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SYNTHESIS OF PYRIDINE DERIVATIVES. INTRAMOLECULAR CYCLIZATION OF δ-OXONITRILES (REVIEW)

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Literature data on cyclization of δ-oxonitriles to pyridine derivatives are analyzed and generalized.

INTRODUCTION

Synthesis of pyridine derivatives by cyclization of δ-oxonitriles has a number of advantages over other methods for obtaining pyridine bases. Cyclization of δ-oxonitriles to pyridine derivatives is simple to carry out, in most cases leads to good yields of the target compounds, and has the important advantage that it allows us to obtain pyridine derivatives containing different substituents in any positions on the pyridine ring.

We should note the importance of this method for synthesis of halo-substituted pyridines. The traditional method of obtaining such compounds by direct halogenation of pyridine bases has a number of important disadvantages. The reactions used are nonselective (which generally leads to a mixture of products and significantly complicates isolation of the target compounds in pure form), are nonecological (the need arises for utilization of large amounts of byproducts), and are technologically complicated (expensive special equipment is needed, capable of operating in aggressive media at high temperatures). On the other hand, the method for synthesis of pyridine derivatives by cyclization of δ-oxonitriles is highly selective, significantly more ecological, and allows us to obtain pyridine derivatives with a precise, preplanned position of the halogen and/or other substituents on the heterocyclic ring.

In this review, we have divided all the available literature material on intramolecular cyclization of δ-oxonitriles with formation of pyridine bases into two parts. In the first part, we consider syntheses using presynthesized δ-oxonitriles as the starting compounds. The second part is devoted to conversions in which the δ-oxonitriles formed from unsaturated compounds and substances containing a nitrile or carbonyl group are not isolated but rather are directly converted to the cyclization products. Such a division of the material under consideration is expedient because the indicated two groups of reactions generally are carried out under different conditions.

Despite the great interest in the synthesis of pyridine derivatives based on δ-oxonitriles, the results of investigations in this area so far have not been the subject of systematic treatment and generalization, but rather the material obtained has been briefly and very incompletely presented only in the monographs [1-3].

1. SYNTHESIS OF PYRIDINE DERIVATIVES BY INTRAMOLECULAR CYCLIZATION OF PRESYNTHESIZED Δ-OXONITRILES

Conversion (heterocyclization) of δ-oxonitriles to pyridine bases can be accomplished by treatment with various reagents (hydrogen halides, bromine, acids and their derivatives, bases, complex compounds, aluminum oxide, elemental sulfur), and also hydrogenation or reduction.

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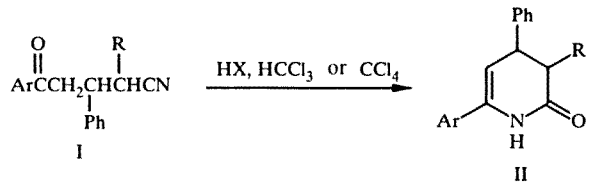
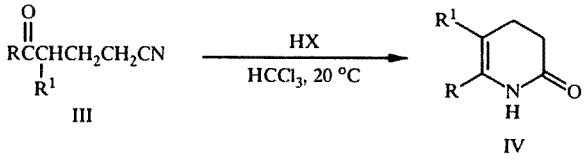
1.1. Heterocyclization by Treatment with Hydrogen Halides

In early work, heterocyclization of δ-oxonitriles I to 3,4-dihydropyridone derivatives II was done using treatment with hydrogen chloride or bromide in chloroform or carbon tetrachloride [4-7]:



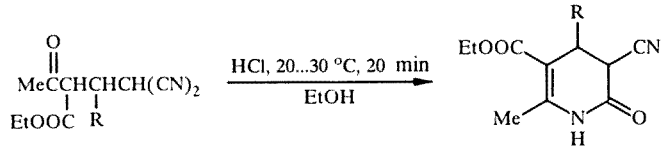
Ar, R, X, yield in %: Ph, COOMe, Cl, —; 4-ClC$_6$H$_4$, COOMe, Br, 90 [4]; Ph, Ph, Br, 90 [5]; Ph, 4-O$_2$NC$_6$H$_4$, Br, 92 [6]; 4-MeOC$_6$H$_4$, Ph, Br, 91 [7]

This technique has also been successfully used for conversion of δ-ketonitriles III to 3,4-dihydro-2-pyridone derivatives IV with another arrangement of the substituents on the heterocyclic ring [8, 9]:



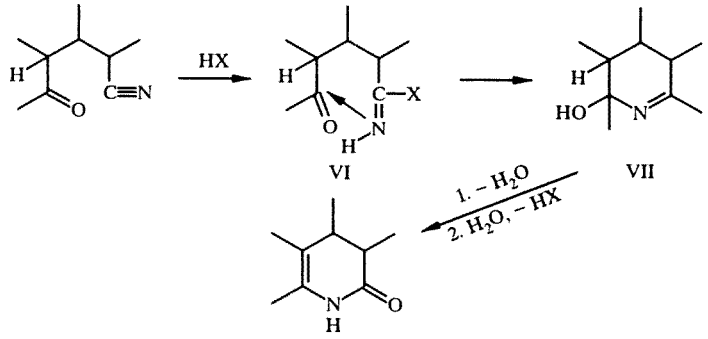
R, R^1, X, yield in %: Me, Me, Cl, 54; Me, Pr, Cl, 36; Me, *i*-Pr, Cl, 25; Me, Bu, Cl, 60 [8]; Ph, MeSO$_2$, Br, 45 [9]

According to patent data [10-13], δ-ketodinitriles can be converted to 3,4-dihydro-2-pyridone derivatives V by treatment with hydrogen chloride in alcohol:

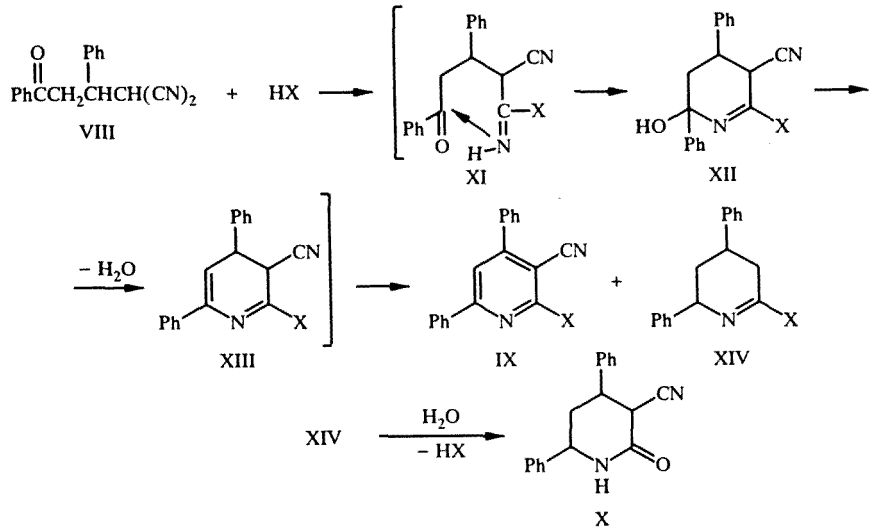


R = Me$_2$CH, Ph, CH$_2$OPh

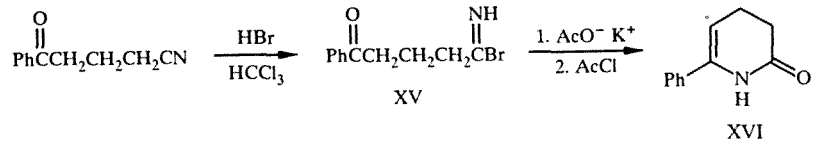
All the indicated conversions occur in an anhydrous medium, and accordingly we need to explain the formation of dihydropyridone derivatives under these conditions. From data in the considered papers, it follows that in the first stage of the process, iminohalides VI are formed which undergo cyclization to compounds VII. The water eliminated from the latter hydrolyzes the chlorine atom located in the 2 position, which leads to the 3,4-dihydro-2-pyridone end product:



The authors of [14] studied cyclization of compound VIII when treated with hydrogen halides and established that the reaction products are mixtures of the pyridines IX and the piperidone X. They proposed the following scheme for the process: cyclization of the iminohalides XI (generated from the ketodinitrile VIII and HX) leads to the compounds XII; as a result of elimination of water from the latter and then disproportionation of the 2-halo-3-cyano-4,6-diphenyl-3,4-dihydropyridines XIII formed due to dehydration, a mixture of pyridine derivatives IX and tetrahydropyridine XIV is formed; in compounds XIV, the chlorine atom in the 2 position is hydrolyzed by the liberated water, which leads to 2-cyano-4,6-diphenyl-2-piperidone (X).



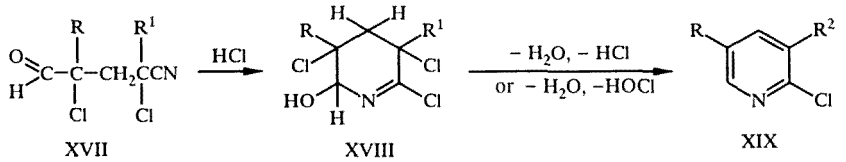
Intermediate formation of iminohalides of type XI was confirmed by obtaining the iminobromide XV and converting it to 6-phenyl-3,4-dihydro-2-pyridone (XVI) [15]:



Hydrogen chloride is widely used in synthesis of halosubstituted pyridine bases from the corresponding δ-oxonitriles. By such a route it is possible to obtain compounds with a precisely fixed position on the heterocyclic ring both for the halogen atoms and other substituents. As already noted above, this favorably distinguishes this method from the method of direct halogenation of pyridine and its derivatives.

A series of papers appearing from 1976 to 1985 [16-21] systematically studied the reactions of cyclization of adducts of *gem*-polychloro-substituted aldehydes with acrylonitrile, methacrylonitrile, or α-trifluoromethylacrylonitrile.

Cyclization of the adducts XVII was accomplished by heating at 180°C in the presence of hydrogen chloride. Under these conditions, pyridine was obtained rather than pyridone (as in the previous cases described). The authors did not study the reaction mechanism, but give the following suggested scheme for the process:

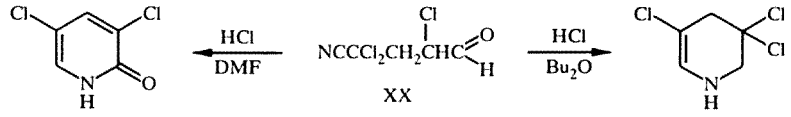


R, R^1, R^2, yield in %: Cl, Me, Me, — [18]; CF_3, H, Cl, 55 [19]; Cl, H, Cl, 65; Me, H, Cl, 53; CF_3, H, Cl, 60; Et, H, Cl, 49; CH_2CH_2Cl, H, Cl, 57; CH_2CHCl_2, H, Cl, 50; CH_2CCl_3, H, Cl, 46; Pr, H, Cl, 35; Me_2CH, H, Cl, 33; Bu, H, Cl, 52; C_5H_{11}, H, Cl, 51 [20]; Cl, H, Cl, —; Cl, Me, Me, — [21]

It is suggesed that the intermediates XVIII, obtained from the nitriles XVII where R^1 = H, under the reaction conditions eliminated an HCl molecule from the 3 and 4 positions and an H_2O mlecule from the 2 and 5 positions and are converted to the products XIX (R^2 = Cl). For R^1 = Me or CF_3, in the adducts XVII the compounds XIX (R^2 = Me, CF_3) are formed as a result of elimination of HCl from the 4 and 5 positions and HOCl from the 2 and 5 positions.

