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QUINOLINE OXIMES: SYNTHESIS, REACTIONS, AND BIOLOGICAL ACTIVITY. (REVIEW)

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Data on the production and the reactions of quinoline aldoximes and ketoximes and their derivatives are reviewed. The synthesis of new heterocycles based on quinoline oximes is examined separately. The main results from investigation of the biological activity of quinoline oximes are presented.

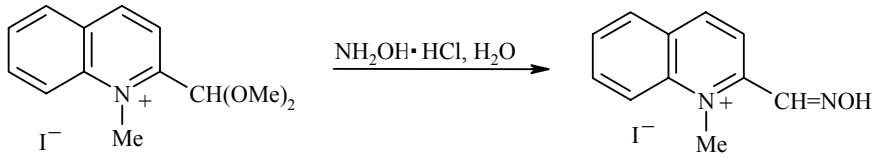
Keywords: oximes, quinoline, biological activity.

Quinoline oximes are widely used as intermediates in organic synthesis. In the present paper the principal methods for the production of quinoline oximes and their reactions are reviewed. Methods for the synthesis of new heterocyclic systems from derivatives of these oximes are considered under a separated heading. The principal methods for investigation of the structure of quinoline oximes with regard to isomerism are also briefly discussed. In the last section the results from investigation of the biological activity of the derivatives of quinoline oximes are described.

1. SYNTHESIS AND STRUCTURE OF QUINOLINE OXIMES

1.1. Synthesis of Quinoline Oximes

The classical method for the synthesis of quinoline oximes is based on the reaction of an aldehyde or ketone with hydroxylamine hydrochloride [1, 2] in the pyridine/ethanol [3, 4], NaOH/EtOH [5], Na_2CO_3 or K_2CO_3/EtOH/H_2O [6, 7], KOH/EtOH [8], KOH/EtOH/H_2O [9], NaOH/H_2O/dioxane [10], or NaOH/EtOH/H_2O [11, 12] systems. A quinoline oxime salt **2** was obtained from the corresponding acetal **1** and hydroxylamine hydrochloride in aqueous hydrochloric acid or sodium carbonate [13].



1 **2**

The reaction of 2-(2-chloro-3-quinolyl)-1-cyano-1-ethoxycarbonylethylene (**3**) with hydroxylamine hydrochloride in ethanol leads to the aldoxime **4** with a yield of 50% [14].

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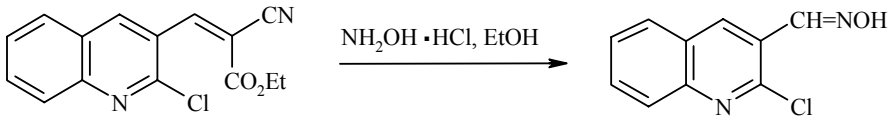
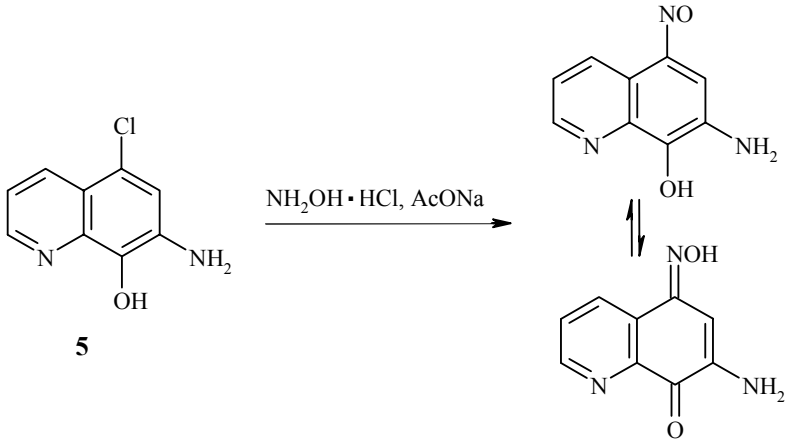


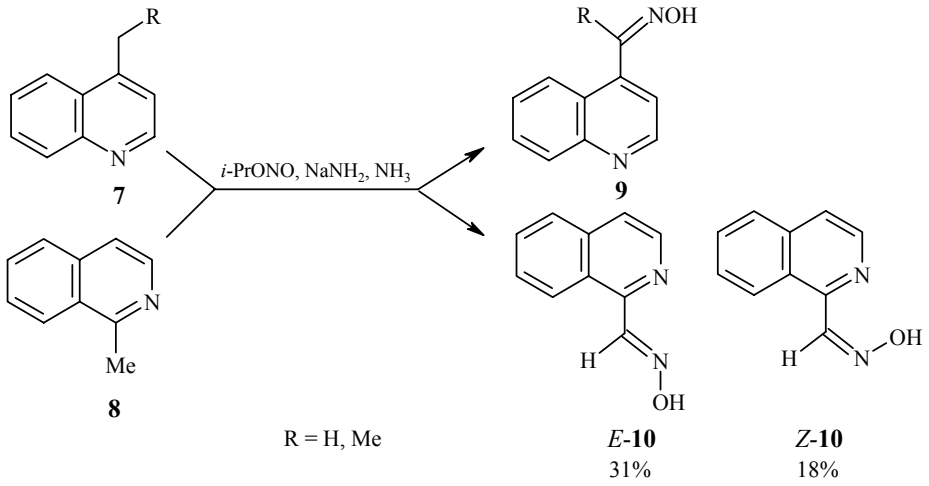
3 **4**

The reaction of 7-amino-5-chloro-8-hydroxyquinoline (**5**) with hydroxylamine hydrochloride in the presence of sodium acetate leads to tautomeric forms of the oxime **6** with a yield of 70% [15].

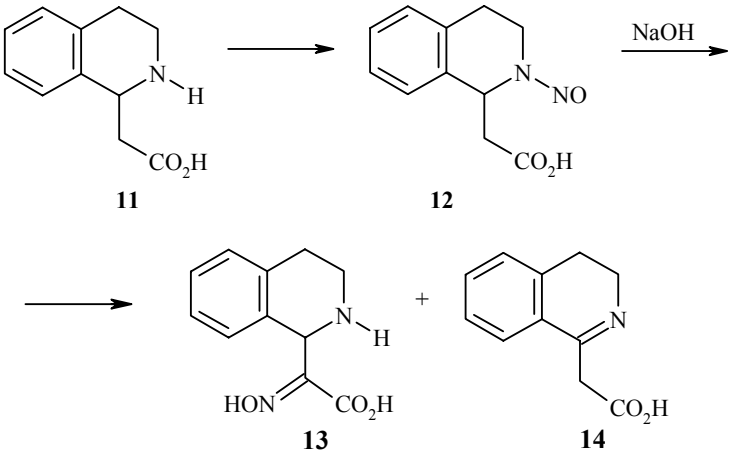


5 **6**

A series of methods for the synthesis of quinoline and isoquinoline oximes are based on nitrosation of the alkyl side chain in the corresponding alkyl derivatives. For example, in the $NaNH_2/NH_3/i$-PrONO system 4-alkylquinolines **7** [16] and 1-methylisoquinoline (**8**) [17] give the oximes **9** or **10** respectively with yields of up to 63%.

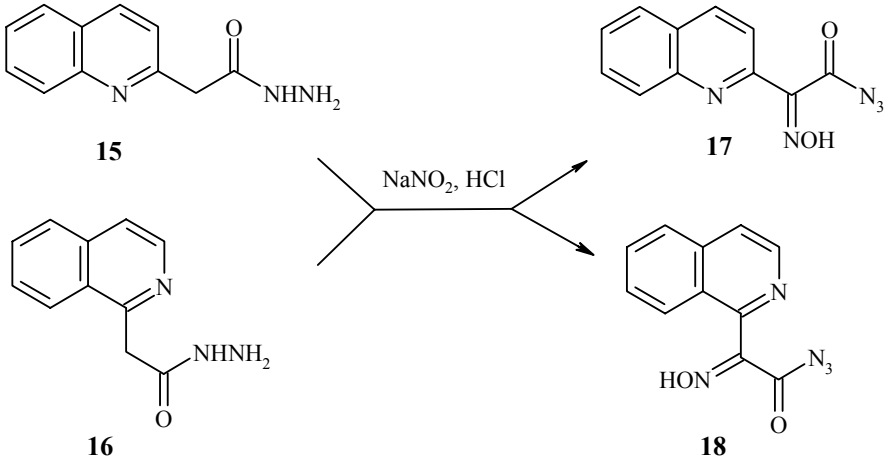


1,2,3,4-Tetrahydroisoquinoline **11** is readily nitrosated by isoamyl nitrite or $NaNO_2$/HCl, forming the N-nitroso derivative **12**, which in aqueous alkali gives a mixture of the oxime **13** (yield 70%) and dihydroisoquinoline **14** (yield 20%) [27].



