Kurdistan Regional Government-Iraq
Ministry of Higher Educational & scientific research
Salahaddin University-Erbil (SUE)
Science College
Chemistry Department

Chemistry of Oxime

A Project Submitted to the Scientific Committee in the Chemistry Department in Partial Fulfilment of the Requirement for the Degree of Bachelor Science in Chemistry

Prepared by

Shanaz Ibrahim Hawez

Supervised by

Dr. Karzan Khaleel Hameed

April,2023 Newroz ,2723 Ramadan ,1444

Acknowledgement

First of all, I thank ALLAH for this opportunity and blessing over me I wish to express my deep gratitude and sincere thanks to my supervisor Dr. Karzan.Kh. Hameed, for his encouragement and provided facilities for this research project. I cannot forget to offer me since thanks to my family, friends and classmates who helped me to carry out this project successfully and for their valuable advice and support which I have received all the time.

List of content

List of Tables

List of figures

List of schemes

Abstract

Oximes and their derivatives have found their application in organic synthesis back in the 19th century and as analytical reagents, in the beginning of the 20th century, Oximes are important functional groups in organic chemistry but in particular they feature as protecting groups for carbonyl groups and as intermediates in the Beckmann rearrangement devoted to the chemistry and biological activity of oximes, The oxime function can rather easily be introduced into an organic molecule. This may involve oximation of a carbonyl group with hydroxyl amine, nitrosation of hydrocarbons, reduction of nitro compounds, oxidation of amines, oxidative ammonolysis etc. On treatment with bases, oximes undergo deprotonation to give oximate anions. Several procedures for the preparation of oximes exist, but most of them have not addressed the green chemistry issue, hence, bismuth compounds are very useful as they are cheap in general, commercially available, air stable crystalline solids, safe, and non-toxic, hence easy to handle, prepared by reaction of an aldehyde or ketone with hydroxylamine with no other additives.

Keywords: oxime, bismuth compounds, Beckmann Rearrangement, oximation

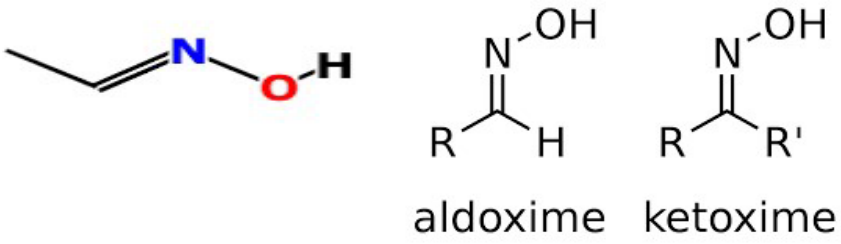
1.Introduction

It is well known that oximes have very interesting reactivity and are often used as intermediates for the preparation of a great variety of compounds. Oximes and their derivatives have found wide use, for example, as anticancer agents, as dyes and bacteriostatic agents. There is also a large number of oximes with other important practical applications, such as photographic sensitizers and developers, vulcanization accelerators in the rubber industry and as valuable intermediates in synthesis. Therefore, a great variety of compounds such as nitriles, amines, substituted amides, hydroxylamines, a-aminoalcohols, nitrones and nitro compounds can be produced from oximes. They can also serve as precursors in the synthesis of a number of heterocycles such as aziridines, furazans, Benz isoxazole N-oxides, quinazoline-3-oxides, pyrazole and pyrazoline 1,2-dioxides. The successful application of oximes and their use as materials in synthetic chemistry stems from their structure and their configuration and especially from the appropriate combination of oximino group with a variety of functional groups as amino, hydroxyl, oximino and others. An interesting case of this is that of dioximes. The presence of two oximino groups in a molecule in appropriate positions allows for the formation of interesting heterocycles by interaction of the functional groups. An important member of this class of molecules is the 1,3-dioximes, and they form the subject of this review which aims at presenting an integrated picture of their chemistry. This research attempts to detail all the aspects about oximes, including their synthesis, configuration, physical and chemical properties as well as their applications.

Synthesis of oximes is an important reaction in organic chemistry because these versatile oximes are used for protection, purification, and characterization of carbonyl compounds. Nitriles, amides via Beckmann rearrangement, nitro compounds, nitrones, amines, and azaheterocycles can be synthesized from oximes. They also find applications for selective activations. In inorganic chemistry, oximes act as a versatile ligand. Several procedures for the preparation of oximes exist, but most of them have not addressed the green chemistry issue. They are associated with generation of pollutants, requirement of high reaction temperature, low yields, lack of a generalized procedure, etc. Hence, there is a demand for developing an efficient, convenient, and non-polluting or less polluting alternative method for the preparation of oximes. (Saikia 2011).

1.1 Definition

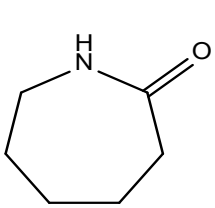
Oximes **1** are the chemical compounds that belong to the class of imines, having the general formula of $R^1R^2C=N-OH$. Oximes are also called nitrogen possessing organic compounds which are obtained from hydroxylamine, ketone, and aldehyde. These compounds are also derived from the reaction of hydrogen-donating reagents with the nitro compounds or another way is by the process of isomerization of the nitroso compounds. Oximes that are obtained from aldehydes called aldoximes can also be dehydrated forming nitriles. The other chemical reactions are the conversion of it to amines by treating it with hydrogen or other reducing agents and by converting it to amides.



1 structures of oxime

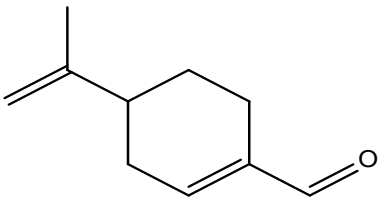
1.2 Applications

Oximes and their derivatives exhibit a wide range of activities. In industries, oximes are used in the production of an organic compound called Caprolactam **2**, which is a precursor for the polymer named Nylon 6. In Organic chemistry are utilized in catalytic reactions. The compounds of oximes are also used as antidotes which are used to serve as nerve agents. In Japan, the oxime naming perillaldehyde **3** is used as an arterial sweetener. In oil paints, the oxime called Methyl ethyl ketoxime is used as a skinning agent. The oxime called Acetone oxime is used as a de-oxidant or a corrosion inhibitor which lowers the toxicity. uses as nerve agent poisoning the class of chemical warfare agents known as nerve agents are organophosphorus compounds that are extremely potent inhibitors of the enzyme acetylcholinesterase. The toxic manifestations of nerve agent exposure are therefore those of excess acetylcholine in vivo. (Byju 2023).



