Translated from *Uspekhi Khimii*, **50**, 1072 - 1104 (1981) U.D.C. 547.821

Advances in the Chemistry of α,α'-Disubstituted Pyridines

L.N.Yakhontov and D.M.Krasnokutskaya

The methods of synthesis of α,α'-disubstituted pyridines are surveyed and recent advances in this field are indicated. Various ways of constructing the α,α'-disubstituted pyridine ring and of replacing one set of α,α'-substituents by another are described. The characteristics of the chemical behaviour of α,α'-disubstituted pyridines due to the steric and inductive effects of the substituents and their influence on the reactivity of the nitrogen atom and processes involving electrophilic substitution in the pyridine ring are examined. The chemical behaviour of the various functional groups in pyridine systems with α,α'-substituents as well as the characteristic features of the tautomerism and the dual reactivity of substances of this class are discussed.
The bibliography includes 254 references.

CONTENTS

I Introduction 565
II. Methods of synthesis of α,α'-disubstituted pyridines 565
III. Chemical characteristics of α,α'-disubstituted pyridines 572

I. INTRODUCTION

The introduction of α,α'-substituents into nitrogen-containing heteroaromatic compounds alters significantly their chemical properties. Together with the usual inductive and mesomeric effects of the substituents in aromatic systems, their influence on the ring heteroatom is in this case manifested and frequently becomes of primary importance.

The mechanism of this influence has been by no means completely investigated and according to many authors is not restricted to steric and inductive factors but includes additional effects characterised by different investigators as "effects of the proximity to the heteroatom", "the effect of the mutual influence of atoms transmitted through space and not through bonds", "the field effect", etc. The physical significance of these effects is not adequately clear but in one way or another the nature of the heterocyclic nitrogen atom changes markedly under the influence of α,α'-substituents. In many cases its nucleophilic properties and its capacity for protonation, complex formation, and solvation are significantly suppressed. This frequently leads to the loss of specificity in the chemical behaviour of the compounds as nitrogen heterocycles and to the appearance of properties typical for aromatic systems without a heteroatom.

It is noteworthy that the effects of α,α'-substituents in various chemical reactions can be extremely varied. These include the destabilisation of the intermediate carbanions, the ease of chelate formation with the interacting reagents, the suppression of processes proceeding via "conjugate acids", etc. The nature of the mutual influence of the α- and α'-substituents transmitted through the ring heteroatom is complex and to a large extent still remains uninvestigated.

So far as we are aware, there are no reviews in the literature dealing with the influence of α,α'-substituents on the properties of azine systems. The aim of the present review is an attempt to fill this gap to some extent and to survey the available information for the simplest case of α,α'-disubstituted nitrogen-containing heterocycles, namely α,α'-disubstituted pyridines. The review surveys also the methods of synthesis of α,α'-disubstituted pyridines described in numerous scattered articles and reviews devoted to specific problems and the advances achieved in this field in recent years.

II. METHODS OF SYNTHESIS OF α,α'-DISUBSTITUTED PYRIDINES

α,α'-Disubstituted pyridines can be obtained by various methods:

(1) By constructing the pyridine ring from aliphatic compounds.

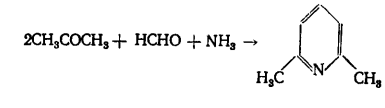
(2) By converting a wide variety of cyclic non-pyridine compounds into α,α'-disubstituted pyridines.

(3) By replacing one set of substituents in α,α'-disubstituted pyridines by another.

The methods of synthesis of new compounds involving a change in the nature of the substituents only in the β-, β'-, or γ-positions of the pyridine ring and not involving the α,α'-substituents constitute a special group, which will not be discussed in this review.

1. Synthesis of α,α'-Disubstituted Pyridines from Aliphatic Compounds

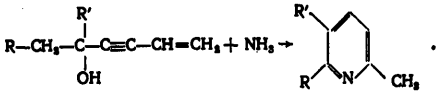
The classical method of synthesising α,α'-disubstituted pyridines with alkyl or aryl residues is the Chichibabin reaction, widely used in the pyridine chemistry and based on the condensation (usually in the gase phase) of ammonia with ketones, aldehydes, nitriles, acetylene derivatives, or their mixtures[1,2]. A series of 2,4,6-triarylpyridines have been synthesised by this method from aromatic aldehydes, aryl methyl ketones, and ammonium acetate[3]. The Chichibabin reaction is used also on an industrial scale to obtain synthetic 2,6-dimethylpyridine (2,6-lutidine) via the mechanism[4]



The synthesis of α,α'-dialkylpyridines by the interaction of aliphatic ketones with ammonia in the gas phase on a platinum catalyst has been recently reported[5].

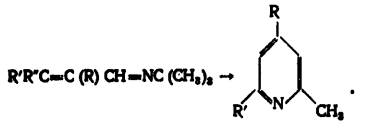
A number of 6-alkyl(aryl)-2-methylpyridines have been obtained by the condensation of vinylacetylenic alcohols

with ammonia[1]:

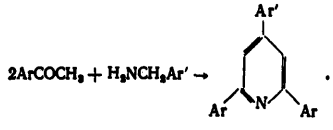


A mixture of the corresponding ketone with vinylacetylene can also be used in the reaction with ammonia.

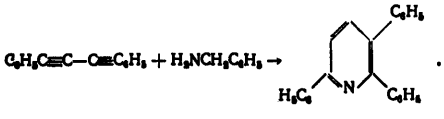
The reaction of unsaturated imino-compounds with chromium and aluminium salts has been used to obtain 4-ethyl-2,6-dimethylpyridine and its analogues via the mechanism[6]



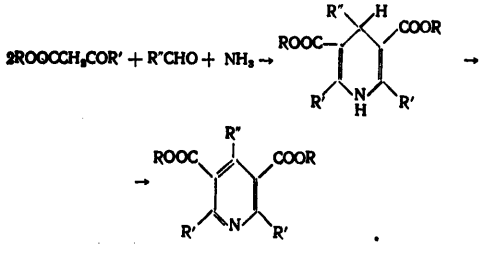
2,4,6-Triarylpyridines are obtained by Reddelin's method involving the condensation of acetophenone with benzylamines in the presence of traces of hydrogen bromide[7,8]:



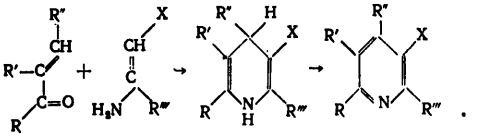
Refluxing of diphenylbutadiyne with benzylamine leads to 2,3,6-triphenylpyridine[9]:



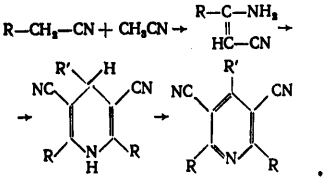
The Hantzsch reaction[10], involving the cyclocondensation of β-ketoesters with aldehydes and ammonia and subsequent oxidation of the 1,4-dihydropyridine derivatives formed, is of practical importance in the synthesis of α,α′-disubstituted pyridines:



Many modifications of Hantzsch's method are known. Instead of ammonia, ammonium acetate, formamide, urotropine, and more rarely primary amines are introduced into the reaction. Together with acetoacetic esters, the esters of cyanoacetic and malonic acids and their various derivatives are used as the carbonyl components: enol acetals, enol esters, iminoethers, etc. In many instances, particularly in the synthesis of asymmetric compounds, it is convenient to begin with α,β-unsaturated ketones, which are intermediates in the Hantzsch reaction formed on condensation of aldehydes with β-dicarbonyl compounds or from substances of analogous structure: methylene aldehydes, methylene ketimines and esters, acetylenic amidines[11], β-chlorovinyl ketones[12], etc. Another possible intermediate in the Hantzsch synthesis—β-aminocrotonic ester or substance of analogous structure (enaminoketones, enaminonitriles, etc.)—are frequently used as second components in these reactions[10,11]:

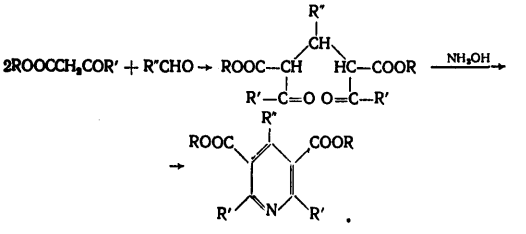


One of the variants of the Hantzsch synthesis is the Meyer–Mohr reaction[13], involving the cyclocondensation of aldehydes or ketones with enaminonitriles obtained on interaction of various nitriles with acetonitrile in the presence of strong bases:



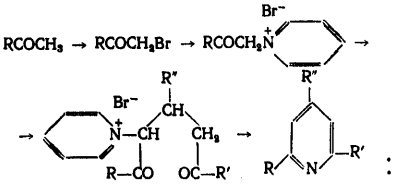
Another variant consists of the condensation of β-aminocrotonic ester with 1,3-enynylamines[14], sodioformylacetone, the acetal of ethoxycrotonaldehyde, or α-ethynylcarbonyl compounds[15].

The isolation of the intermediate product of the condensation of acetoacetic ester with an aldehyde (a derivatives of a 1,5-diketone) and its treatment with hydroxylamine constitute a modification of the initial Hantzsch synthesis[253]:

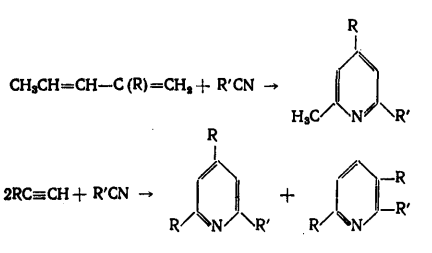


The direct cyclisation of 1,5-diketones and their oximes or imines has also been described[1,11,16].

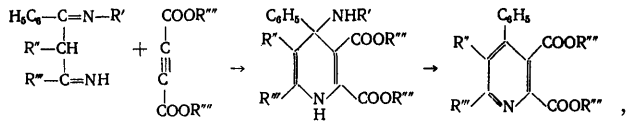
The synthesis of α,α′-disubstituted pyridines from *N*-acetonylpyridinium salts, unsaturated ketones, and ammonium acetate via 1,5-dicarbonyl compounds, proposed by Kröhnke,[17,18] is of considerable preparative interest:



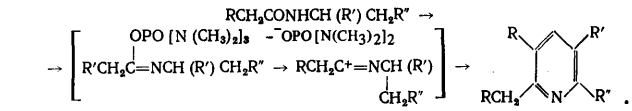
Certain α,α′-disubstituted pyridines have also been obtained by the reaction of nitriles with dienes[19] or acetylenes[20]:



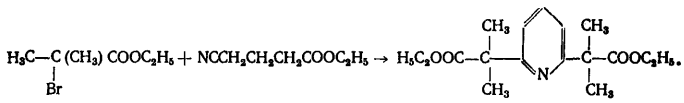
or of 1,3-di-imines with acetylenedicarboxylate esters[21]:



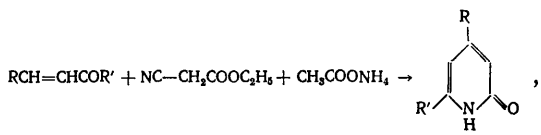
by the cyclisation of secondary carboxamides involving cautious heating in hexamethylphosphoramide[22]:



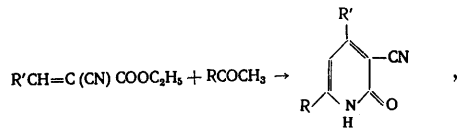
or by the condensation of α-bromoesters with γ-alkoxycarbonylnitriles under the conditions of the Reformatzky reaction[23]:



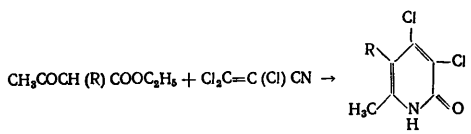
A method of synthesis of 6-substituted 2-pyridones, which follows directly from the Hantzsch reaction, is based on the condensation of the derivatives of malonic ester or malononitrile with enamines[24-28] and also of cyanoacetic ester with α,β-unsaturated ketones and aminoacetate[29]:



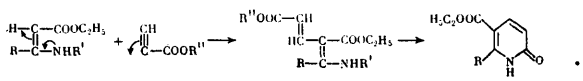
of cyanoacrylic esters with ketones[30]:



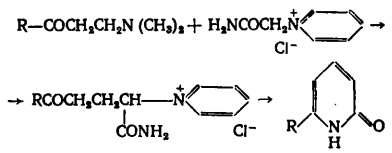
or of β-ketoesters with trichloroacrylonitrile[31]:



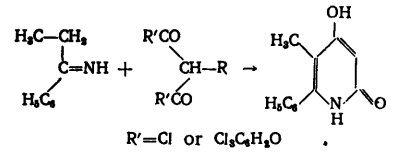
When enaminoesters react with propiolic acid esters, dienamines, which are also capable of cyclising to 6-substituted 2-pyridones, are formed readily[32]:



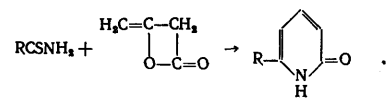
The condensation of α,β-unsaturated ketones or the corresponding products of the Mannich reaction with *N*-carbamoylmethylpyridinium salts also leads to 6-substituted 2-pyridones[33]:



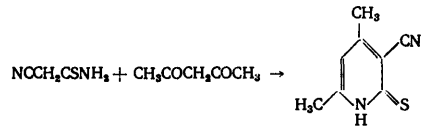
The 2-pyridones are likewise obtained when propiophenoneimine interacts with monosubstituted malonyl chlorides[34] or malonic esters[35]:



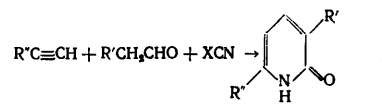
Another way of synthesising 6-substituted 2-pyridones containing in addition a hydroxy-group in the 4-position consists in the condensation of thioamides with diketen[36]:



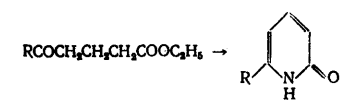
The cyclocondensation of cyanothioacetamide with acetylacetone yielded 3-cyano-4,6-dimethyl-2-pyridinethione:



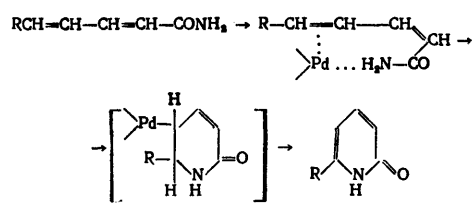
while the condensation of acetylenic compounds with aldehydes and nitriles gave rise to 3,6-disubstituted 2-pyridones[37]:



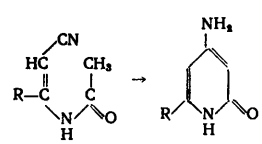
By analogy with the cyclisation of 1,5-diketones discussed above, the interaction of 5-oxoalkenecarboxylic acids or their derivatives (amines, nitriles, etc.) with ammonia or primary amines also leads to the formation of 2,6-disubstituted pyridines—in the given instance 6-substituted 2-pyridones[11]:



The methods of synthesis of 6-substituted 2-pyridones by the cyclisation of 2,4-pentadienamides with lithium chloropalladate(II) in acetonitrile in the presence of triethylamine[38], i.e.

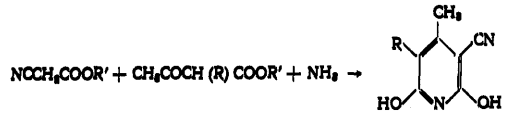


and the Dieckmann cyclisation of certain *N*-substituted amides via the mechanism[11]



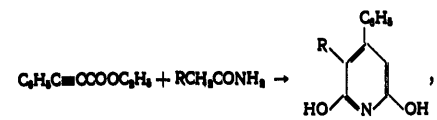
occupy a special place.

The most general and most widely used method of synthesis of α,α'-dihydroxypyridines is the Guareschi–Thorpe reaction[11,39,40], which is based on the cyclocondensation of cyanoacetic and α-alkylacetoacetic esters with ammonia:

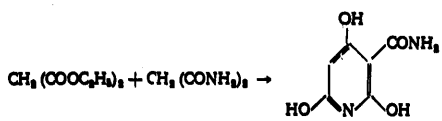


The corresponding amides are frequently used in this reaction instead of esters. The alkyl substituent R may contain different functional groups and multiple bonds. The cyclocondensation is usually carried out in water at room temperature, but reactions without a solvent or in non-aqueous media have also been described[39]. α,β-Unsaturated carbonyl compounds have been used instead of acetoacetic ester or amide[11]. Cyclocondensation with cyanoacetic ester or cyanoacetamide is carried out in this case in the presence of alkali metal alkoxides. One of the variants of the synthesis involves the interaction of cyanoacetic ester with aldehydes and ammonia, whereupon α,β-unsaturated carbonyl derivatives are formed as intermediates as a result of the reaction of the aldehydes with cyanoacetic ester.

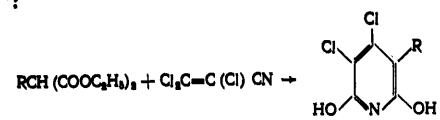
The cyclocondensation of phenylpropiolic ester with amides leads to 3,4-disubstituted 2,6-dihydroxypyridines[41,42]:



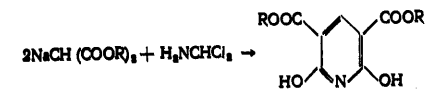
that of malonic ester with malonodiamide in the presence of sodium methoxide produces 3-carbamoyl-2,4,6-trihydroxypyridine[43]:



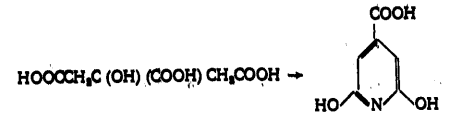
and that of substituted malonic ester with trichloroacrylonitrile under the influence of potassium t-butoxide results in the formation of 3-substituted 4,5-dichloro-2,6-dihydroxypyridines[44]:



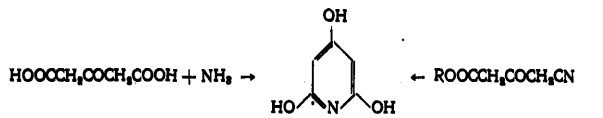
The Gattermann–Skitta reaction, involving the formation of 2,6-dihydroxypyridines by the cyclocondensation of sodiomalonic ester with dichloromethylamine, is a variant of the Hantzsch synthesis[254]:



Different variants of the cyclisation of glutaric acid and its substituted derivatives are widely used for the synthesis of α,α'-dihydroxypyridines. β-Oxo-, β-hydroxy-, and β-imino-derivatives of glutaric acid as well as substituted β-carboxy-β-hydroxyglutaric (citric) acid are most often used for this purpose[11]. An example is provided by the synthesis of 2,6-dihydroxyisonicotinic (citrazinic) acid from citric acid and its conversion into isonicotinic acid (the method has found industrial application)[45]:

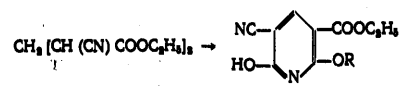


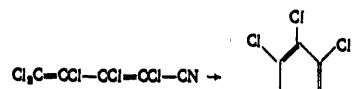
as well as the cyclisation with ammonia of β-oxoglutaric (acetonedicarboxylic) acid, its esters, or mononitrile[11]:

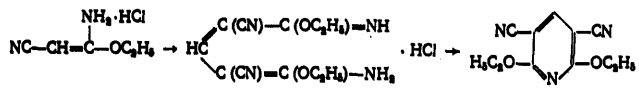


Aryl isothiocyanates or aryl isocyanates have also been used as nitrogen-containing components in these reactions[46].

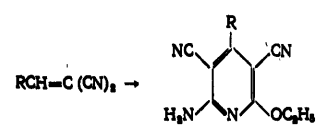
The reactions of methylenebiscyanoacetic esters[11] and pentachloropentadienonitrile[47] with alkali metal oxides as well as the interaction of acid α-methylene derivatives with symmetrical triazine[48] have been used for the closure of a pyridine ring containing 2-alkoxy-6-hydroxy(alkoxy) substituents:





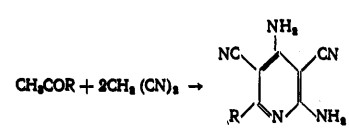


The most general method of synthesis of 2-alkoxy-6-aminopyridines, based on the closure of the pyridine ring, is the condensation of substituted methylenemalonodinitriles with alkali metal alkoxides[49–52]:

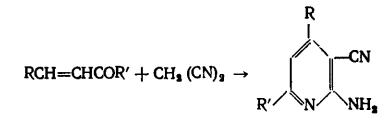


The reactions of acetoacetic or malonic esters with methylene amidines, methyleneimidates, and 5-aminopyrazolones[53], the cyclisation of acetonedicarboxylic ester with ammonia[54], and the condensation of acetylenic compounds with cyanamide[20] are used for these purposes.

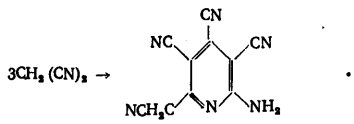
Malonodinitrile has been widely used in recent years in the synthesis of 6-substituted 2-aminopyridines[55]; the condensation of the dinitrile with methyl ketones in the presence of an excess of ammonium acetate leads to 6-alkyl-2-aminopyridines[56,57]:



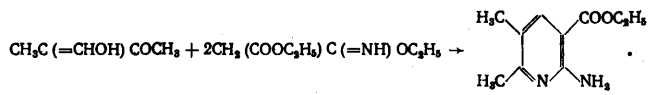
The reaction with unsaturated ketones proceeds in a somewhat different manner[56] via the mechanism



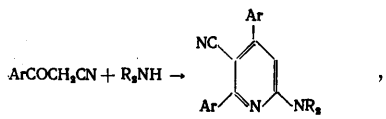
Under the influence of zinc chloride, malonodinitrile trimerises[55]:



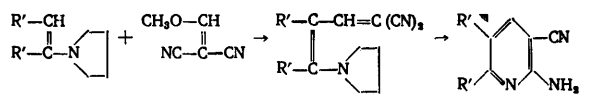
Substituted 2-amino-6-methylpyridine has been obtained by the condensation of ethyl α-hydroxymethylenemethyl ketone with monoiminomalonic ester[58]:



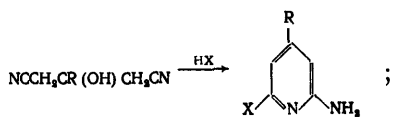
The analogous 6-aryl derivatives are formed on condensation of ω-cyanoacetophenones with secondary amines[59]:



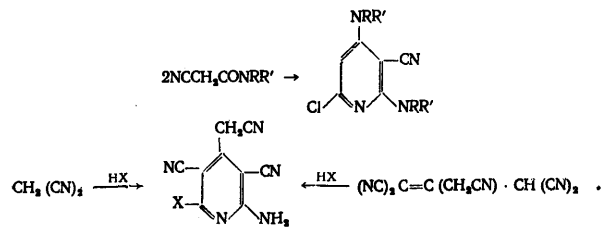
while 6-alkyl derivatives are formed when enamines interact with methoxymethylenemalonodinitrile via intermediate dienamines[60]:



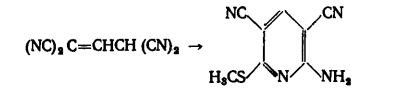
The reactions of 3-hydroxyglutarodinitrile with primary and secondary amines lead to substituted α,α'-diaminopyridines[61]. The use of anhydrous hydrogen bromide or iodide in analogous processes makes it possible to obtain high yields of 2-amino-6-halogenopyridines[62,63]:



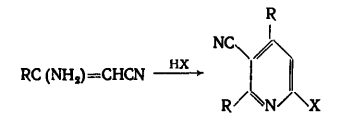
Both possible 2,6-disubstituted isomers are obtained from asymmetric starting materials[64]. Instead of the hydroxy-derivative, the corresponding unsaturated dinitrile can be used in the reaction[65]. Substituted 2-amino-6-chloropyridines have been obtained by the interaction of cyanoacetyldialkylamines with phosphoryl chloride[66] and also by treating malonodinitrile[67], 1,1,3,3-tetracyanopropene, or 2-cyanomethyl-1,1,3,3-tetracyanopropene[63] with hydrogen halides:



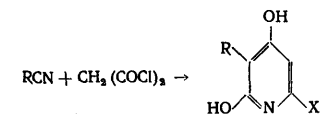
The condensation of 1,1,3,3-tetracyanopropene with methylisothiourea leads to substituted 2-amino-6-methylthiopyridine[68]:



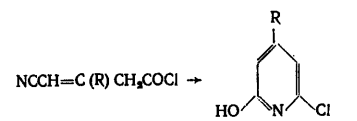
The interaction of enamines with methoxymethylenemalonodinitrile and treatment of the intermediate dienamines with hydrogen halides instead of ammonia made it possible to obtain 6-substituted 2-halogenopyridines[60]. Analogous compounds are also formed on cyclisation of the nitriles or esters of 6-aminocinnamic and β-aminocrotonic acids in the presence of hydrogen halides[70,71]:



2-Halogeno-6-hydroxypyridines have been synthesised by the condensation of malonyl chloride with nitriles[71]:

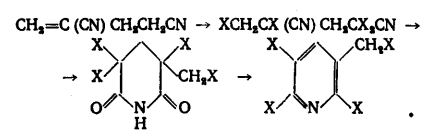


Another method of synthesising compounds of this type consists in the cyclisation of the chlorides of unsaturated γ-cyanoacids under the influence of hydrogen halides[72]:



6-Alkoxy-2-halogenopyridines are formed on cyclisation of perchloropentadienonitrile under the influence of a Grignard reagent[73].

