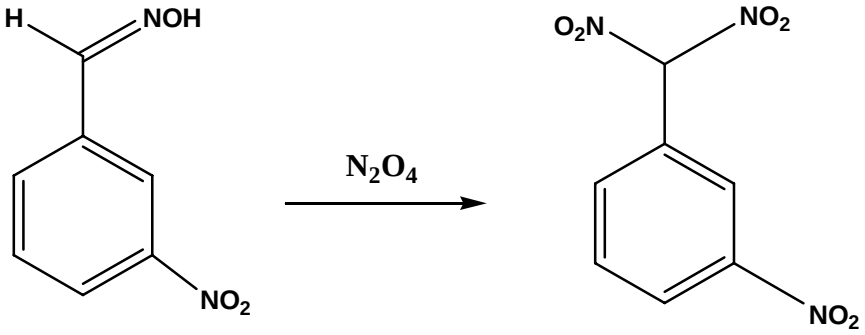
Oximes are used for aziridine synthesis. Treatment of ketoximes with Grignard reagent and subsequent hydrolysis of organometallic complex yields aziridines. This reaction is known as Hoch-Campbell aziridine synthesis[5]. Aziridines are three-membered nitrogen containing heterocycles that have found extensive use in organic synthesis. Moreover large numbers of aziridine appended natural products have been isolated, many with potent and interesting biological properties like mitomycin, azinomycin, porfiromycin.



Phenyl ethyl oxime **3-methyl-2,2-diphenylaziridine**

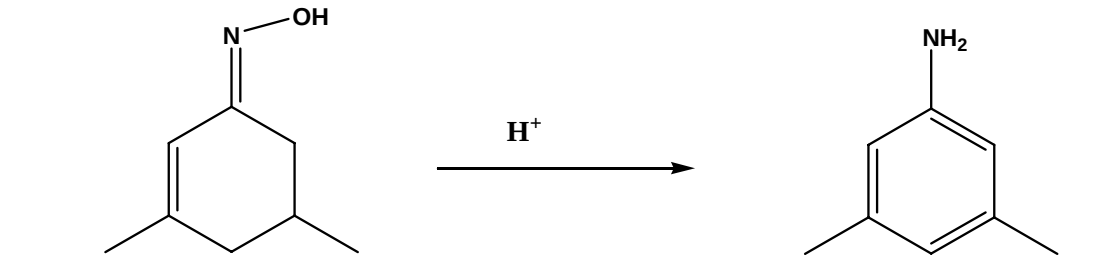
Scheme 5 Hoch-Chambell aziridine systhesis

Another usage of oximes in organic synthesis is formation of dinitrophenylmethanes from benzaloximes. This procedure is known as Ponzio reaction[6]. Oxidation of benzaloximes derivatives with N_2O_4 in ether yields dinitrophenylmethanes.



Scheme 6 Ponzio Reaction

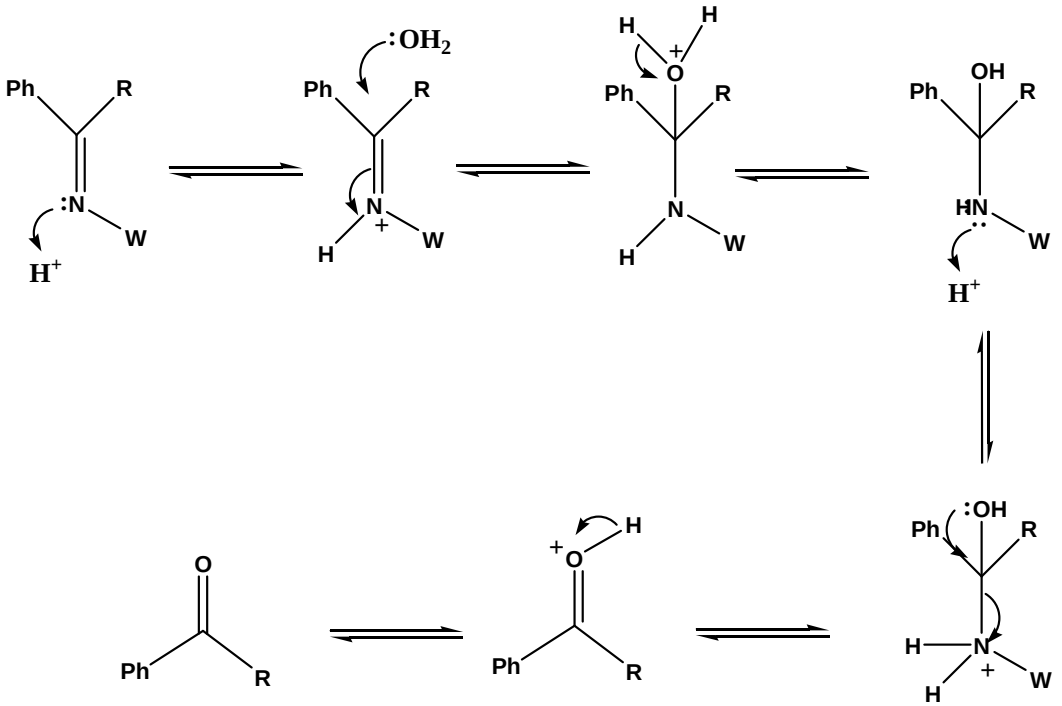
With Semmler-Wolff reaction[7], α,β-unsaturated cyclohexenyl oximes rearranged into aromatic amines under acidic conditions. In this reaction aromatization of cyclohexen ring and reduction of oxime to amine occurs together. This reaction is very important for total synthesis of biological active natural substances.



3,5-dimethylcyclohex-2-enone oxime **3,5-dimethylbenzenamine**

Scheme 7 Semmler-Wolf Reaction

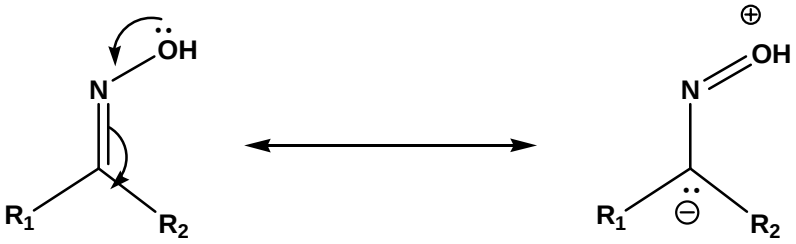
Methods for regeneration of carbonyl compounds from oximes are very important for purification and characterization studies. Regeneration of aldehydes and ketones from imines is a simple hydrolysis reaction.



Scheme 8 acid catalyzed imine hydrolysis

Hydrolysis of oximes is not as easy as imines. When N atom carries an electronegative group C=N become more stable. Oxime, hydrazone and semicarbazone structures require strong acidic or basic mediums for hydrolysis. Often a reactive aldehyde (formaldehyde) is added to combine with liberated amine.

Oxime, hydrazone and semicarbazone are more stable because of electronegative substituent can participate in delocalization of C=N bond. Delocalizations deceases the δ^+ charge on the carbon and raise the energy of LUMO, this makes it less susceptible to nucleophilic attack. As a result of the occupied non-bonding orbital and δ^- charge on carbon, nucleophilic addition become impossible. Carbon side of the molecule is no more electron deficient part[8].



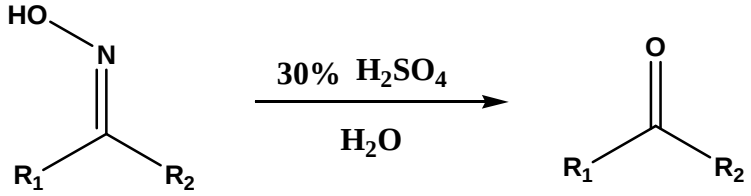
scheme 9 oxime participation of O to C=N bond

1. 1 Traditional methods of carbonyl regeneration

Oximes are frequently used to protect carbonyl compounds and hence considerable attention has been given to develop methods for their deprotection. The Classical methods of carbonyl regeneration hydrolytic cleavage require the use of strong mineral acids and often results low yields due to formation of polymeric by-products. Moreover, unsaturated oximes give saturation or substitution reactions. Oxime with α' hydrogen produces olefins in these conditions.

a) Regeneration of carbonyl compounds by hydrolysis in H_2SO_4

Acidic hydrolysis is the first type of carbonyl regeneration. H_2SO_4 is used for this reaction.

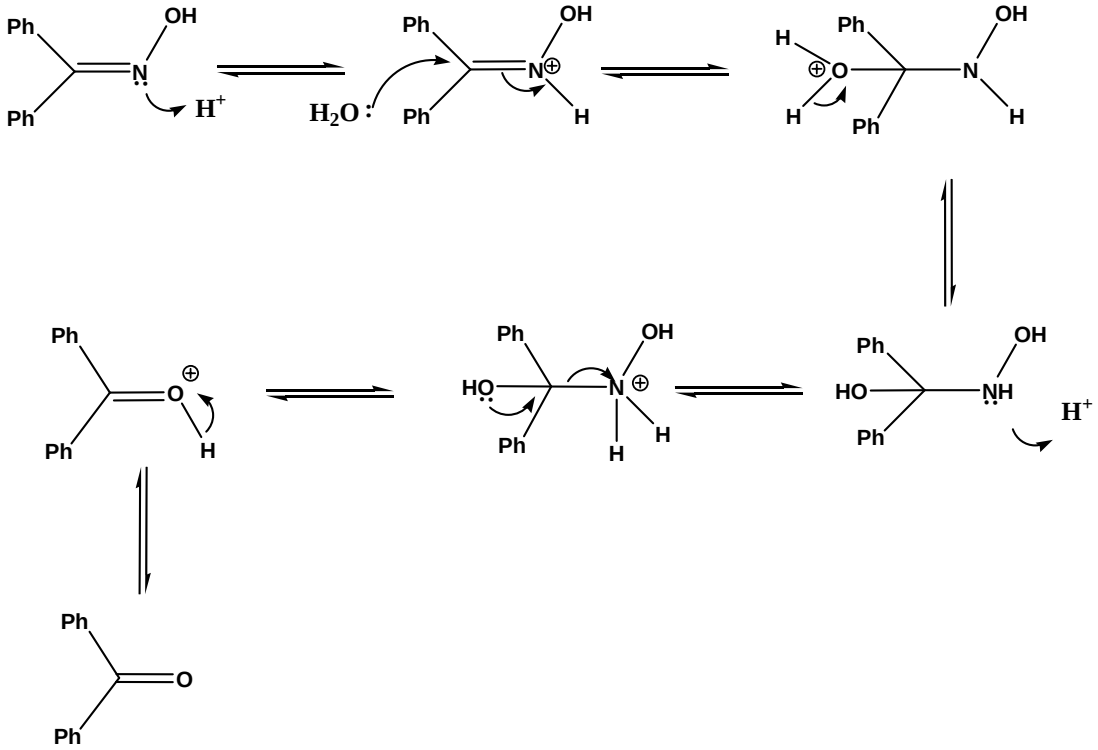


70-80% yield

Scheme 10 Acidic hydrolysis

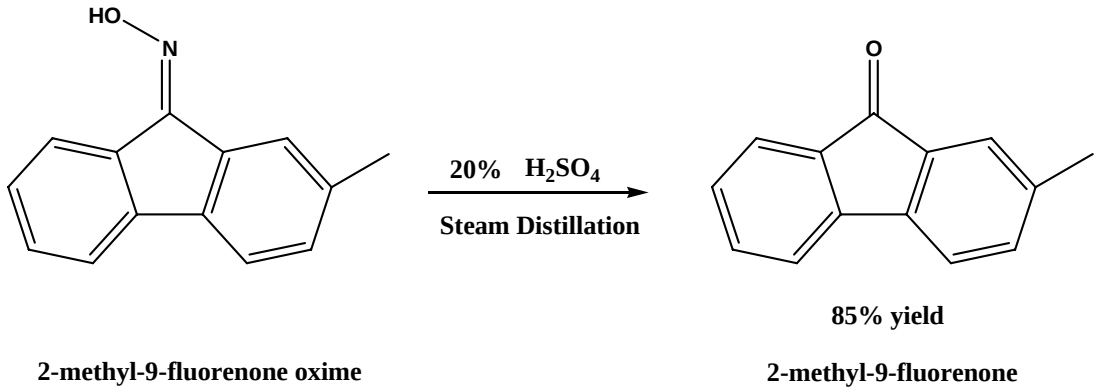
The hydrolysis of carbon-nitrogen double bond involves initial addition of water to carbon side. This addition is not takes place easily like imines. Electro negative hydroxyl substituent on nitrogen participate in delocalization of C=N and making it less susceptible to water addition. In order to prevent participation of this group strong acid is used. First, H^+ is added to nitrogen and than hydrolysis

occurs. *(Scheme11).* As a result of this strong acidic condition, yields are not high and method can be used for stable aryl oximes[9].



