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PROPERTIES OF 2,3-DIHYDRO-IMIDAZOLO[1,2-*a*]PYRIDINES. (REVIEW)

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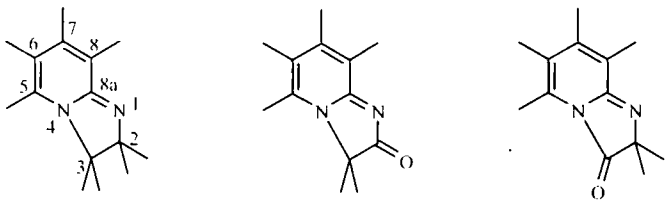
Published data on the physical and chemical characteristics of 2,3-dihydroimidazo[1,2-a]pyridines to 1998 are reviewed.

Keywords: 2,3-dihydroimidazo[1,2-*a*]pyridines, reduction, nucleophilic reactions, oxidation, electrophilic reactions.

From our previous review [1], in which we discussed the synthesis, structure, tautomerism, and nomenclature of 2,3-dihydroimidazo[1,2-*a*]pyridines, it follows that compounds of type **A-C** have wide-ranging practical applications.



A **B** **C**

Data on the chemical properties of 2-oxoimidazopyridines **B**, which have amphoteric characteristics and form water-soluble salts with mineral acids and alkalies, were studied in detail and analyzed in [2]. They were used to obtain many dyes [3-5], which were also synthesized [6] from 3-oxoimidazo[1,2-*a*]pyridines **C**. Their solutions can fluoresce [7, 8] and sometimes exhibit chemiluminescence [9]. However, there is considerably less information on the 3-oxo derivatives, and this is explained by their relative instability – many of them are sensitive to nucleophiles [6, 10-17] and to light [13, 18], are readily oxidized by atmospheric oxygen [13, 18], and decompose when heated [19] and sometimes even at room temperature [20]. More stable are the mesoionic 1-substituted 3-oxoimidazo[1,2-*a*]pyridines, which dissolve in water [8, 13, 19] and can form hydrates [13, 21].

1. PHYSICAL CHARACTERISTICS OF 2,3-DIHYDROIMIDAZO[1,2-*a*]PYRIDINES

A characteristic feature of 2,3-dihydroimidazo[1,2-*a*]pyridines **A** and their 2- and 3-oxo derivatives **B** and **C** is the clearly defined basicity of the nitrogen atom $N_{(1)}$. This is demonstrated by the pK_a values of compound **A** (pK_a 12.51) [22] and also by the fact that salts of 2-oxoimidazopyridines do not give bases **B** when treated with triethylamine [4, 23], although the latter is a sufficiently strong base for the production of 3-hydroxyimidazopyridines from the respective salts [7]. The mobile hydrogen atom in the molecules of

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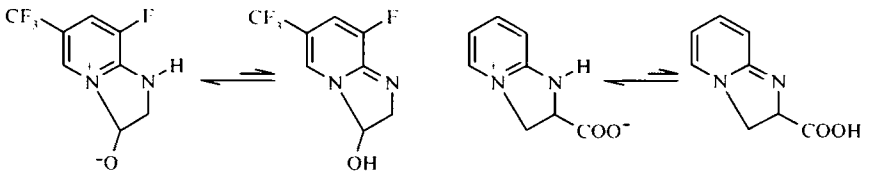
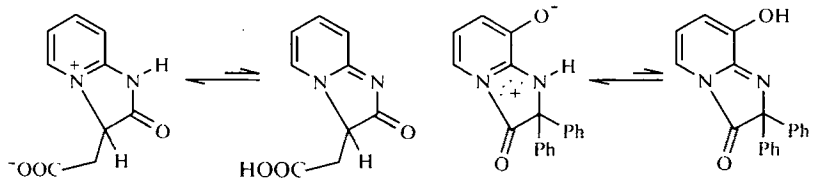
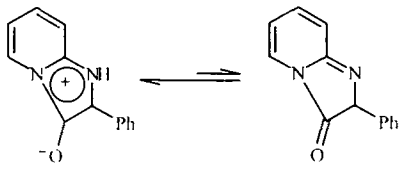
compounds **A-C** are usually at the exocyclic nitrogen atom in the respective zwitterions (e.g., **1a** [24], **2a** [25, 26], **3a** [27], **4a** [12]) or the mesoionic structures (**5a** [15], **6a** [27, 28]). However, for the unsubstituted 2-oxoimidazo[1,2-*a*]pyridine it was suggested on the basis of the ^{1}H NMR spectra that the compound exists in the keto form **B**. In solutions in D_2O 2-oxoimidazopyridines exist mainly in the $N_{(1)}H$ form of the pyridine compounds, but in DMSO-d_6 the oxo form unprotonated at the $N_{(1)}$ atom is also (or only) observed [9, 21, 27, 29].