The reaction of glutaramides and glutarimides with phosphorus halides and subsequent aromatisation of the cyclic halogeno-derivatives[74,75] as well as the dimerisation of acrylonitrile, the halogenation of the dimer, the cyclisation of the product, and treatment of the substituted glutarimide with phosphoric acid halides[76] have been used to obtain 2,6-dihalogenopyridines:

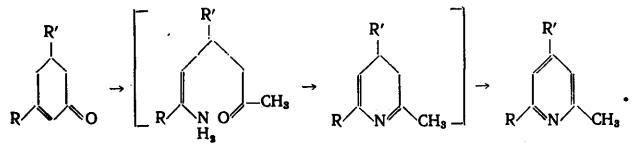


2. The Synthesis of α,α'-Disubstituted Pyridines from Other Cyclic Compounds

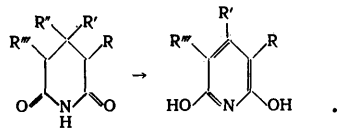
Methods based on the conversion of various non-pyridine cyclic systems into pyridine systems have played an important role in the synthesis of α,α'-disubstituted pyridines.

6-Substituted 2-methylpyridines have been obtained[77] in low yields by heating cyclohexanones with ammonia or ammonium chloride under pressure at 250 °C.[77] It was assumed that the process proceeds via the intermediate formation of

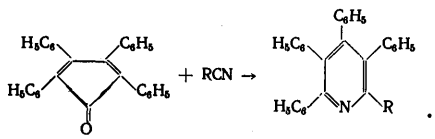
enamines derived from 1,5-dicarbonyl compounds:



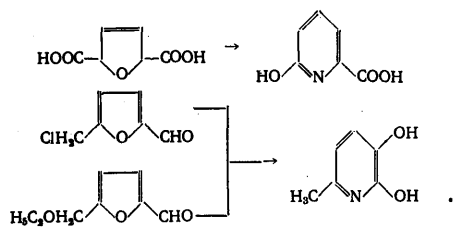
The synthesis of α,α′-dihydroxypyridines (derivatives of glutaconimide) by the oxidation of the corresponding glutarimides has been described[11]:



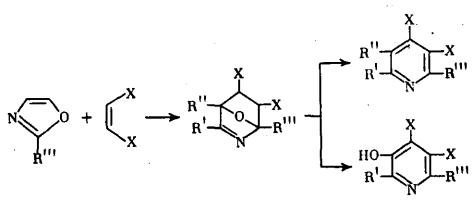
High yields have been achieved in the Diels–Alder condensation of tetraphenylcyclopentadienone with nitriles[78]:



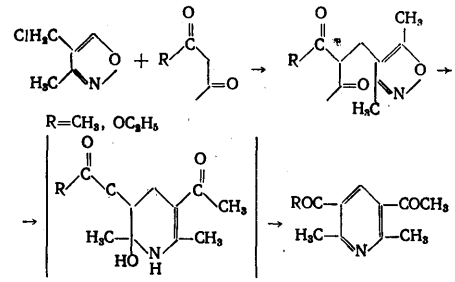
6-Hydroxypicolinic acid has been obtained from 2,5-dicarboxy-2,5-dihydrofuran on heating to 160 °C with aqueous ammonia and ammonium bromide[79]. The reactions of 5-chloromethyl- and 5-ethoxymethyl-furfurals with aqueous ammonium chloride result in the formation under the same conditions of 2,3-dihydroxy-6-methylpyridine together with other products, while 5-substituted 2-acetylfurans are converted into 2,6-disubstituted 3-hydroxypyridines[80–82]:



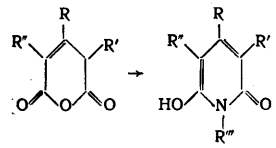
The azadiene condensation of substituted oxazoles with dienophiles (the Kondrat'eva reaction), discovered at the end of the 1950's, constitutes an interesting method of synthesis of α,α′-disubstituted pyridines[83]:



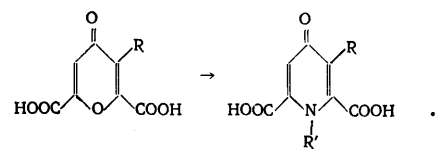
α,α′-Disubstituted pyridines have been synthesised from isoxazoles by catalytic hydrogenation via the mechanism[84,85]



The transformations of the corresponding six-membered oxygen-containing heterocycles occupy a definite place in the synthesis of α,α′-disubstituted pyridines. For example, 6-substituted α-pyrones, obtained by the reaction of malonyl chloride with isocyanates, are converted by treatment with ammonia or amines into the corresponding 6-substituted 2-hydroxypyridines[11,86]. Reactions of this type have been examined in a review[87]:

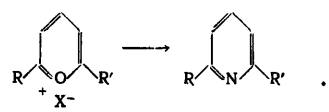


α,α′-Disubstituted γ-pyrones of the type of chelidonic acid are converted into α,α′-disubstituted γ-pyridones (derivatives of chelidamic acid) on treatment with ammonia or amines[88]:

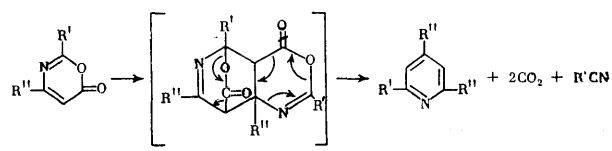


α,α′-Dihalogeno-γ-pyrones give rise similarly to α,α′-dihalogeno-γ-pyridones[89].

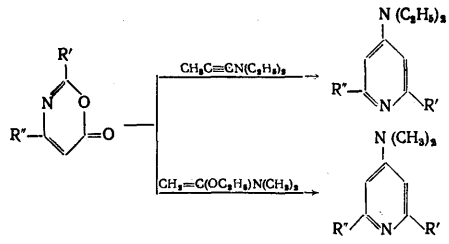
Numerous 2,6-disubstituted pyridines [including 2,6-di(t-butyl)pyridines, which are difficult to obtain by other methods[90]] have been synthesised by the reaction of 2,6-disubstituted pyrylium salts with ammonia or amines[91–93]:



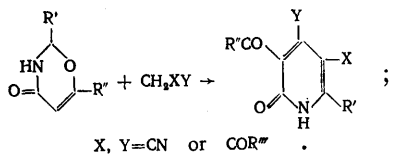
A group of methods is based on the use of oxazine and diazine derivatives as starting materials. These include the pyrolytic cleavage of 6-hydroxy-6*H*-1,3-oxazines[94]:



on interaction with ynamines and keten *O*,*N*-acetals[95]:

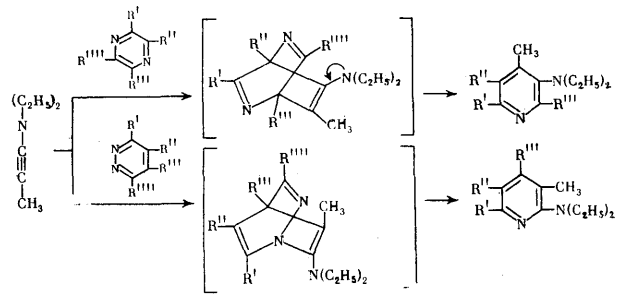


and also the reactions of 2-aryl(alkyl)-4-hydroxy-4*H*-1,3-oxazines with β-dicarbonyl or β-cyanocarbonyl compounds[96]:

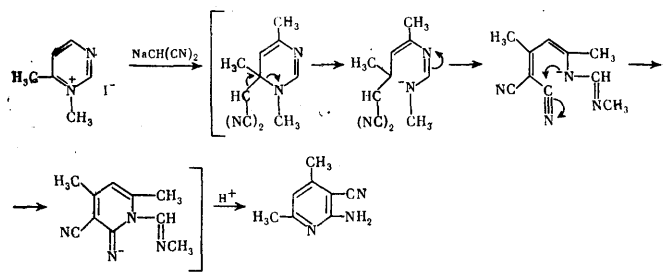


X, Y=CN or COR‴ .

The Diels–Alder condensation of 1-diethylaminopropyne with pyrazine[97] and pyridazine[98] derivatives, i.e.



and the rearrangements of 4-substituted pyrimidines and their quaternary derivatives under the influence of nucleophiles[99–101], i.e.



belong to the same group.

3. Methods of Transforming α,α′-Substituents in the Pyriding Ring

Reactions involving the classical transformation of one set of α,α′-substituents in pyridine structures into another occupy an important place in the synthesis of α,α′-disubstituted pyridines[1,11].

2,6-Dihydroxypyridines are obtained by the hydrolysis of 2,6-diamino, 2,6-dihalogeno-, or 2,6-dialkoxy-pyridines; 6-chloro-2-hydroxypyridines are synthesised by the diazotisation of 2-amino-6-chloropyridine and by the hydrolysis of 2,6-dichloro- or 2-alkoxy-6-chloro-pyridines. 2,6-Dialkoxypyridines are synthesised by the reaction of 2,6-dihalogenopyridines with alkali metal alkoxides[102] or by the alkylation of 2,6-dihydroxypyridines[103]. Under milder conditions, 2,6-dihalogenopyridines react with alkali metal alkoxides to form 6-alkoxy-2-halogenopyridines.

2,6-Dihalogenopyridines are obtained by the reaction of the corresponding 2,6-dihydroxy-derivatives with phosphoric acid halides or hydrogen halides, by the direct halogenation of pyridine bases, their *N*-oxides, or carboxylic acids[104,105], by the substitution of one halogen by another on interaction with hydrogen halides or their salts[106,107], by the arrangement of 2-chloropyridine *N*-oxide on interaction with phosphoryl chloride[108], and by the replacement of nitro-groups by a halogen in the reaction with hydrogen halides.

The reactions of various α,α′-disubstituted pyridines with hydroxy- or halogeno-groups as substituents with P_2S_5 yielded α,α′-dimercaptopyridines[109].

2-Amino-6-halogenopyridines have been synthesised from 2,6-dihalogenopyridines by the substitution of one halogen by an amino-group and from 2-amino-6-hydroxypyridine by the substitution of the hydroxy-group by a halogen; 2,6-diaminepyridines have been synthesised by the corresponding reactions of 2,6-dihalogenopyridines or 6-alkoxy-2-chloropyridines, by the direct Chichibabin amination of pyridines[110], or from dipicolinic acid via the Curtius or Hofmann reactions[111].

6-Alkoxy-2-aminopyridines are obtained by substituting the halogen by an amino-group in 6-alkoxy-2-halogenopyridines; 2-amino-6-nitropyridines are synthesised by the substitution of the bromine atom by the amino-group in 2-bromo-6-nitropyridines; 2-amino-6-hydroxypyridines are obtained by the Chichibabin reaction from α-pyridone or by the hydrolysis of 2,6-diaminopyridine. An interesting instance of the direct amination of 3-azido-2-nitropyridine with formation of a 6-amino-2-nitropyridine derivative and of 2,3,6-triaminopyridine from the latter has been described recently[112].

Direct nitration of pyridine in the α,α′-positions with formation of the 2,6-dinitro-derivatives is possible only in the presence of a strong electron-donating substituent such as an alkoxy-group in the β-position[113]. 3-Methoxy (or hydroxy)-6-methylpyridines are converted on nitration into 3-methoxy(or hydroxy)-6-methyl-2-nitropyridines[114]; the nitration of 3-hydroxy-2-nitropyridine leads to 2,6-dinitro- and 3-hydroxy-2,4,6-trinitropyridine[115]. Kinetic studies have shown that the nitration process involves in these instances the protonated form and that the partial nitration rate constants are 4×10^{-10} for the 2-position and 1×10^{-11} for the 6-position in the 3-methoxypyridinium cation[116]. The halogenation of 3-alkoxy(or hydroxy)pyridines leads similarly to 2,6-dihalogeno-derivatives[113,117], aminomethylation gives rise to 3-alkoxy(hydroxy)-2,6-di(aminomethyl)pyridines[113,118,119], and hydroxymethylation leads to 3-alkoxy-2,6-di-(hydroxymethyl)pyridines[113].

The aminomethylation of 3-hydroxypyridines containing alkyl, alkoxy-, hydroxy-, or nitro-groups in the 2-position, takes place in the 6-position[113,120–124] and the hydroxymethylation of 3-hydroxy-6-methylpyridine involves the 2-position [123,125]; 5-hydroxypicolinic acid is converted as a result of an analogous reaction into 5-hydroxy-6-hydroxymethylpicolinic acid[126]. The azo-coupling of 2,3-dihydroxy-3-ethoxy-2-methoxy-, or 2,5-dihydroxy-pyridines involves the 6-position[127].

Methods of synthesis of 2,6-di(hydroxymethyl)pyridine from 2,6-lutidine via 2,6-diformylpyridine[128-130] or its *N*-oxide[131], via 2,6-di(chloromethyl)pyridine[132] and 2,6-dicyanopyridine[133], and also on the basis of the Böckelheide reaction repeated twice[134] or the oxidation of 2,6-lutidine to dipicolinic acid with reduction of the esters of the latter by complex metal hydrides have been recommended[135].