Scheme 11 Acid catalyzed hydrolysis mechanism

This procedure can be good choice for stable oximes that can be transferred to parent carbonyl compounds by steam distillation. *(Scheme12).*

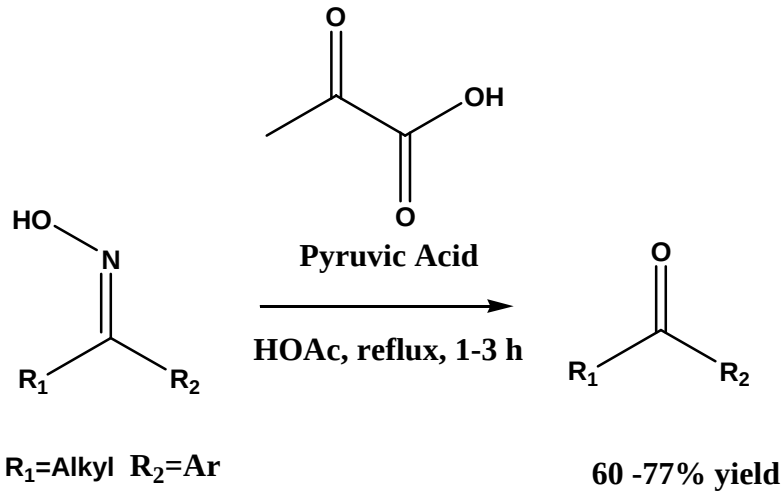


2-methyl-9-fluorenone oxime **2-methyl-9-fluorenone**

Scheme 12 Steam distillation

b) Pyruvic acid hydrolysis

The Pyruvic acid has been employed to regenerate carbonyl compounds from oximes for many years[10]. In the laboratory, pyruvic acid may be prepared by heating tartaric acid mixed with potassium hydrogen sulphate, or by the hydrolysis of acetyl cyanide formed from acetyl chloride, by reaction with potassium cyanide. Typically two molecular equivalents of pyruvic acid are reacted with one equivalent of oxime at reflux temperature of acetic acid to form parent carbonyl compound of oxime.*(Scheme 13)*

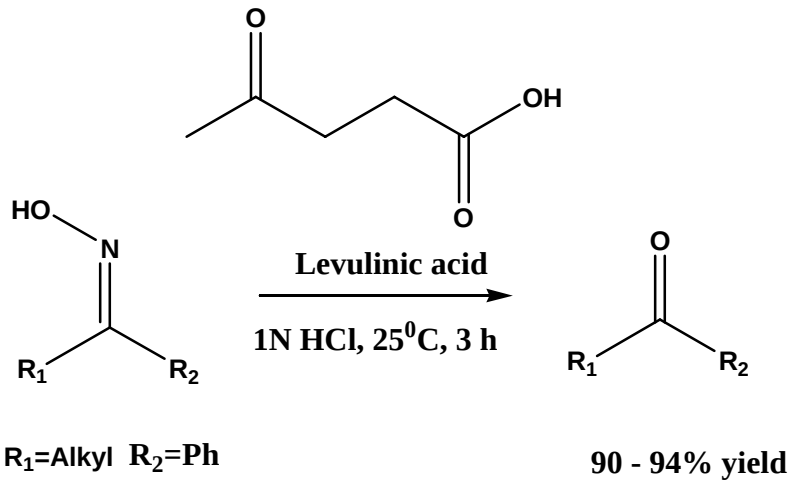


Scheme 13

Advantages of this hydrolysis are the pyruvic acid is contains a carbonyl group to react with liberated hydroxyl amine and more functional groups can tolerate this condition. On the other hand, yield of reaction is still low. The presence of substituents which give elimination products, lover the over all yield greatly.

c) Levulinic acid hydrolysis

This procedure is closely related to the pyruvic acid hydrolysis. Levulinic acid (4-oxopentanoic acid) hydrolysis of oximes is developed to improve regeneration yield of pyruvic acid hydrolysis[11]. Levulinic acid is weaker than pyruvic acid and as a result of this by product formation is lower than former procedure. In a typical procedure, two molecular equivalents of Levulinic acid and one equivalent of oxime were mixed together in 1N HCl at 25^0C for 3 hours to form parent carbonyl compound of oxime *(Scheme 14)*



Scheme 14

This regeneration is still functional group dependent and can not be used for oximes with olefinic bonds and hydroxyl functionality.

d) Regeneration of carbonyl compounds by Sodium Hydrosulfite

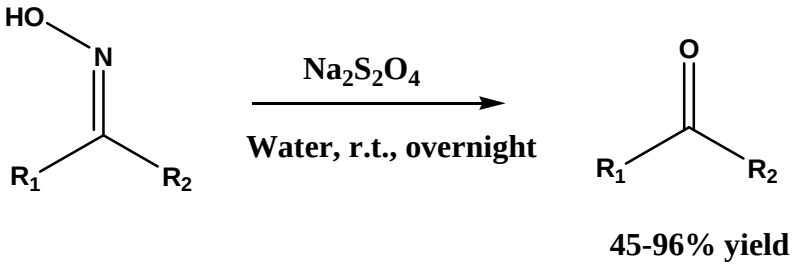
Sodium hydrosulfite (sodium dithionite) is a powerful reducing agent. When oximes are treated at room temperature with aqueous sodium dithionite, either alone or in the presence of sodium hydrogen carbonate or sodium acetate, the organic material gradually dissolves. The parent carbonyl compound is obtained from this mixture by the addition of acid, preferably, or base.

Two possible mechanisms for the deoximation follow. Firstly, solutions of the dithionite anion are not very stable and decompose in a complex manner to the hydrogen sulfite ion. Hence, the cleavage of oximes with sodium dithionite can occur by a hydrolytic pathway analagous to the reaction of oximes with sodium hydrogen sulfite described by Pines[13] and coworkers.

Alternatively, the cleavage might occur by a reductive pathway, the oxime is first reduced to the imine which is immediately hydrolyzed to the carbonyl compound.

The latter mechanism is supported by the observation that addition of a base apparently increases the rate of the deoximation reaction. Under these conditions, sodium dithionite is known to be a powerful reducing agent. Furthermore, the dithionite deoximations take place under conditions milder than those reported for the hydrogen sulfite reaction.

General procedure; the oxime one equivalent was mixed with water containing two equivalent sodium dithionite. The suspension was stirred overnight at room temperature. (Warming to 40°C reduced reaction times to several hours.) *(Scheme 15)*

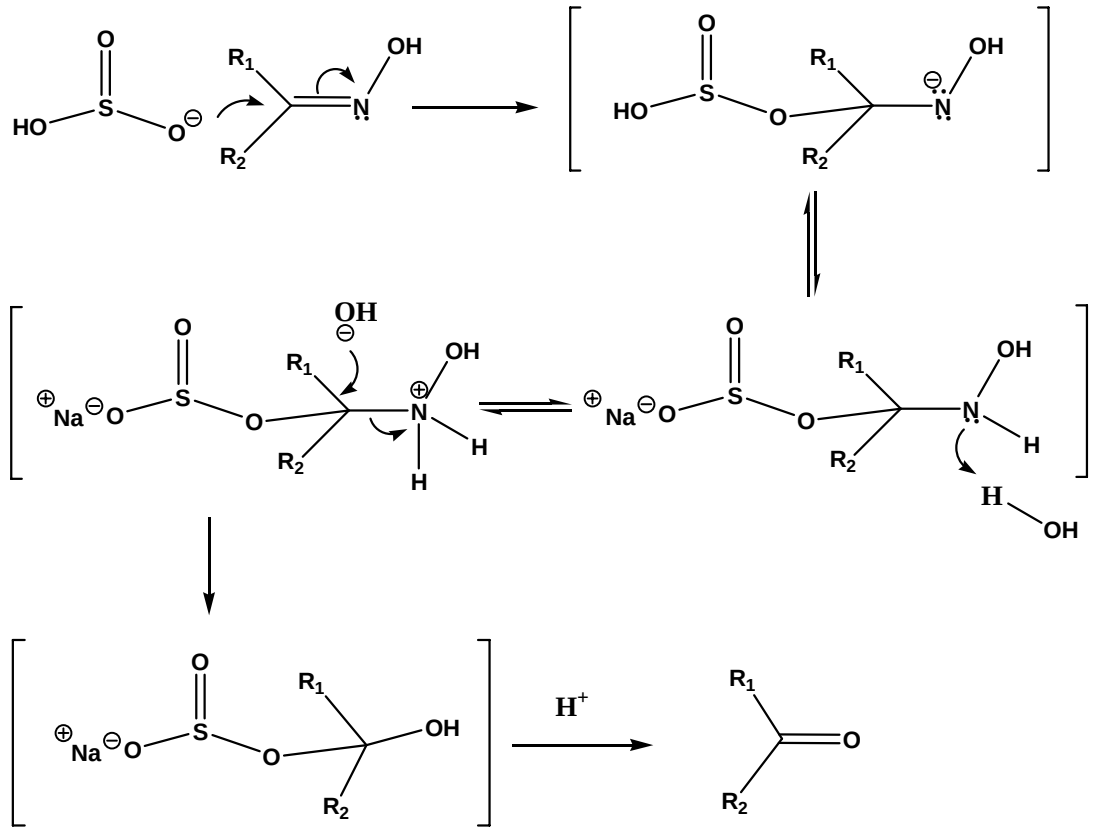


Scheme 15

Limitation of this reaction is regeneration works well with simple ketoximes for example cyclohexanone oxime or acetophenone oxime (over 90% yield). On the other hand, even with aldoximes like benzaldehyde oxime (54%) or butanal oxime(46%) regeneration is not satisfactory.

e) Regeneration of carbonyl compounds by sodium bisulphite

Pines, Chemerda and Kozlowski reported new regeneration procedure for oximes to carbonyl compounds in 1966. Reaction involves nucleophilic addition to the oxime group, followed by hydrolysis. At the first part of reaction, bisulphite ion, provided by sodium bisulphite, added in the presence of water, then acidic hydrolysis by hydrochloric acid yields related carbonyl compound[14]. In general procedure, mixture of oxime (1 mmol) and $NaHSO_3$ (2 mmol) refluxed in EtOH-H_2O for 2-16 h. After cooling, diluted HCl is added to the mixture and stirred for 30 min at room temperature.