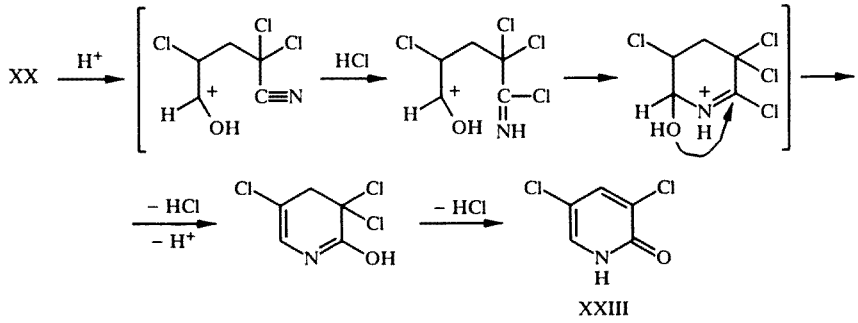
The reactions of the products of addition to α,β-unsaturated aldehydes and ketones of nitriles of α-*gem*-polychlorocarboxylic acids have been systematically investigated.

Different compounds were obtained from the adduct XX of trichloroacetonitrile XXI and acrolein when carrying out the reactions in different solvents: in dibutyl ether, the derivative 3,4-dihydro-2-pyridone XXII was formed, while in DMF the reaction product was the 2-pyridone derivative XXIII [22-24].



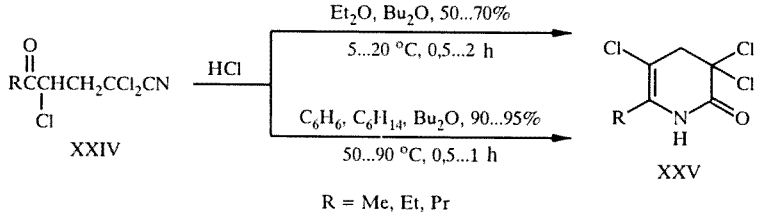
XXIII XX XXII

Compound XXIII, 3,5-dichloro-2-pyridone, would logically be considered the product of hydrolysis of the chlorine atom in the 2 position of the initially formed 2,3,5-trichloropyridine [16, 17]. But the latter is not converted to XXIII when reacted with water under the conditions used in synthesis of the pyridone XXII. In order to explain the formation of product XXIII upon cyclization in DMF, the following scheme has been suggested [22, 23]:



XXIII

Cyclization of trichloroketonitriles XXIV obtained from the nitrile XXI and alkylvinylketones proceeds in an interesting and unique way [23-25]. Thus compounds XXIV when treated with HCl in diethyl or dibutyl ethers, hexane, or benzene are converted in high yields to the 3,4-dihydro-2-pyridone derivatives XXV [23-25]:

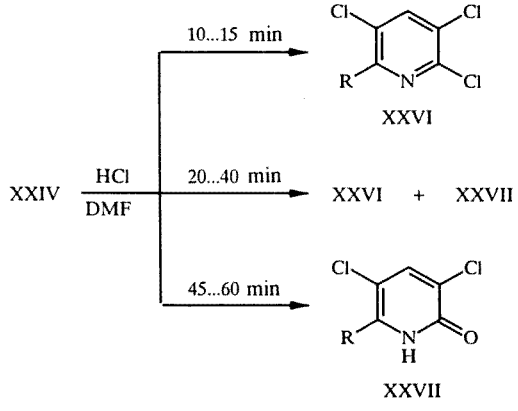


XXIV XXV

R = Me, Et, Pr

When a bulky substituent (R = Ad) is present in the original adduct XXIV, the corresponding compound XXV could be obtained only when carrying out the cyclization in an autoclave at 190°C [23, 26].

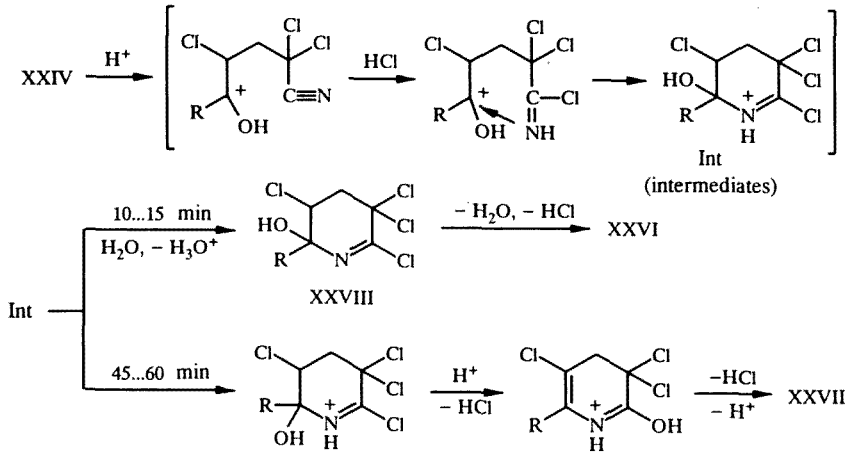
Cyclization of the nitriles XXIV (R = Me, Et, Pr) in DMF proceeds in an unusual manner. Thus when passing HCl through their solutions in DMF for 10-15 min followed by pouring the reaction mass into water, the major reaction products were the pyridine derivatives XXVI, along with which compounds XXVII were also formed in small amounts (~5%). If the hydrogen chloride is passed through the solutions for 45-60 min, then the 2-pyridone derivatives XXVII are the only reaction products (~90% yields). When carrying out the process for 20-40 min, mixtures of compounds XXVI and XXVII are formed.



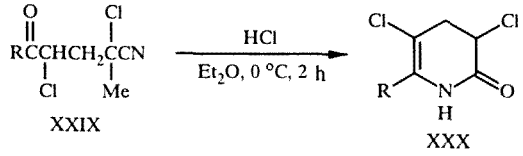
XXVI XXVII

In order to explain the enumerated facts, obviously we should establish the formation of the intermediates (Int). In fact, if the reaction mass is poured into a large volume of water 10-15 min after the HCl begins to pass through the solution, then under the action of the water the intermediates are deprotonated, forming the tetrahydro-6-hydroxypyridines XXVIII, which

eliminate the water molecule and the HCl, being converted to the pyridine derivatives XXVI. When the reaction is carried out for a longer period, an intramolecular attack by the OH group on the chlorine atom in the 2 position occurs, and also elimination of two HCl molecules from the 2 and 5 and the 3 and 4 positions, which leads to the compounds XXVII [23].

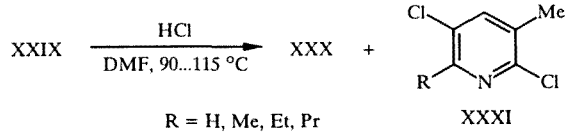


If heterocyclization of the δ-ketonitriles XXIX is carried out in diethyl ether at 0°C, then the 3,4-dihydro-2-pyridone derivatives XXX formed do not undergo dehydrochlorination and are the only reaction products [23, 27]:



R, yield (%) : H ,81; Me ,93; Et ,86; Pr ,92

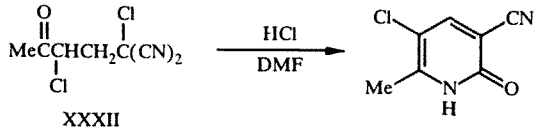
When carrying out cyclization of the ketonitriles XXIX in DMF, mixtures of the compounds XXX and the pyridine derivatives XXXI are obtained [23, 27]:



The overall yield and the ratio of the products XXX:XXXI vary depending on the reaction time and are respectively 12-15% and 1:1 after 10-15 min; 40% and 2:1 after 45-60 min; 70% and 5:1 after 3 h.

Cyclization of the nitrile of 4,4-dichloro-5-ketocaproic acid to 2,5-dichloro-6-methylpyridine was carried out by treatment with HCl at 145-160°C in [28].

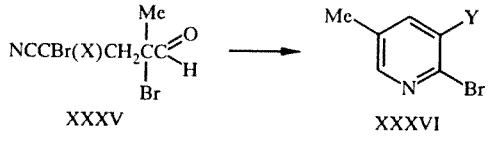
Upon treatment of the ketodinitrile XXXII with hydrogen chloride (110-115°C, 10-45 min), a derivative of nicotinonitrile is formed in 55% yield, 3-cyano-5-chloro-6-methyl-2-pyridone [23]:



The 2-chloropyridine derivatives XXXIII are obtained in high yields by cyclization of the ketonitriles XXXIV in DMF by treatment with HCl in the presence of $POCl_3$ [23]:

R, R^1, yield in %: H, Cl, 79; H, Me, 76; Me, Me, 84; Et, Me, 81; Pr, Me, 88

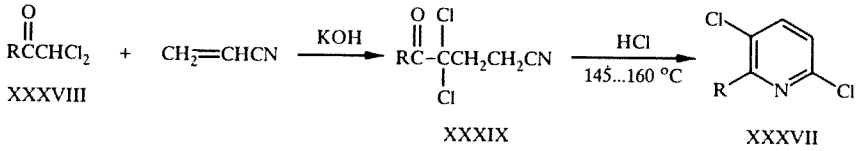
Cyclization of ketonitriles containing other halogen atoms along with the chlorine atoms has also been studied in [28, 29]. In this case, it has been observed that the dichlorofluoroketonitrile $NCC(Cl)FCH_2C(Cl)MeCHO$ cannot be converted to the corresponding substituted pyridine, while the chlorofluoroketonitrile $NCC(F)HCH_2C(Cl)MeCHO$ is converted to 2-chloro-3-fluoro-5-methylpyridine in 44% yield as a result of treatment with hydrogen chloride at 180°C [29]. In the same paper, it is established that the adducts XXXV cannot be obtained in pure form from methacrolein and dibromoacetonitrile: when their distillation is attempted, the pyridine derivatives XXXVI are formed.