2

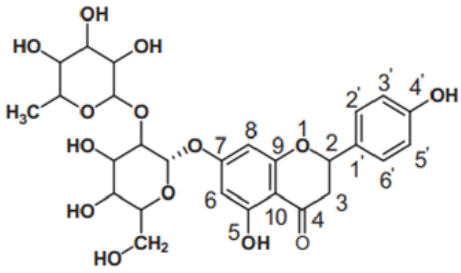
Structure **2** Caprolactam



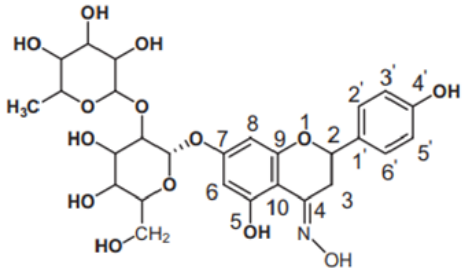
3

structure **3** perillaldehyde

Naringin **4** is one of the major flavanones in citrus and grapefruit. synthesize naringin oxime **5** from naringin. Antioxidant capacity of naringin oxime, as measured by the cupric reducing antioxidant capacity (CUPRAC) method, was found to be higher than that of the parent compound naringin. (Özyürek 2014)

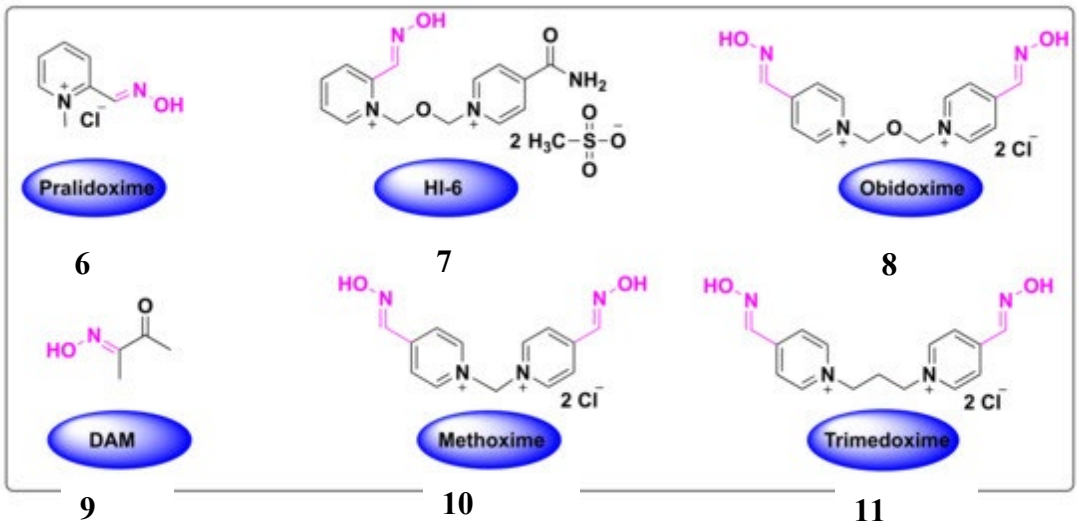


Structure **4** Naringin



Structure **5** Naringin oxime

Oximes represent the most important class in medicinal chemistry, renowned for their widespread applications as OP antidotes, drugs and intermediates for the synthesis of several pharmacological derivatives. Common oxime-based reactivators or nerve antidotes include pralidoxime **6**, HI-6 **7**, obidoxime **8** DAM **9** and methoxime **10**, trimedoxime **11**. (Dhuguru,2022)



6 **7** **8**

9 **10** **11**

Figure 1. Chemical structures of oxime-based nerve antidotes.

2.Characteristices

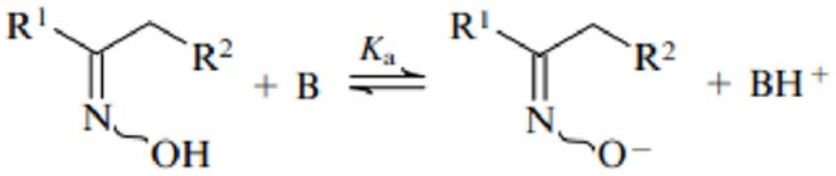
These compounds are found in the form of colorless crystals and are considered to have less solubility in water. The temperature of these compounds gets affected by the salts of acid. Aliphatic groups of oximes are said to be resistant to the hydrolysis process more than the analogous hydrazones. Oximes are toxic, and they show properties of both weakly acidic and basic. Oximes can decompose in the form of an explosion when heated further. If the two side chains on the central carbon atom different from one another, either a ketoxime or an aldoxime with distinct R groups, the oxime can often possess two unique geometric stereoisomeric shapes as per the E/Z configuration.

2.1. Spectral Information

Oximes have three characteristic bands with wave number estimating 3250 cm^{-1}(O-H), 945 cm^{-1} (N-O), and 1665cm^{-1} (C=N) in the infrared spectrum. In ^{1}H NMR spectra, the -OH signal of oximes appeared within δ = 8.5-10.0. (Palm.1953)

2.2. Acidity of oximes

On treatment with bases, oximes (12) undergo deprotonation to give oximate anions (13) **(scheme 1).**



12 **13**

Scheme.1. R1, R2=H, Alk, Ar

Oximes that contain hydrogen atoms in the a-position relative to the oxime function exhibit sufficiently high CH-acidity together with OH-acidity. (Mikhaleva 2006).

2.3. OH-Acidity

Studies of acid ± base properties of mono- and dioximes of diketones are associated with their wide use in analytical chemistry. OH-Acidity of oximes and its correlation with their configuration was the subject of several studies Table. Acidity constants of certain oximes. (Mikhaleva 2006)

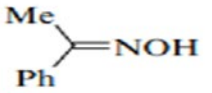
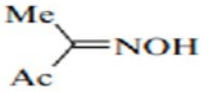
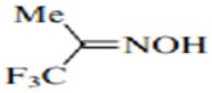
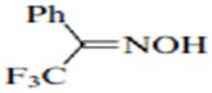
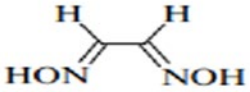
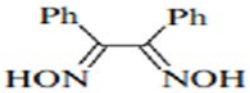
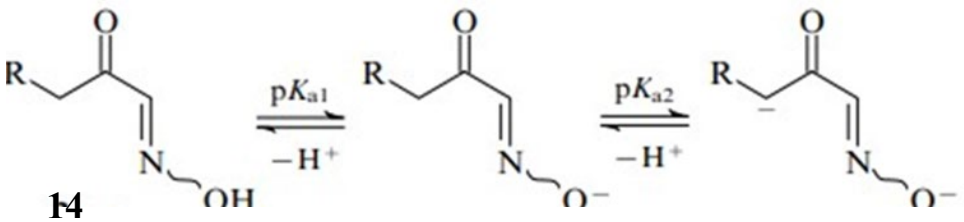
Oxime	pK_a
	11.48
	9.38
	9.76
	9.05
	9.94, 11.49
	10.29, 11.91

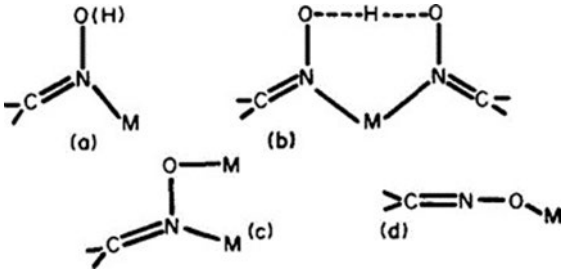
Table.1. shows the data on the acidity of certain oximes. The pKa values depend on the effect of substituents at the oxime function. A substantial increase in the oxime acidity is observed for an oxo aldoximes **14**. For these compounds, the latter oxime being among the most acidic oximes known



Scheme.2. {R = {H (a), MeS (b), MeSO (c), $MeSO_2$ (d), $Me2S^+$ (e)}.