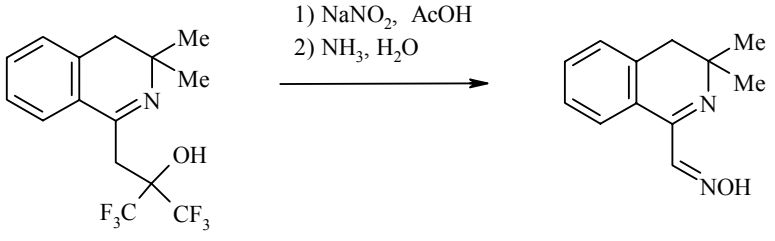
11 **12** **13** **14**

Under the conditions of nitrosation ($NaNO_2/HCl/H_2O$) the acetylhydrazides **15** and **16** give the azide derivatives of oximes **17** and **18** with yields of 92 and 89% respectively [28].



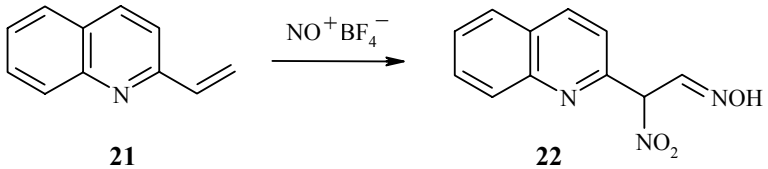
15 **17** **16** **18**

The reaction of 1-(2-hydroxy-2-trifluoromethyl-3,3,3-trifluoropropyl)-3,3-dimethyl-3,4-dihydro-isoquinoline (**19**) with $NaNO_2$/AcOH and then with aqueous ammonia leads to the oxime **20** with a yield of 81% [29].



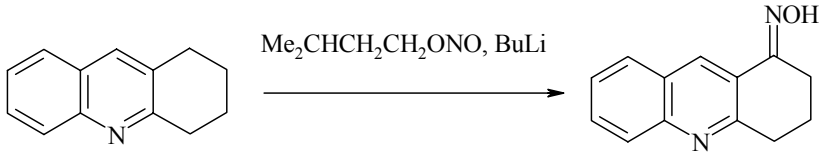
19 **20**

Nitrosonium tetrafluoroborate has been used successfully as nitrosating agent. Thus, the reaction of 2-ethenylquinoline (**21**) with $NO^+BF_4^-$ leads to the formation of α-nitro-2-quinolylacetaldehyde (**22**) as the only product with a yield of 90% [30].



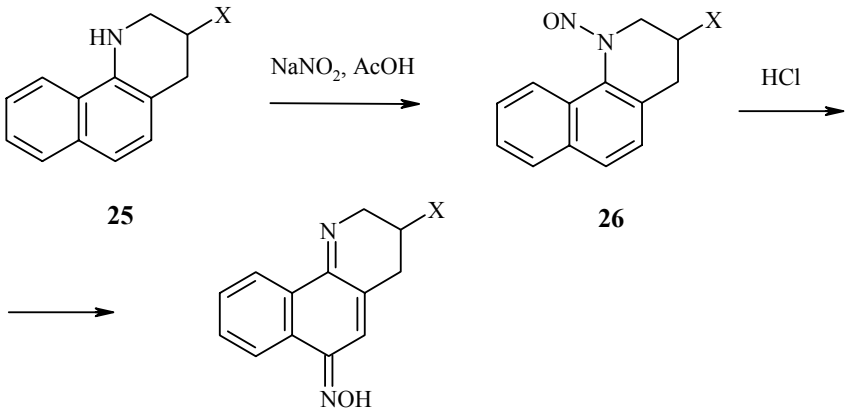
21 **22**

A few methods for the synthesis of quinoline and isoquinoline oximes are based on nitrosation of the ring in the corresponding heterocycle. The oxime of 1,2,3,4-tetrahydroacridine (**23**) was successfully obtained in this way from the corresponding acridine **24** in the isoamyl nitrite/butyllithium/ether system [31].



24 **23**

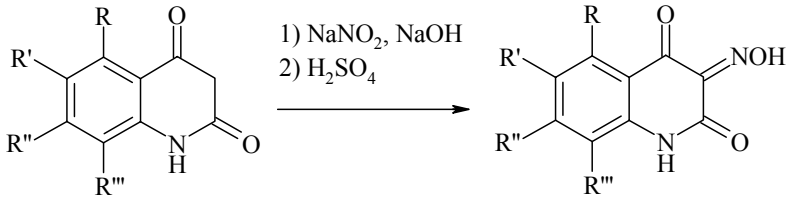
The reaction of 2,3,4,6-tetrahydrobenzo[*h*]quinolines **25** with $NaNO_2$/AcOH leads to the N-nitroso derivatives **26**. Compounds **26** are easily transformed into the corresponding oximes **27** in the presence of HCl [32].



25 **26** **27**

X = Cl, Br, I

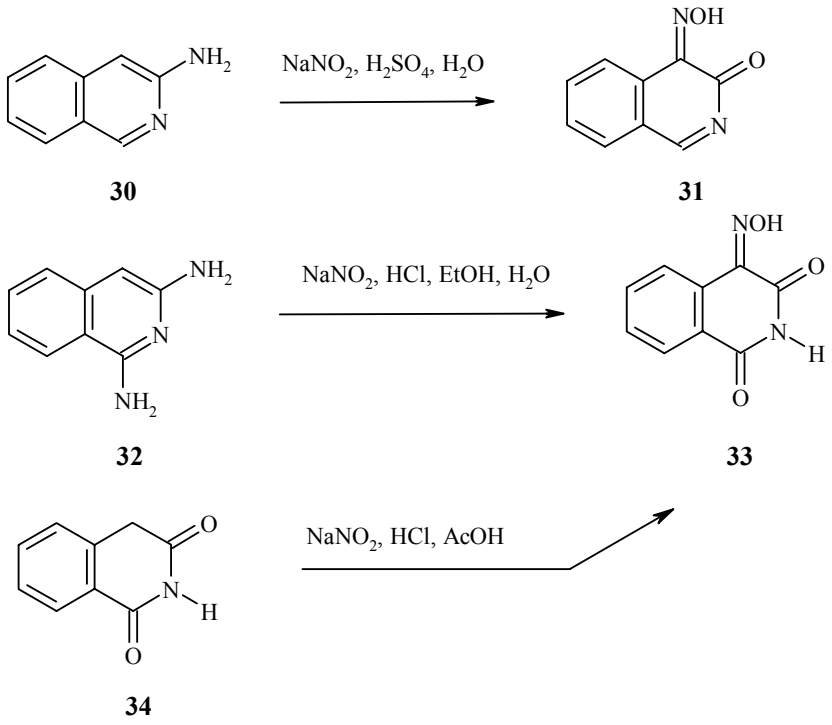
The quinoline-2,4-diones **28** are easily nitrosated in the presence of sodium nitrite [33-35]. The products – 1,2,3,4-tetrahydroquinoline-2,3,4-trione 3-oximes **29** – have been used as bactericides [33], exhibited antiviral activity [34], and were studied as agents that affect central nervous system [35].



28 **29**

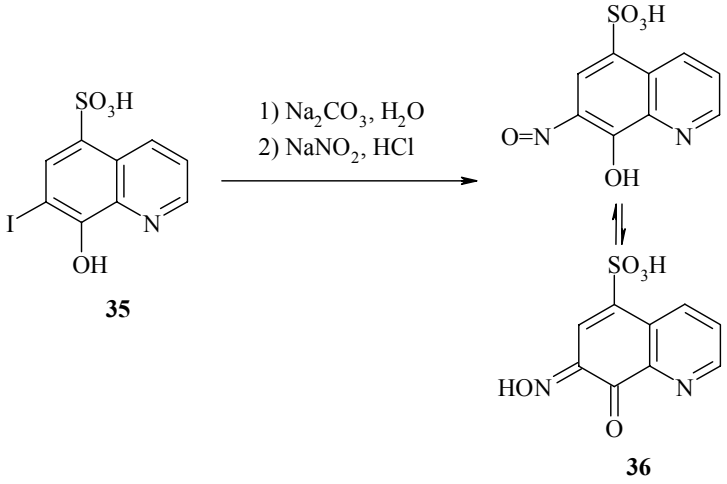
R-R''' = H, Cl, F, Me

3-Aminoisoquinoline (**30**) in the $NaNO_2$/HCl/EtOH/H_2O system gives the oxime **31** with a yield of 88% [36]. The product **31** was used as a fungicide [37]. 1,3-Diaminoisoquinoline (**32**) in the $NaNO_2$/HCl/EtOH/H_2O system gives the oxime **33** with an 86% yield. This oxime was also obtained by nitrosation of isoquinoline-1,3-dione (**34**) [38].