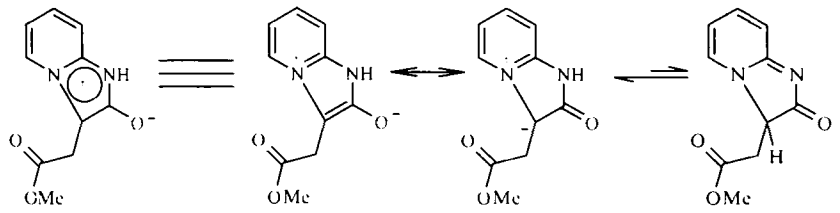
1a **1b** **2a** **2b**



3a **3b** **4a** **4b**

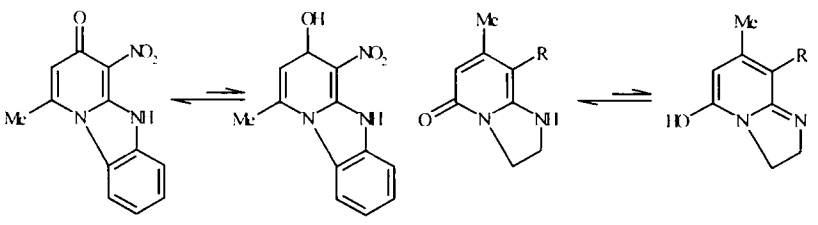


5a **5b**



6a **6b** **6c** **6d**

The acidity of 2-oxoimidazopyridines with a hydrogen atom at position 3 is close to the pK_a value of carboxylic acids (pK_a 3.5-4.1 [21, 27, 31]), and the 2-oxo derivatives therefore exhibit the characteristics of pyridinium ylides. The high basicity of the $N_{(1)}$ atom clearly also gives rise to the fact that the compounds that could exist in hydroxypyridine of pyridone form were only characterized as oxo derivatives (e.g., **7a** [32], **8a** [33]).



7a **7b** **8a** **8b**

X-ray crystallographic analysis [21, 27, 34] of 2-oxoimidazopyridines capable of forming the NH form confirmed that they exist in the form of mesoionic compounds or zwitterions. The lengths of the C–N and C–C bonds in the five-membered ring of the mesoions are almost equal, indicating delocalization of the positive charge in the imidazole ring. The negative charge is at the oxygen atom, but it is necessary to take account of the weighty contribution from the resonance form of pyridinium ylide, as indicated by the length of the $C_{(2)}$–O bond (1.224-1.280 Å) [27, 34]. X-ray crystallographic analysis of the above-mentioned mesoionic structures, 2-oxoimidazopyridines **B** [21, 35], their 3-spiro derivatives [36, 37], and compounds of type **A** [38] and **C** [11] showed that the bicyclic system is close to planar. Due to this the unshared electron pair at the $N_{(4)}$ atom is capable of delocalization, as a result of which the C–O bond in 2-oxoimidazopyridines becomes somewhat longer than in the 3-oxo derivatives [35].

Mass-spectral analysis [7, 21, 30, 37] showed that there are differences between the fragmentation of oxoimidazopyridines and the mesoionic compounds, which are characterized by initial cleavage of the bond between the carbonyl carbon atom and the nitrogen; the dissociation paths of the mesoionic 2- and 3-oxoimidazopyridines also differ [30].