Scheme 16

Yields of this procedure are about 75-85% for stable oximes. Since the reaction conditions include high temperature, alkali and acidic mediums functional groups that can not tolerate these conditions increase by product formation.

1. 2 Oxidative methods for regeneration of carbonyl compounds from oximes

The limited viability and low yields of traditional methods resulted studies on new procedures. Number of oxidative methods have been developed for the cleavage of oximes. However, many of these procedures include reagents corrosive or difficult to handle. Same of the oxidants can not work both ketoximes

and aldoximes. In some cases, reagents are functional group dependent or can not work with hindered oximes. For all these reasons, new mild oxidative regeneration methods are needed.

1.2.a. Regeneration by chromium compounds

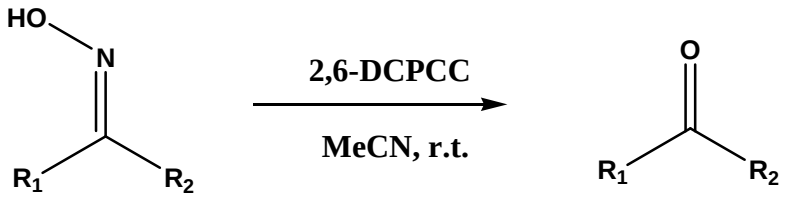
Number of oxidative deoximation methods have been developed which involve chromium (VI) compounds like; chromous acetate[15], trimethylammonium chlorochromate[16], triethylammonium chlorochromate[17], chlorotrimethysilane-(chromium)[18], pyridinium chlorochromate[19], pyridinium fluorochromate[20], quinolinium dichromate[21], quinolinium fluorochromate[22], pyridinium chlorochromate-H_2O_2[23], 3-carboxypyridinium chlorochromate[24], trimethylsilyl chlorochromate[25], bis(trimethylsilyl)chromate[26], chromium trioxide[27], 2,6-dicarboxypyridinium chlorochromate[28], and polymer supported chromium trioxide[29].

First chromium compound used for regeneration of carbonyl compounds from oximes is chromous acetate. This reagent was reported by E.J.Corey and J.E.Richman in1970. Actually, reaction is not oxidation, but reduction in aqueous tetrahydrofuran. Oxime reacts with chromous acetate in THF-H_2O. Reaction temperature differs for aldoxime and ketoxime. The former reacts at 25^0C, the latter needs higher temperatures. Yield of this reaction is 75-95%.

Generally, oxidative cleavage of oximes by chromium compounds is efficient for ketoximes. On the other hand, procedures are not effectual on aldoximes. Benzaldoxime, for example, is regenerated in poor yields by pyridinium chlorochromate, 35% yield by pyridinium chlorochromate-H_2O_2, in 56% yield by triethylammonium chlorochromate and in 72% yield by chromic anhydride-chlorotrimethyl silane.

Derivatives of chromium compounds are being prepared to improve these yields. One of them is 2,6-dicarboxypyridinium chlorochromate. Reagent is

prepared by the reaction of pyridine 2,6-dicarboxylic acid with chromium trioxide in 6N HCl. 2,6-dicarboxypyridinium chlorochromate is soluble in polar solvents such as acetone and acetonitrile and slightly soluble in THF, chloroform and dichloromethane and insoluble in benzene, hexane and CCl_4. General procedure for this regeneration; to solution of oxime (2 mmol) in acetonitrile (20 ml), 2,6-dicarboxypyridinium chlorochromate (4 mmol) is added and the mixture stirred at room temperature. *(Scheme 17)*



80-94% yield

R_1, R_2=alkyl, aryl or H

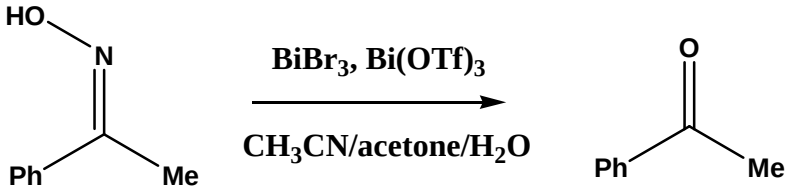
Scheme 17

Works on this derivative of PCC shows interesting results. This reagent is less active than other chromium compounds and reported to not over oxidize aldoximes to carboxylic acids. Unsaturated oximes underwent regeneration without rearrangement of the C=C bond. Main disadvantage of 2,6-DCPCC is reagent needed to be prepared before, it is not commercially available.

b) Bismuth (III) reagents

Recently, bismuth compounds[30] have become attractive candidates for regeneration of carbonyl compounds from oximes. Bismuth has an electron configuration of $[Xe]4f^{14}5d^{10}6s^{2}6p^{3}$. due to the weak shielding of 4f bismuth(III) compounds exhibits Lewis acidity.

In this regeneration, reaction is carried out using 20-40 mol% $BiBr_3$ and 5 mol% $Bi(OTf)_3.4H_2O$ as co-catalyst in CH_3CN/acetone/H_2O. *(Scheme 18)*



68% yield

Scheme 18

Reason for using mixture of $BiBr_3$ and $Bi(OTf)_3$ is; while $BiBr_3$ alone is effective in deprotection, addition of $Bi(OTf)_3$ accelerates the reaction considerable. The use of 5 mol% $Bi(OTf)_3$ is almost ineffective in deprotection. However, When 40 mol% $Bi(OTf)_3$ is used alone, the deprotection takes place but best results will observed with mixture of reagents.

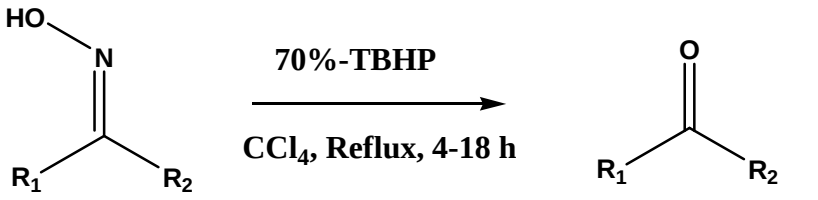
Procedure gives best yield when 1,3 diphenyl 2-propanone oxime is regenerated with 40 mol% $BiBr_3$ and 5 mol% $Bi(OTf)_3.4H_2O$ in CH_3CN/acetone/H_2O as 85%.

Main disadvantage of this reaction is not regenerate carbonyl compounds from aldehydes. The deprotection works with ketoximes but, aldoximes are more resistant to the reaction conditions. Procedure reached 50% yield for benzaldehyde oxime.

c) *tert*-Butyl hydroperoxide (TBHP)

TBHP is a peroxide compound with t-butyl group. This large alkyl moiety makes it soluble in organic solvents and peroxide functionality makes it oxidant.

Oximes When refluxed in CCl_4 with TBHP give the corresponding carbonyl compounds respectively[31]. In typical procedure a mixture of oxime with 1 mol equivalence and 70% TBHP 1.1 mol equivalence in carbon tetra chloride was refluxed for 4-18 hours. *(Scheme 19)*



30-100 % yield

Scheme 19

Similarly, transformation should be completed with hydrogen peroxide. But, yield of regeneration is lower than the case when TBHP is used. Percentage of TBHP is also important in oxidation yield. In order to achieve better transformation, 70% TBHP is required.

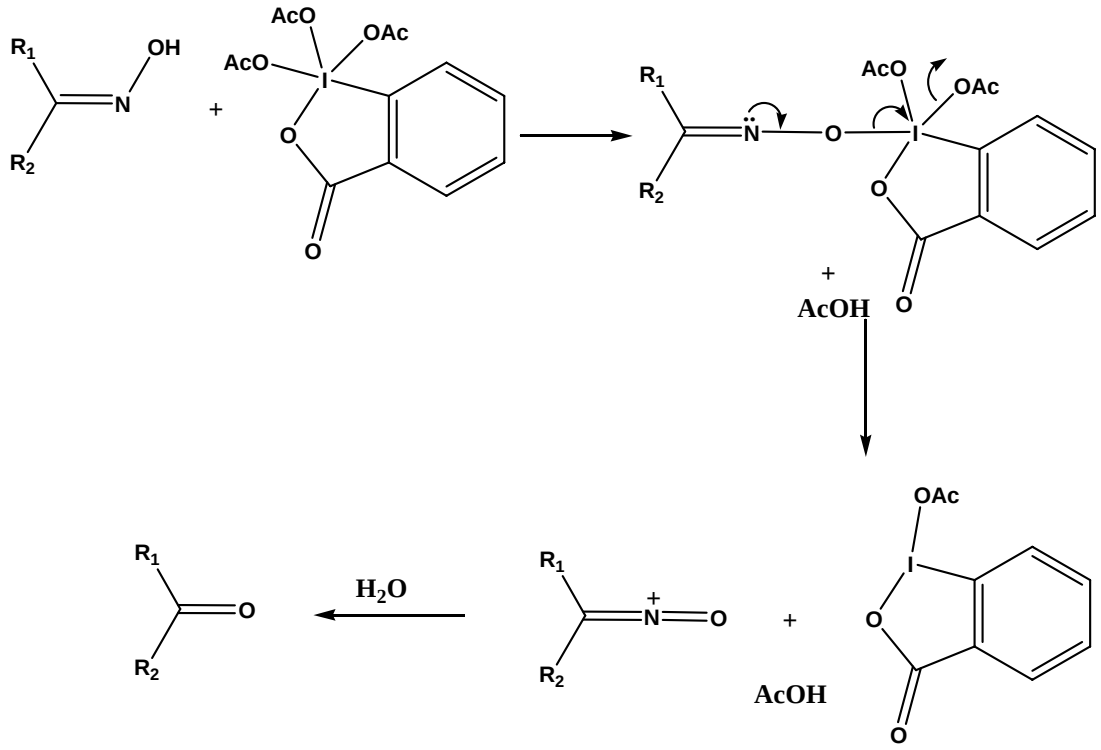
Mechanistically, the reaction appears to be initiated via electrophilic oxidation of C=N of oxime with TBHP to oxaziridines which will be converted immediately into the carbonyl compounds by fragmentation.

Main problem of this procedure is it can not be used for regeneration of aldoximes. TBHP is a kind of strong oxidant for them. When aldoximes react with TBHP they yield carboxylic acid as over oxidation product mainly.

d) Oxidative regeneration by Dess-Martin Periodinane

Dess-Martin Periodinane is known to be a mild oxidant for more than 25 years. It is used for oxidation of primary and secondary alcohols to the

corresponding aldehydes and ketones respectively. This led researchers to consider Dess-Martin Periodinane reagent for degeneration of carbonyl compounds from oximes *(Scheme 20)*[32].