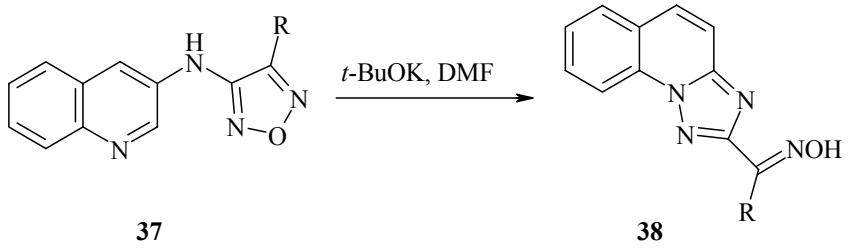
30 **31** **32** **33** **34**

The reaction of 8-hydroxy-7-iodo-5-quinolinesulfonic acid (**35**) with sodium nitrite in the presence of aqueous hydrochloric acid leads to the tautomeric forms of the product **36** [39].



35 **36**

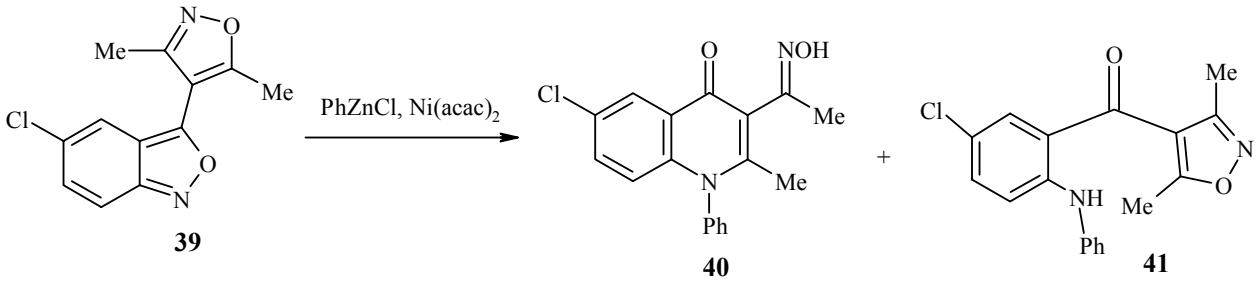
3-(2-Quinolylamino)-1,2,5-oxadiazoles **37** rearrange in the presence of potassium butoxide to the oximes of 2-acyl-1,2,4-triazolo[1,5-*a*]quinolines **38** (yields 66-70%) [40].



37 **38**

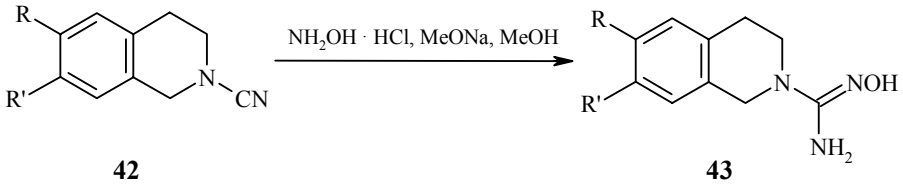
R = Me, Ph

In the PhZnCl/Ni(acac)$_2$/THF system the isoxazole derivative **39** gives a mixture of the oxime **40** (41%) and the aniline derivative **41** (49%) [41].



39 **40** **41**

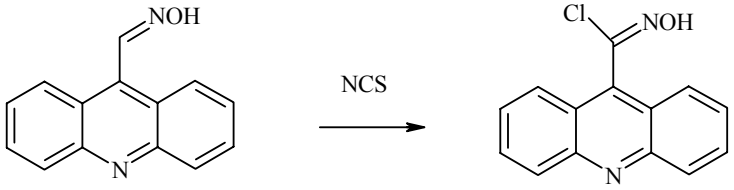
Quinoline aldoximes have been known for more than a hundred years [42]. They were usually obtained by the reaction of pyridine nitriles with hydroxylamine hydrochloride in the Na_2CO_3/DMF [43], Na_2CO_3/H_2O/pyridine [44], or Na/MeOH [45, 46] systems. In the $NH_2OH{\cdot}HCl$/MeONa/MeOH system the N-cyano derivatives of quinolines (e.g., 3,4-dihydro-2-(1H)-isoquinolinecarbonitrile **42**) are also transformed into the corresponding amidoximes **43** [47].



42 **43**

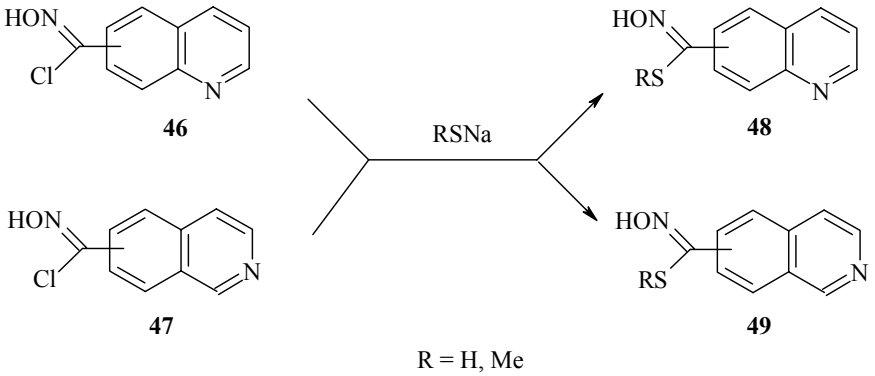
R = H, OH, OMe

The hydroximoyl chloride of acridine **44** is readily formed from the aldoxime **45** in dimethylformamide in the presence of N-chlorosuccinimide (NCS) [12].



45 **44**

In reaction with the salts of thiols [48] the hydroximoyl chlorides **46** and **47** are easily transformed into the corresponding sulfide derivatives of oximes **48** and **49**.



1.2. The Structure of Quinoline Oximes

One of the most reliable methods of determining the structure of quinoline oximes is NMR spectroscopy. The ^{1}H NMR spectra of the monoximes of 3,3-dialkyl-3,4-dihydro-1-isoquinolyl aryl ketones and diketones [26], the ^{1}H NMR spectra of 3-hydroxyiminoquinolin-2-ones [49], and the ^{15}N NMR spectrum of quinoline amidoxime [50] were investigated in greater detail.

It should be mentioned that quinoline 2-aldoxime is used in the spectrophotometric determination of palladium [51]. Quinoline oximes also form complexes with Co(II) [52-55], Ni(II) [48, 52, 53, 55], Fe(II) [54], Cu(II) [48, 54, 55], Mn(II) [54, 55], Al(III) [55], Cd(II) [55], Hg(II) [55], Pb(II) [55], V(IV) [55], U(VI) [55], and Zn(II) [55].

The structure of the quinoline oximes is also supported by data from investigations into the kinetics of the formation of quinoline 2-aldoxime [56] and the hydrolysis of methylquinoline ketoximes in sulfuric acid [57].

The structure of 3-(1-hydroxyiminoethyl)-4-hydroxyquinolin-2(1H)-one [49] and 2-(3,3-dimethyl-3,4-dihydro-1-isoquinolyl)-2-(hydroxyimino)acetamide [58] was recently investigated by X-ray crystallographic analysis.

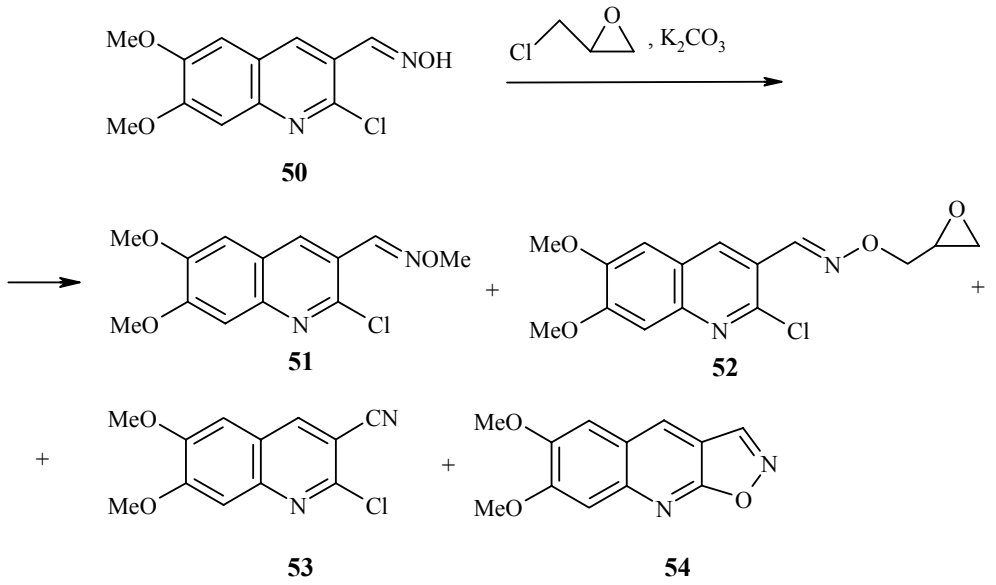
UV [59, 60] and IR [61] methods and also mass spectroscopy [36, 62] were used to study the structure of quinoline oximes. In addition, the effects of the solvent and the substituents on the shifts in the electronic spectra of quinoline oximes containing an azo group were investigated [63].