2.4.N- and O-nucleophilicity of the oxime function

Nucleophilicity of oximes is their most important chemical property that manifests itself most clearly in basic media. The oxime function contains three nucleophilic reaction sites, N, O and C atoms. The neutral molecule usually plays the role of an N-nucleophile, while an anion (oximate) plays the role of a strong O-nucleophile Nucleophilicity of the carbon atom is determined by the contribution of a nitroso tautomer into the equilibrium. (Mikhaleva 2006). Oximes are usually associated the solid state by hydrogen-bonding, O—H. N. Isomerism in the oximes was first described by Werner. Il Owing to the restricted rotation around double bonds the oximes exhibit geometrical isomerism. Occurrence of two isomers in monoximes and three in dioximes the isomers are usually identified by chromatographic or spectroscopic methods. TLC has successfully been used by Toul et al. to separate and identify benzil-a-monoxime, furilmonoxime, furil dioxime and their isomers, and dimethyl monoxime in dimethylglyoxime. Soules et al. separated and identified various isomers of 2,2'-pyridiloximes. It is interesting to note that the different geometrical isomers for the vic-dioximes have been isolated only in the aromatic series. Modes of bonding the oxime group has two donor atoms, N and O, and may co-ordinate to a metal atom through either or both, thus acting as unidentate or bidentate, respectively. The following structures may arise from the different modes of co-ordination of an oxime. (Singh, R.B 1979)



Structures 15 different modes of co-ordination of an oxime

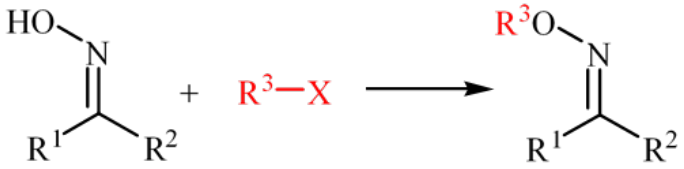
3. Derivatives

3.1. Oxime ethers

oxime have many derivatives the more common are Oxime ethers have that attracted much attention due to their potential biological activities and wide variety of synthetic applications. The name oxime ether is an abbreviation of oxy-imine ether. As one of the prominent medicinal motifs, the oxime ether group is featured in a large number of pharmaceutically important compounds and is widely applied in variety pesticides. For example, oxiconazole Oxime ethers are important and versatile intermediates in organic synthesis. These compounds were successfully transformed into amines, 1,2aminoalcohols, α- and βamino acides, hydroxylamines, nitriles, pyridines, benzofuranes, indoles, pyrroles, pyrazines, isoquinolines isoxazolesm, 8hydroxytetrahydroquinolines, aminocyclopentitols, aziridines, fluorenones, diarylmethylidenefluorene and phenanthrene. Furthermore, oxime ether is an elegant directing-group for activation of aromatic or vinylic C-H bonds for construction of new C-O, C-X and C-N bonds by metal-catalyzed cross coupling reactions Synthesis of oxime ethers from oximes and alkyl(aryl) halides.

3.1.1. Oxime ethers from oximes and alkyl halides

The best-known method for synthesis of acyclic oxime ethers **17** is the reaction of oximes with alkyl- and aryl halides **16**



16 **17**

Scheme.3. Synthesis of oxime ethers from oximes and alkyl(aryl) halides.

The alkylation of the oxygen atom of oxime moiety with alkyl halides has been performed using various base, such as sodium hydride, sodium hydroxide, potassium hydroxide, and potassium carbonate. As well as, the system Na/alcohol has also been utilized. Using potassium carbonate as base and acetonitrile as solvent clearly accelerated the alkylation of the oxime moiety compared to other bases/solvents, and the desired products were synthesized in good yields

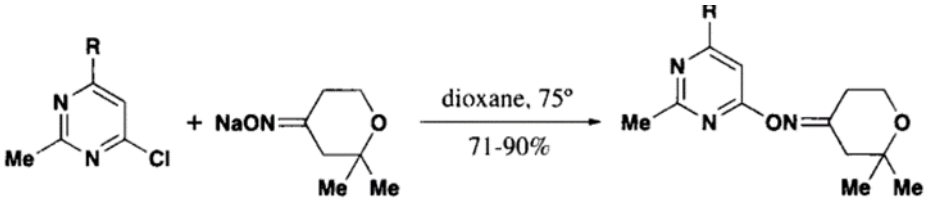
Entry	Solvent	Base	time (h)	Yield (%)
1	CH_2Cl_2	K_2CO_3	24	-
2	1,4-Dioxan	K_2CO_3	24	15
3	THF	K_2CO_3	18	30
4	DMF	K_2CO_3	18	40
5	Acetonitrile	K_2CO_3	8	70

Table.2. Synthesis of oxime ether from oxime and methy-l ,2-chloroacetate in the presence of K_2CO_3 in MeCN Recently, an excellent method for generation of oxime ethers from oximes and epichlorohydrin have been reported using acetone/water/K_2CO_3 system.

However, the high yields of corresponding oxime O-ethers are obtained only when alkyl iodides or bromides are used as alkylating agents

3.1.2. using oxime salts

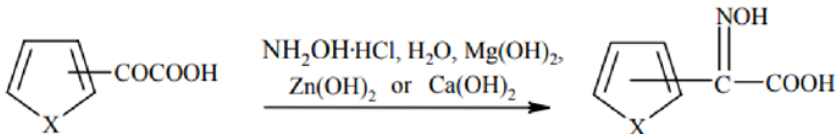
Oxime salts usually are used in the preparation of O-aryl or O-hetaryl oxime ethers. Thus, reaction of chloropyrimidines **18** with sodium salt of 2,2-dimethyltetrahydro-4-pyranone oxime **19** in dioxane leads to corresponding 0-pyrimidinyl oximes **20** in good yields (Abele, E 2003). **(Scheme 4)**



18 **19** R = Me, ON=CMe$_2$ **20**

3.2. Furan oximes

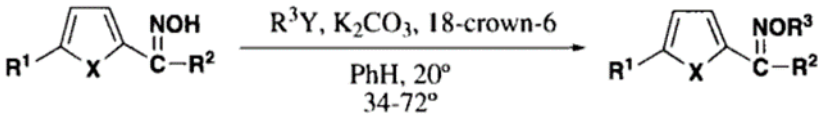
The classical method for the synthesis of furan oximes is based on the reaction of the aldehyde or ketone with hydroxylamine in the presence of NaOH/H2O2 N aqueous KOH/EtOH, K_2CO_3/EtOH, or NaOAc. Magnesium, zinc, and calcium hydroxides are used as bases in the synthesis of the oximes. (Abele, E 2001).



21 **22**

Scheme 5 reactions of furyl- and phenylglyoxal acids **21** with $NH_2OH{\cdot}HCl$ in water in the presence of magnesium, zinc, or calcium hydroxide give (2-hydroxyimino) acetic acids **22**

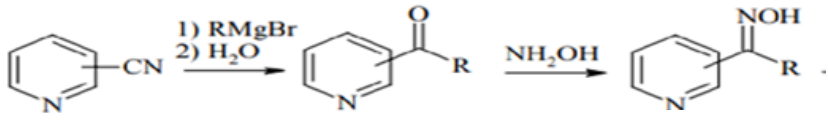
Thiophene and furan containing oximes **23** can be transformed to corresponding O-ethers **24** in two phase system R_3Y/solid K, CO, / 18-crown-6/benzene at room temperature (**scheme 6**). Similar PTC system was used also for the O-acylation of furan and thiophene ketoximes (Abele, E 2003).



23 **24**

3.3. Pyridine oximes

The classical method for the synthesis of pyridine oximes is based on the reaction of the aldehyde or ketone with hydroxylamine in methanol or with hydroxylamine hydrochloride in ethanol, isopropyl alcohol, pyridine, NaOH/EtOH/H_2O, Na_2CO_3/EtOH/H_2O, NaOMe/MeOH, $NaHCO_3$/MeOH, NaOAc/MeOH, NaOAc/H_2O, or Na/EtOH By a modification of these methods it is possible to obtain the pyridine ketoximes from the corresponding nitriles. Thus, the reaction of the nitrile **25** with Grignard reagents (RMgBr) **(scheme 6)** followed by reaction with $NH_2OH{\cdot}HCl$ leads to the formation of the oximes **26**. The pyridine oxime was obtained by a five-stage synthesis from the bipyridyl derivative. The reactions of pyridine nitriles **27** in the H_2/Pd−C/HCl/H_2O/$NH_3OH{\cdot}HSO_4$ system also lead to pyridine aldoximes **28 (scheme 7)** (Abele, E 2003).