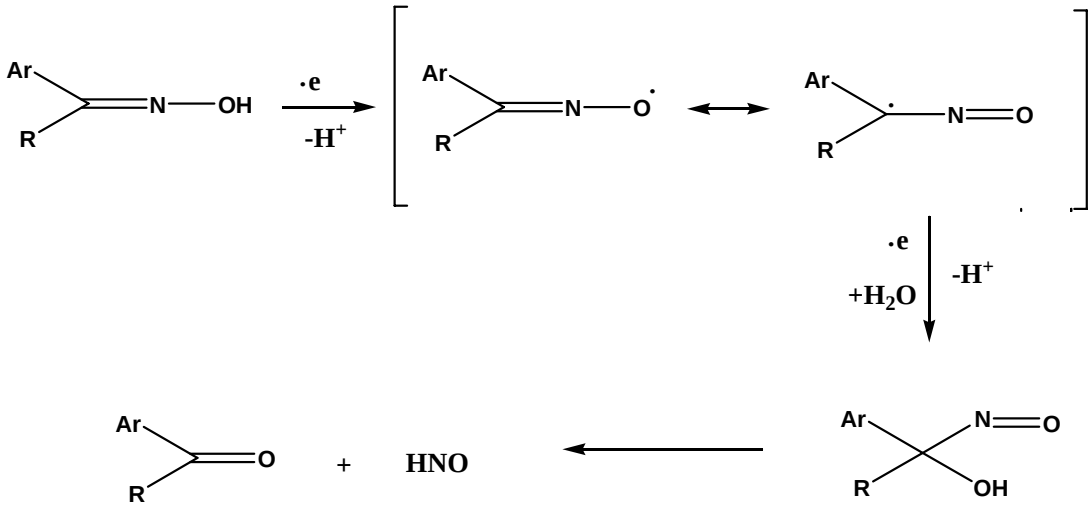
Scheme 20

Yield of reaction is 88-100% for ketoximes, but procedure must be done carefully. When the reaction is carried out using dichloromethane as it is, rather than saturated with water, some by-products will produce. In addition to that, procedure is not effective on aldoximes. During regeneration aldoximes give other products. On the other hand, water is needed to increase the oxidizing power of dess-martin periodinane, but most of functional groups lost their activity in aqueous media. Finally, DM periodinane is reported to be explosive under excessive heating.

1.3 Other methods for carbonyl regeneration form oximes

a) Electrochemical deoximation reaction

Steckhan reported the possibility of oxidative cleavage of various oximes[33]. After that anodic behavior of aromatic oximes studied. The experiments are carried out in acetonitrile containing 10^{-1}M of tetrabutylammonium tetrafluoroborate as supporting electrolyte. Voltammograms are registered at 0.1V s^{-1} at a platinum anode from 5.10^{-3}M solutions of substrate. General procedure for reaction, after a pre-electrolysis, at +2.2 V *sce*, 6.10^{-3} mol of oxime and 10 ml water is added to 60 ml of anolyte. Oxidizing is carried out up to disappearance of starting material. The anolyte is evaporated under reduced pressure. Extraction and column chromatography yield carbonyl compound. Mechanism for reaction is given; initial formation of an iminoxy radical by monoelectronic transfer and deprotonation, transfer of second electron and water addition leading to an α-hydroxy nitroso intermediate, decomposition of the latter with ketone formation. *(Scheme 21)*



Scheme 21

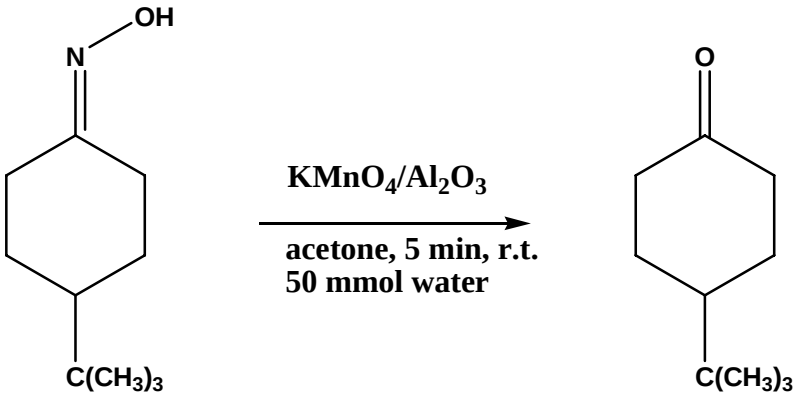
Electrochemical procedure regenerate ketones from ketoximes in 50-93% yield[34]. On the other hand, this procedure is not suitable for aldoxime transformations. This type of oximes regenerated to related carboxylic acid compounds instead of aldehydes.

Main handicap of this reaction is procedure substrate dependent; it only works with aromatic ketones. Electron withdrawing groups on aromatic side also affect the all over yield.

b) Regeneration with solid supported oxidants

The solid supported reagents can be used for regeneration of carbonyl compounds from oximes. Various solid supports are studied such as alumina montmorillonite K 10 clay, zeolites and silica gel. These reagents are being studied to develop 'dry media' procedures that include microwave assisted reactions[34].

Alumina supported potassium permanganate[35] is one of the reagents that is used for regeneration of carbonyl compounds. Oxidizing power of this reagent is less than the homogeneous, aqueous reactions. In that way, reagent supposed to be mild oxidant for oximes. A representative procedure is; alumina (neutral, 150 mesh) is dehydrated by heating to 300^0C after cooling, alumina is ground together with potassium permanganate in a mortar. To solution of oxime (5 mmol) in diethyl ether, alumina supported potassium permanganate (6 mmol $KMnO_4$) is added at 0^0C. Then water (50 mmol) is added to reaction medium. *(Scheme 22)*

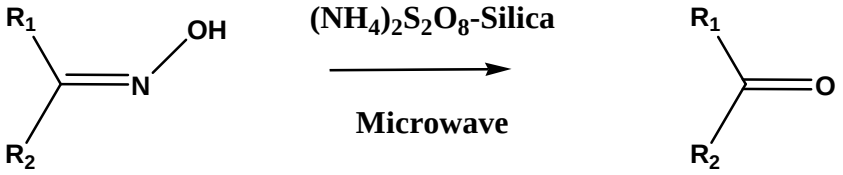


yield 82%

Scheme 22

Reaction was optimized by adding water in to the reaction medium. But, water makes regeneration not suitable for unsaturated oximes. On the other hand steric congestion near C=N bond increase the reaction time dramatically. Alumina supported potassium permanganate appears to work better with the less hindered oximes. Main disadvantage of this regeneration is reagent is still oxidize aldoximes to the related carboxylic acid instead of aldehyde.

Silica gel supported ammonium persulfate is another reagent for deprotection of oximes[36]. This reagent regenerate carbonyl compounds with microwave assistance. When microwave is used for a reaction, it resulted in very short time. In general procedure, oxime (1 mmol) is combined with silica gel (10 times, w/w), for homogeneous mixture dissolved in dichloromethane, and ammonium persulfate is added to the mixture. The contents are irradiated at full power in an alumina bath inside a microwave oven (2450 MHz, 800 Watts) for 0.8 – 2.5 minutes. After extraction and column chromatography yields 59-83% of related carbonyl compound. *(Scheme 23)*



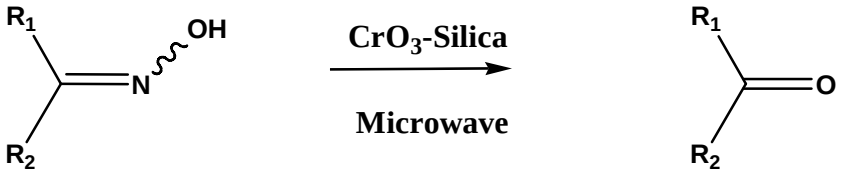
59-83% yield

Scheme 23

Results of the reaction shows that, even stable ketoxime like acetophenone oxime is yield 65% yield. Such low yields mat be resulted from short reaction time with high energy

.

Some reagents are adapted to solid supported microwave assisted regeneration procedures like chromium trioxide[37]. This reagent is known to be effective for oximes with strong functional groups. Silica gel supported form of CrO_3 is used reactions as follows; dry powder obtained by evaporating dichloromethane from a well stirred mixture of oxime (5 mmol), 5 ml dichloromethane and SiO_2-CrO_3 (5 mmol) is irradiated in a microwave oven for 0.75-2 minutes. After elution with dichloromethane, carbonyl compound recovered in 57-95%.*(Scheme 24)*



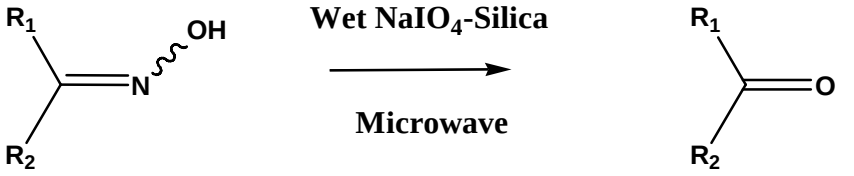
57-95% yield

Scheme 24

Result shows that, silica supported chromium trioxide is not more effective than free oxidant. In addition, reagent still yields low values with aldoximes.

Low yields of microwave assisted 'dry' solid supported oxidant procedures force researchers to develop new methods in this area. First

experiment are done with wet silica supported oxidants like sodium periodate[38]. The reagent is prepared by adding silica gel to a stirred solution of $NaIO_4$ in water. After removal of water resulting white powder is dried in an oven at 120^0C for 12 h. Regeneration procedure; $NaIO_4$-silica gel (2.14 mmol) is wetted with water (0.6 ml) and mixed with the neat ketoxime (1 mmol) in a small beaker. The beaker is placed in a alumina bath inside a microwave oven an irradiated for 0.75 to 2.5 minutes depending on the nature of oxime. Extraction with dichloromethane and purification yields related ketone 68-93%. *(Scheme 25)*



Scheme 25

The reaction does not from a Schiff's base in the case of aromatic amine. But, the regeneration of aldoximes under similar reaction conditions results in a complex mixture of products with consumption of all the starting material.

Among the various solid supports examined silica gel is likely to be the better one. In the absence of silica, however, mixtures of products are obtained. The reactions on clay predominantly result in the formation of Beckmann rearranged products. The optimum ratio of substrate to reagent is found to be 1:5; the reaction remains in complete with lower amounts even after extended exposure to microwaves (5 min).

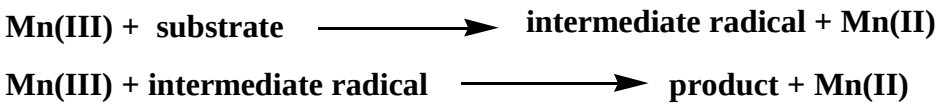
1. 4 $Mn(OAc)_3$ mediated transformations

Highly oxidized transition metals have long been used in organic synthesis and their synthetic and mechanistic chemistry has been thoroughly studied. Even so new uses are being discovered every year for these standard reagents. Milder transition metal oxidant (i.e. Mn(III) species) have been far less commonly employed by synthetic chemists.