2. REACTIONS OF QUINOLINE OXIMES

2.1. Synthesis of Ethers of Quinoline Oximes

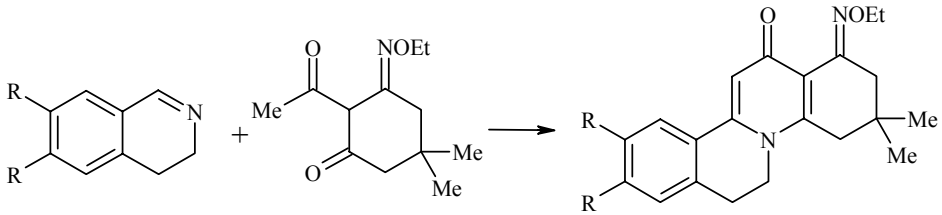
Many of the methods of O-ethers for the synthesis of quinoline oximes are based on reaction of the O-alkyl derivatives of hydroxylamines (or their hydrochlorides) with carbonyl derivatives in methanol [64], ethanol [65], or DMSO [66].

In addition, reactions of the respective oximes with alkyl halides in the NaH/DMF [67, 68] or K_2CO_3/PEG-1000/MeCOMe [68] systems have also been widely used. However, the reaction of the quinoline oxime **50** with epichlorohydrin in the K_2CO_3/MeOH system leads to a mixture of the ethers **51** (10%) and **52** (20%), the nitrile **53** (30%), and the isoxazole **54** (5%) [69].



50 **51** **52** **53** **54**

The [2+4] cyclocondensation of 3,4-dihydroisoquinolines **55** with 2-acetyl-3-ethoxyimino-5,5-dimethyl-cyclohexanone **56** gives the oxime ethers **57** with yields of 71-74% [70].



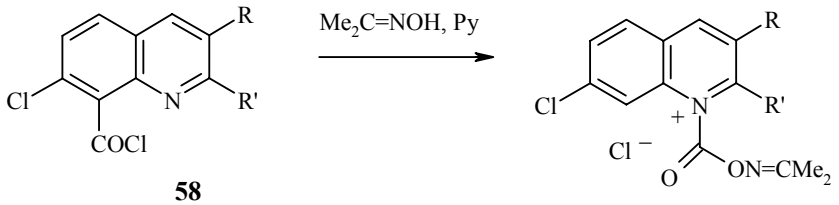
55 **56** **57**

R = H, OMe

The O-benzyl derivatives of quinoline oximes were obtained by acylation of the oximes with benzoyl chloride in the presence of pyridine [32].

The O-carbamoyloximes of 2,3-dihydro-4-quinolinones were successfully obtained from the oximes and phenyl isocyanate in benzene [71].

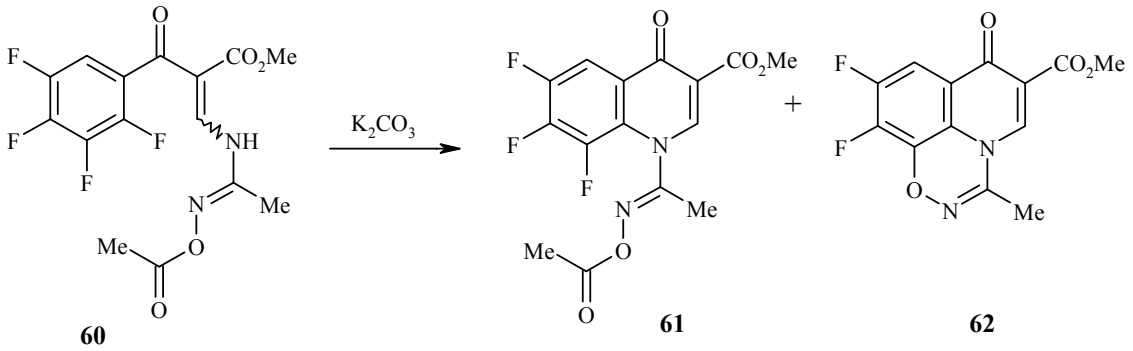
It is interesting that the reaction of 3,7-dichloro-8-quinolylcarbonyl chlorides **58** with acetone oxime in pyridine gives the products from migration of the ester group **59** [72].



58

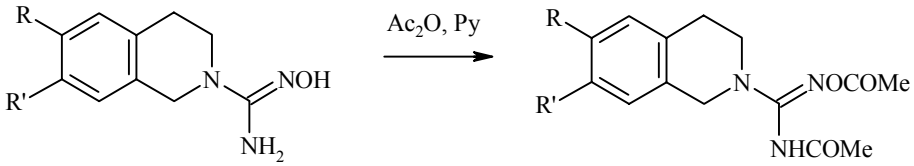
R = H, Alk, Cl; R' = H, Me **59**

Cyclization of ethyl 3-[(1-acetoxyiminoethyl)amino]-2-(2,3,4,5-tetrafluorobenzoyl)-2-propionate **60** in the presence of potassium carbonate leads to a mixture of the acylated oxime **61** (14%) and the tricyclic derivative of oxadiazine **62** (22%) [73].



60 **61** **62**

The acylation of the amidoximes of 2,4-dihydro-2(1H)-isoquinoline acids **43** with acetic anhydride in pyridine takes place in an interesting way; the diacylated products **63** were isolated as a result of the reaction [47].

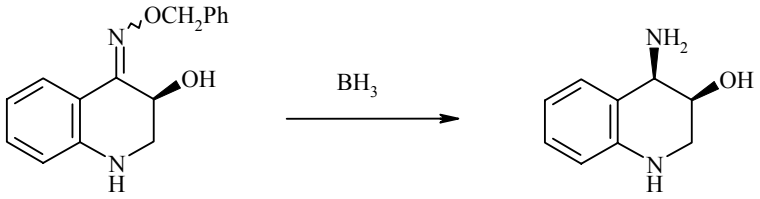


43 **63**

2.2. Reactions of Quinoline Oxime Groups and Rings

The dehydration of oximes was described comprehensively in the review [74]. In addition, quinoline aldoximes are easily transformed into the corresponding nitriles in the presence of acetic anhydride [75-79] phosphorus oxychloride [17, 25], montmorillonite KSF and silica gel [80], and montmorillonites K-10 or KSF with microwave treatment [81]. 9-Cyanoacridine was successfully obtained from the corresponding aldoxime in boiling water or in the presence of formalin [82].

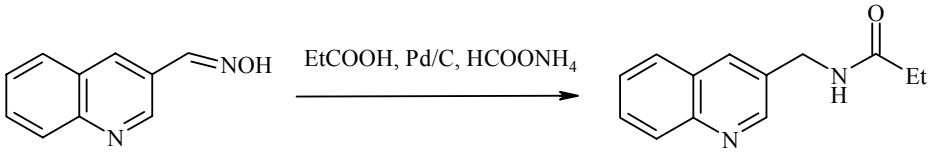
Quinoline aldoximes and ketoximes were reduced to the corresponding derivatives of primary quinoline amines in the H_2/Raney nickel/ethanol [24], Pd/ammonium formate [83], Na/EtOH [84], $Zn/NH_3/H_2O$ [31], ZnO/AcOH [85], or $LiAlH_4/Et_2O$ systems. Stereoselective reduction of the oxime ether **64** with borane gave the *cis*-1,2-amino alcohol **65** [87].



64 **65**

It should also be noted that reduction of the methyl ethers of quinoline ketoximes in the presence of Raney nickel gives the corresponding imines [88].

Reductive acylation of 3-quinolylaldoxime (**66**) in the $HCOONH_4$/10% Pd/C/EtCOOH system leads to formation of the amide **67** with a yield of 67% [89].

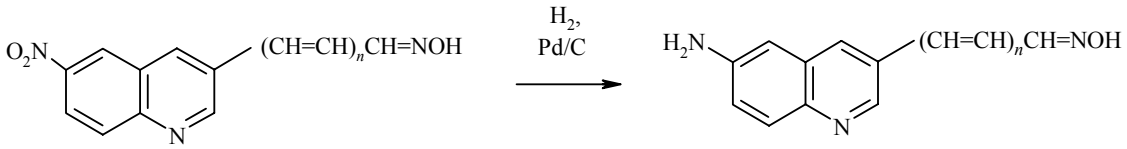


66 **67**

In the reaction of the O-(methylsulfonyl)oximes of 2,3-dihydro-1-(methylsulfonyl)-2-phenyl-4(1H)-quinolines with sodium ethoxide in ethanol the only products are 4-amino-2-phenylquinolines [90].