2,6-Di(bromomethyl)pyridine has been obtained from 2,6-di(hydroxymethyl)pyridine[136] and also by the direct radical bromination of 2,6-lutidine[137]. 2,6-Diformyl pyridine has been synthesied by the catalytic oxidation of 2,6-lutidine[128, 130,138]. 6-Formylpicolinic acid has been obtained similarly from 6-methylpicolinic acid[11].

The Claisen condensation of dipicolinic ester with ethyl acetate has been used to synthesise 2,6-diacetylpyridine[139], while 2,6-dibenzoylpyridine has been obtained by the Friedel–Crafts condensation of dipicolinic acid dichloride with benzene[11]. 2,6-Diacylpyridines have been reduced by the Kishner method to 2,6-dialkylpyridines[140].

The reaction of pyridine *N*-oxide with phenylmagnesium bromide gave a low yield of 2,6-diphenylpyridine together with 2-phenylpyridine[11]. The synthesis of 2,6-dicyanopyridine from 2,6-dibromopyridine and copper cyanide has been described[141].

Potassium permanganate[142], selenium dioxide or its complexes[143], nitrogen oxides in the presence of selenium dioxide[144], sodium dichromate and chromic anhydride[145] have been used as oxidants for the conversion of 2,6-lutidine into 6-methylpicolinic and dipicolinic acids. Dipicolinic acid has also been obtained by the carboxylation of pyridine[146] or picolinic acid[147] and by the oxidative ammonolysis of 2,6-lutidine[148,149] with subsequent hydrolysis of 2,6-dicyanopyridine[150].

III. CHEMICAL CHARACTERISTICS OF α,α′-DISUBSTITUTED PYRIDINES

1. The Influence of α,α′-Substituents on the Reactivity of the Nitrogen of the Pyridine Ring

In the complex mechanism of the influence of α,α′-substituents on the pyridine nitrogen atom steric effects, which have been studied in greatest detail in relation to 2,6-dialkylpyridines, play an important role. Brown and coworkers[151-153] and then other investigators[154,155] showed that, when α,α′-methyl groups are introduced, steric hindrance to the protonation of the pyridine nitrogen is not observed. However, on passing to 2,6-di(t-butyl)pyridine, the pK_a and the heats of neutralisation with methanesulphonic acid in nitromethane (ΔH) clearly indicate a significant steric hindrance in the protonation process. In the analogous reaction with picric acid steric hindrance is manifested even in 6-(t-butyl)-2-isopropylpyridine, which, like 2,6-di(t-butyl)pyridine is incapable of forming a picrate.

On passing from protonation to complex formation involving more bulky reagents—the Lewis acids [BH_3, BF_3, and $B(CH_3)_3$]—steric hindrance becomes appreciably more significant. For example, the heats of formation of complexes with BF_3 decrease in the sequence pyridine > α-picoline > 2,6-lutidine by 9.2 and 35.6 kJ mol^{-1} respectively. In the analogous reaction in $B(CH_3)_3$ the value of $\Delta\Delta H$ is 24.7 kJ mol^{-1} even for α-picoline, while 2,6-lutidine does not form a complex with this reagent at all.

The above steric effects are not only of theoretical but also of preparative interest in a number of instances; the methods of separation of 2,6-lutidine from other components of the β-picoline fraction[156] and the methods of separation of protic and Lewis acids[157] are based on them.

Analogous steric effects are observed also in the interaction of α,α′-disubstituted pyridines with alkyl halides. For example, 2,6-di(t-butyl)pyridine does not form a quaternary salt even with methyl iodide. 2,6-Dimethyl-, 2,6-diethyl, and 2,6-di-isopropylpyridines are converted under identical conditions into methiodides in yields of 99, 74, and 45% respectively[140].

α,α′-Functional substituents exert a more complex influence on the heterocyclic nitrogen atom. For example, in the case of 2,6-dihalogenopyridines the substituents exhibit, in addition to a definite steric effect, a much stronger inductive electron-accepting influence[158]. In contrast to compounds without halogen atoms or α-monohalogeno-derivatives[158-160], 2,6-dihalogenopyridines do not form stable salts with inorganic acids, do not give rise to picrates or complexes with Lewis acids[74,158,161], form quaternary salts with very great difficulty even after prolonged heating at high temperatures under pressure, and are virtually not oxidised to N-oxides[158].

In contrast to 6-methylpicolinic acid, dipicolinic (pyridine-2,6-dicarboxylic) acid is a very weak base and, for example, does not combine with cation-exchange resins in the H^+-form. This permits the esterification of dipicolinic acid by various alcohols in the presence of ion exchangers in high yields[135].

2. The Influence of α,α′-Substituents on the Transformations of the Functional Groups in Other Positions in the Pyridine Ring

The change in the basicity of the pyridine nitrogen under the influence of α,α′-substituents influences not only the processes involving the heteroatom but also the reactivity of the entire pyridine system.

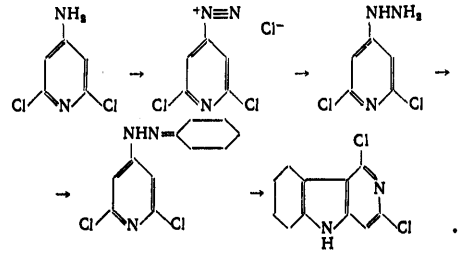
Significant differences between the reactions of pyridines and the analogous benzene derivatives are known to be related both to the change in the distribution of electron densities in the aromatic system owing to the electron-accepting influence of the pyridine nitrogen and to the fact that many electrophilic reactions do not involve the free pyridine bases but take place with participation of the corresponding "conjugate acids", which are characteristed by an even greater electron-accepting effect of the positively charged heteroatom[162,163].

The introduction of α,α′-substituents into the pyridine ring affects both the distribution of electron density in the system and the ease of formation of the corresponding "conjugate acids". The influence of the ring heteroatom is therefore to a large extent blocked in many reactions of pyridines having electron-accepting or sterically hindered substituents in the 2- and 6-positions and compounds of this type begin to behave like the analogous benzene derivatives.

Pyridines are sulphonated with fairly considerable difficulty, forming more readily complexes with SO_3 via the nitrogen atom[11]. 2,6-Di(t-butyl)pyridine, in which the nitrogen heteroatom is sterically hindered and is incapable of forming the "conjugate acid" under the reaction conditions, proved to be capable of being sulphonated in the 3-position under very mild conditions—by reaction with sulphur trioxide in liquid SO_2 below 0 °C.[151,152] In contrast to the corresponding dehalogenated compounds, the γ-methyl group in α,α′-dihalogeno-γ-methylpyridines does not condense with aldehydes and mesoxalic ester and is not oxidised by selenium dioxide even under very severe conditions[158]. The chlorides of 2,6-dihalogenopyridine carboxylic acids readily undergo the Rosenmund reaction to aldehydes[164], like the chlorides of

aromatic acids; the corresponding 2,6-dehalogenated derivatives of pyridine are not converted into aldehydes by this procedure.

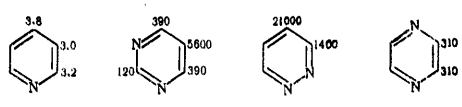
In contrast to the usual 4-aminopyridines, which do not form stable diazonium salts, 4-amino-2,6-dichloropyridine is easily converted on treatment with sodium nitrite into a fairly stable diazonium salt[165], which is reduced in a high yield by tin(II) chloride to 2,6-dichloro-4-pyridylhydrazine. The thermal conversion of the corresponding 4-pyridylhydrazones into indoles in methylene glycol, in which a positively charged pyridinium nitrogen is not formed, actually proceeds with greater difficulty and is less unambiguous for 2,6-dichloropyridines than for the analogous substances without halogen atoms[165]:



Apparently the smaller capacity of α,α'-dihalogenopyridine derivatives for solvation by ethylene glycol has an effect in this instance.

Interesting results were obtained in the study of the quantitative effects of α-substituents by the method of correlation analysis. Determination of a series of such compounds led Zuman[166] to assert that such substances exhibit the "effect of proximity to the heteroatom" with a deviation from the correlation. A study of different series showed that, in contrast to *ortho*-substituted anilines, for α-substituted pyridines the correlation is better in terms of σ_{meta} and σ_{ortho} constants; on this basis, the author[167] concluded that there is virtually no transmission of the influence of α-substituents in terms of the conjugation effect. Owing to the short distances between the α-substituent and the nitrogen, the mutual influence of these reaction centres is exerted through space and not through the bonds. The field effect is taken into account by σ' and σ* constants and less rigorously by the σ_{meta} constant. A field effect decaying rapidly with distance is virtually atypical for the analogous benzene derivatives, where the distance between the reaction centres in the *ortho*-positions is much greater.

For a quantitative estimate of the influence of α-substituents in *N*-heteroaromatic systems, measurements were made[168] of the rate of deuterium isotope exchange in an alkaline medium for different positions of the heterocycles (the rate constants for the exchange of the corresponding hydrogen atoms at 164.6 °C multiplied by a factor of 10^6 are indicated below):



It was found that the hydrogen atoms located near the carbon atoms between the two nitrogen atoms or at the carbon atoms adjoining the nitrogen atoms usually exhibit the smallest capacity for deuterium exchange under these conditions. In pyridine, for example, the base-catalysed deuterium exchange takes place most readily in the 4-position[169], although according to the calculations of charges by the Hückel method the 2-position should be the most "acid"[168].

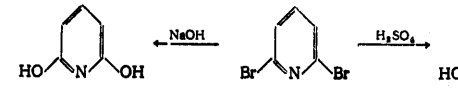
The reduced activity of the α-positions in isotope exchange reactions[170] is apparently the result of the operation of two factors: the decrease of the amount of *s* character of the hydrogen bond with the carbon adjoining the atom of the nucleophile and the repulsion between the electron pairs of the nitrogen and the carbanion being generated. These factors were studied theoretically by various investigators from the standpoint of the theory of hetarynes[171] and α-effects[168, 172].

The above effects should apparently be taken into account also in the study of the characteristics of the chemical behaviour of α,α'-disubstituted pyridines, but as yet there is no information in the literature about this subject.

3. Comparative Reactivities of α,α'- and γ-Substituents in the Pyridine Molecule

The differences between the reactivities of α- and γ-substituents in the pyridine ring, on the one hand, and β-substituents, on the other, have been studied in fair detail[11]. At the same time the comparative reactivities of α-, α'-, and γ-substituents in pyridine compounds have been little investigated. There are as yet no theoretical generalisations in this field and the problem is still mainly in the stage of the accumulation of experimental data. Unfortunately in the series of pyridines, including α,α'-disubstituted and α,α',γ-trisubstituted derivatives, a detailed analysis of the effect of specific solvation and of the influence of various solvents on the reaction mechanism, of the kind carried out, for example, for pyrimidine derivatives[173], has not been performed.

It has been established experimentally that, on heating with an aqueous solution of sodium hydroxide, 2,6-dibromopyridine is fairly smoothly converted into 2,6-dihydroxypyridine, while heating with 70% sulphuric acid even at 160 °C leads only to 6-bromo-2-hydroxypyridine[11]:

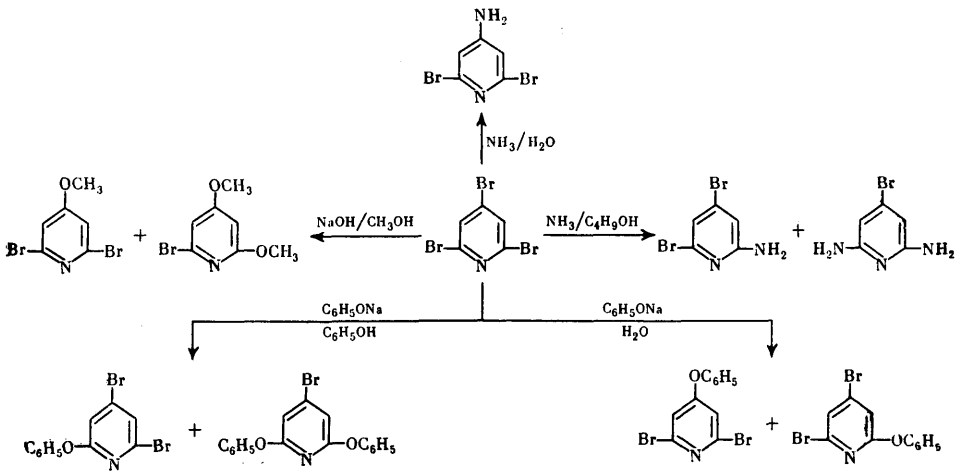


Nucleophilic substitution of 2,4,6-tribromopyridine takes place in the 4- and 2,4-positions in a methanol solution of sodium hydroxide, in the 2- and 2,6-positions in the presence of sodium phenoxide with an excess of phenol, in the 2- and 4-positions in an aqueous solution of sodium phenoxide, in the 4-position in an aqueous solution of ammonia, and in the 2- and 6-positions in a butanol solution of ammonia[11] (see scheme at the top of page 574).

Analogous effects are observed also in the reactions of polyhalogenopyridines. For example, pentachloropyridine reacts with magnesium and butyl-lithium in ether in the 4-position[174]; in methylcyclohexane the same reaction with butyl-lithium takes place only in the 2-position[175-177].