XXXV XXXVI

X, Y : H, Br; F, F

A synthesis of 6-substituted 2,5-dichloropyridines XXXVII has been patented by means of cyanoethylation of the dichloroketones XXXVIII followed by cyclization of the ketonitriles XXXIX formed upon heating in the presence of HCl [30, 31]:

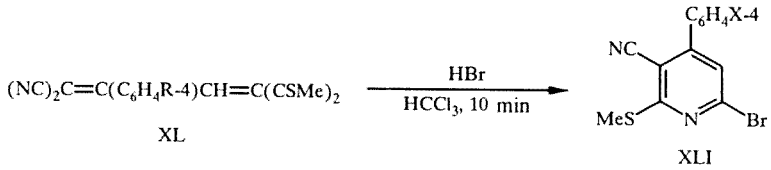


XXXVIII XXXIX XXXVII

R = $C_{1...8}$- alkyl $C_{3...8}$- cycloalkyl , $C_{4...8}$- cycloalkylalkyl

2,3,5-Trichloropyridine was synthesized in 85% yield as a result of treatment of 2,2,4-trichloro-4-cyanobutyral with HCl at 180°C [17].

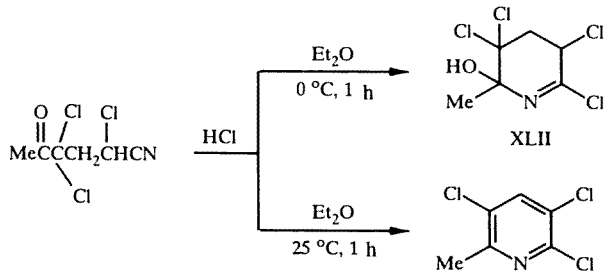
The pyridine derivatives XLI are obtained in high yield when the ketodinitrile dithioketals XL are treated with hydrogen bromide [32]:



XL XLI

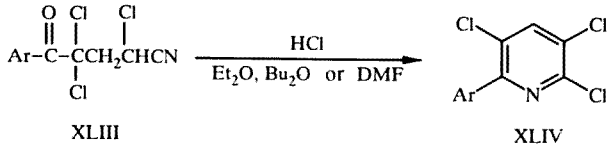
X, yield (%) : H, 85; Cl, 94; Br, 91; MeO, 96

The temperature conditions are quite important for heterocyclization of the nitrile of 2,4,4-trichloro-5-ketocaproic acid in diethyl ether: at 0°C, the tetrahydropyridine derivative XLII is formed (82% yield); and at 25°C, 2,3,5-trichloro-6-methylpyridine is formed (90% yield) [33]. The same trichloroketonitrile in DMF at 120-130°C after 45 min is converted to 2,3,5-trichloro-6-methylpyridine in 65% yield [33].



XLII

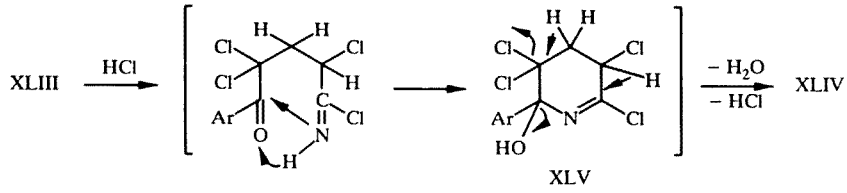
While derivatives of pyridine, 2-pyridone, or 3,4-dihydro-2-pyridone can be synthesized by cyclization of δ-oxonitriles of the aliphatic series using various solvents and hydrogen halide treatment times, both in DMF and in Et_2O or Bu_2O the pyridine derivatives XLIV were obtained from the arylketonitriles XLIII (adducts of trichloromethylaryl ketones with acrylonitrile) as the only reaction products in 80-90% yields [33-35]:



XLIII XLIV

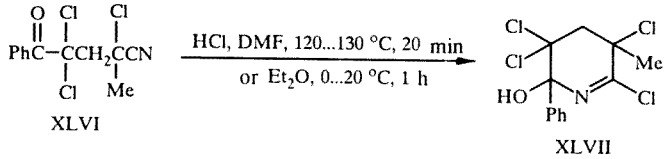
Ar = Ph, 4-HOC_6H_4, 4-MeC_6H_4, 4-$O_2NC_6H_4$

From the reaction schemes proposed below, we can see that in the intermediates XLV there is no hydrogen atom in the 5 position and elimination of the elements of water from the 5 and 6 positions is not possible. Obviously, in this case the reactions of dehydrochlorination from the 4 and 5 positions and dehydration from the 3 and 6 positions occur synchronously (according to a 1-4 elimination scheme) [33]:



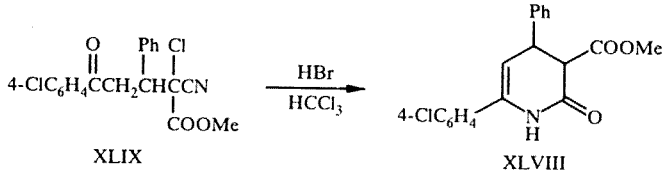
XLV

Evidence in favor of the proposed scheme is the fact that in cyclization of the ketonitrile XLVI, the reaction stops at formation of the tetrahydropyridine derivative XLVII (80% yield). In this case, elimination of the water is impossible, since there is no hydrogen atom in the 3 position [33]:



XLVI XLVII

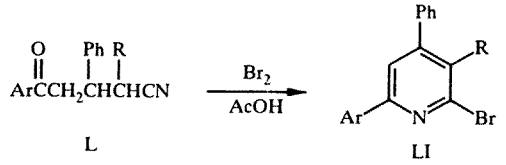
The synthesis of compound XLVIII has been described (90% yield) when boiling the ketonitrile XLIX with hydrogen bromide in chloroform [4]:



XLIX XLVIII

1.2. Heterocyclization of δ-Ketonitriles by Treatment with Bromine

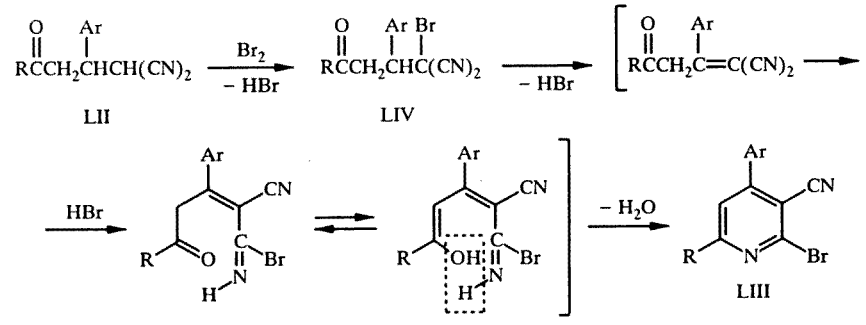
In a number of papers [4-7, 9, 15, 36], cyclization of δ-ketonitriles was carried out using treatment with bromine. Thus when the ketonitriles L were reacted with bromine in acetic acid, the 2-bromopyridine derivatives LI were synthesized [4-6]:



L LI

Ar, R, yield (%) : Ph, COOMe, 97 [4]; Ph, Ph, 90 [5]; Ph, 4-$O_2NC_6H_4$, – [6]

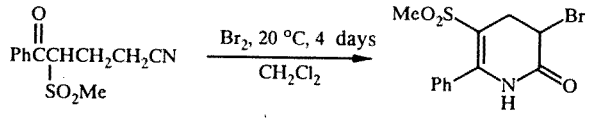
Later cyclization of the ketodinitriles LII in glacial acetic acid at 65-80°C was described, leading in high yields to the corresponding 2-bromo-3-cyano-6-(2-thienyl)-pyridines LIII [36]. The authors of this paper proposed the following reaction scheme:



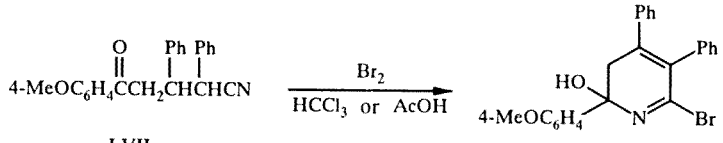
R = 2-thienyl;Ar, yield (%) : Ph, 73; 4-FC_6H_4, 80; 4-ClC_6H_4, 69; 4-BrC_6H_4, 79; 4-$O_2NC_6H_4$, 86

For confirmation of the proposed scheme, the bromo derivative LIV was synthesized (R = Ar = Ph), converted to 2-bromo-3-cyano-4,6-diphenylpyridine LIII by heating in acetic acid [36].

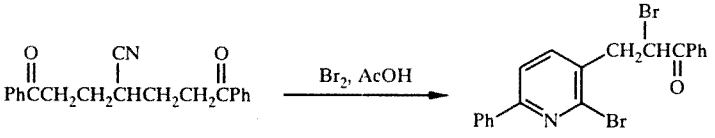
According to the data in [15], when treated with bromine, 4-benzoylbutyronitrile is converted to 6-phenyl-2-pyridone. However, when 4-methylsulfonyl-4-benzoylbutyronitrile (LV) is treated with bromine at room temperature, the 3,4-dihydro-2-pyridone derivative (LVI) was obtained (in 62% yield) [9]:



When the ketonitrile LVII is reacted with bromine, the compound LVIII is formed in low yield (10%), containing an hydroxyl group in the 6 position [7]:

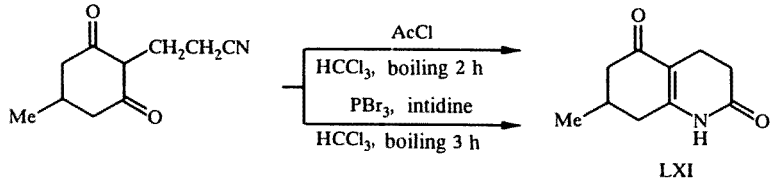


In the case of the diketonitrile LIX under similar conditions, along with cyclization the reaction of bromination of the side chain of the pyridine derivative formed occurs, leading to the dibromide LX [37]:

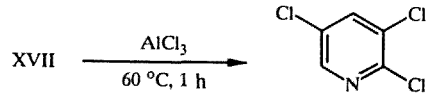


1.3. Heterocyclization by Treatment with Different Lewis and Bronsted Acids

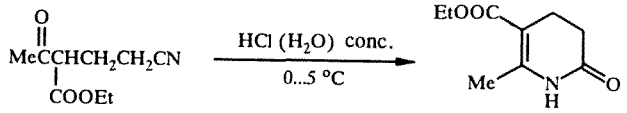
2-(2-Cyanoethyl)-5-methylcyclohexane-1,3-dione is converted to the compound LXI when treated with acetyl chloride (28.8% yield) or phosphorus tribromide (20% yield) [38]:



Heating the ketonitrile XVII (R = R^1 = Cl) with aluminum chloride leads in high yield (83%) to 2,3,5-trichloropyridine [17]:

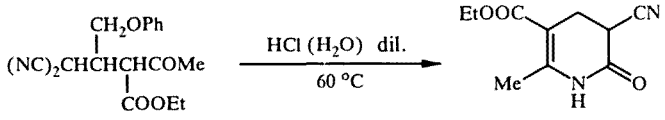


For cyclization of oxonitriles, mineral acids are also used rather often. When 4-ethoxycarbonyl-5-ketocapronitrile is treated with concentrated hydrochloric acid, the 3,4-dihydro-2-pyridone derivatives LXII is formed and the ester group does not undergo hydrolysis [39]:



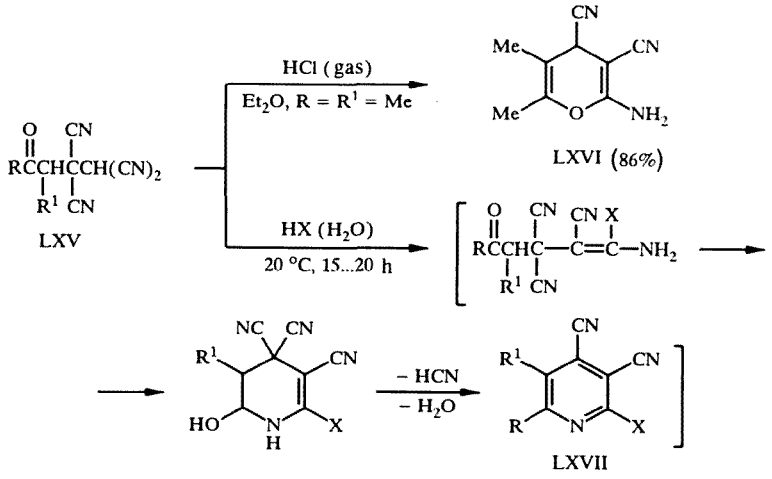
LXII

Hydrolysis is also not observed during cyclization of compound LXIII containing an ethoxycarbonyl group to the 3,4-dihydro-2-pyridone derivative LXIV by heating with dilute hydrochloric acid [11]:



LXIII LXIV

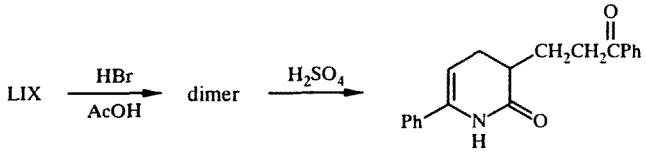
Different compounds were obtained as a result of treatment of tetracyanoketones LXV with hydrogen halides or their aqueous solutions: in treatment with the former, 86% pyran derivative LXVI is formed, while using hydrochloric or hydrobromic acids leads to the pyridine derivatives LXVII [40, 41]:



LXV LXVI (86%) LXVII

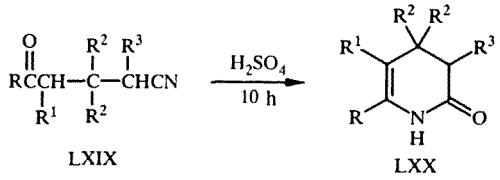
R, R^1 (or R + R^1), X, yield LXVII (%) : Me, H, Cl, 73; Me, Me, Cl, 84; Me, Me, Br, 61; $(CH_2)_4$, Cl, 62; $(CH_2)_3$, Cl, 70; Et, H, Br, 71

According to the data in [37], when treated with hydrogen bromide the diketonitrile LIX is converted to a dimer, from which the 3,4-dihydro-2-pyridone derivative LXVIII is obtained by treatment with concentrated sulfuric acid:



LXVIII

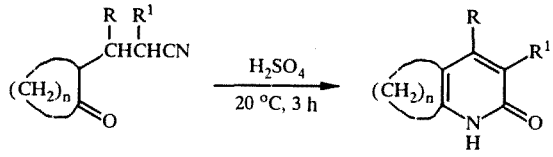
Depending on the structure of the starting ketonitriles, by treatment with concentrated sulfuric acid we can obtain mono-, di-, and tricyclic nitrogen-containing heterocyclic compounds. Thus the 3,4-dihydro-2-pyridone derivatives LXX were synthesized from the ketonitriles LXIX [42, 43]:



LXIX LXX

R, R^1, R^2, R^3, yield (%) : Ph, H, Me, Me, 48; Ph, H, Me, Ph, 79; Ph, H, Ph, Me, 12; Ph, H, Ph, Ph, 70; Ph, Me, H, Me, 74 [42]; Me, 4-pyridine, H, H, 37 [43]

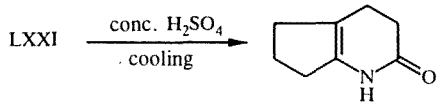
When alicyclic ketones LXXI containing a $-CH(R)CH(R^1)CN$ group in the position adjacent to the keto group were treated with concentrated sulfuric acid, the compounds LXXII were obtained [44]:



LXXI LXXII

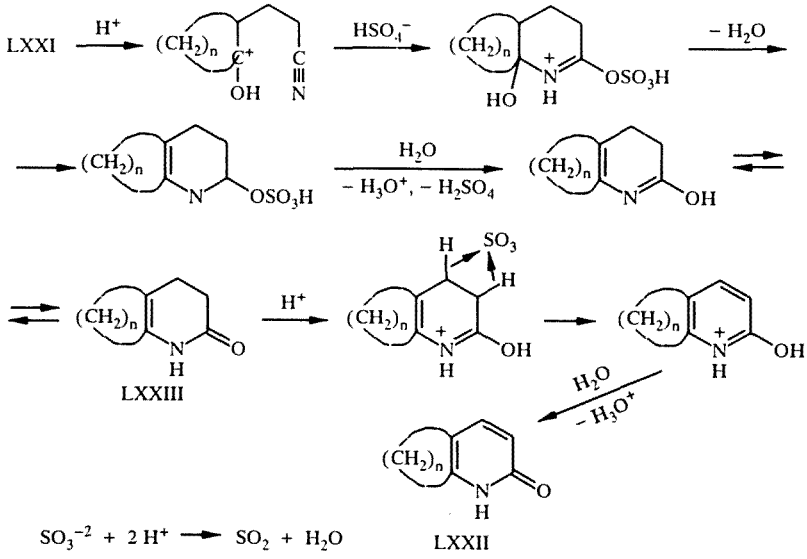
R, R^1, n, yield (%) : H, H, 4, 54; H, Me, 4, 54; H, H, 5, 45

In the case of the ketonitrile LXXI (R = R^1 = H, n = 3), similar treatment at 20°C led to the more saturated product LXXIII [44]:



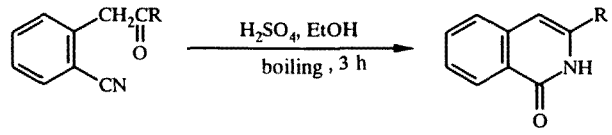
LXXIII

Compounds of the LXXIII type when treated with concentrated sulfuric acid in a nitrogen atmosphere at 20°C are converted to the pyridone derivatives LXXII, and liberation of SO_2 is observed. Monitoring this process by UV spectroscopy, the authors observed that in 96% H_2SO_4 after less than 10 min the peak in the 252 nm region (compound LXXII) disappears and two peaks appear in the 282 nm region (SO_2) and the 294 nm region (ε 8600) (compound LXXIII). In [44], a hypothetical scheme is presented for the conversions LXXI (R = R^1 = H, n = 3-5) → LXXIII and LXXIII → LXXII:



$SO_3^{-2} + 2\,H^+ \longrightarrow SO_2 + H_2O$

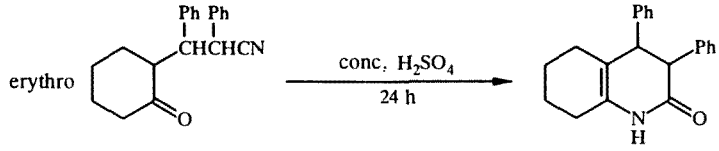
When heating benzonitriles LXXIV containing the $-CH_2COR$ group in the *o* position with concentrated sulfuric acid in ethanol, 3-substituted 1-isoquinolones (LXXV) are synthesized [45]:



LXXIV LXXV

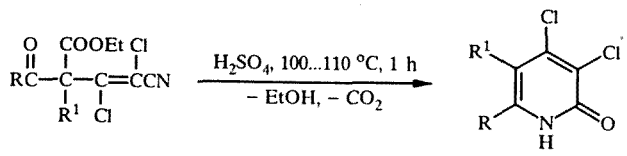
R, yield (%) : Ph, 90; 4-MeC$_6$H$_4$, 87; Et, 82

In 1989, a stereoselective synthesis of the hexahydro-2-quinolone derivative LXXVI was described (50% yield) from 2-(1,2-diphenyl-2-cyanoethyl)cyclohexanone by treatment with concentrated sulfuric acid [46]:



LXXVI

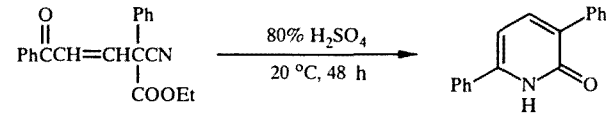
In cyclization of ketonitriles LXXVII by heating with concentrated sulfuric acid, hydrolysis of the ethoxycarbonyl group occurs followed by decarboxylation. As a result, the 3,4-dichloro-2-pyridone derivatives LXXVIII were synthesized [47]:



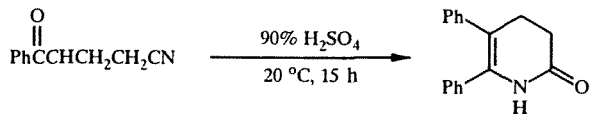
LXXVII LXXVIII

R, R^1 (or R + R^1), yield (%) : Me, Me, 94; Me, Et, 87; Me, Bu, 92; Me, H, 30; $-CH_2CH_2CH_2-$, 64

For cyclization of ketonitriles to 2-pyridone derivatives LXXIX (90% yield) or 3,4-dihydro-2-pyridone LXXX (65% yield), a less concentrated acid was used [48, 49]:

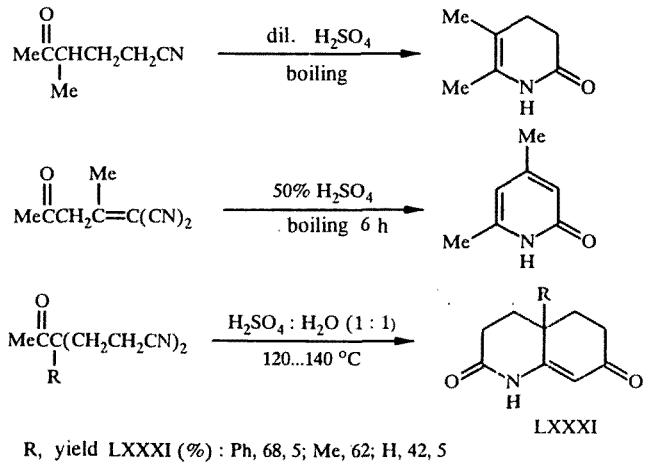


LXXIX



LXXX

The use of even more dilute acid has also been described [50-52] for synthesis of 5,6-dimethyl-3,4-dihydro-2-pyridone (84% yield), 4,6-dimethyl-2-pyridone, or the compounds LXXXI:

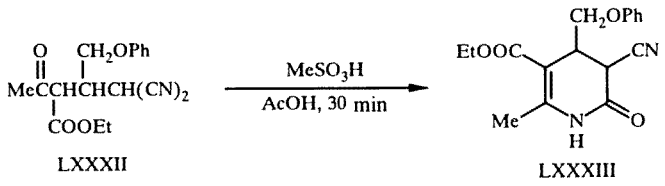


LXXXI

R, yield LXXXI (%) : Ph, 68, 5; Me, 62; H, 42, 5

Dilute sulfuric acid converts 4,4,5,5-tetracyano-3-methylpentan-2-one to 3,4-dicyano-5,6-dimethyl-2-pyridone with 10% yield [41].