Deoximation of 3-quinolinealdehyde oximes to the corresponding aldehydes takes place readily in the presence of pyridinium chlorochromate and dicyclohexylcarbodiimide [91].

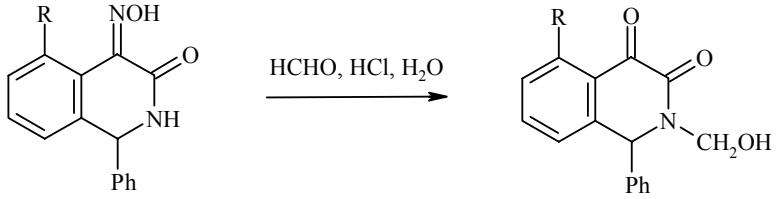
It is interesting that only the nitro group is reduced during hydrogenation of the 6-nitroquinoline oximes **68** in the presence of 10% Pd/C in ethanol giving compound **69**. The oxime group is not reduced under these conditions [91].



68 **69**

n = 0, 1

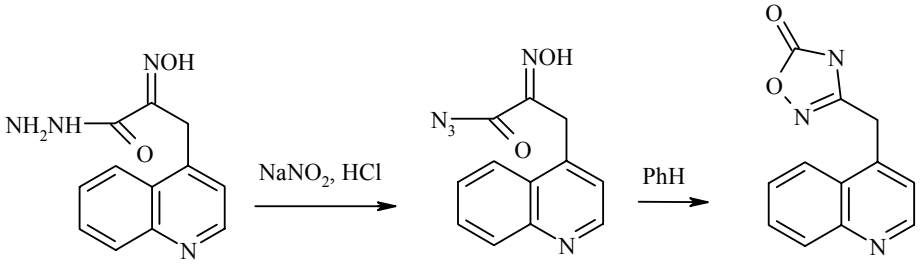
The reaction of 4-hydroxyimino-1-phenyl-1,4-dihydroisoquinolin-3(2H)-ones **70** with formaldehyde in an acidic medium gives isoquinoline-3,4-diones **71** with yields up to 66% [93].



70 **71**

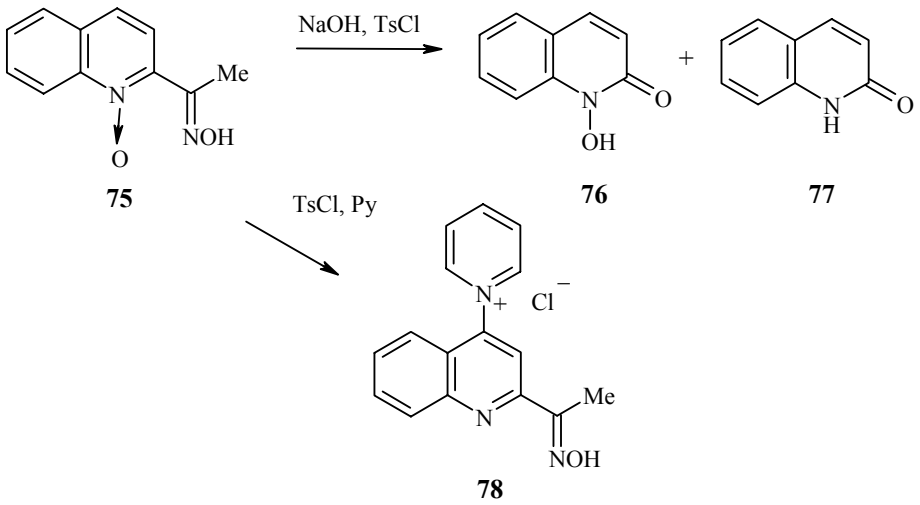
R = H, Me

Under the conditions of nitration ($NaNO_2$/HCl/H_2O) the oxime **72** forms the azide **73**. In boiling benzene **73** is converted into the oxadiazolone **74** as the only product [94].



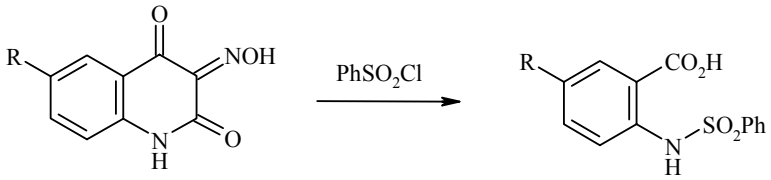
72 **73** **74**

In the TsCl/NaOH/H_2O/THF system the N-oxide of 2-acetylquinoline oxime (**75**) gives a mixture of quinolones **76** and **77** (yields 46 and 24% respectively). In the reaction of the oxime **76** with tosyl chloride in pyridine the product is the pyridinium salt **78** (yield 84%) [23].



75 **76** **77** **78**

The reaction of the quinolinedione oximes **79** with $PhSO_2Cl$ leads to 2-(phenylsulfonylamino)benzoic acids **80** [33].



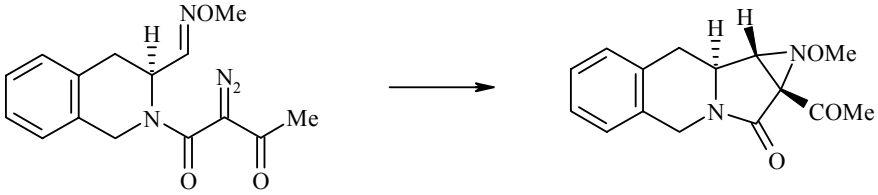
79 **80**

R = H, Me, Br, Cl

2.3. Synthesis of New Heterocyclic Systems from Quinoline Oximes

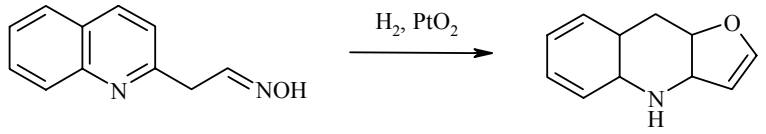
Recent achievements in the synthesis of heterocyclic systems from oximes were reviewed in [95]. In this section the specific reactions of quinoline oximes will be set out in greater detail.

With methyl acrylate in the presence of the metal complex [$Cu(acac)_2$ or $Rh_2(OAc)_4$] the quinoline oxime O-ether **81**, containing a diazo group, undergoes cyclization and forms the aziridine **82** [96].



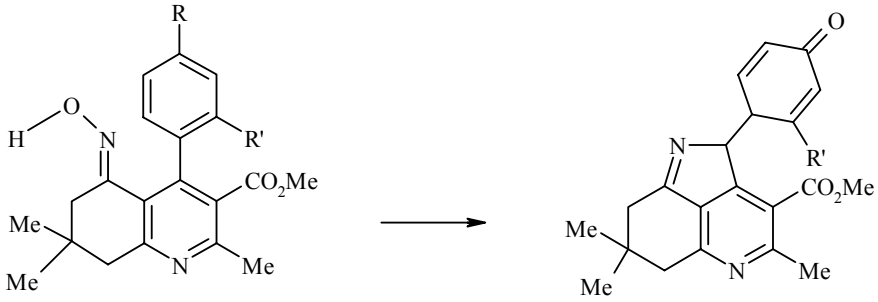
81 **82**

Hydrogenation of 2-quinolineacetaldoxime (**83**) at PtO_2 as catalyst gives 1,2,3,4-tetrahydrofuro-[3',2':2,3]quinoline (**84**) as the main product [97].



83 **84**

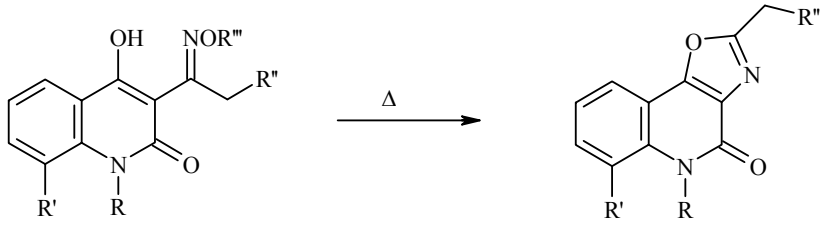
In polyphosphoric acid the oximes of 4-aryl-3-ethoxycarbonyl-2,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydroquinolines **85** are transformed into the pyrroloquinolines **86** with yields of 28-31% [98].