The interaction of pentachloro-,[74] pentabromo-,[178] and pentafluoropyridines[179] with a series of nucleophiles proceeds selectively at the $C_{(4)}$ atom. On the other hand, pentachloropyridine reacts with certain amines only at the $C_{(2)}$ atom[180], while in others it gives rise to a mixture of products of substitution at the $C_{(2)}$ and $C_{(4)}$ atoms[181]. It has been shown recently[182] that the reaction of pentafluoropyridine with pentafluorophenol in the presence of potassium fluoride and 18-crown-6-ether proceeds selectively with substitution of fluorine in the 2-position, although normally this mode of reaction is atypical for pentafluoropyridines[183-185].

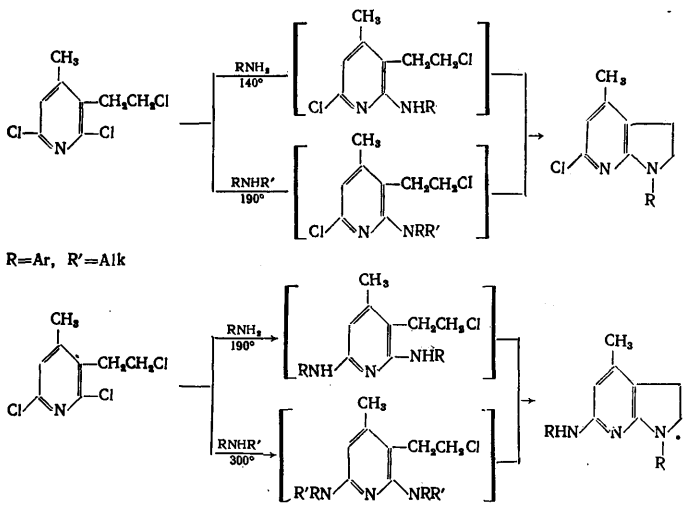
The *N*-sodio-derivative of α-aminopyridine formed in the Chichibabin reaction as a result of the interaction of pyridine with sodium amide is again aminated with sodium amide at a



higher temperature to give 2,6-diaminopyridine. The same compound is also formed on interaction of 2-dimethylaminopyridine with sodium amide; the dimethylamino-group is split off in the form of an *N*-sodio-derivative[186].

In contrast to aromatic diamines, forming 1 : 2 complexes with Lewis acids, 2,6-diaminopyridine combines with only one BF_3 molecule (like 2,4,6-triaminotriazine) to form a 1 : 1 adduct[187]. The hydrolysis of 2,6-diaminopyridine yields only 6-amino-2-hydroxypyridine[11].

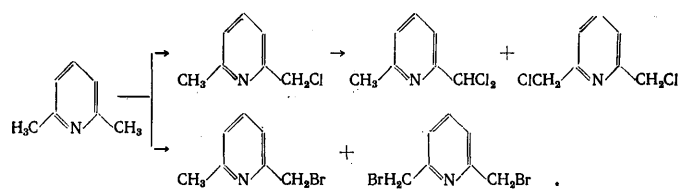
The products of the interaction of substituted 2,6-dichloropyridine (trichlorocollidine) with primary and secondary amines indicate different reactivities of the α- and α'-chlorine atoms in this compound:



The α- and α'-chlorine atoms interact with aromatic amines at 140° and 190 °C respectively[188]; the α-chlorine atom begins to interact with secondary amines of the type of *N*-alkylanilines at 190 °C, while the α'-chlorine atom does not react until 300 °C, *N*-dealkylation occurring in both cases[188-190]. The processes are very sensitive to steric hindrance and the reaction with t-butylamine does not occur at all[188]. After the substitution of the α- or α,α'-chlorine atoms in trichlorocollidine by amine residues, cyclisation involving the β-chloroethyl side chain takes place readily and 7-azaindoline derivatives are formed[189].

Kinetic studies of the oxidation of 2,6-lutidine with potassium permanganate in an aqueous medium showed that the process takes place stepwise and the products corresponding to all oxidation stages are formed even in the earliest stages: 2,6-lutidine → 6-methylpicolinic acid → dipicolinic acid → oxalates → carbonates[142].

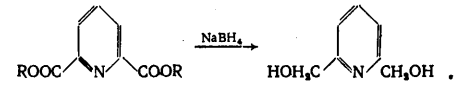
On bromination of 2,6-lutidine with *N*-bromosuccinimide, the monobromo-derivative and the symmetrical dibromo-derivative were isolated in low yields[137]. Further halogenation in CCl_4 at 60 °C in the presence of added sodium carbonate and water of 2-chloromethyl-6-methylpyridine, obtained by the chlorination of 2,6-lutidine, leads to the formation of the asymmetric dichloro-product at a rate which is 3.7 times faster than the formation of the symmetrical product[191]. The opposite results have been described for the reactions of 2,6-lutidine with organolithium compounds[192]:



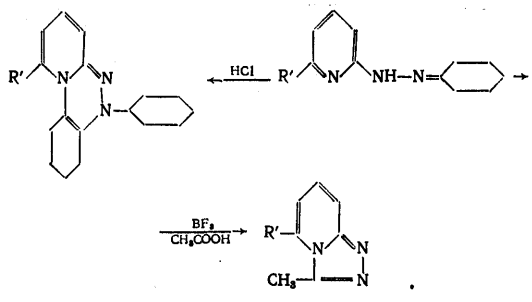
Analysis of the differences between the reactivities of the α,α'- and γ-substituents in the pyridine ring has shown that in many cases the differences are caused by the formation of intermediates with participation of the α,α'-substituents and the pyridine nitrogen atom. For example, it has been established[193] that, in the reduction of isomeric bisalkoxycarbonylpyridines with di-isobutylaluminium hydride, the ester residues in the α,α'-positions of the pyridine ring are the first to be converted into aldehyde groups. This is apparently caused by the favourable energetic factors in the formation of intermediate cyclic products with participation of the complex hydride, the ester groups, and the pyridine nitrogen.

The formation of an intramolecular complex also explains the tendency of pyridine-2,6-dicarboxylate (dipicolinate) esters to be reduced by sodium tetrahydroborate, used in the large-scale industrial synthesis of the medicinal preparation paramidin[135]. Sodium tetrahydroborate does not usually interact with ester groups but dipicolinate esters are reduced by this reagent to 2,6-di(hydroxymethyl)pyridine

in high yields:



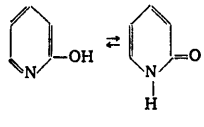
Processes in which the cyclic substances formed are the final reaction products also belong to the class of reactions involving the formation of new rings with participation of the α,α′-substituents and the pyridine nitrogen atom. For example, when 6-bromo- and particularly 6-methyl-2-pyridinylhydrazones of cyclohexanone are treated with hydrochloric acid or the etherate of boron trifluoride in acetic acid, cyclisation via the pyridine nitrogen atom takes place under the conditions of the Fischer reaction. This results in the formation of derivatives of 1*H*-benzo[1,2-*e*]pyrido[2,1-*c*]-*asymm*-triazine and triazolo[4,3-*c*]pyridine:[194–196]



4. Problems of the Tautomerism and the Dual Reactivity of α,α′-Disubstituted Pyridines

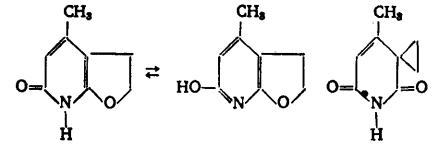
The characteristics of the distribution of electron density in α,α′-disubstituted pyridines, the nature of the protonation and solvation of these compounds have a significant influence on the lactam–lactim tautomerism of 6-substituted 2-hydroxypyridines.

It is known[197–199] that the lactam–lactim tautomeric equilibrium involving α- and γ-hydroxypyridines in aqueous solutions is greatly displaced towards lactams. The enthalpy characterising the extent to which the oxo-form is favoured by energy factors amounts to 14.2 kJ mol^{-1} for α-pyridone[200], while the tautomeric equilibrium constant is 3.0.[197]

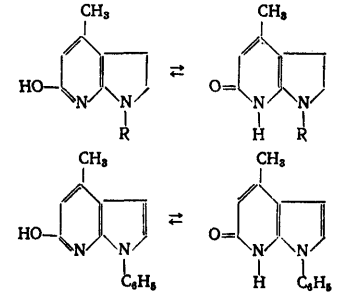


The formation of associated species via intermolecular hydrogen bonds[201–204] and solvation effects[205,206] apparently play an important role. The decrease of the concentration of the test substance in non-polar solvents and an increase of temperature displace somewhat the tautomeric equilibrium in the direction of lactims even in more concentrated solutions [201,207]. For example, at an α-pyridone concentration in cyclohexane of 1.25×10^{-7} M, pK_T decreases to 1.6.[201] However, in this case too the oxo-tautomer predominates[201,208]. It has been established recently by ultraviolet[209] and infrared[213–217] spectroscopy and mass spectrometry[210–212] that only in the gas phase is the tautomeric equilibrium involving α-pyridone displaced towards the hydroxy-form with an equilibrium constant of ~0.4.[201,207,218]

Up to 1966 very little was known about the influence of substituents in α-pyridones in the 6-position on the prototropic lactam–lactim tautomeric equilibrium. Only a report about the differences between the ultraviolet spectra of perchloro-2-pyridone and its *N*-methyl derivative, indicating different chromophoric systems in these compounds, was published[219]. Furthermore, there has been a report, which aroused a wide controversy, concerning the preparative separation of the oxo- and hydroxy-tautomers of 6-hydroxy-4-methyl-2,3-dihydrofuro[2,3-*c*]pyridine, which have different solubilities in ethyl acetate, different melting points, different ultraviolect spectra, and different colour reactions with iron(III) chloride[220]. However, further investigations [221–223] disproved the possibility of isolating individual stable hydroxy- and oxo-tautomers and showed that the second compound is an isomeric product with a spiro-structure:



It was discovered in 1966 [224] that, on passing from α-pyridone to the analogous derivatives of dihydropyrrolo-[2,3-*c*]pyridine (6-hydroxy-7-azaindolines), there is an appreciable shift of the lactam–lactim equilibrium towards lactims. Comparable amounts of both tautomeric forms have been detected in solutions of these compounds by ultraviolet and infrared spectroscopy, but, as a result of a change in the solvent polarity, the equilibrium can be displaced reversibly towards the oxo- or hydroxy-tautomer until it predominates:



On passing from 7-azaindolines to 7-azaindoles, the equilibrium is displaced still more towards the hydroxy-form[225]. For example, infrared spectroscopy failed to detect the lactam form of 6-hydroxy-4-methyl-1-phenyl-7-azaindole either in the crystalline form or in dioxan solution and a weak absorption due to the lactam carbonyl begins to be manifested at 1642 cm^{-1} only in the spectrum of a solution in a more polar solvent—carbon tetrachloride—together with the intense band due to the hydroxy-group of the lactim at 3580 cm^{-1}. Concordant results have been obtained also by ultraviolet spectroscopy using as a reference "fixed" *N*- and *O*-methyl derivatives[225]. The prototropic tautomeric equilibrium is displaced towards the lactim even more in the case of the oxygen analogues of 7-azaindolines—derivatives of 7-azabenzofuran[226].

A change in the junction between the rings, namely the transition from 6-hydroxy-7-aza-compounds to 6-hydroxy-5-azaindoles or benzofurans, causes a sharp weakening of the influence of the heteroatom of the five-membered ring on the position of the tautomeric equilibrium: the predominance of the oxo-form characteristic of α-pyridones is restored for the compounds in the crystalline state and in solutions of different polarity[226]. This permitted the conclusion that a

decisive factor in the effect of the heteroatom of the five-membered ring is its inductive influence, which rapidly decays with distance.

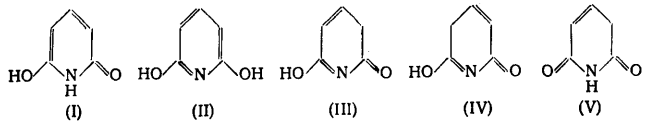
The study of the lactam–lactim equilibria involving monocyclic 6-substituted α-pyridones showed that the tautomeric equilibria of 6-amino- and 6-chloro-2-hydroxy-pyridines are also significantly displaced towards the lactims[227]. Quantitative analysis demonstrated[227] that the effect of the 6-amino-group is somewhat greater if the latter is incorporated in the five-membered ring condensed to pyridine and the influence of hetero-substituents increases, in conformity with their $-I$ effect, in the sequence Cl > OR > NR_2. When the 6-amino-group is acylated, its $-I$ effect diminishes and the tautomeric equilibrium is greatly displaced towards the lactam[228].

Thermodynamic studies have shown[200,229] that the conversion of the lactam into the lactim is an exothermic process for the majority of the solvents investigated. With decrease of solvent polarity, the process becomes less exothermic and in dioxan, where the lactim formed greatly predominates, the process already becomes endothermic. An increase of temperature favours a decrease of the content of the lactam forms in more polar solvents, while in solvents of low polarity the opposite behaviour is observed.