The mass spectra of compounds of type **A** have been studied less [24, 29]. For 2,3-dihydroimidazopyridines **A** the ^{1}H NMR spectra contain a characteristic signal for the protons of the methylene groups in the imidazole ring in the form of a singlet or a multiplet in the region of 3.52-4.05 ppm. If there are substituents at positions 2 or 3, splitting into two separate signals is observed, and they are shifted to 5.18 [24] or even 7.1 ppm [40], depending on the nature of the substituents. The signals of the carbon atoms of the methylene groups in the imidazole ring in the ^{13}C NMR spectra appear in the region of 44.79-52.74 and 44.00-49.82 ppm [41]. The spectra of the 2- and 3-oxoimidazopyridines **B** and **C** are characterized by signals for the carbonyl carbon atom in the region of 165.2-184.7 for the 2-oxoimidazopyridines **B** [21, 35] and 168.5-181.9 ppm for the 3-oxo derivatives [12, 15]. The signals of the imidazole carbon atoms $C_{(3)}$ and $C_{(2)}$ in compounds **B** and **C** appear in the region of ~60.2-67.7 [21] and 76.5-80.5 ppm respectively [12, 15]. The signal of the amidine carbon $C_{(8a)}$ in imidazopyridines **A** lies in the region of ~149.74-151.62 [41], while in the oxo derivatives **B** and **C** it is in the region of 151.9-167.7 ppm [12, 15, 21, 35]. If the tautomeric 2-oxoimidazopyridines are compared with the corresponding mesoionic compounds, the signals of the $C_{(8a)}$ and $C_{(2)}$ atoms in the spectra of the latter are shifted upfield, while those of $C_{(3)}$ are shifted downfield by 30-35 ppm. The isomeric 2- and 3-oxoimidazopyridines and also their mesoionic forms can be distinguished by their NMR spectra [35, 42]. ^{1}H NMR and ^{13}C NMR spectroscopy were used to study the ring–chain tautomerism of 2-hydroxy- and 3-hydroxy-2,3-dihydroimidazopyridines [43-46] and [24, 40], the position of the positive charge in salts of imidazopyridines **A** [44, 45, 47], the formation of the zwitterions (the NH forms) [12, 21], the "oxoimidazopyridine–hydroxyimidazopyridine" tautomerism [9, 31, 48, 49], and the tautomerism between oxoimidazopyridine (CH form) and the mesoionic imidazopyridine (NH form) [21, 27, 31].

The IR spectra of 2,3-dihydroimidazo[1,2-*a*]pyridines are characterized by absorption bands in the region of 1630-1650 cm^{-1}, corresponding to the vibrations of the C=N bond, and for the oxo derivatives **B** and **C** also by νC=O in the regions of 1710-1750 and 1780-1800 cm^{-1} respectively [1, 12, 20, 31, 35]. In the existing spectral data the largest amount of information has accumulated on the electronic spectra of 2- and 3-oxoimidazopyridine derivatives, and this due to their use as dyes. (Detailed information on the UV spectra of the oxo derivatives is given in the review by Mosby [2] and in the more recent papers [12, 20, 21, 23, 50, 51].) The UV spectra of the mesoionic compounds [8, 13, 18, 21, 28, 42] and 2,3-dihydroimidazopyridines **A** [22, 41, 44, 45, 52-54] have also been studied.

2. CHEMICAL CHARACTERISTICS OF 2,3-DIHYDROIMIDAZO[1,2-*a*]PYRIDINES

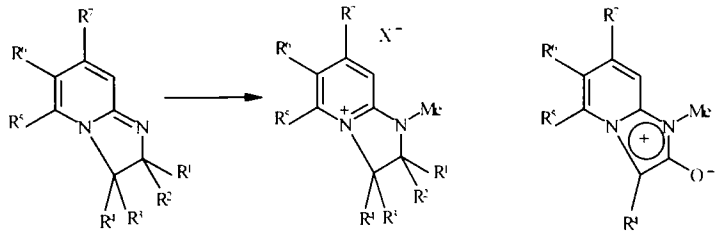
2.1. Electrophilic Reactions

The presented data show that the protonation, alkylation, and acylation of compounds of type **A** must take place at the $N_{(1)}$ atom. The protonation and alkylation of 2-oxoimidazo[1,2-*a*]pyridines of type **B** also take place at the $N_{(1)}$ atom, but in the case of compound **6**, which can be described by formulas **6a-d**, it is seen that $C_{(3)}$ and the