85 **86**

R = Cl, OMe; R' = H, Cl

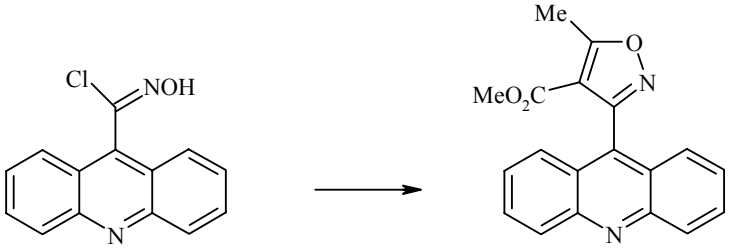
A few publications have been devoted to the synthesis of oxazole [99, 100] and isoxazole [12, 101-104] derivatives from quinoline oximes. The thermal reaction of 4-hydroxyquinolone oximes **87** in 1,2-dichlorobenzene leads to oxazolo[5,4-*c*]quinolones **88** with yields of 52-93% [99]. The products **88** are produced through the intermediate formation of isoxazolo[4,5-*c*]quinolones.



87 **88**

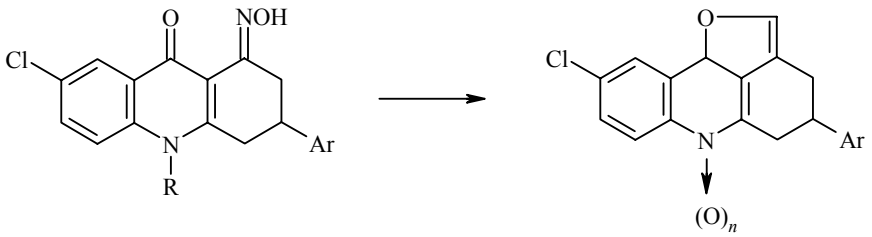
R, R', R", R''' = H, Alk, Ar

A convenient method for the synthesis of isoxazoles is the 1,3-dipolar cycloaddition of nitrile oxides, obtained from quinoline oximes, to alkenes [12, 101-103]. Thus, the reaction of hydroximoyl chloride **45** with the enamine of ethyl acetoacetate gives the isoxazole **89** [12].



45 **89**

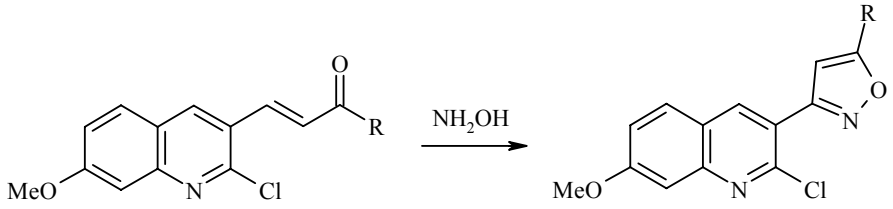
The intramolecular cyclization of 1-hydroxyacridine-1,9-diones (**90**) in the presence of polyphosphoric acid gives 4,5-dihydro-3H-isoxazolo[3,4,5-*kl*]acridines (**91**) with yields of 34-94% [102].



90 **91**

R = OH, OMe; *n* = 0.1

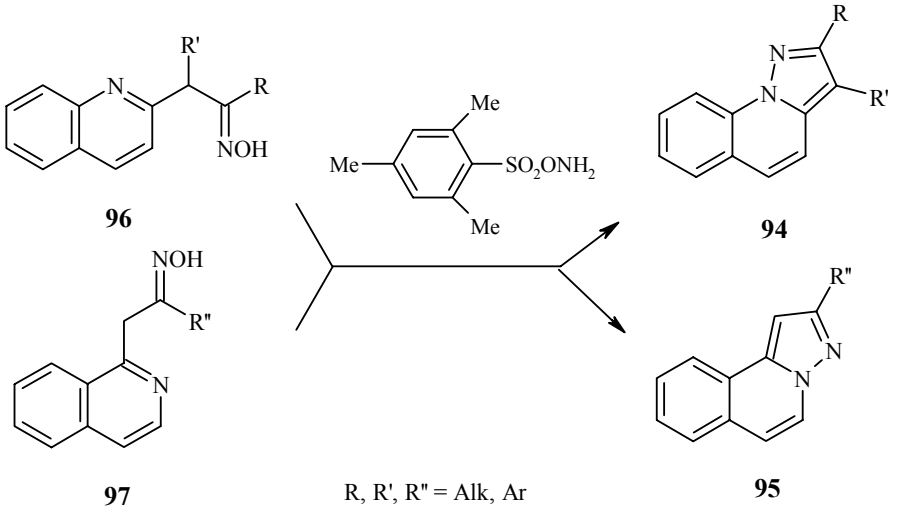
Sometimes quinoline chalcones form isoxazoles instead of the expected oximes in reaction with hydroxylamine. For example, the isoxazole **92** is formed in the reaction of the ketone **93** with hydroxylamine [104].



93 **92**

R = Ar, Het

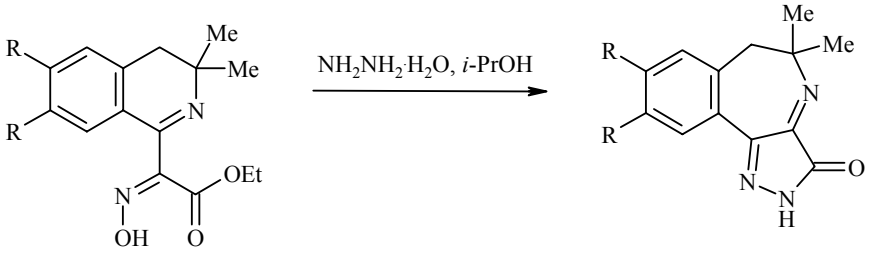
Pyrazolo[1,5-*a*]quinolines **94** and pyrazolo[5,1-*a*]isoquinolines **95** were successfully obtained from the oximes **96** and **97** in the presence of O-mesitylsulfonylhydroxylamine [105].



96 **94**

97 R, R', R" = Alk, Ar **95**

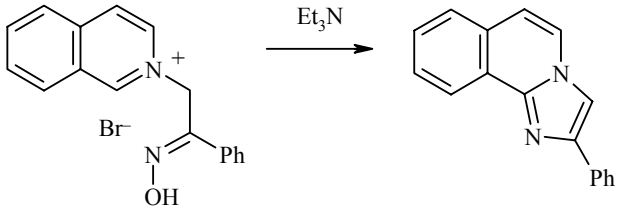
The reaction of 1-(3,4-dihydro-3,3-dimethylisoquinolyl)-1-hydroxyiminoacetates **98** [106] with hydrazine hydrate leads to products from enlargement of the isoquinoline ring – 5,5-dimethyl-2,3,5,6-tetrahydro-3-oxopyrazolo[3,4-*b*]benzo-3-azepines **99** with yields of 47-74% [107].



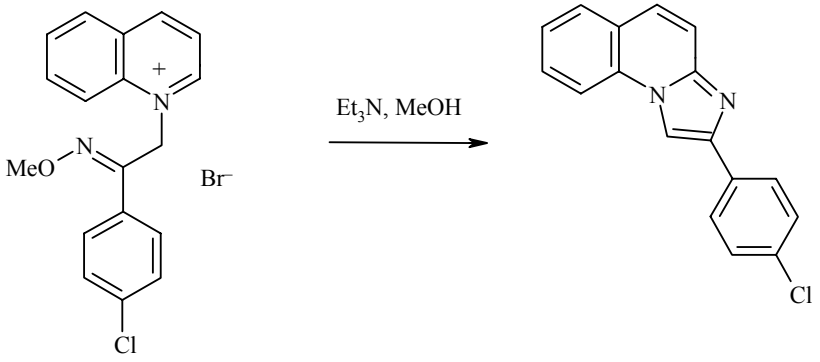
98 **99**

R = H, OMe

A series of papers have been devoted to the synthesis of imidazoles from quinoline oximes [108-114]. In a basic medium the salts of isoquinoline oximes **100** [109] and the ethers of quinoline oximes **101** [110] give good yields of the imidazoles **102** and **103**.

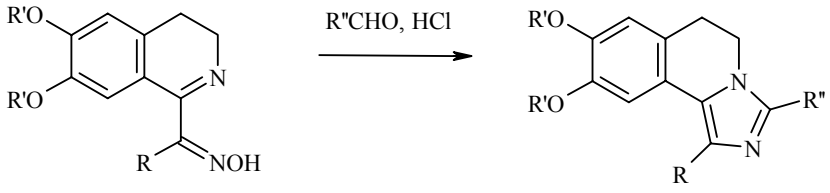


100 **102**



101 **103**

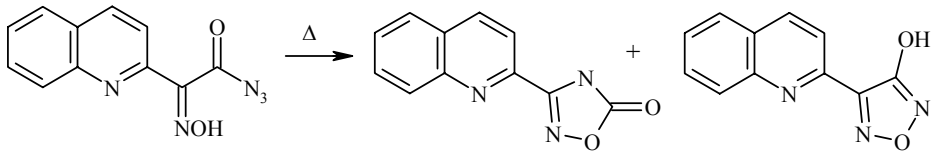
The reaction of dihydroquinoline oximes **104** with aldehydes in the presence of HCl leads to the formation of 5,6-dihydroimidazo[5,1-*a*]isoquinolines **105** [112].