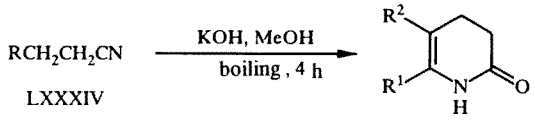
A report is available [53] on the use of the methanesulfonic acid for cyclization of the ketonitrile LXXXII to the 3,4-dihydro-2-pyridone derivative LXXXIII:



LXXXII LXXXIII

1.4. Heterocyclization by Treatment with Bases

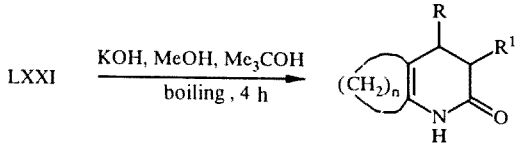
Potassium hydroxide can be used for cyclization of δ-oxonitriles to pyridine bases. Thus the ketonitriles LXXXIV when boiled with this base in methanol are converted to the corresponding heterocyclic compounds LXXXV [54]:



LXXXIV LXXXV

R, R^1, R^2, yield (%) : $-\overline{CH(CH_2)_4CO}$, $(CH_2)_4$, 28; PhCOCH(Ph)–, Ph, Ph, 12; MeCOCH(Ph)–, Me, Ph, 30

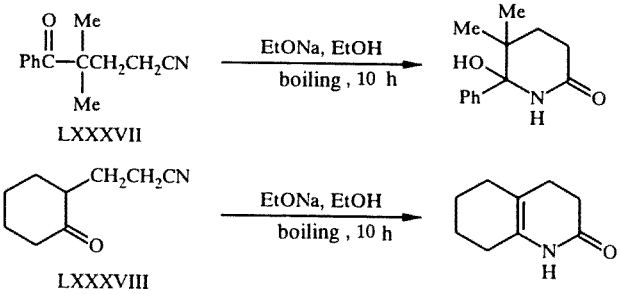
While the pyridones LXIII are formed when the ketonitriles LXXII are reacted with sulfuric acid, heating of the same ketonitriles with potassium hydroxide in a mixture of methyl and *tert*-butyl alcohols leads to the corresponding 3,4-dihydropyridones LXXXVI [44]:



LXXXVI

R, R^1, n, yield (%) : H, Me, 4, 40; Me, H, 4, – ; H, H, 5, 15

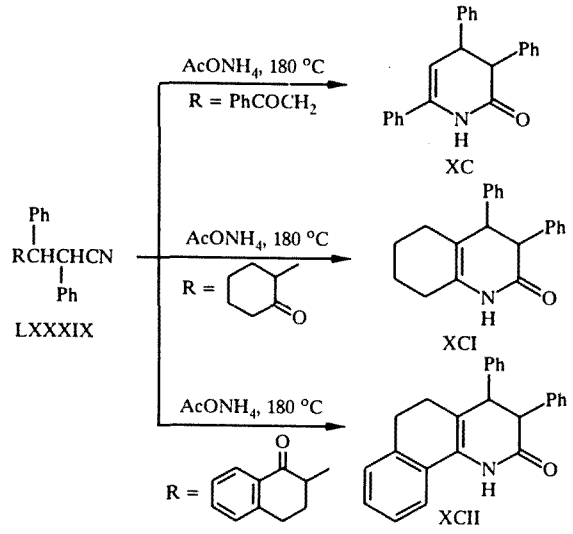
The authors of [55] carried out heterocyclization of the ketonitriles LXXXVII and LXXXVIII by boiling with an alcoholic solution of sodium ethoxide, obtaining the piperidone (50% yield) and 3,4-dihydropyridone (60% yield) indicated in the scheme:



LXXXVII

LXXXVIII

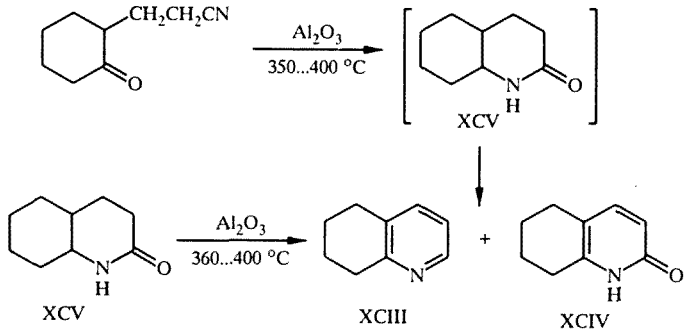
Bulgarian researchers [46] used ammonium acetate for cyclization of the ketonitriles LXXXIX and synthesized monocyclic (XC), bicyclic (XCI), or tricyclic (XCII) compounds in 64%, 68%, and 53% yields respectively:



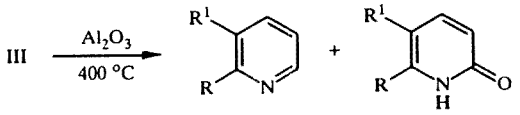
1.5. Other Methods for Heterocyclization of δ-Oxonitriles

In addition to acidic or basic compounds, some other compounds are used for heterocyclization of δ-oxonitriles.

The product of cyanoethylation of cyclohexanone, 2-(2-cyanoethyl)cyclohexanone, when heated with aluminum oxide is converted to a mixture of 5,6,7,8-tetrahydroquinoline XCIII and 5,6,7,8-tetrahydro-2-quinolone XCIV. The occurrence of the reaction through the intermediate XCV is confirmed by the fact that under the same conditions, a mixture of the products XCIII and XCIV is obtained from specially synthesized 3,4,5,6,7,8,9,10-octahydro-2-quinolone XCV [56, 57]:



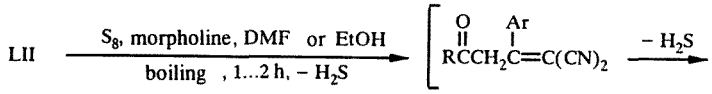
The ketonitriles III behave similarly under these conditions [57, 58].

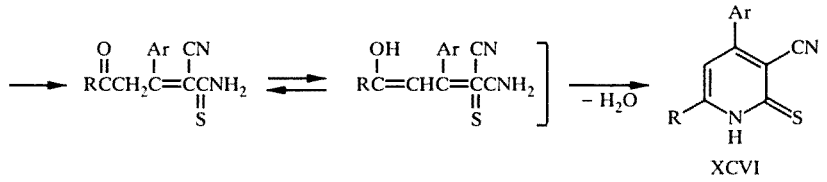


R, R^1, yield (%) : Me, Me, 6,6 and 23; Me, Pr, 10 and 11; Ph, H, 31, –

Heterocyclization of the same ketonitriles can also be carried out over Cr_2O_3/Al_2O_3 at 300-310°C [57].

An original method for heterocyclization of ketonitriles LII to the compounds XCVI by heating with sulfur (in the presence of morpholine) has been described by the authors of [36]:





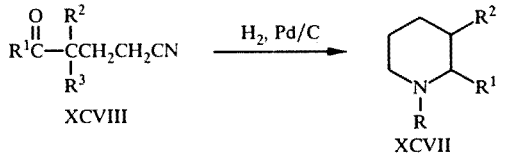
XCVI

R = 2-thienyl; Ar, yield XCVI (%) : Ph, 69; 4-FC_6H_4, 77; 4-ClC_6H_4, 65; 4-BrC_6H_4, 68; 4-$O_2NC_6H_4$, 64

By heterocyclization of 2,4-dichloro-5-cyano-2-methylbutyral in the presence of the complex catalyst $NiCl_2 \cdot PPh_3$ and isopropylamine in acetonitrile, 2,3-dichloro-5-methylpyridine was synthesized in high yield (86%) [60].

δ-Oxonitriles can also be converted to pyridine bases by hydrogenation in the presence of catalysts.

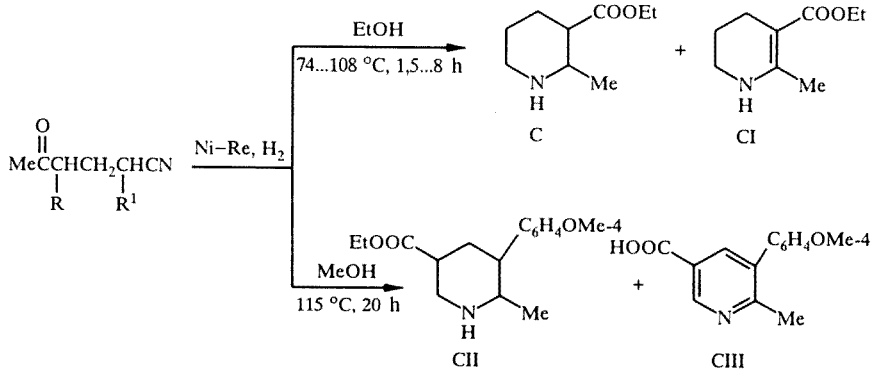
A whole series of piperidine derivatives XCVII was obtained by hydrogenation of the ketonitriles XCVIII over palladium on carbon. In this case, if the process was carried out in an aqueous solution of formaldehyde, the products XCVII contain a methyl group on the nitrogen atom (R = Me, in the absence of CH_2O R = H) [61]:



XCVIII XCVII

R, R^1, R^2, R^3 (or : $R^2 + R^3$, $R^1 + R^2$), yield in %: H, Me, H, H, 85; H, Me, H, COOEt, 86; Me, Me, H, COOEt, 98; H, Me, Me, COOEt, 89; Me, Me, Me, COOEt, 58; H, Me, *i*-Pr, COOEt, 84; Me, Me, *i*-Pr, COOEt, 82; H, Me, *i*-Bu, COOEt, 91; Me, Me, *i*-Bu, COOEt, 84; H, Me, C_6H_{13}, COOEt, 85; Me, Me, C_6H_{13}, COOEt, 80; H, Me, C_7H_{15}, COOEt, 63; Me, Me, C_7H_{15}, COOEt, 33; H, Me, $PhCH_2$, COOEt, 85; Me, Me, $PhCH_2$, COOEt, 81; H, Me, $PhCH_2$, COOMe, 75; Me, Me, $PhCH_2$, COOMe, 75; H, Me, Ph, COOEt, 57; H, Me, $-CH_2CH_2OCO$, 30; Me, Me, $-CH_2CH_2OCO-$, 70; H, $(CH_2)_3$, COOEt, 73; Me, $(CH_2)_3$, COOEt, 85; H, Me, CH_2CH_2COOMe, COOEt, 43; H, Me, CH_2CH_2COOEt, COOEt, 65; Me, Me, CH_2CH_2COOEt, COOEt, 86; H, Me, $(CH_2)_3NH_2$, Me, 77; H, Ph, H, H, 80; H, Ph, H, COOEt, 73; Me, Ph, H, COOEt, 94