The existence in solutions of comparable amounts of the hydroxy- and oxo-tautomers of 6-chloro-2-hydroxypyridine has been demonstrated, their ratio being proportional to the solvent polarity[72,227,230,231]. The addition of an anionic surfactant (sodium lauryl sulphate) to an aqueous solution of 6-chloro-2-hydroxypyridine has little effect on the tautomeric equilibrium, while the addition of a cationic detergent (cetyltrimethylammonium bromide) shifts the equilibrium towards the lactim form[232].

The predominance of the lactim form has also been described for 5,6-dichloro-2-hydroxy-3,4-diphenylpyridine[233]. Problems concerning the protonation of 6-amino-2-hydroxy-pyridines have been examined in detail[234].

Of the five theoretically possible tautomeric forms (I)–(V) of 2,6-dihydroxypyridine,



(I) (II) (III) (IV) (V)

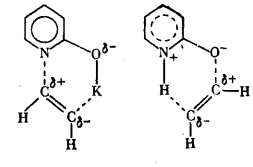
apparently three forms exist in aqueous solutions: (I), (II), and (V) in proportions of 60 : 25 : 15.[222,235–237] The oxolactim (I) predominates not only in water, alcohols, and dimethyl sulphoxide but also in cyclohexane with 5% of added alcohol. The tautomeric equilibrium is displaced towards the lactim to an even greater extent for 2-hydroxy-6-methoxypyridine[238]. The lactam–lactim tautomerism involving comparable amounts of the tautomeric forms has been described also for 2,3,6-dihydroxypyridines[239].

The 5,6-annelation of γ-pyridone via condensation with the dihydrofuran ring leads to a shift in the tautomeric equilibrium towards the lactim, which is greater than for the monocyclic 6-substituted α-pyridones; on the other hand, following condensation with the six-membered tetrahydropyran ring, the shift of the tautomeric equilibrium towards the lactim is smaller than for the monocyclic 6-substituted α-pyridones[240–242].

The displacement of the tautomeric equilibria of α,α'-disubstituted pyridines to the region where there are comparable amounts of the lactam and lactim tautomeric forms made it possible to investigate the more refined influence of the β- and γ-substituents in the pyridine ring on this process[238]. Usually, after the almost complete displacement of the tautomeric equilibria of α-pyridones towards lactams, such influences of the β- and γ-substituents cannot be detected[197,231,243,244]. It has been found that γ-substituents affect mainly the conjugation effect. For example, whereas the introduction of the hydroxy-group in the 6-position of the α-pyridone system displaces the tautomeric equilibrium towards the lactim owing to its $-I$ effect, the same group in the 4-position of the pyridine ring causes some displacement of the equilibrium towards the lactam by virtue of its $+M$ effect, i.e. it exerts the directly opposite effect[238,245]. Electron-accepting substituents in the β-position of the pyridine molecule shifts the tautomeric equilibrium towards the lactam in the absence of additional effects due to intramolecular hydrogen bonds, etc.[238]

It is noteworthy that the mode of the *N*- or *O*-alkylation processes involving 6-substituted 2-hydroxypyridines is not correlated with the position of the lactam–lactim tautomeric equilibrium[224–226]. α-Pyridone is alkylated at the nitrogen atom by dimethyl sulphate in an aqueous alkaline medium. The alkylation of 6-hydroxy-7-azaindolines under the conditions where the tautomeric equilibrium is displaced towards the lactim leads to high yields of the corresponding *O*-methyl derivatives. However, treatment of 6-hydroxy-7-azabenzofurans, whose tautomeric equilibrium is displaced towards the lactim to an even greater extent, with dimethyl sulphate in an aqueous alkaline medium again gives rise to high yields of *N*-methyl derivatives[227]. A similar behaviour has been observed also in the reactions with diazomethane. α-Pyridone forms virtually only the *O*-methyl derivative, 6-amino-2-hydroxypyridine gives rise to a mixture of equal amounts of the *O*- and *N*-methylated products, while 6-chloro-2-hydroxypyridine, whose tautomeric equilibrium is displaced towards the lactim to an even greater extent, is methylated predominantly at the nitrogen atom[227].

Evidently dynamic reaction factors and not the position of the tautomeric equilibrium play a decisive role in the alkylation of α-hydroxy-derivatives of *N*-heteroaromatic compounds. The view, which remained current for a long time, that the ratio of the amounts of methylation products can indicate the position of the tautomeric equilibrium in the initial compound is therefore erroneous. This claim is also supported by the formation of different proportions of *N*- and *O*-vinyl derivatives when α-pyridones react with acetylene, as a function of the catalyst employed—from 66 : 1 (in the presence of potassium hydroxide) to 23 : 75 (in the presence of cadmium acetate). Shostakovskii et al.[246] assumed that this is associated with the existence of two types of intermediate cyclic vinylation products.



Quantitative determination of the positions of alkylotropic equilibria of the type of 2-methoxypyridine–1-methyl-2-pyridone from the heats and the equilibrium constants showed that in all cases the lactam forms predominate, the enthalpy differences amounting to 50.6 ± 3.3 and 32.2 ± 9.6 kJ mol^{-1} for the liquid and gas phases respectively[247,248]. The introduction of the methyl group in the 6-position of the pyridine ring has little effect on the equilibrium position. On passing to the 6-chloro-derivative, the enthalpy difference decreases significantly owing to the electron-accepting effect of the chlorine atom: to 17.2 ± 9.2 kJ mol^{-1} for the liquid phase and to 1.3 – 15.5 kJ mol^{-1} for the gas phase.

Calculation of the aromaticity of 2-methoxypyridine and 1-methyl-2-pyridone showed that it amounts to ~20% of that of benzene[249], which is consistent with the values of the aromaticity of α-pyridone calculated previously[217,250]. Unfortunately quantum-chemical calculations based on the geometrical optimisation of the α-pyridone system did not yield results in agreement with experiment[251,252].

Thus studies on the chemistry of α,α'-disubstituted pyridines revealed in recent years new features which are of general theoretical interest. At the same time these investigations have also posed new problems associated with the mechanism of the transmission of the effects of α,α'-substituents in heteroaromatic systems, the nature of the mutual influence of the α- and α'-functional groups, etc. The solution of these problems has an importance going quite far beyond the framework of the individual types of pyridine derivatives.

REFERENCES

1. L.I.Vereshchagin and I.L.Kotlyarevskii, Usepkhi Khim., 1961, **30**, 982 [Russ.Chem.Rev., No.8 (1961)].
2. A.P.Ivanovskii, V.A.Shikhanov, A.M.Kut'in, and M.A.Korshunov, "Gazofaznyi Kataliticheskii Sintez Piridina i Ego Metil'nykh Gomologov" (The Gas-Phase Catalytic Synthesis of Pyridine and Its Methyl Homologues), Symposium, "Kataliticheskii Sintez i Prevrashcheniya Geterotsiklicheskikh Soedinenii (Geterogennyi Kataliz)" [Catalytic Synthesis and Reactions of Heterocyclic Compounds (Heterogeneous Catalysis)], Izd.Zinatne, Riga, 1976, p.98.
3. P.M.Carbateas and G.L.Williams, J.Heterocycl.Chem., 1975, **11**, 819.
4. V.A.Shikhanov, A.P.Ivanovskii, A.M.Kut'in, and M.A.Korshunov, Khim.Prom., 1975, 828.
5. R.Hamilton, M.McKervey, and J.Rooney, Chem.Comm., 1976, 1038,
6. Yu.S.Dol'skaya, V.S.Bogdanov, and G.Ya.Kondrat'eva, Izv.Akad.Nauk SSSR, Ser.Khim., 1978, 1691.
7. G.Reddelin, Chem.Ber., 1920, **53**, 334.
8. L.Amoros-Marin and R.B.Carlin, J.Amer.Chem.Soc., 1959, **81**, 733.
9. A.J.Clark, Tetrahedron Letters, 1972, 3487.
10. U.Eisner and J.Kuthan, Chem.Rev., 1972, **72**, 1.
11. E.Klingsberg (Editor), "Pyridine and Its Derivatives", Interscience, New York–London, 1960.
12. N.K. Kochetkov, Uspekhi Khim., 1955, **24**, 46.
13. A.Courts and V.Petrow, J.Chem.Soc., 1952, 334.
14. M.A.Kirilova, Yu.A.Zaichenko, I.A.Maretina, and A.A.Petrov, Zhur.Org.Khim., 1972, **8**, 1575.
15. F.Bohlmann and D.Rahtz, Chem.Ber., 1957, **90**, 2265.
16. M.N.Tilichenko, Zhur.Obshch.Khim., 1961, **31**, 1558.
17. W.Zecher and F.Kröhnke, Chem.Ber., 1961, **94**, 690, 698, 707.
18. F.Kröhnke, Synthesis, 1976, 1.
19. G.J.Janz and W.J.H.McCulloch, J.Amer.Chem.Soc., 1955, **77**, 3143.
20. H.Bönnemann, Angew.Chem., 1978, **90**, 517.
21. J.Barluenga, S.Fustero, and V.Gotor, Synthesis, 1975, 191.
22. F.Freid, E.B.Pederson, and S.O.Lawesson, Tetrahedron, 1973, **29**, 4215.
23. V.Assenljevic, H.Lapin, and A.Horeau, Compt.rend., 1959, **248**, 3309.
24. K.Schreiber and G.Adam, Chem.Ber., 1960, **93**, 1848.
25. A.Dornow and H.Plessen, Chem.Ber., 1966, **99**, 244.
26. U.Schmidt, Angew.Chem., 1957, **79**, 138.
27. H.Junek, Monatsch., 1964, **95**, 1453.
28. E.Gudriniece and A.V.Nikitenko, Izv.Akad.Nauk Latv. SSR, 1872, 569.
29. A.Sakurai and H.Midorikawa, Bull.Chem.Soc.Japan, 1967, **40**, 1680.
30. S.Kambe, K.Saito, A.Sakurai, and T.Hayashi, Syntheis, 1977, 841.
31. K.Grohe and A.Roedig, Chem.Ber., 1967, **100**, 2953.
32. N.Anghelide, C.Draghici, and R.Raileanu, Tetrahedron, 1974, **30**, 623.
33. J.Thesing and A.Müller, Chem.Ber., 1957, **90**. 711.
34. E.Ziegler and K.Belegratis, Monatsh., 1967, **98**, 219.
35. T.Kappe, M.A.Chirazi, H.P.Stelzel, and E.Ziegler, Monatsh., 1972, **103**, 586.
36. T.Kappe, I.Maninger, and E.Zielger, Monatsh., 1968, **99**, 85.
37. L.E.Overman and S.Tsuboi, J.Amer.Chem.Soc., 1977, **99**, 2813.
38. A.Kasahara and T.Saito, Chem.Ind.(London), 1975, 745.
39. B.M.Ferrier and N.Campbell, J.Chem.Soc., 1960, 3513.
40. J.S.A.Brunskii, J.Chem.Soc., Perkin Trans.I, 1972, 2946.
41. H.N'Al-Yallo and F.H.Al-Hajjar, J.Chem.Soc.C, 1971, 3916.
42. M.Y.Shandala and N.H.Al-Jobour, J.Chem.Eng.Data, 1976, **21**, 120.
43. K.E.Schulte and R.Mang, Arch.Pharm., 1963, **296**, 501.
44. A.Roedig, K.Grohe, and W.Mayer, Tetrahedron, 1968, **24**, 1851.
45. E.E.Mikhlina, V.Ya.Furshtatova, and M.V.Rubtsov, Zhur.Obshch.Khim., 1956, **28**, 946.
46. H.Junek, A.Metallidis, and E.Ziegler, Monatsh., 1969, **100**, 1937.
47. A.Roedig, K.Grohe, and D.Klaff, Chem.Ber., 1966, **99**, 2818.
48. R.Hoffman, F.Schaefer, and F.Pefers, J.Org.Chem., 1962, **27**, 551.
49. A.S.Alvarea-Insua, M.Lora-Tamayo, and J.L.Soto, J.Heterocyclic Chem., 1970, **7**, 1305.
50. M.A.Cabrerizo and J.L.Soto, An.Quim., 1974, **70**, 951.
51. L.Fuentes and J.L.Soto, An.Quim., 1977, **73**, 1349.
52. L.Fuentes, A.Lorente, and J.L.Soto, J.Heterocyclic Chem., 1979, **16**, 273.
53. M.Ridi, P.Papinis, and S.Cheechi, Gazzetta, 1961, **91**, 973.
54. H.N.Pydon and K.Undheim, J.Chem.Soc., 1962, 4676.
55. A.J.Fatadi, Synthesis, 1978, 165.
56. A.Sakurai and H.Midorikawa, Bull.Chem.Soc.Japan, 1968, **41**, 430.
57. A.J.Fatadi, Synthesis, 1978, 191.
58. A.Dornow and O.Hahmann, Arch.Pharm., 1957, **290**, 298.
59. G.Purrello and A.Vullo, J.Heterocyclic Chem., 1974, **11**, 481.
60. H.Kurihara and H.Mishima, J.Heterocyclic Chem., 1977, **14**, 1077.
61. US P.3 225 041 (1965); Chem.Abs., 1966, **64**, 6623.
62. F.Johnson, J.P.Panella, A.A.Carlson, and D.H.Hunneman, J.Org.Chem., 1962, **27**, 2473.
63. J.P.Atkinson and M.C.Johnson, J.Chem.Soc., 1968, 1252.
64. F.Johnson and W.A.Nasutavicus, J.Org.Chem., 1962, **27**, 3953.
65. US P.3 096 337 (1963); Chem.Abs., 1963, **59**, 12 768.