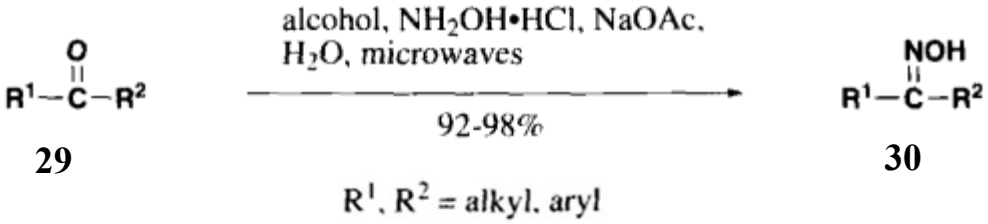
25 **Scheme 6** **26**

27 **Scheme 7** **28**

4. Synthesis of Oximes

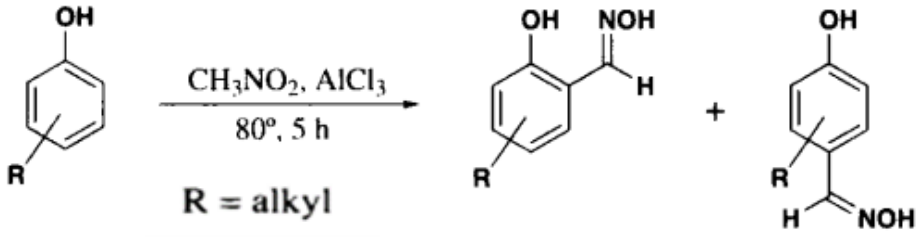
4.1 Synthesis of Aldoximes and Ketoximes

Aldoximes and ketoximes usually are obtained by oximation reaction of corresponding carbonyl compounds with hydroxylamine salts in the presence of a base in alcohols. The reaction of carbonyl compounds with hydroxylamine hydrochloride is accelerated by using of phase transfer catalyst such as polyethylene glycol-600 or alkyl phenol (nonylphenol or dodecylphenol). Formation of oximes **29** is dramatically enhanced by microwave heating. For example, ketones **30** are easily oximate by $NH_2OH.HCl$ in the presence of sodium acetate in alcohol/water medium under microwave irradiation. **(Scheme 8)**



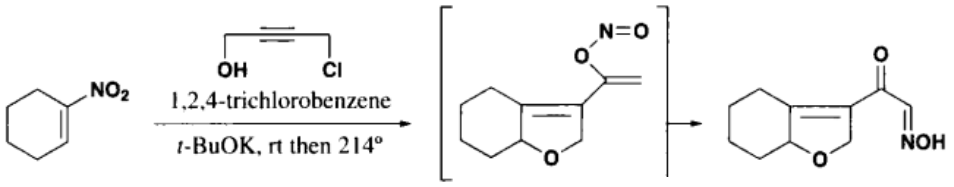
29 **30**

Mild synthesis of phenolic oximes **32** and/or **33** has been performed by heating of suitable phenol **31** with $AlCl_3$ in nitro methane. The ortho-oxime **32** is produced as a single E-isomer whereas the para-oxime **33** is obtained as a mixture of *E* and *Z* isomers. **(Scheme 9)**



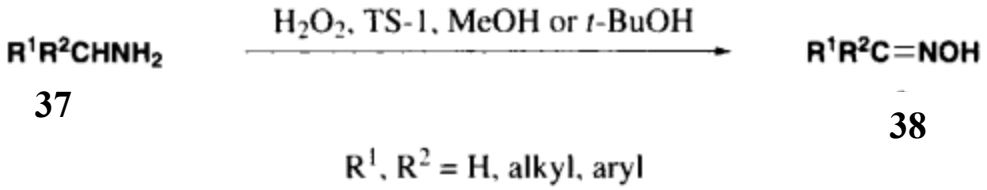
31 **32** **33**

Cyclic nitroalkene **34** in the presence of chlorobutynol and *t*-BuOK afforded dihydrofuran derived keto oxime **36**. The formation of **36** proceeds via novel [1,3]-sigma tropic rearrangement of intermediate vinyl nitrite **35. (Scheme 10)**



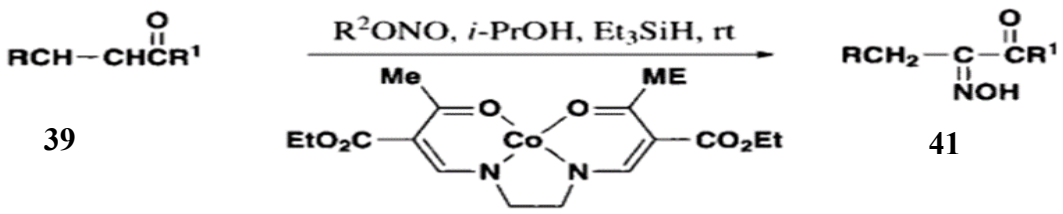
34 **35** **36**

Primary amines **37** with a-hydrogens are oxidized with hydrogen peroxide in the presence of catalytic quantities of titanium silicate molecular sieves (TS-1) to give corresponding oximes **38** as main products. The latter formed with good substrate selectivity (up to 88%) and peroxide efficiency (Abele and lukevics 2000). **(Scheme 11)**



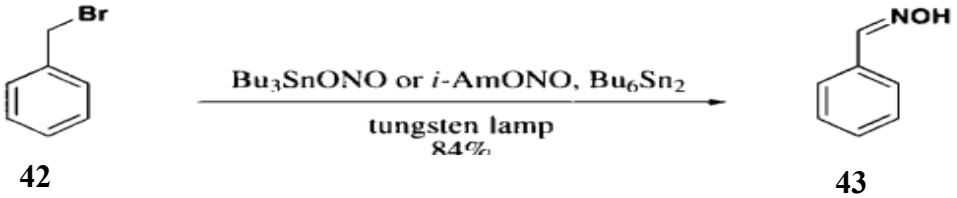
37 **38**

Oximes are successfully prepared by nitrosation of various activated C-H bonds. Thus, α-ketoximes **40** are prepared by reaction of alkenes **39** with nitrites in the presence of Et, SiH and cobalt complex catalyst. (Abele and lukevics 2000). **(Scheme 12)**



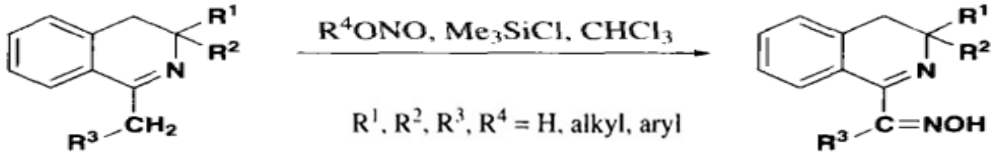
39 **41**

Exposure of benzyl bromide **42**, isoamyl nitrite and hexabutylidin under a tungsten lamp for 5 h afforded 84% of Benz aldoxime **43**. The formation of product occurs via radical process. (Saikia, L 2011). **(Scheme 13)**



42 **43**

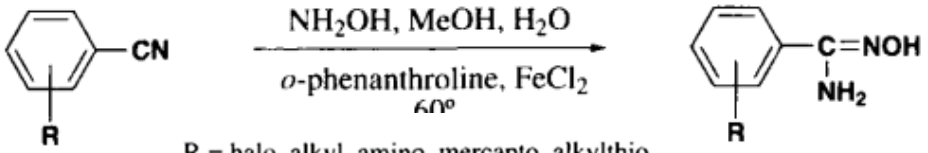
A novel synthesis of imino oximes from Schiff bases via nitrosation. 1-Alkyl-3,4-dihydroisoquinolines **44** in the presence of reagent Me_3SiCl/alkyl nitrite in chloroform afforded imino oximes **45** in yields up to 98%. The process of synthesis of 3,4- dihydroquinolines **45** probably includes N-nitrosation prior to subsequent NO migration to carbon. (Saikia, L 2011). **(Scheme 14)**