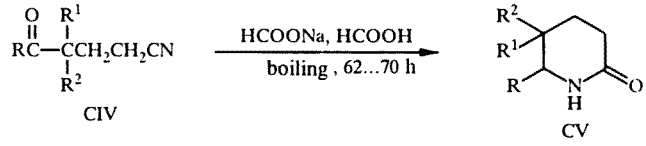
As a result of hydrogenation of the ketonitriles XCIX in the presence of Raney nickel catalyst, depending on the nature of the substituent R and R^1, either a piperidine derivative (C) (10% yield) and a tetrahydropyridine derivative (CI) (76% yield) [39] or a piperidine derivative (CII) (25.2% yield) and a pyridine derivative (CIII) (12% yield) are formed [62]:



C CI CII CIII

R, R^1 : COOEt, H; C_6H_4OMe-4, COOEt

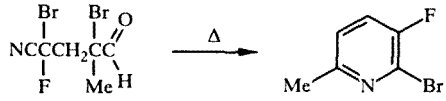
Reductive cyclization of the ketonitriles CIV to the 2-piperidone derivatives CV is accomplished by treatment with sodium formate in formic acid [63, 64]:



CIV CV

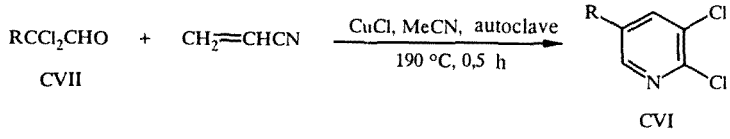
R, R^1 (or , $R^1 + R^2$), R^2, yield (%) : Me, H, H, 68; Me, Me, H, 74; Me, Et, H, 50; $(CH_2)_4$ H, 72; 2-selenolyl-2, Me, Me, 68, 5

Cyclization of ketonitriles is known simply by heating, without introducing condensing agents [65]:



2. SYNTHESIS OF PYRIDINE DERIVATIVES FROM *gem*-POLYHALO DERIVATIVES AND UNSATURATED COMPOUNDS (WITHOUT ISOLATION OF THE INTERMEDIATE δ-OXONITRILES)

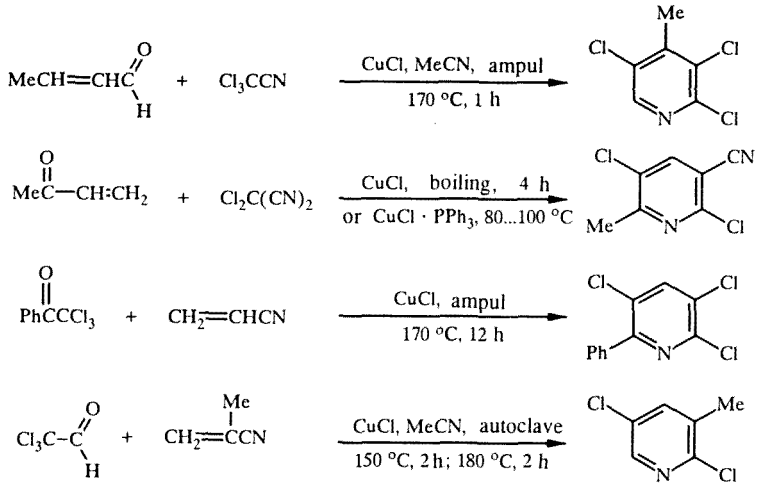
A number of pyridine derivatives CVI have been synthesized from aldehydes CVII and acrylonitrile in the presence of copper chloride (I) without isolation of the intermediate adducts [17, 20]:



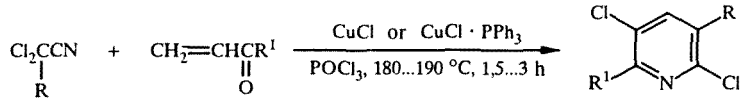
CVII CVI

R, yield (%): Cl, 65; Me, 53; CF_3, 60; Et, 49; CH_2CH_2Cl, 57; CH_2CHCl_2, 50; CH_2CCl_3, 46; Pr, 35; *i*-Pr, 33; Bu, 52; C_5H_{11}, 51

Other chloropyridines have been obtained similarly in 51%, 51%, and 45% yields respectively [23, 33, 34, 18]:

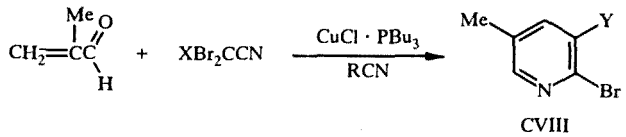


In some cases, $POCl_3$ was introduced in addition to the CuCl [22, 23, 27]:



R, R^1: Cl, H; Me, H; Me, Me; Me, Et; Me, Pr

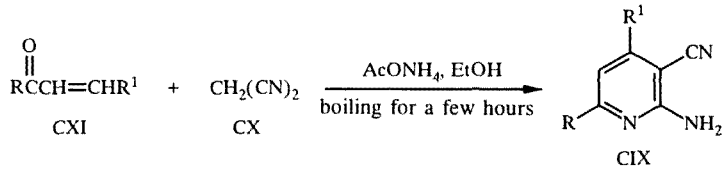
Under rather mild conditions, formation of halo-substituted pyridines (CVIII) from methacrolein and polyhaloacetonitriles occurs in the presence of the complex $CuCl \cdot PBu_3$ in RCN [29]:



CVIII

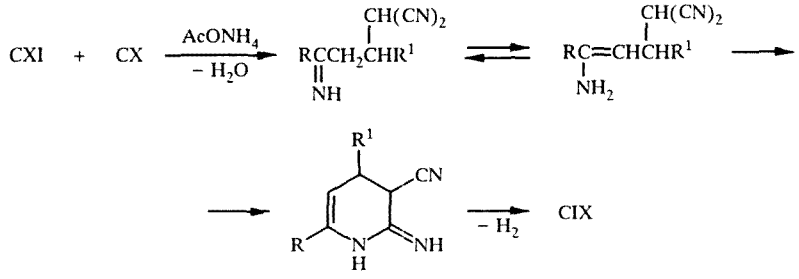
R, X, Y, reaction temperature (°C), reaction time (h), yield (%): Me, H, Br, 90, 14,5, 40; Et, F, F, 110, 12, 30

A large number of alkyl-, aryl-, and hetaryl-substituted 2-amino-3-cyanopyridines (CIX) have been synthesized by reaction of the dinitrile of malonic acid (CX) with α,β-unsaturated ketones (CXI) in the presence of ammonium acetate [66-69]:



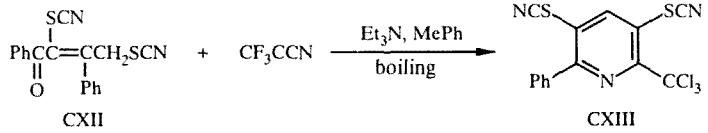
R, R^1, yield (%): Me, Ph, 24; Et, Ph, 34; Pr, Ph, 15; Ph, Ph, 33 [66]; Ph, 2-furyl-2, 72; 4-$MeOC_6H_4$, 2-furyl-2, 73; 4-ClC_6H_5, 2-furyl-2, 67; Ph, 2-thienyl, 69; 4-$MeOC_6H_4$, 2-thienyl, 65; 4-ClC_6H_4, 2-thienyl, 65 [67]; Ph, Ph, 33; 4-MeC_6H_4, Ph, 34; 4-$MeOC_6H_4$, Ph, 36; 4-BrC_6H_4, Ph, 28; 4-ClC_6H_4, Ph, 30; 4-$O_2NC_6H_4$, Ph, 28; 4-ClC_6H_4, Ph, 38; 4-ClC_6H_4, 4-ClC_6H_4, 30; 4-$O_2NC_6H_4$, 4-ClC_6H_4, 50 [68]; for the remaining compounds R = 2-HO-4-$BuOC_6H_3$ и 2-HO-4-BuO-5-$O_2NC_6H_2$; R^1 = Ph, 2-BrC_6H_4, 4-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 2-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 4-MeC_6H_4, 3,4-$(OCH_2O)C_6H_3$, 4-$Me_2NC_6H_4$, 2-ClC_6H_4, 4-BrC_6H_4, 3,4,5-$(MeO)_3C_6H_2$, 33...50 [69]

In [67], the following scheme is proposed for this process:

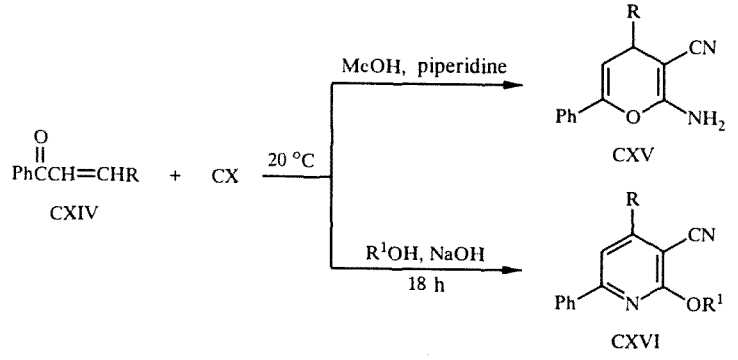


The compounds CIX, where R = Ph or 4-MeC_6H_4, and R^1 = 4-$MeOC_6H_4$ or 3,4-$(CH_2O_2)-C_6H_3$, were obtained from the dinitrile CX and the corresponding chalcones by heating without a solvent (120-150°C) in the presence of ammonium acetate [70].