Manganese(III) acetate deals with the addition reactions of compounds, mostly bearing a hydrogen atom alpha to a carbonyl group, to olefinic and aromatic unsaturated systems. Demir and Jeganathan reviewed a variety of selective oxidations of α,β-unsaturatedketones and the α'-position[38].

The fate of the primary adduct radical strongly depends on the reaction conditions and the nature of the substrate. Substrates that are less reactive to common oxidants are more interesting since here the unique properties of Manganese (III) acetate as a free radical generator can be more fully exploited.

It is often observed that owing to its lower reactivity, higher selectivity's can be obtained with manganese (III) acetate as compared with the other oxidizing agents. Many of these reactions proceed according to the simplified. *(Scheme 26)*



Scheme 26

1. 5 Aim of the work

Because of the high importance of the carbonyl compounds which form the central core in a large number of natural products and are constituents of a variety of biologically active compounds there is a constant need for the development of new methods for regeneration of carbonyl compounds from related oximes, which are mild and highly tolerant towards a wide range of functional groups.

In literature there are more than 30 methods known for regeneration of carbonyl compounds. These methods called as regeneration, deprotection or cleavage. Most of them are functional group dependent or only effective for only one type of oxime. Same of them can not be used for both aldoximes and ketoximes. Moreover, lots of reagents are expensive, sensitive or must be synthesize before use.

As a result of all these handicaps, we wanted to use mild oxidative character of manganese(III) acetate to generate carbonyl compounds from both aldoximes and ketoximes in the presence of different functional groups.

As shown in scheme 26 we suggest that $Mn(OAc)_3$ is one electron oxidant and it is possible to generate iminoxy-nitroso radical which can be converted to carbonyl compounds.

CHAPTER II

RESULTS AND DISCUSSION

2.1 The synthesis of oximes from aldehydes and ketones for the regeneration

Before regeneration studies, oximes were synthesized from selected carbonyl compounds with representing functional groups. Such as, aldehyde, ketone, α,β-unsaturated carbonyl compounds, α-hydroxy ketones, aromatic and hetero aromatic aldehyde and ketone, sterically hindered ketone, oximes with defined geometry. For this purpose lots of procedures are present. In our study, we used a procedure as mixture of NaOAc and $NH_2OH.HCL$ in EtOH, reacted with aldehyde or ketone. Reactions are monitored by TLC and IR spectra are given excellent information (C=N absorption) about the formation of oximes. After completion of the reaction, extraction and recrystallization furnished desired oxime with high yield.

The acetophenone(**2a**) was converted to its oxime form **1a** using Wargha procedure[39] described before. Recrystallization from hexane-methanol resulted pure white crystals of **1a**. IR spectrum of this crystals with KBr shows 3233 (br s, OH), 1645 (m, C=N), 1005 (s, N-O) cm^{-1}. Melting point of this oxime found 57-58^{0}C (lit[40] mp 59-60^{0}C). These values are same of the reported one's in literature.

The methyl ethyl oxime(**1b**) was prepared, same as **1a**, from ketone **2b**. After completing the reaction and work-up, colorless oil **2b** obtained. IR spectrum of this oil(neat) shows 3203 (br s, OH), 1656 (m, C=N), 963 (s, N-O) cm^{-1}.

Boiling point of this oxime found 149-153^{0}C (lit[40] bp 152^{0}C) these values are same of the reported one's in literature.

The 2-furyl methyl ketone(**2c**) was converted to its oxime form **1c** using procedure described before[39]. Recrystallization from hexane resulted pure white crystals of **1a**. IR spectrum of this crystals with KBr shows 3226 (br s, OH), 1633 (m, C=N), 997 (s, N-O) cm^{-1}. Melting point of this oxime found 26-28 ^{0}C (lit[41] mp 28^{0}C).

The benzaldoxime(**2d**) was converted to 4**a** using Wargha procedure[39] described before. Recrystallization from hexane-methanol resulted pure white crystals of **1d**. IR spectrum of this crystals with KBr shows 3263 (br s, OH), 1611 (m, C=N), 1027(s, N-O) cm^{-1}. Melting point of this oxime found 129^{0}C (lit[42] mp 130^{0}C).

The furfural(**2e**) was converted to **1e** using Wargha procedure[39] described before. Recrystallization from hexane-methanol resulted pure crystals of **1e**. IR spectrum of this crystals with KBr shows 3275 (br s, OH), 1638 (m, C=N), 998(s, N-O) cm^{-1}. Melting point of this oxime found 89^{0}C (lit[40] mp 90^{0}C).

The 4-metoxy benzaldehyde(**2f**) converted to **1f** using Wargha procedure[39] described before. Recrystallization from hexane-methanol resulted pure crystals of **1d**. IR spectrum of this crystals with KBr shows 3453 (br s, OH), 1587 (m, C=N), 1023 (s, N-O) cm^{-1}. Melting point of this oxime found 133-134^{0}C (lit[43] mp 133^{0}C).

The cyclohexanone(**2g**) was converted to 7**a** using Wargha procedure[39] described before. Recrystallization from hexane-methanol resulted pure white crystals of **1d**. IR spectrum of this crystals with KBr shows 3191 (br s, OH), 1665 (m, C=N), 994 (s, N-O) cm^{-1}. Melting point of this oxime found 88-89^{0}C (lit[40] mp 89.5-90.5^{0}C).

The isobutyl methyl oxime(**1h**) was prepared, same as **1a**, from ketone **2h**. After completing the reaction and work-up, colorless oil **2h** obtained. IR spectrum of this oil(neat) shows 3255 (br s, OH), 1666 (m, C=N), 1385 (s, CH_3), 1382 (s, CH_3) 935 (s, N-O) cm^{-1}. Boiling point of this oxime found 68-70^{0}C (lit[40] bp 69-71^{0}C).

The 4-hydroxy acetophenone(**2i**) was converted to its oxime form **1i** using Wargha procedure[39] described before. Recrystallization from hexane-methanol resulted pure white crystals of **1a**. IR spectrum of this crystals with KBr shows 3293 (br s, OH), 1615 (m, C=N), 1005 (s, N-O) cm^{-1}. Melting point of this oxime found 85-87^{0}C (lit[44] mp 86-88^{0}C). These values are same of the reported one's in literature.

The camphor(**2j**) was converted to **1j** using Wargha procedure[39] described before. Recrystallization from methanol resulted pure white crystals of **1j**. IR spectrum of this crystals with KBr shows 3306 (br s, OH), 1685 (m, C=N), 923 (s, N-O) cm^{-1}. Melting point of this oxime found 117^{0}C (lit[40] mp 116.5-117.5^{0}C).

The 1,2di(furan-2yl)-2-hydroxy ethanone(**2k**) was converted to **1k** using Wargha procedure[39] described before. Recrystallization from methanol resulted pure white crystals of **1k**. IR spectrum of this crystals with KBr shows 3566 (br s, OH), 1605 (m, C=N), 998 (s, N-O) cm^{-1}. Melting point of this oxime found 147^{0}C (lit[40] mp 146.5-148.5^{0}C).

The (E)-1,3-di(furan-2yl)-prop-2-en-1-one(**2l**) was converted to **1l** using Wargha procedure[39] described before. Recrystallization from methanol resulted pale yellow crystals of **1l**. IR spectrum of this crystals with KBr shows 3361 (br s, OH), 1666 (m, C=N), 1008 (s, N-O) cm^{-1}. Melting point of this oxime found 107^{0}C (lit[40] mp 105-108^{0}C).

2.2 Manganese (III) acetate mediated regeneration of carbonyl compounds from oximes

Commercially available $Mn(OAc)_3$ has been used for the majority oxidative reactions. Manganese(III) acetate deals with the addition reactions of compounds. The reactivity of the primary adduct radical strongly depends on the reaction conditions and the nature of the substrate. Substrates that are affected by strong oxidants, give interesting results with manganese(III) acetate as a free radical generator and Lewis acid.

The results are summarized in Table 1. Aromatic oximes with various functional group: **1a**, **1d**, **1f**, **1i**. Heteroaromatic oximes: **1c**, **1e**. Aliphatic oximes: **1b**, **1g**, **1h**. Sterically hindered oxime: **1j**. α-Hydroxy ketoxime: **1k**. α,β-Unsaturated oxime: **1l**. Oximes with defined geometry: **1m**, **1n**.

Table 1. The regeneration of carbonyl compounds from related oximes.

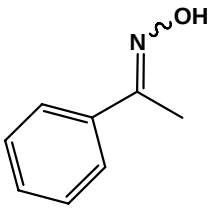
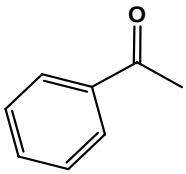
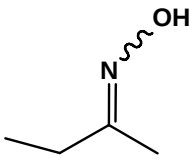
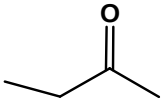
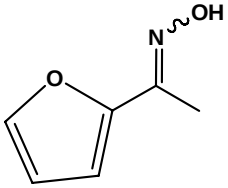
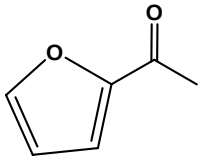
	Oxime 1	**Carbonyl 2**	**Yield (%)**	**Time(h)**
a			**96**	**1**
b			**92**	**1**
c			**92**	**1**

Table 1 continuous.