44 **45**

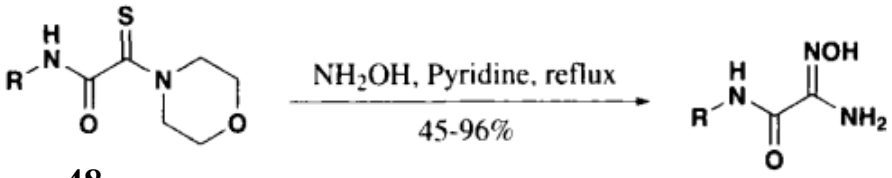
4.2 Synthesis of amidoxime derivatives

Amidoximes are of interest as intermediates in the preparation of pesticides and drugs. Chemistry of amidoximes and related compounds is reviewed by Eloy and Leaners. Some modification of classical method of synthesis of amidoximes from nitriles is described in patent. Thus, benzonitriles **46** in the presence of hydroxylamine solution and chelating agent (*0*-phenanthroline and ferrous chloride) in a mixture of water and methanol at 60° afford corresponding amidoximes **47** in good yields. (Saikia, L 2011). **(Scheme 15**)



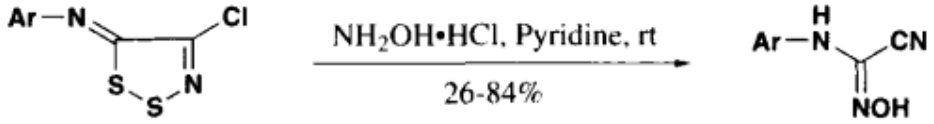
46 **47**

A convenient method of carbamoyl amidoxime **48** syntheses by the reaction of *N, S*-substituted mono thiooxamides **49** with hydroxylamine in pyridine is presented. (**Scheme 16)**



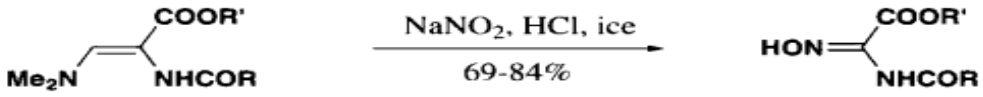
48 **49**

The reaction of 5-arylimino-4-chloro-5H- 1,2,3-dithiazoles **50** with hydroxylamine hydrochloride in pyridine at room temperature gave N-arylcyanoformamidoximes **51** in yields up to 84%. (**Scheme 17**)



50 **51**

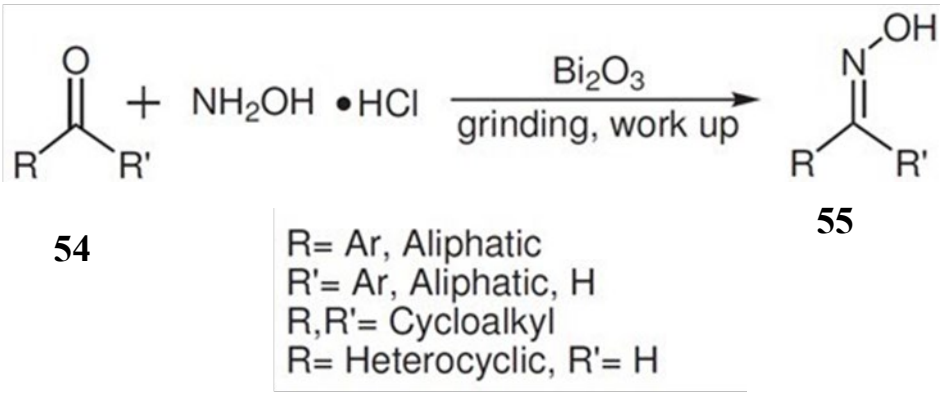
Treatment of 2-(substituted cinnamoyl amino)-3-dimethylaminopropenoates **52** with sodium nitrite in aqueous hydrochloric acid at 0 produced alkyl N-cinnamoyl oxalic acid hydroxyimide amides **53** in good yields (Abele, E. and Lukevics, 2000). **(Scheme 18)**



52 **53**

R = aryl, R' = alkyl

Bismuth compounds are very useful as they are cheap in general, commercially available, air stable crystalline solids, safe, and non-toxic, hence easy to handle. Classically, oximes **55** are prepared by refluxing an alcoholic solution of a carbonyl compound aldehyde or ketone **54** with hydroxylamine hydrochloride. The method has multiple drawbacks such as low yields, long reaction time, toxicity of pyridine, and effluent pollution caused by the use of organic solvent. In recent times, solvent free reactions have drawn considerable attention and popularity, not only from an environmental point of view, but also for synthetic advantages in terms of yield, selectivity and simplicity of the reaction procedure. Since chemical industry deals with larger quantity of materials, these factors are particularly very important therein. be efficient (Saikia, L 2011).



Scheme 19 In the present solvent-free method, the effectiveness of Bi_2O_3 in oxime synthesis under grinding condition is demonstrated using a broad spectrum of aldehydes and ketones with hydroxylamine hydrochloride in the absence of a base or any other additives.

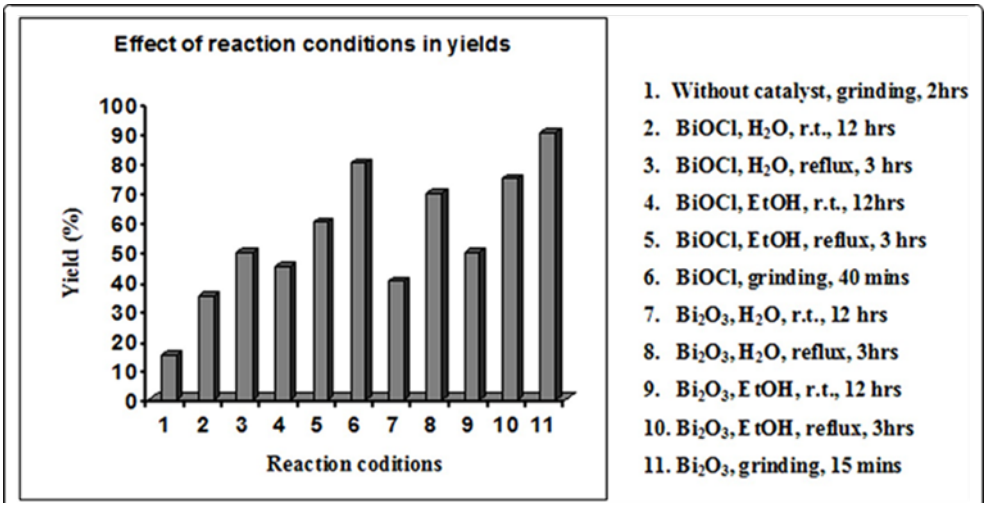
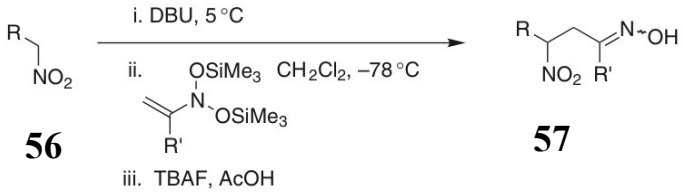


Figure 2 effect of reaction conditions in yields

4.3 Synthesis of oximes from noncarbonyl compounds

Reduction of nitro compounds has been the major route for synthesis of oximes other than from carbonyl compounds. Reduction of secondary nitronates **56** with hexadimethyldisilane gives oximes **57** in 40–73% yields. Cross-coupling of N, N-bis(silyloxy)enamines with primary or secondary nitronates yields nitrooximes (scheme 21, Table 4) For secondary nitronates the reaction must be carried out in diethyl ether at 0C to avoid side reactions. (Robertson, G.M., 1996).