When the unsaturated nitrile CXII was boiled with trichloroacetonitrile in toluene in the presence of triethylamine, the corresponding substituted pyridine CXIII is formed [71]:

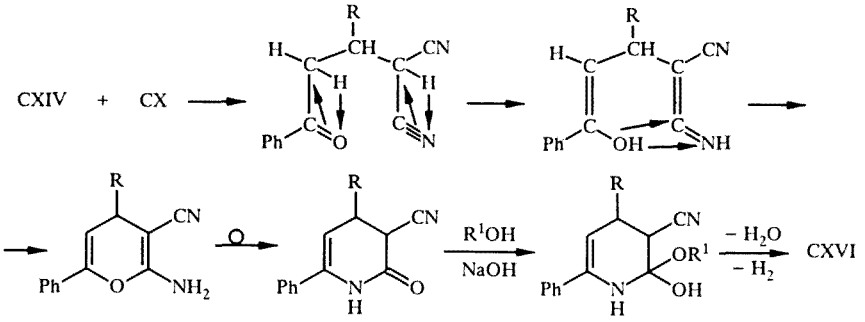


The reaction of the unsaturated ketones CXIV with the dinitrile CX in the presence of compounds with different basicities leads to different products. Thus, when using piperidine, the pyrone derivatives CXV are formed (yields 15.8%-31.7%); and when a stronger base is used, the pyridine derivatives CXVI are formed [72, 73]:

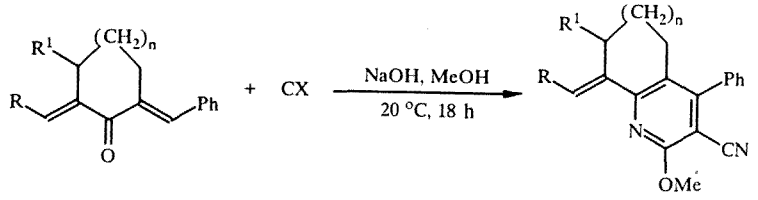


R, yield CXVI (%): Ph, 40,5; PhCH=CH, 18,7; 1-naphthyl 43,6; R^1 = Me, Et, Pr, Bu

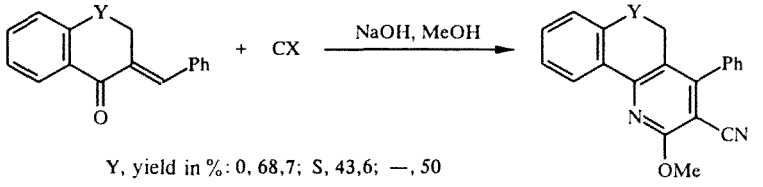
Formation of the compounds CXVI is explained by the authors using the following scheme [72]:



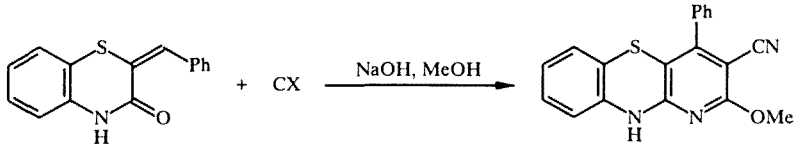
When this reaction is carried out with cyclic ketones in which along with the −C=O group there is a semicyclic double bond, bicyclic and also tricyclic compounds were obtained (25% yield) [73]:



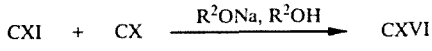
R, R^1, *n*, yield (%): Ph, H, 0,58, 9; Ph, H, 1, 23, 4



Y, yield in %: 0, 68,7; S, 43,6; —, 50

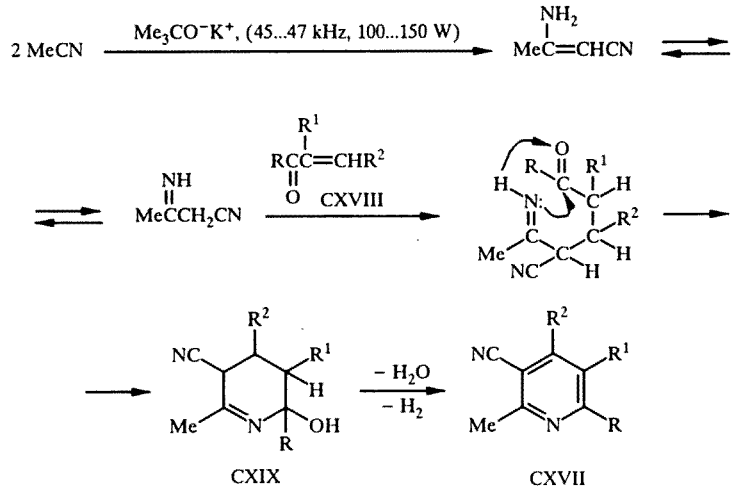


The series of 2-alkoxy-3-cyano-4,6-disubstituted pyridines CXVI was synthesized from the chalcones CXI and the dinitrile CX in the presence of sodium methoxide or sodium ethoxide [74]:



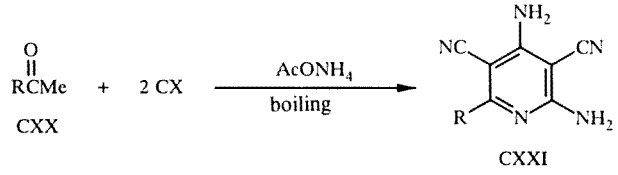
R, R^1, R^2, reaction time in min, yield (%): Ph, Ph, Et, 25, 71; 4-MeC_6H_4, 4-MeC_6H_4, Et, 120, 66; 4-ClC_6H_4, 4-MeC_6H_4, Et, 30, 74,; 4-BrC_6H_4, 4-MeC_6H_4, Et, 25, 78; 2-thienyl, 4-MeC_6H_4, Et, 15, 80; 2-thienyl , 4-$MeOC_6H_4$, Et, 20, 77; Ph, 4-$MeOC_6H_4$, Et, 35, 64; 2-thienyl -2, 4-ClC_6H_4, Et, 45, 65; 2-thienyl , 3-BrC_6H_4, Et, 50, 61; 2-pyridyl, 3-ClC_6H_4, Et, 70, 75; Ph, 2,4-$Cl_2C_6H_3$, Et, 40, 58; Ph, 3,4-$Cl_2C_6H_3$, Et, 45, 60; 4-BrC_6H_4, 4-ClC_6H_4, Me, 15, 58; 4-$MeOC_6H_4$, 4-MeC_6H_4, Me, 35, 58; Ph, 4-$MeOC_6H_4$, Me, 50, 78; 2,4-$(MeO)_2C_6H_3$, 4-MeC_6H_4, Me, 35, 56; 4-ClC_6H_4, 2,4-$(MeO)_2C_6H_3$, Me, 45, 70; 4-$MeOC_6H_4$, 3,4-$Cl_2C_6H_3$, Me, 45, 72; Ph, Ph, Me, 30, 70; 4-ClC_6H_4, 4-MeC_6H_4, Me, 25, 76; 2-pyridyl, 4-MeC_6H_4, Me, 20, 62; 2-pyridyl-2, 4-$MeOC_6H_4$, Me, 25, 61; Ph, 4-$MeOC_6H_4$, Me, 40, 75

An original and promising method for obtaining the pyridine derivatives CXVII, containing alkyl, aryl, ferrocenyl, and/or hetaryl radicals, was developed by Japanese researchers [75-77]. They carried out the reaction of the chalcones CXVIII with acetonitrile in the presence of potassium *tert*-butoxide under the action of ultrasound. From the data obtained, at first the dimer of acetonitrile is formed. Then this dimer is added to the chalcone and the addition products undergo cyclization to the tetrahydropyridine derivatives CXIX. The latter are converted to the compounds CXVII by eliminating a water molecule and a hydrogen molecule:



R, R^1, R^2, yield (%): Ph, H, 4-ClC_6H_4, 70; Ph, H, Ph, 93; 4-$MeOC_6H_4$, H, Ph, 93; Me_3C, H, Ph, 97; Me, H, Ph, 66; Ph, Ph, Ph, 59; Ph, H, Ph, 29; Ph, Me, Ph, 32; H, H, Ph, 40; Ph, H, 4-ClC_6H_4, 30 [75]; Fc (ferrocenyl), H, Ph, 82; Fc, H, 2-furyl, 55; Fc, H, 2-thienyl, 63; Fc, H, 2-pyridyl, 89; Fc, H, 4-ClC_6H_4, 80; Fc, H, 4-$MeOC_6H_4$, 85; Fc, H, 1-naphthyl, 60; Fc, H, Fc, 80; Me_3C, H, Fc, 74; Ph, H, Fc, 82; 2-furyl, H, Fc, 85; 2-thienyl, H, Fc, 88; 2-pyridyl, H, Fc, 68; 4-ClC_6H_4, H, Fc, 63; 4-$MeOC_6H_4$, H, Fc, 76 [76]; Ph, H, 2-furyl, 87; Ph, H, 2-thienyl, 80; Ph, H, 2-pyrrolyl, 62; Ph, H, 2-pyridyl, 54; 4-ClC_6H_4, H, 2-furyl, 85; 4-ClC_6H_4, H, 2-thienyl, 71; 4-ClC_6H_4, H, 2-pyrrolyl, 86; 4-$MeOC_6H_4$, H, 2-furyl, 36; 4-$MeOC_6H_4$, H, 2-thienyl, 69; 4-$MeOC_6H_4$, H, 2-pyrrolyl, 62; 4-$MeOC_6H_4$, H, 2-pyridyl, 70; 2-furyl, H, Ph, 77; 2-furyl, H, 2-thienyl, 66; 2-furyl, H, 2-pyrrolyl, 63; 2-thienyl, H, Ph, 59; 2-thienyl, H, 2-furyl, 71; 2-thienyl, H, 2-thienyl, 86; 2-thienyl, H, 2-pyrrolyl, 74; 2-pyridyl, H, Ph, 63; 2-pyridyl, H, 2-furyl, 63; 2-pyridyl, H, 2-thienyl, 67; 2-pyridyl, H, 2-pyrrolyl, 75 [77]

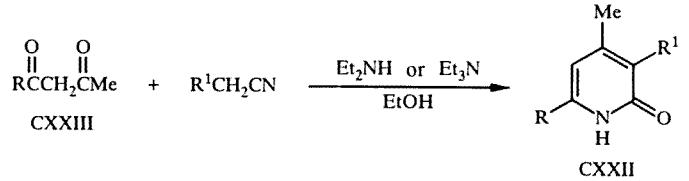
In a number of papers, synthesis of pyridine bases from saturated ketones and nitriles is described. Obviously in these reactions, unsaturated ketonitriles are formed as intermediates which are converted *in situ* to heterocyclic compounds. Thus, 2,4-diamino-3,5-dicyano-6-alkylpyridines CXXI were obtained by boiling the ketones CXX with the dinitrile CX in the presence of ammonium acetate [66]:



R, reaction time in h, yield (%): Me, 3, 24; Et, 5, 32; Pr, 5, 34; C_5H_{11}, 6, 21; $C_{16}H_{13}$, 6, 25; C_9H_{19}, 4, 19,; Me_2CHCH_2, 7, 4

Under the same conditions (reaction time 7 h), 3-cyano-4,6-diphenyl-6-methyl-5,6-dihydro-2-pyridone is obtained from PhCOMe and the dinitrile CX [66].