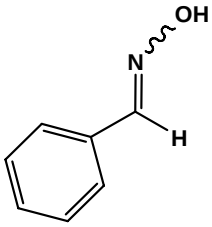
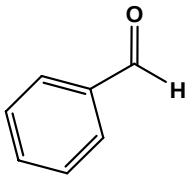
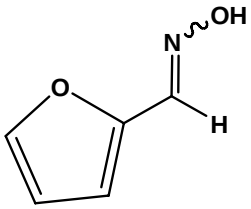
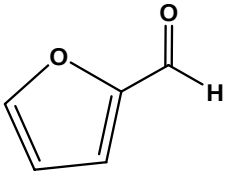
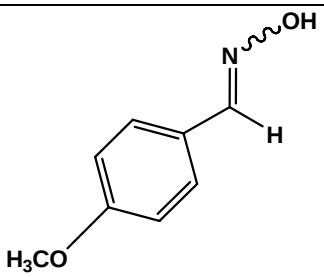
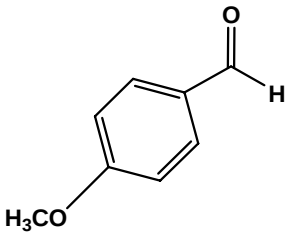
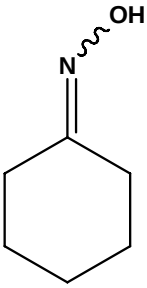
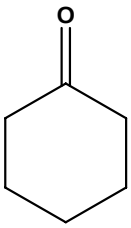
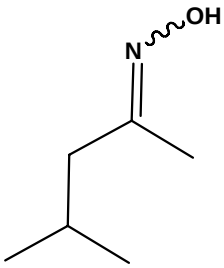
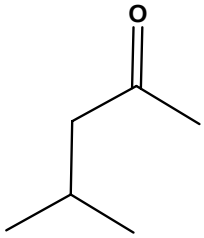
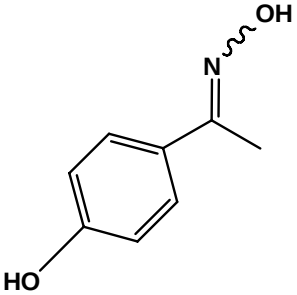
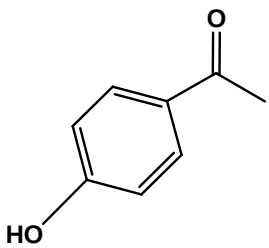
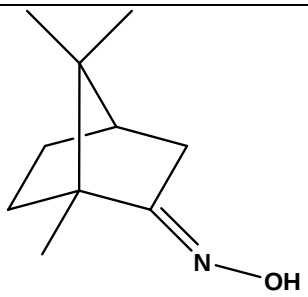
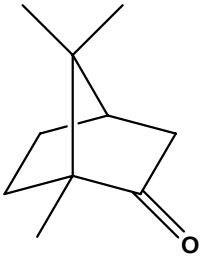
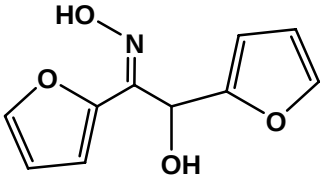
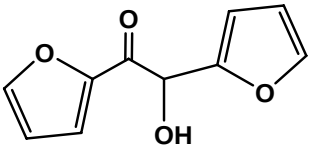
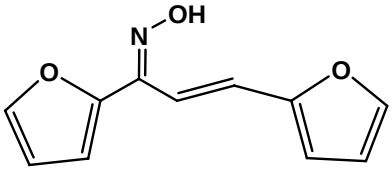
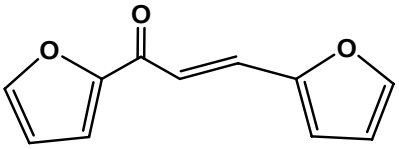
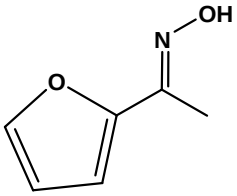
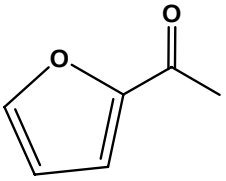
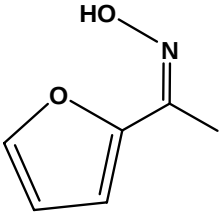
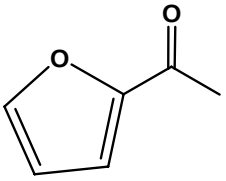
d			**89**	**30min**
e			**86**	**1**
f			**93**	**2**
g			**94**	**1**
h			**91**	**1**
i			**96**	**2**

Table 1 continuous.

j			**91**	**1**
k			**87**	**1**
l			**88**	**1**
m			**94**	**2**
n			**93**	**2**

[a]All products were identified by their IR spectra and mp's.

In an initial reaction, a solution of 10 mmol oxime and 12 mmol $Mn(OAc)_3$ in 30 ml benzene was stirred under reflux (Dean-Stark apparatus) during which the dark brown color of $Mn(OAc)_3$ disappeared by time which was also monitored by GC-MS and TLC. After all starting material was consumed, the reaction mixture was diluted with ether and washed with brine. Resulting organic phase was dried over $MgSO_4$ and concentrated under vacuum. If necessary, crude

products were purified by column chromatography using EtOAc:Hexane as eluent. In some cases, direct filtering of the reaction mixture through a pad of silica provide pure carbonyl compounds.

Later we focus our attention to find out how many equivalence of oxidant is needed to complete this regeneration. For this purpose, reaction repeated with 1.5 equivalence of manganese(III) acetate which was dried over phosphorous pentoxide and 1 equivalence of compound **1a**. Complete formation of carbonyl compound **1a** shows that, less than 2 equivalence of oxidant is needed for regeneration. Reactions with 1.2 and 1 equivalences of dry manganese(III) acetate and 1 equivalence of oxime **1a** resulted in better yields than the reactions were done with higher equivalences of oxidant. These results also shows that, 1 equivalence of dry manganese(III) acetate is enough for this regeneration.

A control experiment was done with 0.5 equivalence of manganese(III) acetate and 1 equivalence of oxime **1a** at the same conditions. This experiment resulted with 46% regeneration of oxime **1a** to ketone **2a** and 47% of staring oxime **1a** as unchanged. After all these studies, we conclude that, 1:1 ratio between manganese(III) acetate and oxime is required to complete this transformation.

In order to find effect of procedure on alkyl oximes, reaction repeated with 2-butanone oxime **1b** and manganese(III) acetate. Results show that, regeneration of alkyl ketone **2b** from related oximes can be done with high yield.

Effectiveness of procedure was checked by repeating it with another aromatic ketoxime **1c.** Reaction with ketoxime **1c** and manganese(III) acetate smoothly afforded the desired ketone **2c** in 92% yield.

In the light of these observations, we applied this procedure for regeneration of aldehydes from aldoximes. Firstly, reaction between benzaldehyde oxime **1d** and manganese(III) acetate was examined. Total regeneration of

aldehyde **2d** achieved with 1:1 ratio of reactants in 30 minutes of reflux under dean-stark trap. Secondly, procedure was applied to furfural oxime **1e**. Desired regeneration product **2e** was afforded with 86% isolated yield. Thirdly, more reactive aldoxime, 4-metoxybenzaldehyde oxime transferred to related aldehyde **2f** in high isolated yield.

These results proved that, regeneration of aldehydes from oximes can be done successfully with our method. This procedure can be applied to aldoximes and regeneration of them completed in shorter reflux time. Oxidation of aldehydes to carboxylic acid was not observed with manganese(III) acetate.

After regeneration of alkyl ketone **2b** from related oxime with high yield, more examples were studied. Transformation of cyclohexanone oxime **1g** to cyclohexanone **2g** proved that cyclic alkyl oximes can be transferred to their ketones successfully.

Manganese(III) acetate based regeneration of isobuyhyl methyl ketone **2h** from it's oxime **1h** form completed with high yield. This result shows efficiency of procedure with bulky groups around C=N. After this observation, more complex structures like (1R)-camphor oxime **1j** was converted to its ketone form **2j** with out any change in configuration. This result indicates impressive mild oxidant behavior of manganese(III) acetate.

Selectivity and facile character of procedure forced us to examine more functional group containing oximes. Regeneration of 1,2di(furan-2yl)-2-hydroxy ethanone **1k** from its oxime form **2k** performed smoothly with 87% yield. Hydroxy group at α position was preserved trough the reaction. After this impressive result, α-β unsaturated oxime **1l** was afforded to give related ketone **2l** in 88% yield. Olefin functionality was preserved during the regeneration. ^{1}H-NMR (80 MHz):δ ppm 6.75-6.74 (m, 1H, furan) 6.61-6.60 (m, 1H, furan) 6.54-6.53 (m, 1H, furan) 7.34 (d, 1H, olefinic, J=16 Hz) 7.32-7.33 (m, 1H, furan)

7.551-7.548 (m, 1H, furan) 7.65 (d, 1H, olefinic, J=16 Hz) 7.66-7.67 (m, 1H, furan)

Deprotection ability of manganese(III) acetate was studied for E/Z isomers separately. For this purpose, E and Z isomers of 2-furyl methyl oxime were separated by column chromatography. Isomers are identified by ^{1}H NMR (200 MHz): the E isomer displays three multiplets of furane ring at δ 6.35, 6.61 and 7.41 ppm(C-4, C-3, C-5 H) and Z isomer displays the signal of C-3 H down field shift by 7.4 ppm. Procedure was repeated for both E and Z isomers separately, after 2 hours of reflux under dean-stark trap, regeneration to furyl methyl ketone completed with 94% and 93% yields respectively.

Functional group studies were followed by temperature dependency investigations. Different reaction temperatures were examined for regeneration of **1a** to ketone **2a**. mixture of acetophenone oxime and manganese(III) acetate was stirred at room temperature and controlled by TLC. At the first 3 hours of experiment, trace amount of regenerated ketone observed and system left for stirring overnight. At the 30 hours of stirring, noticeable amount of ketone was regenerated and reaction was left for complete regeneration. After 120 hours of stirring at room temperature, all oxime **1a** was converted to acetophenone **2a**. This result shows that regeneration of ketoximes can be completed at room temperature.

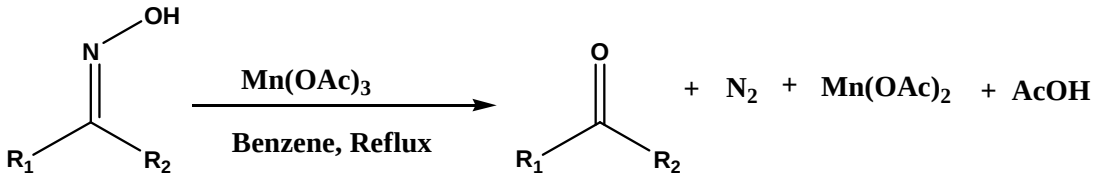
Since regeneration of ketoximes at room temperature gives full conversion. Same condition was investigated for aldoximes. Furfural oxime **1e** was chosen for that purpose which gives the lowest yield at reflux temperature. Mixture of **1e** and manganese(III) acetate was stirred at room temperature and reaction controlled by TLC. At the first 2 hours of experiment regeneration started. During the first 8 hours important amount of aldehyde was regenerated. At that point regeneration speed decreased. Complete regeneration of oxime **1e** to

aldehyde **2e** took 24 hours. Moreover, conversion was completed with lower side product formation.

Regeneration of carbonyl compounds from related oximes were studied in different solvents. Dichloromethane and cyclohexane were used for those experiments. Both aldoximes and ketoximes give poor results in these solvents. Toluene gives better results that dichloromethane and cyclohexane. But, the best yield comes when benzene used as solvent. This result conclude that, regeneration of carbonyl compounds from related oximes carried out by radical path way.