56 **57**

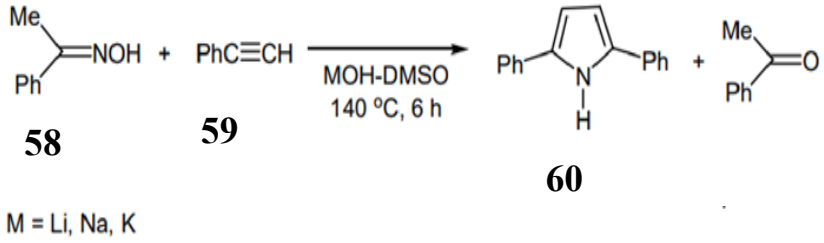
R	*R′*	*Yield* (%)
Et	Me	78
H	Me	64
CO_2Me	Me	64
CH_2CO_2Me	H	88
CO_2Me	$(CH_2)_2CO_2Me$	78

Scheme 20, Table 3 Yields of -nitro oximes from the cross-coupling of N, N bis(silyloxy)enamines with nitronates.

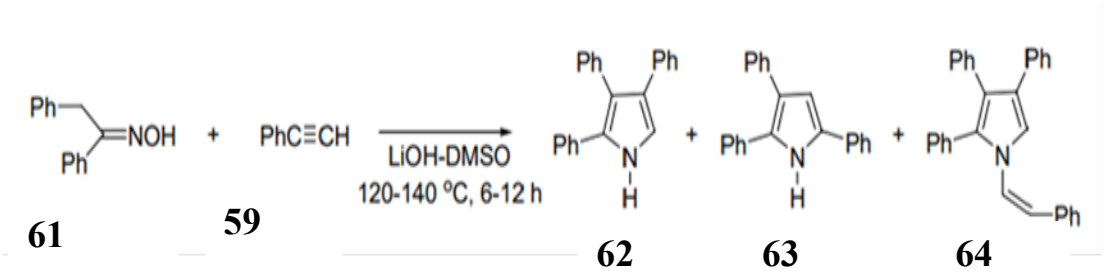
5. Reactions

5.1. Reaction with 1,3-diketones

the reaction of 1,3-diketones with different nitrogen-containing compounds (ammonium acetate, aromatic imines, oximes) followed by cyclization of the intermediates formed. The reaction of ketoximes **58** with phenylacetylene **59** (the Trofimov reaction) in the superbase systems MOH-DMSO, where M = Li, Na, K, makes it possible to prepare a wide series of substituted pyrroles **60** in one preparative step. (Hyun, H. and Trofimov 2009) (**Scheme 21**)



Under analogous conditions (LiOH-DMSO, 140 oC, 6 h), the reaction of benzylphenylketoxime **61** with acetylene **59** delivers (2,3,4-triphenyl- **62**, 2,3,5-triphenyl-1Hpyrroles **63** and 2,3,4-triphenyl-1-[(Z)-2-phenylethenyl]-1H-pyrrole **64**. (Hyun, H. and Trofimov 2009) (**scheme 22**)



Scheme 21,22: reactions of oximes with deferent reaction condition.

5.2. Oximes with different compounds

Oximes are successfully transformed into amines, 1,2-aminoalcohols, α- and βamino acids, hydroxylamines, nitriles, pyridines, benzofuranes, indoles, pyrroles, pyrazines, isoquinolines, isoxazolesm, 8-hydroxytetrahydroquinolines, aminocyclopentitols, aziridines, fluorenones, diarylmethylidenefluorene and phenanthrene. (Mirjafary, Z 2016)

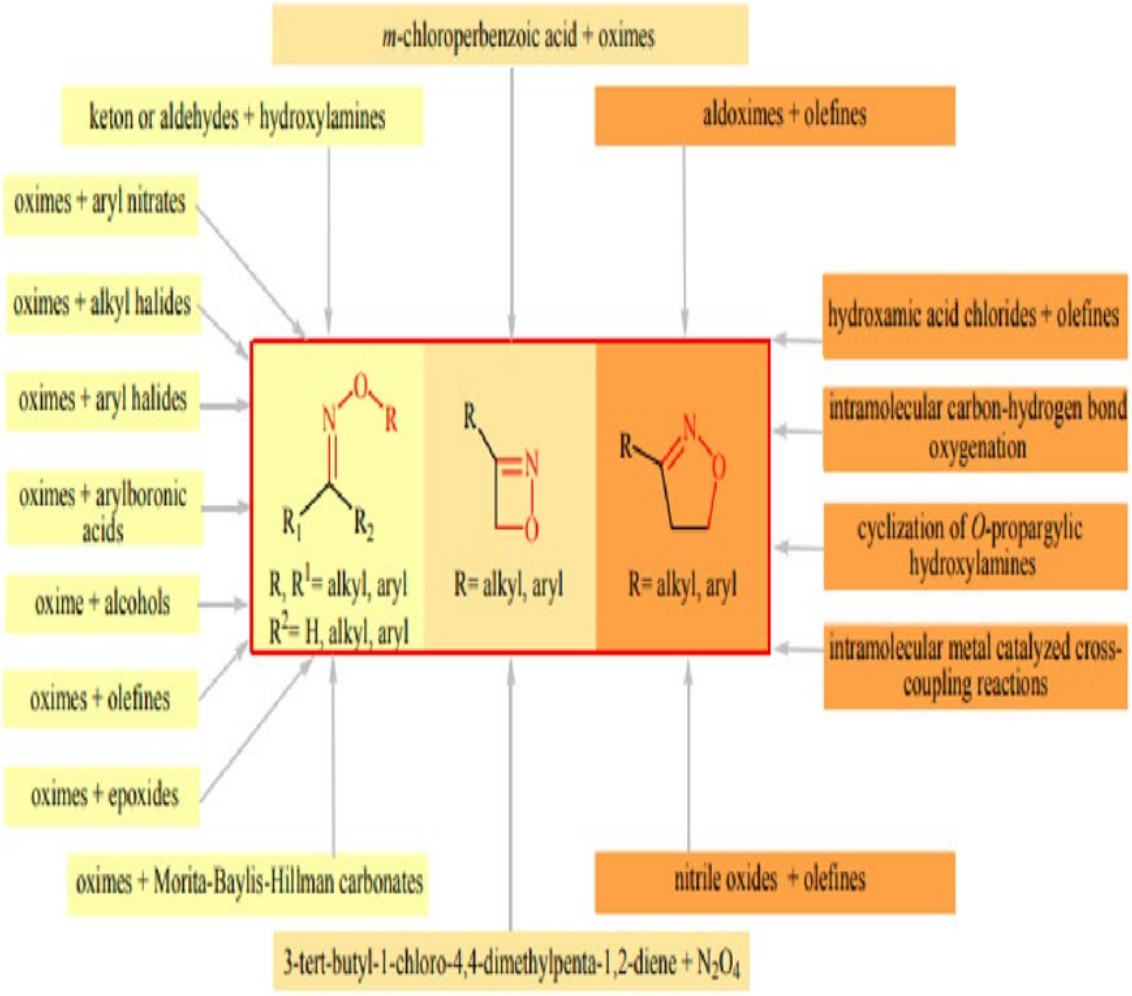
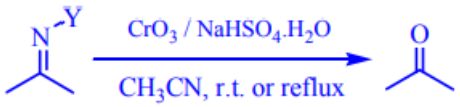