66. A.L.Cossey, R.L.N.Harris, J.L.Huppatz, and J.N.Phillips, Angew.Chem., 1972, **84**, 1183.
67. T.Onoda and H.Masai, Japan Kakai, 1975, 75 690 210; Chem.Abs., 1975, **83**, 178 380.
68. S.G.Cottis and H.Tieckelmann, J.Org.Chem., 1961, **26**, 79.
69. E.Bulleck and B.Gregory, Canad.J.Chem., 1965, **43**, 332.
70. P.D.Klemmensen, J.Z.Mortensen, and S.O.Laweson, Tetrahedron, 1970, **26**, 4641.
71. J.A.Elvidge and N.A.Zaidi, J.Chem.Soc., 1968, 2188.
72. G.Simchen, Chem.Ber., 1970, **103**, 389.
73. A.Roldig, K.Grohe, D.Klatz, and H.Kleppe, Chem. Ber., 1966, **99**, 2813, 2818.
74. A.Roldig and K.Grohe, Chem.Ber., 1965, **98**, 923.
75. R.W.Meikle and E.A.Williams, Nature, 1966, **210**, 523.
76. H.Fritz, C.Weis, and T.Winkler, Helv.Chim.Acta, 1976, **59**, 179.
78. W.Polaczkowa, T.Jaworski, and J.Wolinski, Roczniki Chem., 1953, **27**, 468.
79. H.J.Bray, F.C.Neale, and W.V.Thorpe, Biochem.J., 1950, **46**, 506.
80. W.Gruber, Chem.Ber., 1955, **88**, 178.
81. L.D.Smirnov, V.P.Lezina, V.F.Bystrov, and K.M.Dyumaev, Izv.Akad.Nauk SSSR, Ser.Khim., 1963, 752.
82. L.D.Smirnov, S.I.Sholina, E.E.Kruglyakova, and K.M.Dyumaev, Izv.Akad.Nauk SSSR, Ser.Khim., 1963, 890.
83. M.Ya.Karpeiskii and V.L.Florent'ev, Uspekhi Khim., 1969, **38**, 1244 [Russ.Chem.Rev., 1969, No.7].
84. M.Ohashi, H.Kamachi, H.Kakisawa, and G.Stork, J.Amer.Chem.Soc., 1967, **89**, 5460.
85. P.Caramella, R.Metelli, and P.Grünanger, Tetrahedron, 1971, **27**, 379.
86. A.Butt, M.Hasan, and Z.Manawar, Tetrahedron, 1967, **23**, 2461.
87. N.P.Shusherina, N.D.Dmitrieva, E.A.Luk'yanets, and R.Ya.Levina, Uspekhi Khim., 1967, **36**, 458 [Russ.J. Chem.Rev., 1967, No.3].
88. R.F.Toomey and E.R.Piegel, J.Org.Chem., 1952, **17**, 1492.
89. I.S.Belonosov and A.A.Konstantinov, Zhur.Prikl.Khim., 1953, **25**, 1233.
90. A.G.Anderson and P.J.Stang, J.Org.Chem., 1976, **41**, 3034.
91. G.N.Dorofeenko, S.V.Krivun, V.I.Dulenko, and Yu.A.Zhdanov, Uspekhi Khim., 1965, **34**, 236 [Russ. Chem.Rev., 1965, No.2].
92. S.V.Krivun, O.F.Alferova, and S.V.Sayapina, Uspekhi Khim., 1974, **43**, 1739 [Russ.Chem.Rev., 1974, No.10].
93. N.F.Ewess, A.R.Katritzky, P.L.Nie, and C.A.Ramaden, Synthesis, 1977, 634.
94. E.Buschmann and W.Steglich, Angew.Chem., 1974, **86**, 414.
95. W.Steglich, E.Buschmann, and O.Hollitzer, Angew. Chem., 1974, **85**, 596.
96. T.Kato, Y.Yamamoto, and M.Kondo, Chem.Pharm.Bull. (Tokyo), 1975, **23**, 1873.
97. H.Neunhoeffer and G.Werner, Annalen, 1972, **761**, 39.
98. H.Neunhoeffer and G.Werner, Annalen, 1973, 437.
99. A.Albert and W.Pendergast, J.Chem.Soc., Perkin Trans.I, 1973, 1794.
100. E.A.Oestveen and H.C.Plas, Rec.Trav.chim., 1974, **93**, 233.
101. A.N.Kost, R.S.Sagitullin, and G.G.Danagulyan, Khim. Geterotsikl.Soed., 1978, 1400.
102. G.R.Newkome, A.Nayak, G.L.McClure, F.Danesh-Khoshboo, and J.Bronssard-Simpson, J.Org.Chem., 1977, **42**, 1500.
103. D.E.Ames, R.E.Bowman, and T.F.Grey, J.Chem.Soc., 1953, 3008.
104. K.Lewiska and E.Plozer, Roczniki Chem., 1966, **40**, 1875.
105. I.S.Belonosov and A.A.Konstantinov, Zhur.Prikl.Khim., 1952, **25**, 1233.
106. M.M.Bondakian, J.Heterocyclic Chem., 1968, **5**, 683.
107. N.A.Akhmetova, V.M.Vlasov, and G.G.Yakobson, Izv. Akad.Nauk SSSR, Ser.Khim., 1978, 949.
108. M.Hamana and M.Jamazaki, Yakugaku Zasshi, 1961, **81**, 574; Chem.Abs., 1961, **55**, 24 743.
109. J.S.Brunskii, J.Chem.Soc.C, 1968, 960.
110. A.F.Pozharskii and A.M.Simonov, "Aminirovanie Geterotsiklov po Chichibabinu" (The Chichibabin Amination of Heterocyles), Izd.Rostov.Univ., Rostov-on-Don, 1971.
111. B.S.Gorton and W.Shive, J.Amer.Chem.Soc., 1957, **79**, 670.
112. G.A.Mokrushin, S.K.Kotovskaya, and I.Ya.Postovskii, Khim.Geterotsikl.Soed., 1979, 131.
113. K.M.Dyumaev and L.D.Smirnov, Uspekhi Khim., 1975, **44**, 1788 [Russ.Chem.Rev., 1975, No.10].
114. L.D.Smirnov, M.R.Avezov, V.P.Lezina, G.P.Kartasheva, and K.M.Dyumaev, Izv.Akad.Nauk SSSR, Ser. Khim., 1971, 845.
115. W.Czuba and E.Plazek, Rec.Trav.chim., 1958, **77**, 92.
116. A.R.Katritzky, H.O.Tarhan, and S.Tarhan, J.Chem. Soc.B, 1970, 114.
117. L.D.Smirnov, L.G.Stolyarova, L.G.Shirokova, and V.P.Lezina, Izv.Akad.Nauk SSSR, Ser.Khim., 1977, 452.
118. L.D.Smirnov, V.P.Lezina, V.F.Bystrov, and K.M.Dyumaev, Izv.Akad.Nauk SSSR, Ser.Khim., 1968, 198.
119. K.M.Dyumaev, L.D.Smirnov, V.P.Lezina, and V.F.Bystrov, Teor.Eksper.Khim., 1965, 290.
120. N.S.Kamiya, Chem.Pharm.Bull.(Tokyo), 1968, **16**, 1466.
121. K.M.Dyumaev, L.D.Smirnov, M.R.Avezov, and B.E.Zaitsev, "Nauchnye Trudy Samarkandskogo Gosudarstvennogo Universiteta" (Transactions of the Samarkand State University), 1971, Vol.II, p.108.
122. L.D.Smirnov, M.R.Avezov, V.P.Lezina, B.E.Zaitsev, and K.M.Dyumaev, Izv.Akad.Nauk SSSR, Ser.Khim., 1971, 2338.
123. L.D.Smirnov, V.P.Lezina, V.F.Bystrov, and K.M.Dyumaev, 1965, 1836.
124. L.D.Smirnov, T.P.Kartasheva, V.P.Lezina, and K.M.Dyumaev, Izv.Akad.Nauk SSSR, Ser.Khim., 1967, 2742.
125. C.D.Weiss, J.Heterocyclic Chem., 1978, 15, 29.
126. L.D.Smirnov, S.I.Sholina, K.E.Kruglyakova, and K.M.Dyumaev, Izv.Akad.Nauk SSSR, Ser.Khim., 1963, 899.
127. B.E.Zaitsev, G.V.Sheban, L.D.Smirnov, and K.M.Dyumaev, Khim.Geterotsikl.Soed., 1973, 224.
128. W.Mathes, W.Sanermilch, and J.Klein, Chem.Ber., 1953, **86**, 584.
129. Yu.Sh.Gol'dberg, L.Ya.Leitis, and M.V.Shimanskaya, Izv.Akad.Nauk Latv.SSR, Ser.Khim., 1976, 698.
130. S.Hillers, M.V.Shimanskaya, L.Leitis, A.Avots, E.Simansone, J.Gavars, and G.Glemite, USSR P. 507 569 (1969); Byul.Izobret., 1976, No.11.
131. Japanese P.7 200 059 (1970); Chem.Abs., 1972, **76**, 72 214.