Suggested mechanism:

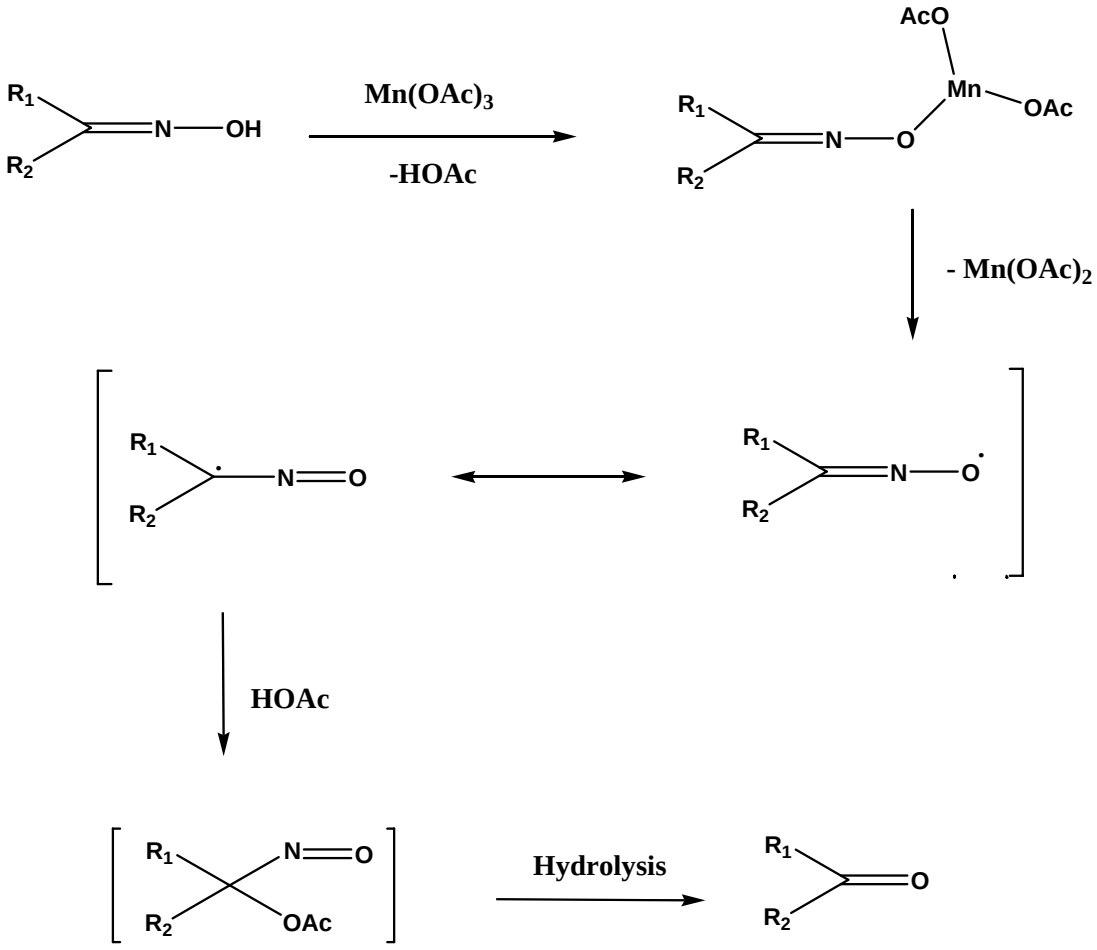
In this reaction manganese(III) acetate would act toward oximes as an oxidizing agent. We suggest that the reaction of aldoximes and ketoximes with manganese tri acetate proceeds smoothly, with evolution of nitrogen, to give the corresponding carbonyl compounds and manganese diacetate.*(Scheme27)*



Scheme 27 Suggested mechanism

According to our studies, we observe that reaction is working in different solvents like, dichloromethane, cyclohexane, toluene and benzene. Both aldoximes and ketoximes give the best results in benzene. That means, regeneration of carbonyl compounds from related oximes carried out by single electron transfer path way. $Mn(OAc)_3$ is one electron oxidant and as known from the literature it gives no chain propagation after radical formation.

Reaction starts as addition of manganese triacetate to the hydroxy side of the oxime by loose of acetic acid. Formation of an iminoxy radical was forced by single electron transfer from manganese while reducing to manganese diacetate. Second addition of acetic acid to this radical resulted with formation of α-acetoxy nitroso intermediate. Decomposition of this compound yields related carbonyl compound.*(Scheme 28)*



Scheme 28

This mechanism shows that manganese triacetate can convert oximes to related carbonyl compounds and one equivalence of oxidant is enough for this transformation. This result quite important, In literature manganese(III) acetate known as single electron transfer oxidizing agent and generally two equivalence of it used to complete reaction. In our method, oxidizing fallowed by addition of

acetic acid and former hydrolysis of it resulted complete transformation of oxime to carbonyl compound with 1:1 ratio with manganese(III) acetate.

The other possibility is the trace amount presence of $KMnO_4$ in Mn(III) acetate which can catalyses the formation of Mn(III) from Mn(II), formed during the reaction, in the presence of acetic acid.

CHAPTER III

EXPERIMENTAL

The structure determination of the compounds in this study was done by the instruments mentioned below.

IR spectra were recorded with Perkin Elmer 1600 series FT-IR spectrometer by using CCl_4 and ethyl acetate as solvent or a neat.

Proton magnetic resonance spectra (^{1}H-NMR) were recorded with Bruker AC 80 MHz FT-NMR spectrometer, using tetramethylsilane (TMS) as internal standard and deutereochloroform and deutereomethanol as solvent.

Column chromatography was conducted on silica gel 60 (mesh size 40-63 um). TLC was carried out on aluminum sheets precoated with silica gel $60F_{254}$ (Merck), and the spots were visualized with UV light (λ = 254 nm).

GC results were determined using a Unicam 610 SERIES with ZB-5 capillary column, 30m, 250µm; T_{GC}(injector) = 250°C, T_{FID}(detector) = 280°C, time program (oven): $T_{0\ min}$ =100°C, $T_{3\ min}$ = 100°C, $T_{13\ min}$ = 260°C (heating rate 16°C·min^{-1}), $T_{19\ min}$ = 280°C, $T_{23\ min}$ = 280°C,

Solvents were either technical of higher grade, when necessary they were purified and dried with drying agents and by distillation.

All extracts were dried over anhydrous magnesium sulfate ($MgSO_4$) and solutions were concentrated under vacuum by using rotary evaporator.

Typical procedure:

3.1 The synthesis of acetophenone oxime

To a mixture of NaOAc (11.48 g, 0.14 mol) and $NH_2OH.HCL$ (6.59 g, 0.14 mol) in 300ml EtOH, acetophenone (12.01 g, 11.7 ml, 0.1 mol) was added and the resulting mixture refluxed for 5 hours (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel).

After completion of the reaction, the mixture filtered by suction to remove excess NaOAc and $NH_2OH.HCL$. Organic phase extracted with water and saturated solution of $NaHCO_3$. Condensing of organic phase with rotavapor resulted white crystals of oxime. Recrystallization from ethanol, concentration under reduced pressure furnished acetophenone oxime (**1a**) (12.57g, 93%, white crystals), as confirmed by IR and melting point. (mp 57-58^{0}C, lit[40] mp 59-60^{0}C)

IR (KBr) 3233, 1645, 1005cm^{-1}

3.2 The synthesis of methyl ethyl oxime

To a mixture of NaOAc (5.74 g, 0.07 mol) and $NH_2OH.HCL$ (3.48 g, 0.07 mol) in 150ml EtOH, methyl ethyl ketone (3.60 g, 4.5 ml, 0.05 mol) was added and the resulting mixture refluxed for 4 hours (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel).

After completion of the reaction, the mixture filtered by suction to remove excess NaOAc and $NH_2OH.HCL$. Organic phase extracted with water and saturated solution of $NaHCO_3$. Condensing of organic phase with rotavapor resulted clear liquid oxime. Concentration under reduced pressure yielded methyl ethyl oxime (**1b**) (3.83 g, 88%, clear liquid), as confirmed by IR. (bp 149-153^{0}C, lit[40] bp 152^{0}C)

IR (neat) shows 3203, 1656, 963 cm^{-1}

3.3 The synthesis of 2-furyl methyl oxime

The procedure described for the synthesis of **1a** was repeated using NaOAc (1.64 g, 0.02 mol), $NH_2OH.HCL$ (0.9 g, 0.02 mol), 2-furyl methyl ketone (1.1 g, 0.01 mol) and 150 ml EtOH. Condensing of organic phase with rotavapor resulted white crystals of oxime. Recrystallization from ethanol, concentration under reduced pressure 2-furyl methyl oxime (**1c**) (1.18g, 94%, white crystals), as confirmed by IR. (mp 26-28 ^{0}C, lit[41] mp 28^{0}C).

IR (KBr) 3226, 1633, 997 cm^{-1}

3.4. The synthesis of benzaldoxime

The procedure described for the synthesis of **1a** was repeated using NaOAc (3.28g, 0.04 mol), $NH_2OH.HCL$ (1.98 g, 0.04 mol), benzaldehyde (2.1 g, 2.2 ml, and 0.02 mol) and 150 ml EtOH. Condensing of organic phase with rotavapor resulted white crystals of oxime. Recrystallization from ethanol, concentration under reduced pressure benzaldoxime (**1d**) (2.20g, 91%, white crystals), as confirmed by IR. (mp 129^{0}C, lit[42] mp 130^{0}C).

IR (KBr) 3263, 1611, 1027cm^{-1}

3.5. The synthesis of furfural oxime

The procedure described for the synthesis of **1a** was repeated using NaOAc (1.64 g, 0.02 mol), $NH_2OH.HCL$ (0.9 g, 0.02 mol), furfural (0.9 g, 0.01 mol) and 100 ml EtOH. Condensing of organic phase with rotavapor resulted crystals of oxime. Concentration under reduced pressure furfural oxime (**1e**) (1.02g, 92%, crystals), as confirmed by IR. (mp 89^0C, lit[40] mp 90^0C).

IR (KBr) 3275, 1638, 998cm^{-1}

3.6. The synthesis of 4-methoxy benzaldehyde oxime

The procedure described for the synthesis of **1a** was repeated using NaOAc (1.64 g, 0.02 mol), $NH_2OH.HCL$ (0.9 g, 0.02 mol), 4-methoxy benzaldehyde (1.36 g, 0.01 mol) and 150 ml EtOH. Condensing of organic phase with rotavapor resulted crystals of oxime. Concentration under reduced pressure 4-methoxy benzaldehyde oxime (**1f**) (1.43g, 95%, crystals), as confirmed by IR. (mp133-134^{0}C, lit[43] mp 133^0C).

IR (KBr) 3453, 1587, 1023 cm^{-1}

3.7.The synthesis of cyclohexanone oxime

The procedure described for the synthesis of **1a** was repeated using NaOAc (6.56g, 0.08 mol), $NH_2OH.HCL$ (3.96 g, 0.08 mol), cyclohexanone (3.93 g, 4.2 ml, and 0.04 mol) and 200 ml EtOH. Condensing of organic phase with rotavapor resulted white crystals of oxime. Recrystallization from ethanol, concentration under reduced pressure cyclohexanone oxime (**1g**) (4.3g, 95%, white crystals), as confirmed by IR. (mp 88-89^{0}C, lit[40] mp 89.5-90.5^{0}C).

IR (KBr) 3191, 1665, 994cm^{-1}

3.8.The synthesis of isobutyl methyl oxime

The procedure described for the synthesis of **1a** was repeated using NaOAc (1.64 g, 0.02 mol), $NH_2OH.HCL$ (0,9 g, 0.02 mol), isobutyl methyl (1.1 g, 0.01 mol) and 100 ml EtOH. Condensing of organic phase with rotavapor resulted colorless liquid oxime. Concentration under reduced pressure isobutyl methyl oxime

(**1h**) (1.05g, 89%, colorless liquid), as confirmed by IR. (bp 68-70^{0}C, lit[40] bp 69-71^{0}C).

IR (neat) 3255, 1666, 1385, 1382, 935 cm^{-1}

3.9. The synthesis of 4-hydroxy acetophenone oxime

The procedure described for the synthesis of **1a** was repeated using NaOAc (3.28g, 0.04 mol), $NH_2OH.HCL$ (1.98 g, 0.04 mol), 4-hydroxy acetophenone (2.72 g, 2.45 ml, and 0.02 mol) and 200 ml EtOH. Condensing of organic phase with rotavapor resulted white crystals of oxime. Recrystallization from ethanol, concentration under reduced pressure 4-hydroxy acetophenone (**1i**) (2.66g, 88%, white crystals), as confirmed by IR. (mp 85-87^{0}C, lit[44] mp 86-88^{0}C).