Figure 3. The main methods for synthesis of acyclic and cyclic oxime ethers

5.3. Oxidative cleavage of oximes

5.3.1. using NaHSO4.H2O - supported CrO3

their deoximation provides an alternative pathway to the aldehydes and ketones **Table 5** summarizes the results of the conversion of various oximes, to their corresponding aldehydes and ketones using $NaHSO_4.H_2O$ - supported CrO_3 is used for the efficient oxidative cleavage of oximes cleavage of carbon-nitrogen double bonds to their corresponding carbonyl compounds under mild and completely heterogeneous reaction conditions with good to high yields (**scheme23**) (Shirini, F 2007)



Scheme 23 oxidative cleavage of oxime to ketone

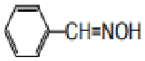
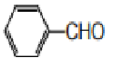
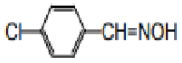
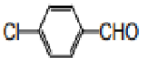
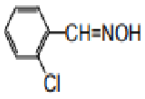
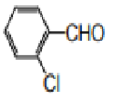
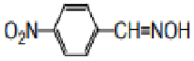
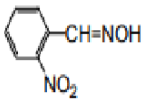
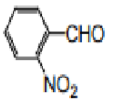
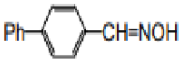
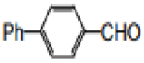
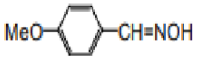
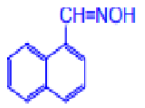
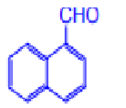
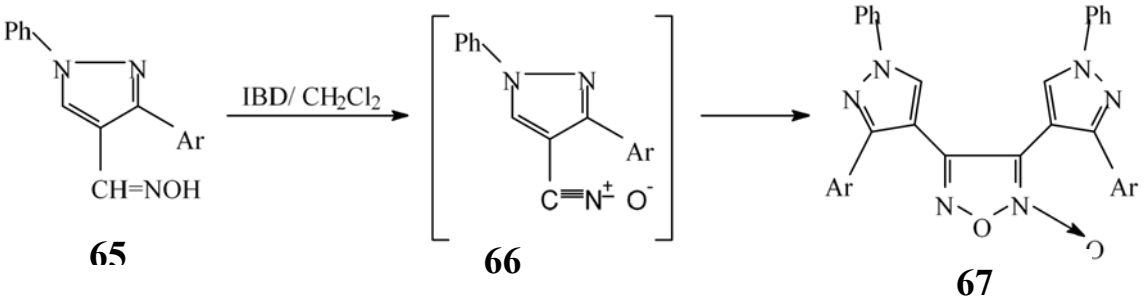
Entry	Substrate	Product	Time (min)	Yield % [b]
1			4	85
2			6	82
3			12	85
4			4	90
5			3	82
6			2	85
7			8	80
8			2	85

Table 4 summarizes the results of the conversion of various oximes, to their corresponding aldehydes and ketones

5.3.2. Using iodine reagents

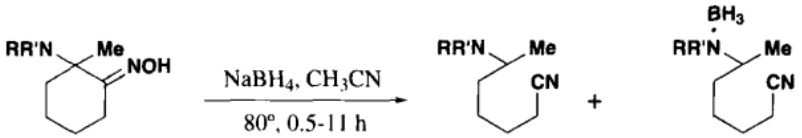
one area of recent interest is the oxidative studies of 'N' containing compounds such as oximes. While ketoximes undergo efficient oxidative cleavage to the parent ketone and acids/esters, mediated reactions of aldoximes offer an easy method for the formation of aromatic nitrile oxides which are valuable intermediates in organic synthesis. the reaction of aromatic aldoximes with oxidizing agents, namely lead tetraacetate, alkali hypohalite, N-bromo succinimide in DMF, etc., it was anticipated that oxidation of the pyrazolyl aldoximes **65** might afford either nitrile oxides **66** or their dimer oxadiazole-N-oxides **67**. (Prakash, O 2007)



Scheme 24 oxime was treated with IBD in dichloromethane at room temperature.

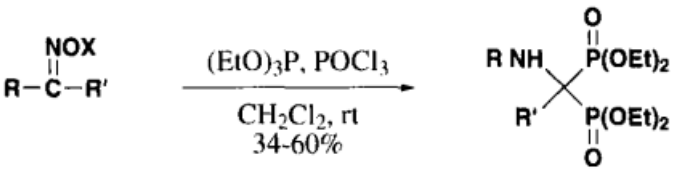
5.4. Beckmann rearrangement of Oximes

Beckmann rearrangement as one of more characteristic reactions of oximes has been used extensively in organic synthesis due to the simplicity of synthesis of different compounds with nitrogen insertion into carbon chain. The Beckmann rearrangement of ketoximes to corresponding amides usually is catalyzed by acids or Lewis's acids. Rearrangement of oximes to amides can be also successfully carried out in the presence of 2-chloro-l,3-dimethylimidazolium chloride', N-Bromo succinimide"', tetrabutylammonium perrhenate/trifluoromethanesulfonic acid', beta zeolites, montmorillonite KSF and K-10 montmorillonite/microwave irradiation1". Unusual reductive Beckmann rearrangement is presented by Petukhov and Tkachev'. Thus, treatment of a-amino oximes **68** with NaBH, in boiling acetonitrile results in Beckmann synchronous fragmentation and formation of o-amino nitriles **69** and corresponding borane-amine complexes **70** in yields up to 87%. (**Scheme 25)**



68 **69** **70**

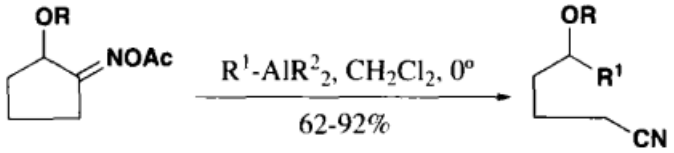
Beckmann rearrangement of oxime derivatives **71** in the presence of P-nucleophiles afforded the corresponding amino methylene gem-diphosphines **72** in moderate yields. (Abele, E. and Lukevics 2000). (**Scheme 26)**



71 **72**

X = H, Ms; R, R' = alkyl, aryl

The reaction of a-alkoxy cycloalkanone oxime acetates **73** with organoaluminium reagents caused Beckmann fragmentation and subsequent carbon-carbon bond formation to give o-cyano-a-alkyl ethers **74** in high yields. (Abele, E. and Lukevics 2000). (**Scheme 27)**

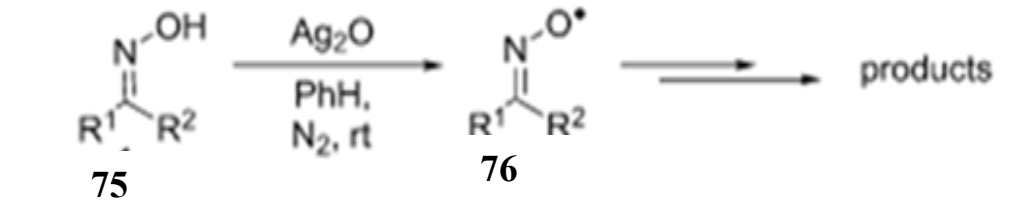


73 **74**

R, R^1, R^2 = alkyl

5.5. Radicals

Iminoxyl radicals were first discovered in 1964 by EPR spectroscopy as short living intermediates formed from the oximes of both aromatic and aliphatic ketones and aldehydes, as well as from the oximes of quinones under the action of a strong single electron oxidant, cerium (IV) ammonium nitrate, in methanol. To record EPR spectra, a flow system was used, which allowed observation of radicals with lifetimes of about 2−10 s. The EPR spectra of iminoxyl radicals are characterized by large values of the hyperfine splitting constants The establishing of the self-decay pathways of iminoxyl radicals is complicated by the formation of a large number of products, some of the initially formed products are not stable. Moreover, participation of the oxidizing agent not only in the radical generation, but also in its decay also possible. The products formed during the decomposition of iminoxyl radicals **75** generated from oximes **76** under the action of Ag_2O(Krylov,2020)**. (Scheme 28).**