132. French P.1 394 362 (1963); Chem.Abs., 1965, **63**, 8326.
133. Japanese P.7 246 069 (1970); Chem.Abs., 1973, **78**, 97 490.
134. V.Böckelheide and W.J.Zinn, J.Amer.Chem.Soc., 1954, **76**, 1286.
135. E.I.Levkoeva, L.I.Mastafanova, D.M.Krasnokutskaya, M.I.Evstratova, Ya.S.Karpman, I.S.Tubina, I.L.Ivanova, and L.N.Yakhontov, Khim.Geterotsikl.Soed., 1976, 233.
136. W.Baker, K.M.Buggle, J.F.McOmie, and D.A.Natkins, J.Chem.Soc., 1958, 3594.
137. W.Offermann and F.Vögtle, Synthesis, 1977, 272.
138. J.Schreiber, Chem.Listy, 1960, **54**, 51.
139. A.P.Terent'ev, E.G.Rukhadze, I.G.Mochalina, and V.V.Rode, Zhur.Vses.Khim.Obshch.im.Mendeleeva, 1961, **6**, 116.
140. R.Lukeš and M.Pergal, Chem.Listy, 1957, **51**, 68.
141. G.A.Pearge and J.Wisowaty, J.Heterocyclic Chem., 1973, **10**, 647.
142. L.N.Yakhontov, E.I.Levkoeva, L.I.Mastafanova, D.M.Krasnokutskaya, M.I.Evstratova, O.N.Volzhina, Z.M.Klimonova, Ya.S.Karpman, I.S.Tubina, I.L.Ivanova, I.G.Markova, and V.A.Kuzovkin, Khim.-Farm.Zhur., 1979(4), 72.
143. T.Slebodzinski, H.Kielczewska, and W.Biernacki, Przem.Chem., 1969, **48**, 90.
144. BRD.P.1 620 174 (1972); Chem.Abs., 1972, **77**, 48 273.
145. D.Kreile, I.A.Milman, D.Eglite, L.Kurmina, D.Sile, A.Strautina, and V.A.Slavinskaya, Zhur.Prikl.Khim., 1978, **51**, 1644.
146. B.P.820 478 (1959); Chem.Abs., 1960, **54**, 9963.
147. US P.3 766 258 (1973); Chem.Abs., 1974, **80**, 14 748.
148. B.V.Suvorov and N.R.Bukeikhanov, "Okislitel'nye Reaktsii v Organicheskom Sinteze" (Oxidative Reactions in Organic Synthesis), Izd.Khimiya, Moscow, 1978.
149. I.A.Milman, E.Dziliuma, A.Strautina, E.Kh.Kochagova, and V.A.Slavinskaya, Izv.Akad.Naul Latv.SSR, Ser. Khim., 1978, 353.
150. D.Sile, I.A.Milman, and D.Kreile, Izv.Akad.Nauk Latv. SSR, Ser.Khim., 1978, 350.
151. H.C.Brown and B.Kanner, J.Amer.Chem.Soc., 1966, **88**, 986.
152. H.C.Brown and X.R.Mihm, J.Amer.Chem.Soc., 1955, **77**, 1723.
153. H.C.Brown, D.Gintis, and L.Domash, J.Amer.Chem. Soc., 1956, **78**, 5387.
154. C.Laurence and M.Lucon, Canad.J.Chem., 1976, **54**, 2021.
155. L.S.Hart, C.R.Killen, and K.D.Sauders, Chem.Comm., 1979, 24.
156. N.D.Rus'yanova, B.E.Kogan, and M.A.Kosareva, Khim.Geterotsikl.Soed., 1976, 1587.
157. H.C.Brown and B.Kanner, J.Amer.Chem.Soc., 1953, **75**, 3865.
158. L.N.Yakhontov, Dokl.Akad.Nauk SSSR, 1957, **113**, 1088.
159. G.Coppens, F.Declarck, C.Gillet, and J.Nasielski, Bull.Soc.chim.belges, 1963, **72**, 25.
160. K.Weisser, F.Rulaček, R.Karliček, J.Sova, J.Čeladnik, and K.Palat, Pharmazie, 1979, **34**, 197.
161. G.C.Finger and L.D.Starr, Nature, 1961, **191**, 595.
162. A.R.Katritzky and B.J.Ridgewell, J.Chem.Soc., 1963, 3753.
163. A.R.Katritzky and B.J.Ridgewell, J.Chem.Soc., 1963, 3882.
164. R.Graf and A.Weinberg, J.prakt.Chem., 1932, **134**, 177.
165. L.N.Yakhontov and M.F.Marshalkin, Khim.Geterotsikl. Soed., 1972, 1638.
166. P.Zuman, Coll.Czech.Chem.Comm., 1962, **27**, 630.
167. M.Charton, J.Amer.Chem.Soc., 1964, **86**, 2033.
168. J.A.Zolotewicz, G.Grahe, and S.L.Smith, J.Amer. Chem.Soc., 1969, **91**, 5501.
169. R.A.Abramovitch, G.M.Singer, and A.R.Vinutha, Chem.Comm., 1967, 55.
170. N.J.Fina and J.O.Edwards, Int.J.Chem.Kinet., 1973, **5**, 1.
171. T.Kauffmann and R.Wirthwein, Angew.Chem., 1971, **83**, 21.
172. A.P.Grekov and V.Ya.Veselov, Uspekhi Khim., 1978, **47**, 1200 [Russ.Chem.Rev., 1978, No.7].
173. V.P.Mamaev, O.A.Zagulyaeva, and S.M.Shein, Khim. Geterotsikl.Soed., 1973, 723.
174. I.F.Mikhailov and V.A.Barkhash, Zhur.Obshch.Khim., 1967, **37**, 2792.
175. J.D.Cook, B.J.Wakefield, and C.J.Clayton, Chem. Comm., 1967, 150.
176. J.D.Cook and B.J.Wakefield, J.Organometal.Chem., 1968, **13**, 15.
177. J.D.Cook, B.J.Wakefield, H.Heaney, and J.Jablonski, J.Chem.Soc.C, 1968, 2727.
178. S.A.Moshchinskii and A.A.Zeikan', Khim.Geterotsikl. Soed., 1978, 1514.
179. R.D.Chambers, J.Hutchinson, and W.K.R.Musgrave, Proc.Chem.Soc., 1964, 83.
180. S.M.Roberts and H.Suschitzky, J.Chem.Soc.C, 1968, 2844.
181. W.T.Flowers, R.N.Haszeldine, and S.A.Majid, Tetrahedron Letters, 1967, 2503.
182. V.M.Vlasov, V.V.Aksenov, N.E.Akhmetova, G.Z.Mustakimova, and G.G.Yakobson, Izv.Sibir.Otd.Akad.Nauk SSSR, 1978, No.6, 130.
183. R.F.Banks, R.N.Haszeldine, J.V.Latham, and L.M.Joung, Chem.Ind.(London), 1964, 835.
184. R.D.Chambers, C.A.Heaton, and W.K.R.Musgrave, J.Chem.Soc.C, 1969, 1700.
185. G.G.Jakobson, T.D.Petrova, and L.S.Kobrina, Fluorine Chem.Rev., 1974, **7**, 115.
186. A.F.Pozharskii, V.V.Kuz'menko, V.A.Azimov, and L.N.Yakhontov, Khim.Geterotsikl.Soed., 1973, 1232.
187. A.Kreutzberger and F.C.Ferris, J.Org.Chem., 1962, **27**, 3496.
188. D.M.Krasnokutskaya and L.N.Yakhontov, Khim. Geterotsikl.Soed., 1974, 650.
189. L.N.Yakhontov, Uspekhi Khim., 1968, **37**, 1258 [Russ.Chem.Rev., 1968, No.7].
190. L.N.Yakhontov and V.M.Rubtsov, Zhur.Obshch.Khim., 1964, **44**, 493.
191. T.Hattory, Japan Kakai, 1974, **74**, 127 977; Chem. Abs., 1976, **84**, 121 665.
192. R.P.Cassity, L.T.Taylor, and J.F.Wofe, J.Org.Chem., 1978, **43**, 2286.
193. G.Queguiner and P.Pastour, Compt.rend., 1969, 268C, 182.
194. L.N.Yakhontov and E.V.Pronina, Khim.Geterotsikl. Soed., 1969, 1121.
195. L.N.Yakhontov, E.V.Pronina, and M.V.Rubtsov, Dokl.Akad.Nauk SSSR, 1966, **169**, 361.
196. L.N.Yakhontov, E.V.Pronina, B.V.Rozynov, and M,V.Rubtsov, Dokl.Akad.Nauk SSSR, 1968, **178**, 127.
197. J.Elguero, C.Marzin, A.R.Katritzky, and P.Linda, "The Tautomerism of Heterocycles. Advances in Heterocyclic Chemistry, Supplement", Acad.Press, New York–San Francisco–London, 1976.

198. A.R.Katritzky, Uspekhi Khim., 1972, **41**, 700 [Russ. Chem.Rev., 1972, No.4.
199. L.Stefaniak, Tetrahedron, 1976, **32**, 1065.
200. M.J.Cook, A.R.Katritzky, L.G.Hepler, and T.Matsui, Tetrahedron Letters, 1976, 2685.
201. P.Beak, J.B.Covington, and S.G.Smith, J.Amer. Chem.Soc., 1976, **98**, 8284.
202. P.Beak, J.B.Covington, and J.M.Zeigler, J.Org. Chem., 1978, **43**, 177.
203. O.Bensaude, M.Dreyfus, G.Dodin, and J.E.Dubois, J.Amer.Chem.Soc., 1977, **99**, 4438.
204. O.Bensaude, M.Chevrier, and J.E.Dubois, J.Amer. Chem.Soc., 1978, **100**, 7055.
205. P.Beak, F.Fry, J.Lee, and F.Steele, J.Amer.Chem. Soc., 1976, **98**, 171.
206. M.Cignitti and L.Paoloni, Gazzetta, 1978, **108**, 491.
207. A.Gordon and A.R.Katritzky, Tetrahedron Letters, 1968, 2767.
208. Yu.N.Sheinker and E.M.Peresleni, Zhur.Fiz.Khim., 1962, **36**, 1705 [Russ.J.Phys.Chem., 1962, No.8].
209. P.Beak and F.Fry, J.Amer.Chem.Soc., 1973, **95**, 1700.
210. T.Gronnebera and K.Undheim, Org.Mass Spectr., 1972, **6**, 823.
211. M.J.Cook, A.R.Katritzky, M.Taagepara, T.D.Singh, and R.W.Taft, J.Amer.Chem.Soc., 1976, **98**, 6048.
212. A.Maquestin, Y.Haverbeke, C.Meyer, A.R.Katritzky, M.J.Cook, and A.D.Page, Canad.J.Chem., 1975, **53**, 490.
213. E.S.Levin and G.N.Rodionova, Dokl.Akad.Nauk SSSR, 165, **164**, 584.
214. E.S.Levin and G.N.Rodionova, Dokl.Akad.Nauk SSSR, 1967, **172**, 607.
215. E.S.Levin and G.N.Rodionova, Dokl.Akad.Nauk SSSR, 1967, **174**, 1132.
216. E.S.Levin and G.N.Rodionova, Dokl.Akad.Nauk SSSR, 1969, **189**, 326.
217. M.J.Cook, A.R.Katritzky, P.Linda, and R.D.Tack, J.Chem.Soc., Perkin Trans.II, 1972, 1295.
218. M.P.Cook, S.El-Abbady, A.R.Katritzky, C.Guimon, and G.Pfister-Guillouzo, J.Chem.Soc., Perkin Trans.II, 1977, 1652.
219. A.Roedig and C.Märkl, Annalen, 1960, **636**, 1.
220. J.R.Stevens, R.H.Beutel, and E.Chamberlin, J.Amer. Chem.Soc., 1946, **64**, 1093.
221. M.Ritchie, Austral.J.Chem., 1956, **9**, 244.
222. E.Spinner and G.B.Yeoh, Tetrahedron Letters, 1968, 5691.
223. D.W.Jones, J.Chem.Soc.C, 1969, 1678.
224. L.N.Jakhontov, D.M.Krasnokutskaya, E.M.Peresleni, Yu.N.Sheinker, and M.V.Rubtsov, Tetrahedron, 1966, **22**, 3323.
225. L.N.Yakhontov, D.M.Krasnokutskaya, E.M.Peresleni, Yu.N.Sheinker, and M.V.Rubtsov, Dokl.Akad.Nauk SSSR, 1967, **172**, 118.
226. L.N.Yakhontov, D.M.Krasnokutskaya, E.M.Peresleni, Yu.N.Sheinker, and M.V.Rubtsov, Dokl.Akad.Nauk SSSR, 1967, **176**, 613.
227. E.M.Peresleni, L.N.Yakhontov, D.M.Krasnokutskaya, and Yu.N.Sheinker, Dokl.Akad.Nauk SSSR, 1967, **177**, 592.
228. Chau-der-Li, L.S.Ritmann, A.S.Tsiftsoglou, K.K.Bhargava, and A.C.Sartorelli, J.Medicin.Chem., 1978, **21**, 874.
229. Yu.N.Sheinker, E.M.Peresleni, I.S.Rezchikova, and N.P.Zosimova, Dokl.Akad.Nauk SSSR, 1970, **192**, 1295.
230. A.R.Katritzky, J.D.Rowe, and S.K.Roy, J.Chem.Soc. B, 1967, 758.
231. J.Frank and A.R.Katritzky, J.Chem.Soc., Perkin Trans II, 1976, 1428.
232. A.Cipiciani, P.Linda, and G.Savelli, Gazzetta, 1975, **105**, 431.
233. P.I.Mortimer, Austral.J.Chem., 1968, **21**, 467.
234. G.B.Barlin and W.Pfleiderer, J.Chem.Soc.B, 1971, 1425.
235. A.R.Katritzky, F.D.Popp, and J.D.Row, J.Chem.Soc. B, 1966, 562.
236. E.Spinner and J.C.White, J.Chem.Soc.B, 1966, 991.
237. E.Spinner and G.B.Yeoh, Austral.J.Chem., 1971, **24**, 2557.
238. E.M.Peresleni, M.Ya.Uritskaya, V.A.Loginova, Yu.N.Sheinker, and L.N.Yakhontov, Dokl.Akad.Nauk SSSR, 1968, **183**, 1102.
239. H.J.Knackmuss, Chem.Ber., 1968, **101**, 2679.
240. E.Spinner and G.B.Yeoh, J.Chem.Soc.B, 1971, 279.
241. E.Spinner and G.B.Yeoh, J.Chem.Soc.B, 1971, 289.
242. E.Spinner and G.B.Yeoh, J.Chem.Soc.B, 1971, 296.
243. J.Pitha and J.Kuthan, Coll.Czech.Chem.Comm., 1963, **28**, 1625.
244. H.Sterk and H.Junek, Monatsh., 1967, **98**, 1763.
245. Chun-Shan Wang, J.Heterocylic Chem., 1970, **7**, 389.
246. M.F.Shostakovskii, G.G.Skvortsova, S.M.Tyrina, Yu.A.Frolov, N.M.Deriglazov, V.K.Voronov, and N.A.Ivanova, Dokl.Akad.Nauk SSSR, 1969, **186**, 620.
247. P.Beak, J.Bonham, and J.T.Lee, J.Amer.Chem.Soc., 1968, **90**, 1569.
248. P.Beak, T.S.Woods, and D.S.Mueller, Tetrahedron 1972, **28**, 5507.
249. A.K.Burnham, J.T.Lee, T.G.Schmalz, P.Beak, and W.H.Frygare, J.Amer.Chem.Soc., 1977, **99**, 1836.
250. A.R.Katritzky, Khim.Geterotsikl.Soed., 1972, 1011.
251. M.Berndt, J.S.Kwiatkowski, J.Budzinski, and B.Szezdzowska, Chem.Phys.Letters, 1973, **19**, 246.
252. M.L.Tosato, M.Cignitti, and L.Paoloni, Gazzetta, 1975, **105**, 385.
253. E.Knoevenagel, Chem.Ber., 1902, **36**, 2180.
254. L.Gattermann and A.Skita, Chem.Ber., 1916, **49**, 494.

Ordzhonikidze All-Union Institute
of Chemistry and Pharmacology,
Moscow