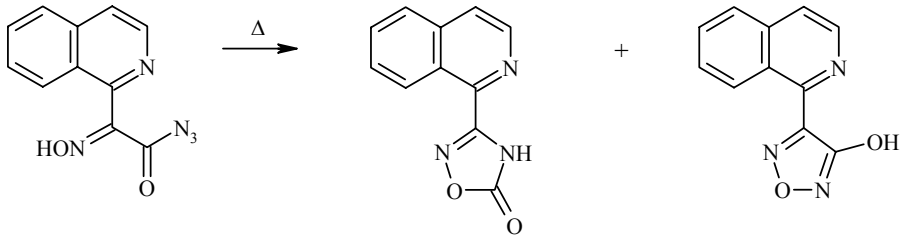
104 **105**

R = CN, $CONH_2$; R' = H, Alk; R" = H, Alk, Ar

1,2,4-Oxadiazoles were successfully obtained from quinoline amidoximes [115] and azido derivatives of quinoline oximes [28]. For example, in boiling ethanol or chloroform the oximes **16** and **18** give a mixture of 1,2,4-oxadiazolin-5-ones **106** and **107** and furazans **108** and **109** respectively [28].

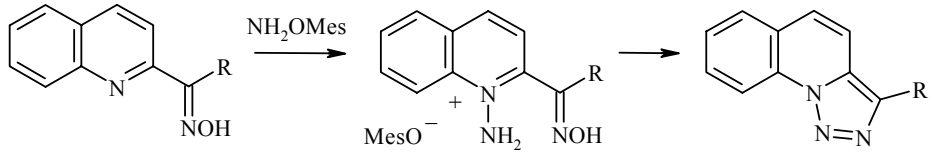


16 **106** 28–77% **107** 5–58%



18 **108** 92 % **109**

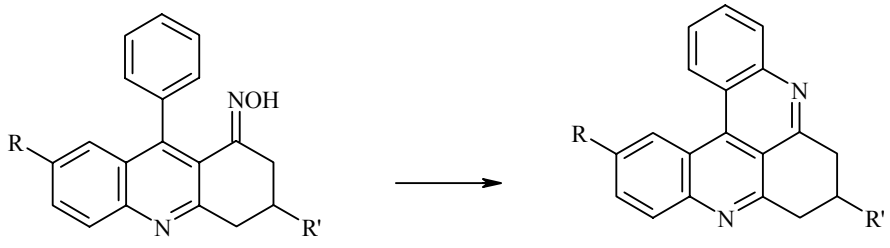
The quinoline oximes **110** and O-mesitylenesulfonylhydroxylamine give N-amine salts **111**, which undergo cyclization in the presence of polyphosphoric acid to triazolo[1,5-*a*]quinolines **112** (yields 72-75%) [116].



110 **111** **112**

R = H, Ph

In polyphosphoric acid 9-phenyl-1,2,3,4-tetrahydro-1-acridinone oximes **113** give dibenzo[*c*,*f*][2,7]naphthiridines **114** with yields of 75-95% [117].

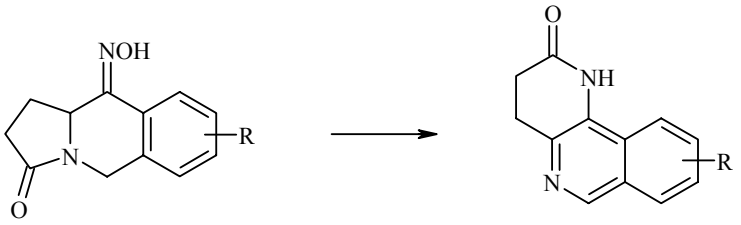


113 **114**

R, R' = H, Cl, Me, Ph

Dibenzo[*a*,*g*]quinolizines were obtained similarly from the respective oximes [118, 119].

The reaction of 1,10a-dihydropyrrolo[1,2-*b*]isoquinoline-3,10-dione oximes **115** with polyphosphoric acid leads to the formation of 1,2,3,4-tetrahydrobenzo[*c*]-1,5-naphthiridines **116** with yields of 44-64% [120-122].

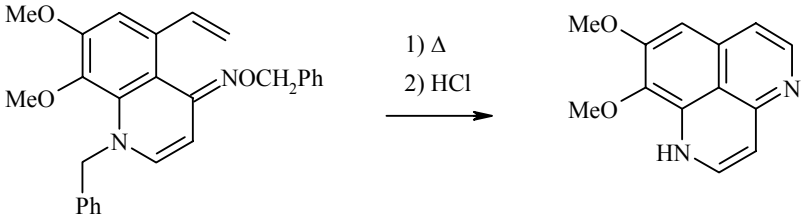


115 **116**

R = H, Cl, Br, Me, OMe

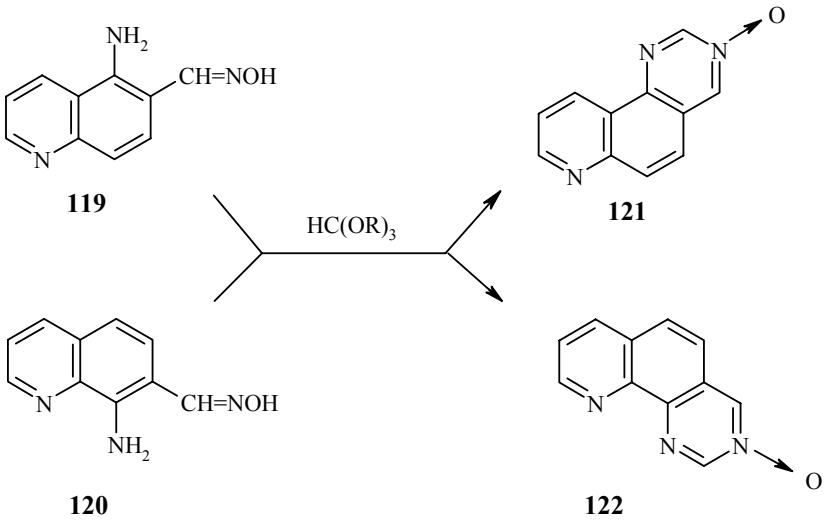
It is interesting that *ortho*-substituted phenylbenz[*a*]acridones in reaction with hydroxylamine form benzoquinacridine N-oxide instead of the expected oximes [123].

The synthesis of the alkaloid aaptamine **117** was realized by thermal cyclization of the quinolone oxime **118** [124].



118 **117**

In the presence of ortho esters the *ortho*-amino oximes **119** and **120** give pyrimidine N-oxides **121** and **122** with yields of 66-90% [125].



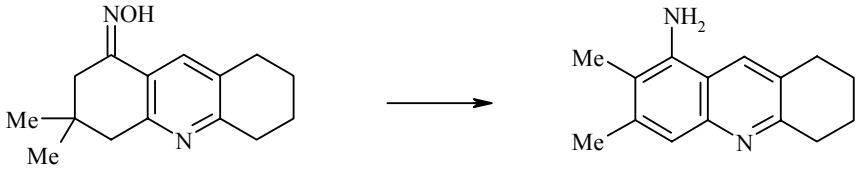
119 **121**

120 **122**

2.4. Beckmann Rearrangement of Quinoline Oximes

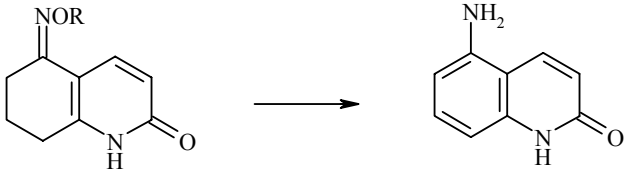
The Beckmann rearrangement is one of the most characteristic reactions of oximes. The rearrangement of oximes to the corresponding amides [126] is usually carried out with concentrated sulfuric acid [85] in the presence of phosphorus pentachloride in chloroform [127] or benzene [128].

In the abnormal Beckmann reaction in the presence of polyphosphoric acid 3,3-dimethyl-1-oxo-1,2,3,4,5,6,7,8-octahydroacridine oxime gives the product from aromatization of the unsaturated ring **124** with migration of the methyl group [129].



123 **124**

Under similar conditions (AcOH, Ac_2O, polyphosphoric acid, HCl, or Cl_2) tetrahydroquinolone oxime **125** is transformed into the amino derivative of carbostyril **126** with yields of 19-36% [130].