The 2-pyridone derivatives CXXII were synthesized by reaction of the diketones CXXIII with the dinitrile CX [78] or the ethyl ester of cyanoacetic acid [78, 79] in the presence of diethylamine [78] or triethylamine [79]:



R, R^1, amine: Ph, CN, Et_2NH (yield 63%); Ph, COOEt, Et_2NH [78]; Me, COOEt, Et_3N [79]

REFERENCES

1. F. Brody and P. R. Ruby, in: Pyridine and Its Derivatives (E. Klingsberg, ed.), Interscience, New York (1960), Vol. 114, Pt. 1, p. 289.
2. N. S. Boodman, J. O. Hawthore, R. X. Msciantonio, and A. B. Simon, in: Pyridine and Its Derivatives (R. A. Abramovitch, ed.), Interscience, New York (1974), Vol. 14, Pt. 1, p. 245.
3. G. Jones, in: Comprehensive Heterocyclic Chemistry (A. R. Katritzky and C. W. Ress, eds.), Pergamon Press, Oxford (1984), Vol. 2, p. 395.
4. E. P. Kohler, A. Graustein, and D. R. Merrill, J. Am. Chem. Soc., **44**, 2536 (1922).
5. E. P. Kohler and Ch. F. H. Allen, J. Am. Chem. Soc., **46**, 1522 (1924).
6. Ch. F. H. Allen, J. Am. Chem. Soc., **47**, 1733 (1925).
7. Ch. F. H. Allen, J. Am. Chem. Soc., **49**, 1112 (1927).
8. N. P. Shusherina, A. V. Golovin, and R. Ya. Levina, Zh. Obshch. Khim., **30**, 1762 (1960).
9. D. Diller and F. Bergmann, J. Org. Chem., **73**, 2147 (1972).
10. F. Hoffman, Brit. Pat. 549,673; Chem. Abstr., **38**, 978 (1944).
11. F. Hoffman, Swiss Pat. 216,943; Chem. Abstr., **42**, 6860 (1948).
12. F. Hoffman, Swiss Pat. 221,820; Chem. Abstr., **43**, 3472 (1949).
13. F. Hoffman, Swiss Pat. 221,621; Chem. Abstr., **43**, 3472 (1949).
14. E. P. Kohler and B. L. Souther, J. Am. Chem. Soc., **44**, 2903 (1922).
15. Ch. F. H. Allen and W. L. Ball, J. Am. Chem. Soc., **59**, 686 (1937).
16. E. Steiner, P. Martin, and D. Bellus, EPV 12117; Chem. Abstr., **93**, 186186 (1980).
17. E. Steiner, P. Martin, and D. Bellus, Helv. Chim. Acta, **65**, 983 (1982).
18. E. Steiner and P. Martin, EPV 46735; Chem. Abstr., **97**, 23629 (1982).
19. E. Steiner and P. Martin, US Pat. 4,469,896; Chem. Abstr., **101**, 21002 (1984).
20. P. Martin, E. Steiner, J. Streith, T. Winkler, and D. Bellus, Tetrahedron, **41**, 4057 (1985).
21. D. Bellus, Pure Appl. Chem., **57**, 1827 (1985); Chem. Abstr., **105**, 171416 (1986).
22. M.-G. A. Shvekhgeimer, K. I. Kobrakov, S. S. Sychev, and V. K. Promonenkov, Khim. Geterotsikl. Soedin., No. 8, 1082 (1987).
23. S. S. Sychev, Dissertation in competition for the academic degree of Candidate of the Chemical Sciences, Moscow (1988).
24. M.-G. A. Shvekhgeimer, K. I. Kobrakov, S. S. Sychev, and V. K. Promonenkov, USSR Pat. 1,182,035; B. I., No. 36 (1985).
25. M.-G. A. Shvekhgeimer, K. I. Kobrakov, S. S. Sychev, and V. K. Promonenkov, USSR Pat. 1,325,045; B. I., No. 27, 95 (1987).
26. M.-G. A. Shvekhgeimer, K. I. Kobrakov, S. S. Sychev, and V. K. Promonenkov, Dokl. Akad. Nauk SSSR, **294**, 893 (1987).
27. M.-G. A. Shvekhgeimer, K. I. Kobrakov, S. S. Sychev, and V. K. Promonenkov, Khim. Geterotsikl. Soedin., No. 4, 514 (1989).
28. Z. Lysenko and R. G. Pews, US Pat. 4,445,573; Chem. Abstr., **100**, 191478 (1984).
29. R. G. Pews and Z. Lysenko, J. Org. Chem., **50**, 5115 (1985).
30. M. E. Halpern, Th. J. Dietsche, J. A. Orvik, and B. J. Barron, EPV 306,547; Chem. Abstr., **111**, 173989 (1989).
31. M. E. Halpern, J. A. Orvik, Th. J. Dietsche, and B. J. Barron, US Pat. 5,084,576; Chem. Abstr., **116**, 194166 (1992).
32. K. Peseke, M. Michalik, U. Schoenhausen, and J. Streichardt, Z. Chem., **28**, 328 (1988).
33. N. A. Toshkhodzhaev, Dissertation in competition for the academic degree of Candidate of the Chemical Sciences, Moscow (1993).
34. M.-G. A. Shvekhgeimer, N. A. Toshkhodzhaev, S. S. Sychev, and K. I. Kobrakov, "Synthesis of chlorine-substituted pyridine bases" in: Abstracts, Fifth All-Union Conference on the Current State and Prospects for Development of Theoretical Principles for Production of Organochlorine Products [in Russian], Baku (1991), p. 43.

35. K. I. Kobrakov, M.-G. A. Shvekhgeimer, S. S. Sychev, and N. A. Toshkhodzhaev, in: Abstracts, Fifth All-Union Conference on the Chemistry of Nitrogen-Containing Heterocyclic Compounds [in Russian], Chernogolovka (1991), p. 87.
36. Yu. A. Sharanin, V. K. Promonenkov, and A. M. Shestopalov, Zh. Org. Khim., **18**, 630 (1982).
37. Ch. F. H. Allen and A. C. Bell, Canad. J. Res., **11**, 40 (1934).
38. R. D. Clark and C. H. Heath, J. Org. Chem., **41**, 636 (1976).
39. N. F. Alberston, J. Am. Chem. Soc., **74**, 3816 (1952).
40. O. E. Nasakin, E. T. Nikolaev, P. B. Terent'ev, A. Kh. Bulai, B. A. Khaskin, and V. K. Mikhailov, Khim. Geterotsikl. Soedin., No. 11, 1574 (1984).
41. O. E. Nasakin, E. T. Nikolaev, P. B. Terent'ev, A. Kh. Bulai, and I. V. Lavrent'eva, Khim. Geterotsikl. Soedin., No. 5, 653 (1987).
42. A. Vigier and J. Dreux, Bull. Soc. Chim. France, No. 10, 2292 (1936).
43. G. Y. Lecher, B. Singh, and Ph. M. Carabateas, US Pat. 4431651; Chem. Abstr., **100**, 174679 (1984).
44. A. J. Meyers and G. Garcia-Minoz, J. Org. Chem., **29**, 1435 (1964).
45. W. T. Boyce and R. Levine, J. Org. Chem., **31**, 3807 (1966).
46. K. Popandova-Yambolieva and C. Jvanov, Dokl. Bolg. Akad. Nauk, **42**, 35 (1989).
47. K. Grohe and A. Roeding, Chem. Ber., **100**, 2953 (1967).
48. D. Münzner, H. Lettau, and H. Z. Schubert, Z. Chem., **7**, 278 (1967).
49. O. Yu. Magidson, Zh. Obshch. Khim., **33**, 2173 (1963).
50. M. Cherubim and F. A. Dagga, BRD Pat. 2,245,097; Chem. Abstr., **80**, 146041 (1974).
51. R. Hull, J. Chem. Soc., No. 4, 1136 (1951).
52. C. F. Koelsch and H. M. Walker, J. Am. Chem. Soc., **72**, 346 (1950).
53. F. Hoffmann, Swiss Pat. 221,822; Chem. Abstr., **43**, 3472 (1949).
54. A. D. Campbell and J. D. R. Stevens, J. Chem. Soc., No. 4, 959 (1956).
55. T. A. Favorskaya, N. Yu. Baron, and S. I. Yakimovich, Zh. Org. Khim., **5**, 1187 (1969).
56. N. P. Shusherina, R. Ya. Levina, and H. Hua-Minh, Zh. Obshch. Khim., **31**, 3477 (1961).
57. N. P. Shusherina, H. Hua-Minh, and R. Ya. Levina, Zh. Obshch. Khim., **33**, 3613 (1963).
58. N. P. Shusherina, R. Ya. Levina, and H. Hua-Minh, Zh. Obshch. Khim., **32**, 3599 (1962).
59. B. D. Simpson, A. M. Schnitzer, and R. L. Cobb, US Pat. 3,007,931; Chem. Abstr., **56**, 4738 (1962).
60. Z. Lysenko and R. G. Pews, EPV 137,415; Chem. Abstr., **103**:177970 (1985).
61. N. F. Albertson, J. Am. Chem. Soc., **72**, 2594 (1950).
62. H. Plieninger, Chem. Ber., **86**, 25 (1953).
63. A. N. Kost, T. A. Shchegoleva, and L. G. Yudin, Zh. Obshch. Khim., **25**, 2264 (1955).
64. Yu. K. Yur'ev, N. K. Sadovaya, and V. V. Titov, Zh. Obshch. Khim., **28**, 3036 (1958).
65. Z. Lysenko and R. G. Pews, EPV 143,465; Chem. Abstr., **104**, 5574 (1986).
66. A. Sakurai and H. Midorikawa, Bull. Chem. Soc. Jpn., **41**, 430 (1968).
67. N. Latif, N. Mishriky, and N. S. Girgis, Indian J. Chem., **20B**, 147 (1981).
68. S. S. Verma, P. Taneja, L. Parkash, and R. Z. Mutal, J. Indian Chem. Soc., **65**, 798 (1988).
69. M. D. Ankhiwala, J. Indian Chem. Soc., **69**, 166 (1992).
70. A. Sammour, Y. Akhnookh, and H. Jahine, Egypt. J. Chem., **13**, 421 (1970); Chem. Abstr., **77**, 101348 (1972).
71. F. M. Abdelzazek, A. W. Erian, and A. M. Torgman, Chem. Ind., No. 1, 30 (1988).
72. T. Al Nakib and M. J. Meegan, J. Chem. Res. Synop., No. 5, 146 (1988).
73. D. V. Tundall, T. Al Nakib, and M. J. Meegan, Tetrahedron Lett., **29**, 2703 (1988).
74. M. M. Al Arab, J. Heterocycl. Chem., **26**, 1665 (1989).
75. K. Shibata, K. Urano, and M. Matsui, Bull. Chem. Soc. Jpn., **61**, 2199 (1988).
76. K. Shibata, J. Katsujama, M. Matsui, and H. Muramatsu, Bull. Chem. Soc. Jpn., **63**, 3710 (1990).
77. K. Shibata, J. Katsujama, M. Matsui, and H. Muramatsu, J. Heterocycl. Chem., **28**, 161 (1991).
78. U. Basu, J. Indian Chem. Soc., **7**, 815 (1930).
79. A. N. Osman, M. Ismail, and M. A. Barakat, Egypt. J. Pharm. Sci., **28**, 87 (1987); Chem. Abstr., **109**, 110211 (1988).