75 **76**

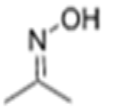
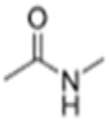
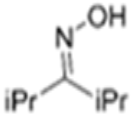
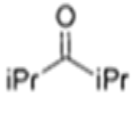
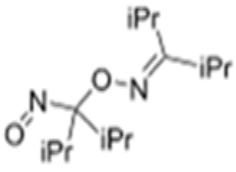
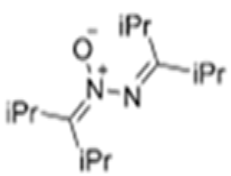
oxime	identified decomposition products
 **1a**	 **3a**, 20%  traces + N_2O, N_2
 **1b**	 **3b**, 2–5%  **4b** up to 75%  **5b**, ca. 20% + N_2O, N_2

Table 5 The products of decomposition of iminoxyl radicals generated from oximes by oxidation with Ag_2O

CONCLUSIONS

The present data indicate that oximes, though strongly hydrophilic, can enter the central nervous system, but that the concentrations reached in the brain are only about 4-10% of the plasma level. Best blood-brain barrier penetration is observed for pralidoxime. It is likely that passage through the blood-brain barrier is at least partly carrier-mediated, possibly by one of the amino acid carriers. Experimental data indicate that oximes can effectively antagonize some of the biological effects elicited by organophosphate intoxication in the central nervous system. However, this effect is unlikely to be sufficient as to protect against organophosphate-induced lethality.

References

Abele, E., Abele, R. and Lukevics, E., 2003. Pyridine oximes: Synthesis, reactions, and biological activity. *Chemistry of heterocyclic compounds*, 39, pp.825-865.

Abele, E. and Lukevics, E., 2001. Furan and Thiophene Oximes: Synthesis, Reactions, and Biological Activity. *Chemistry of Heterocyclic Compounds*, 37, pp.141-169.

Abele, E. and Lukevics, E., 2000. Recent advances in the chemistry of oximes. *Organic Preparations and Procedures International*, *32*(3), pp.235-264.

Byju Raveendran and Divya Gokulnath 2011 byjus.com/chemistry/oximes/ (accessed 17 Feb 2023)

Dawson, R.M., 1994. Review of oximes available for treatment of nerve agent poisoning. *Journal of applied toxicology,* 14(5), pp.317331.

Damljanović, I., Vukićević, M. and Vukićević, R.D., 2006. A simple synthesis of oximes. *Monatshefte für Chemie/Chemical Monthly*, 137, pp.301-305.

Dhuguru, J., Zviagin, E. and Skouta, R., 2022. FDA-approved oximes and their significance in medicinal chemistry. *Pharmaceuticals*, 15(1), p.66.

Hyun, H. and Trofimov, B.A., 2009**.** Reaction of acetophenone and benzylphenylketone oximes with phenylacetylene: a route to di-and triphenylpyrroles. *Arkivoc*, 4, pp.14-20.

Kukushkin, V.Y. and Pombeiro, A.J., 1999. Oxime and oximate metal complexes: unconventional synthesis and reactivity. *Coordination Chemistry Reviews*, 181(1), pp.147-175.

Kotali, A. and Papageorgiou, V.P., 1991. The chemistry of 1, 3-dioximes. A brief review. *Organic Preparations and Procedures International*, *23*(5), pp.593-610.

Krylov, I.B., Paveliev, S.A., Budnikov, A.S. and Terent'ev, A.O**.,** 2020. Oxime radicals: generation, properties and application in organic synthesis. *Beilstein Journal of Organic Chemistry*, 16(1), pp.12341276.

Karapinar, E., Karabulut, O. and Karapinar, N., 2013. Thermal, Electrical, and Optical Properties of Synthesized (1E, 2E)-(4bromophenyl)(hydroxyimino) acetaldehyde Oxime Complexes. *Journal of Chemistry,* 2013.

Mikhaleva, A.I., Zaitsev, A.B. and Trofimov, B.A., 2006. Oximes as reagents. *Russian chemical reviews*, 75(9), p.797.

Mirjafary, Z., Abdoli, M., Saeidian, H., Kakanejadifard, A. and Farnia, S.M.F., 2016. Review of the synthesis of acyclic and cyclic oxime ethers. *RSC advances*, 6(21), pp.17740-17758.

Narasaka, K. and Kitamura, M., 2005. Amination with oximes. *European journal of organic chemistry,* 2005*(*21), pp.4505-4519.

Naik, P.N., Alkobati, N.A. and Kusurkar, R.S., 2015. Beckmann rearrangement for the synthesis of derivatives of β-and γ-carbolinones, dihydropyrrolopyridinone and tetrahydroisoquinolinone. *ARKIVOC: Online Journal of Organic Chemistry, 2015.*

Palm, A. and Werbin, H., 1953. The infrared spectra of alpha and beta oximes. *Canadian Journal of Chemistry*, 31(11), pp.1004-1008.

Özyürek, M., Akpınar, D., Bener, M., Türkkan, B., Güçlü, K. and Apak, R., 2014. Novel oxime-based flavanone, naringin-oxime: Synthesis, characterization and screening for antioxidant activity. *ChemicoBiological Interactions*, 212, pp.40-46.

Prakash, O. and Pannu, K., 2007. Hypervalent iodine oxidation of 1phenyl-3-arylpyrazole-4-carboxaldehyde oximes: a facile and efficient synthesis of new 3, 4-bis (1-phenyl-3-arylpyrazolyl)-1, 2, 5-oxadiazoleN-oxides. *Arkivoc*, 13, pp.28-33.

Robertson, G.M., 1996. Imines and Their N-Substituted Derivatives: Oximes and Their O-R Substituted Analogues. *ChemInform*, 27(31), pp.no-no.
Saikia, L., Baruah, J.M. and Thakur, A.J., 2011. A rapid, convenient, solventless green approach for the synthesis of oximes using grindstone chemistry. *Organic and Medicinal Chemistry Letters*, 1(1), pp.1-6.

Singh, R.B., Garg, B.S. and Singh, R.P., 1979. Oximes as spectrophotometric reagents—a review. *Talanta,* 26(6), pp.425-444.
Sahyoun, T., Arrault, A. and Schneider, R., 2019. Amidoximes and oximes: Synthesis, structure, and their key role as NO donors. *Molecules*, 24(13), p.2470.

Vedantu`s founders Vamsi Krishna, Anand Prakash, Pulkit Jain and Saurabh Saxena 2006 www.vedantu.com(acceced 5 oct 2022)
Shirini, F., Mamaghani, M. and Rahmanzadeh, A., 2007. Efficient oxidative cleavage of C= N using chromium trioxide supported on NaHSO4. H2O. *Arkivoc*, 1, pp.34-39.

حکومەتی هەرێمی کوردستان-عیراق
وەزارەتی خوێندنی باڵا و توێژینەوەی زانستی
زانکۆی سەڵاحەدین-هەولێر
کۆلێژی زانست
بەشی کیمیا

کیمیای ئۆکزایمەکان

پرۆژەیەک پێشکەش بەلیژنەی زانستی کراوە لە بەشی کیمیا لە بەشی جێبەجێکراو پێویستی بۆ پلەی زانستی بەکالۆریۆس لە کیمیا

ئامادەکردنی:

شاناز ابراهیم حوێز

بەسەرپەرشتی:

د.کارزان خلیل حمید

رەمەزان ١٤٤٣ نیسان ٢٠٢٣ نەورۆز ٢٧٢٣