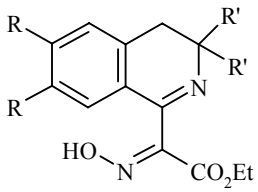
125 **126**

R= H, COAlk, COAr

BIOLOGICAL ACTIVITY OF DERIVATIVES OF QUINOLINE OXIMES

3.1. Action on the Cardiovascular System

A broad spectrum of activity of quinoline oximes acting on the cardiovascular system has been investigated. The 3,3-disubstituted derivatives of 3,4-dihydroisoquinolyl-1-glyoxalic acids **127** showed high vasodilatory and anticoagulative activity [131].



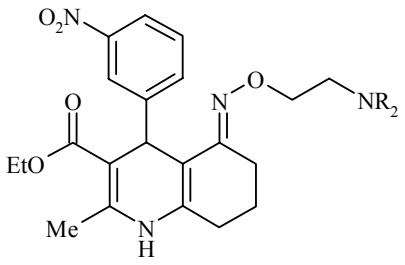
127

R = H, Me, OMe; R' = Me, R'R' = $(CH_2)_4$, $(CH_2)_5$

In addition, it is necessary to mention the hypotensive activity of 4-hydroxyimino-1,2,3,4-tetrahydroquinolines [132] and the antidiabetic activity of the ethers of quinoline oximes containing a thiazolidinedione group [133, 134].

3.2. Sedative, Antidepressant, and Anticonvulsive Activity

The derivatives of quinoline oximes **128** are well known as antidepressants [135]. Oxime ethers of benzo[*a*]quinolizines are sedative and anticonvulsive agents [136].

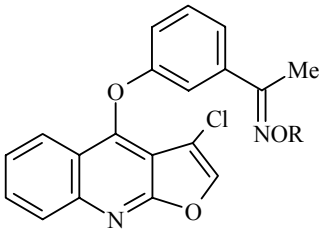


128

The 1,2,3,4-tetrahydroquinoline-2,2,4-trione oximes **29** acted as antagonists of NDMA in glycine receptors [35, 137, 138]. These compounds were used as agents against neurodegenerative diseases (e.g., Alzheimer's disease).

3.3. Analgesic and Anti-inflammatory Activity

The derivatives of isoquinoline amidoximes [139] and the oximes of quinolylaminoacetophenones [140] exhibit analgesic and anti-inflammatory activity. The oximes of furo[2,3-*b*]quinoline **129** and **130** [65, 141] and 9-phenoxy- or 9-anilinoacridine [142] were proposed as anti-inflammatory agents.



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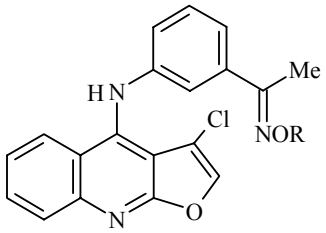
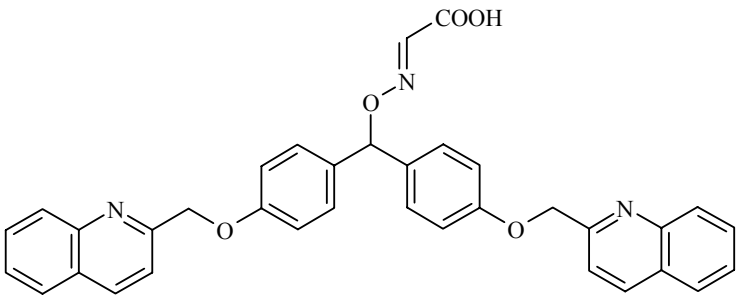


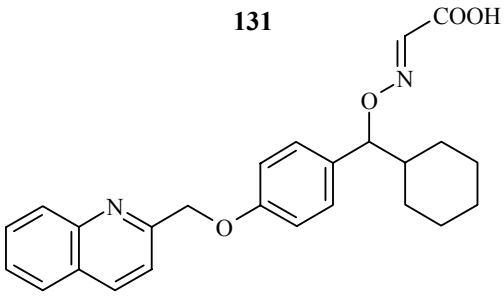
130

R = H, Me

A series of papers were devoted to study of the ethers of quinoline oximes as inhibitors of the biosynthesis of leukotriene [143-148]. These compounds, among which the ethers **131** and **132** should be mentioned, have been used as antiallergic and anti-inflammatory agents.



131

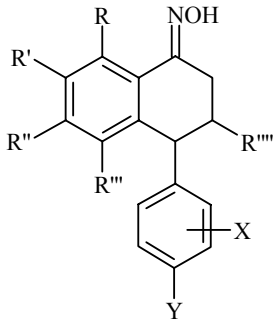


132

In addition, the quinoline-4-carbaldehyde oxime exhibited bronchodilatory activity [149]. Pyrrolo-[3,2-*c*]quinoline oximes have inhibiting activity against interleukin 1 [150] and are used as antiinflammatory agents.

The ethers of quinoline oximes have also exhibited antiallergic activity [151-153].

2,3-Dihydro-1H-quinolin-4-one oximes **133** have been used as inhibitors of protein formation during thermal shock [154].



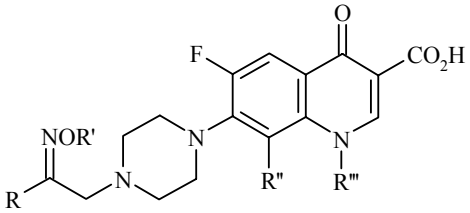
133

R-R'''' = H, Alk, Hal; X, Y = H, Alk

3.4. Cytotoxic, Antitumor, Antiviral, and Bactericidal Activity

Derivatives of quinoline oximes are widely used as cytotoxic and antitumor agents.

Clearly defined cytotoxic and bactericidal activity was recently discovered in oxime derivatives of norfloxacin **134** [155-157].



134

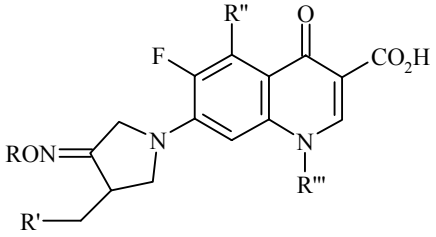
R = Alk, Ar; R' = H, Alk; R" = H, Hal; R"' = Alk, Ar

High cytotoxicity was exhibited by the oxime derivatives of 4-anilinofuro[2,3-*b*]quinoline [158] and indoloquinolines [159]. The range of antitumor activity in the 7-hydroxyiminomethyl derivatives of campthotecin should be noted [160].

The anti-HIV activity of 4-imino- and 4-alkoxyiminoquinolones has been described [161].

High bactericidal activity was found in quinoline aldoximes [162], amidoximes [163, 164], O-dialkylaminoalkyloximes [165], and 2-(1-ethyl-1,4-dihydro-4-oxo-3-quinolyl)-2-alkoxyiminoacetates [68].

The derivatives of norfloxacin **134** and their analogs also displayed high bactericidal activity [166]. Bactericidal activity was recently found in piperazinyl-substituted [167] and pyrrolidinyl-substituted quinolones **135** [168, 169].



135

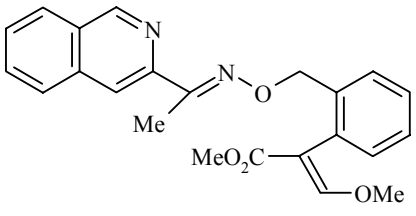
R = Alk, Ar; R' = H, Me; R" = H, NH_2; R"' = Alk

Cephalosporin antibiotics contain quinoline oxime fragments [170, 171].

The high protozoicidal activity of quinoline oximes against *Eimeria tenella* was described in [172, 173].

3.5. Quinoline Oximes as Fungicides and Herbicides

Quinoline and isoquinoline oximes [174, 175] and their O-ethers [176-178] have high fungicidal activity. Among these compounds the ethers **136** and **137**, which exhibit a wide spectrum of fungicidal activity, should be noted.



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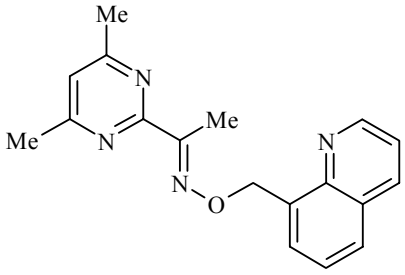

137

Herbicidal activity has also been reported in the ethers of quinoline oximes [179, 180].

3.6. Other Types of Activity

Quinoline oximes have exhibited diuretic activity [181, 182] and have been proposed for the treatment of glaucoma [183]. The antidotal activity of the oximes of 1-phenylacylquinolinium chlorides in poisoning by organophosphorus compounds has also been reported [184].

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