IR (KBr) 3293, 1615, 1005 cm^{-1}

3.10. The synthesis of (1R)-camphor oxime

The procedure described for the synthesis of **1a** was repeated using NaOAc (0,82 g, 0.01 mol), $NH_2OH.HCL$ (0.46 g, 0.01 mol), (1R)-camphor (0,76 g, 5 mmol) and 80 ml EtOH. Condensing of organic phase with rotavapor resulted

crystals of oxime. Concentration under reduced pressure (1R)-camphor oxime (**1j**) (0,74g, 89%, crystals), as confirmed by IR. (mp117^{0}C, lit[40] mp 116.5-117.5^{0}C).

IR (KBr) 3306, 1685, 923 cm^{-1}

3.11. The synthesis of 1,2di(furan-2yl)-2-hydroxy ethanone oxime

The procedure described for the synthesis of **1a** was repeated using NaOAc (0,82 g, 0.01 mol), $NH_2OH.HCL$ (0.46 g, 0.01 mol), 1,2di(furan-2yl)-2-hydroxy ethanone (0,96 g, 5 mmol) and 90 ml EtOH. Condensing of organic phase with rotavapor resulted crystals of oxime. Concentration under reduced pressure 1,2di(furan-2yl)-2-hydroxy ethanone oxime (**1k**) (0,87g, 85%, crystals), as confirmed by IR. (mp 147^{0}C, lit[40] mp 146.5-148.5^{0}C).

IR (KBr) 3566, 1605, 998cm^{-1}

3.12. The synthesis of (E)-1,3-di(furan-2yl)-prop-2-en-1-one oxime

The procedure described for the synthesis of **1a** was repeated using NaOAc (0,82 g, 0.01 mol), $NH_2OH.HCL$ (0.46 g, 0.01 mol), 1,3-di(furan-2yl)-prop-2-en-1-one (0,94 g, 5 mmol) and 80 ml EtOH. Condensing of organic phase with rotavapor resulted crystals of oxime. Concentration under reduced pressure (E)-1,3-di(furan-2yl)-prop-2-en-1-one oxime (**1k**) (0,87g, 85%, crystals), as confirmed by IR. (mp 107^{0}C, lit[40] mp 105-108^{0}C).

IR (KBr) 3361, 1666, 1008 cm^{-1}

3.13. The Regeneration of acetophenone

Typical procedure:

To a solution of acetophenone oxime (200 mg, 1.5 mmol) in 30 ml benzene, $Mn(OAc)_3$ (396 mg, 1.5 mmol) was added and the resulting mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel).

After completion of the reaction, 50 ml ethyl acetate was added. The precipitated $Mn(OAc)_2$ was filtered by suction, then organic phase extracted with water and saturated solution of $NaHCO_3$. Condensing of organic phase with rotavapor and purifying by column chromatography resulted acetophenone (**2a**) (178 mg, 96%), as confirmed by IR.

3.14. The regeneration of methyl ethyl ketone

The procedure described for the regeneration of **2a** was repeated using methyl ethyl oxime(**1b**) (200 mg, 2.29 mmol), $Mn(OAc)_3$ (615 mg, 2.29 mmol) and 40 ml benzene. Mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted methyl ethyl ketone (**2b**) (152 mg, 92%), as confirmed by IR.

3.15. The regeneration of 2-furyl methyl ketone

The procedure described for the regeneration of **2a** was repeated using 2-furyl methyl oxime(**1c**) (200 mg, 1.60 mmol), $Mn(OAc)_3$ (429 mg, 1.60 mmol) and 30 ml benzene. Mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate

3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted 2-furyl methyl ketone (**2c**) (101 mg, 92%), as confirmed by IR.

3.16. The regeneration of benzaldehyde

The procedure described for the regeneration of **2a** was repeated using benzaldoxime (**1d**) (200 mg, 1.65 mmol), $Mn(OAc)_3$ (442 mg, 1.65 mmol) and 50 ml benzene. Mixture was refluxed under dean stark trap for 30 minutes (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted benzaldehyde (**2d**) (154 mg, 89%), as confirmed by IR.

3.17. The regeneration of furfural

The procedure described for the regeneration of **2a** was repeated using furfural oxime(**1e**) (200 mg, 1.80 mmol), $Mn(OAc)_3$ (482 mg, 1.80 mmol) and 40 ml benzene. Mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted furfural (**2e**) (148 mg, 86%), as confirmed by IR.

3.18. The regeneration of 4-methoxy benzaldehyde

The procedure described for the regeneration of **2a** was repeated using 4-methoxy benzaldehyde oxime(**1f**) (200 mg, 1.32 mmol), $Mn(OAc)_3$ (354 mg,

1.32 mmol) and 30 ml benzene. Mixture was refluxed under dean stark trap for 2 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted 4-methoxy benzaldehyde (**2f**) (167 mg, 93%), as confirmed by IR.

3.19. The regeneration of cyclohexanone

The procedure described for the regeneration of **2a** was repeated using cyclohexanone oxime (**1g**) (200 mg, 1.78 mmol), $Mn(OAc)_3$ (474 mg, 1.78 mmol) and 40 ml benzene. Mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted cyclohexanone (**2g**) (164 mg, 94%), as confirmed by IR.

3.20. The regeneration of isobutyl methyl ketone

The procedure described for the regeneration of **2a** was repeated using isobutyl methyl oxime (**1h**) (200 mg, 1.73 mmol), $Mn(OAc)_3$ (465 mg, 1.73 mmol) and 40 ml benzene. Mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted cyclohexanone (**2h**) (157 mg, 91%), as confirmed by IR.

3.21. The synthesis of 4-hydroxy acetophenone

The procedure described for the regeneration of **2a** was repeated using 4-hydroxy acetophenone oxime (**1i**) (200 mg, 1.32 mmol), $Mn(OAc)_3$ (354 mg, 1.32 mmol) and 30 ml benzene. Mixture was refluxed under dean stark trap for 2 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted 4-hydroxy acetophenone (**2i**) (172 mg, 96%), as confirmed by IR.

3.22. The regeneration of (1R)-camphor

The procedure described for the regeneration of **2a** was repeated using (1R)-camphor oxime (**1j**) (200 mg, 1.19 mmol), $Mn(OAc)_3$ (320 mg, 1.19 mmol) and 30 ml benzene. Mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted (1R)-camphor (**2j**) (164 mg, 91%), as confirmed by IR.

3.23. The regeneration of 1,2di(furan-2yl)-2-hydroxy ethanone

The procedure described for the regeneration of **2a** was repeated using 1,2di(furan-2yl)-2-hydroxy ethanone oxime (**1k**) (200 mg, 0.96 mmol), $Mn(OAc)_3$ (258 mg, 0.96 mmol) and 30 ml benzene. Mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted 1,2di(furan-2yl)-2-hydroxy ethanone (**2k**) (160 mg, 87%), as confirmed by IR.

3.24. The regeneration of (E)-1,3-di(furan-2yl)-prop-2-en-1-one from (E)-1,3-di(furan-2yl)-prop-2-en-1-one oxime

The procedure described for the regeneration of **2a** was repeated using (E)-1,3-di(furan-2yl)-prop-2-en-1-one oxime (**1l**) (200 mg, 0.98 mmol), $Mn(OAc)_3$ (263 mg, 0.98 mmol) and 30 ml benzene. Mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted (E)-1,3-di(furan-2yl)-prop-2-en-1-one (**2l**) (162 mg, 88%), as confirmed by IR.

3.25. The regeneration of 2-furyl methyl ketone from E-2-furyl methyl oxime

The procedure described for the regeneration of **2a** was repeated using 2-furyl methyl oxime(**1m**) (200 mg, 1.60 mmol), $Mn(OAc)_3$ (429 mg, 1.60 mmol) and 30 ml benzene. Mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted 2-furyl methyl ketone (**2c**) (162 mg, 92%), as confirmed by IR.

3.26. The regeneration of 2-furyl methyl ketone from Z-2-furyl methyl oxime

The procedure described for the regeneration of **2a** was repeated using 2-furyl methyl oxime(**1n**) (200 mg, 1.60 mmol), $Mn(OAc)_3$ (429 mg, 1.60 mmol) and 30 ml benzene. Mixture was refluxed under dean stark trap for 1 hour (formation of the product was monitored by TLC using n-hexane: ethyl acetate 3:1 /silica gel). After completion of the reaction and work up described for **2a** fallowed by column chromatography resulted 2-furyl methyl ketone (**2c**) (163.8 mg, 93), as confirmed by IR.

CHAPTER 4

CONCLUSION

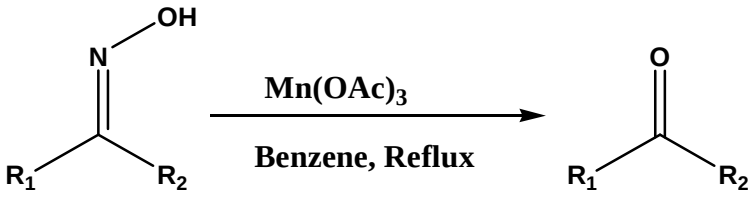
Both Aldoximes and ketoximes can be transferred to parent carbonyl compounds with this facile method. By products of reaction $Mn(OAc)_2$, acetic acid and N_2 are not toxic materials.

Method doesn't required protection like the other reactions. Procedure can be applied to free oxime. Regeneration of aldoximes can be completed at room temperature. On the other hand, reflux decreases the reaction time dramatically.

Method applied to many functional groups and hindered oximes are given deoximation reaction good yield. Both E and Z oximes can be oxidized to parent carbonyl compounds. Isomerization of olefinic double bond geometry of α-β unsaturated oximes is not observed. Oximes of α-β unsaturated ketones and aryl alkyl ketones are given trace amount of α'-acetoxylation products. In order to reduce these side products, reflux speed must be adjusted well. Reaction must be checked by TLC because after cleavage of oximes overoxydation can occur in some cases. Ratio between oxime and $Mn(OAc)_3$ is also important. At conditions that $Mn(OAc)_3$ ratio is higher than oxime, other oxidation products of $Mn(OAc)_3$ observed. Regeneration of aldoximes at room temperature gives less side products than one's refluxed at solvents boiling point.

Consequently; Procedure is suitable for direct conversion of oximes both aldoximes and ketoximes. $Mn(OAc)_3$ can be used for an effective and mild oxidizing agent for the regeneration of carbonyl compounds from oximes in good yield. Many functional groups are tolerated under the reaction conditions. It is noticeable that, side product after the reaction are not toxic. Used oxidant, $Mn(OAc)_3$, is easy to synthesis and cheap. This is superior to the other oxidants. During regeneration, geometry of starting material is not changing. This is important for characterization studies. In this reaction, we suggest that the reaction of aldoximes and ketoximes with $Mn(OAc)_3$ proceeds smoothly, with

evolution of nitrogen, to give the corresponding carbonyl compound and manganese diacetate. This reaction is new, mild, easy and cheap procedure for regeneration of carbonyl compounds from oximes.



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