oxygen at $C_{(2)}$ can be active centers in reactions with electrophiles. In fact acylation, condensation with aldehydes, electrophilic substitution, and azo coupling in 2-oxoimidazo[1,2-*a*]pyridines take place at position 3, while acylation can also take place at the oxygen. The analogous reactions for 3-oxoimidazo[1,2-*a*]pyridines take place at position 2 or at the oxygen atom at $C_{(3)}$.

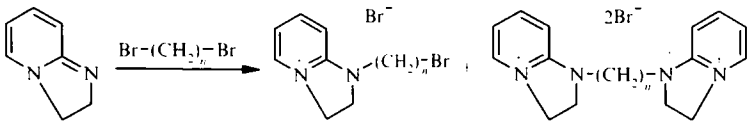
2.1.1. Protonation and Alkylation. During synthesis imidazopyridines are usually isolated in the form of hydrohalides. Other salts – picrates [55], iodides [56], perchlorates [22, 57] – can be obtained by substitution of the anion (most often the chloride ion). 2,3-Dihydroimidazo[1,2-*a*]pyridinium chlorides, perchlorates, picrates, and nitrates have also been synthesized by treatment of the respective bases with acids [22, 38, 58, 59].

The methylation of 2,3-dihydroimidazo[1,2-*a*]pyridines and their 2-oxo derivatives (R^1, R^2 = O) with methyl triflate [39, 60], dimethyl sulfate [23, 28], and methyl iodide [35, 38, 56, 57] gave salts of 1-methylimidazo[1,2-*a*]pyridine **10** or, after treatment with a base, compound **11** (if R^1, R^2 = O, R^3 = H). The reactions of 2,3-dihydroimidazo[1,2-*a*]pyridines **9** with other alkyl halides take place similarly [61].



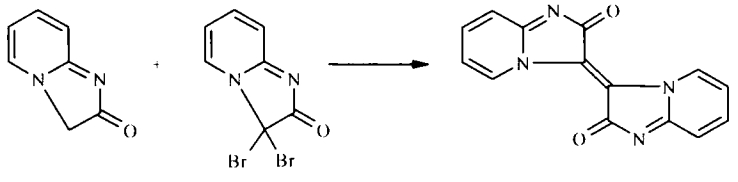
9 **10** **11**

The alkylation of imidazopyridine **12** with 1,2-dibromoethane or 1,3-dibromopropane gave a mixture of mono- and disubstituted ethanes **13** and **14** (*n* = 2) respectively or only the disubstituted salt **14** (*n* = 3) [56].



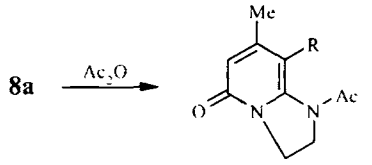
12 **13** **14**

Only one example of the alkylation of 2-oxoimidazopyridines, taking place at the $C_{(3)}$ atom, is known; the dimer **17** is formed in the reaction of hydrochloride of 2-oxoimidazopyridine **15** with the dibromo derivative **16** in the presence of sodium carbonate [62].



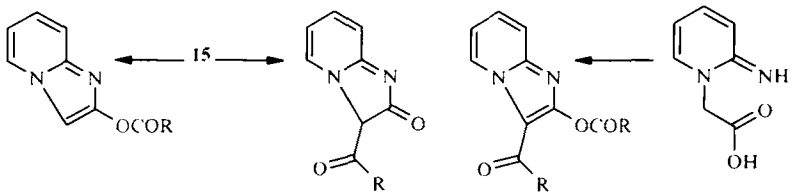
15 **16** **17**

2.1.2. Acylation. Only in one paper [33] was it mentioned that acylation takes place at the $N_{(1)}$ atom; here the acetyl derivative **18** was obtained from compound **8a** and acetic anhydride.



18

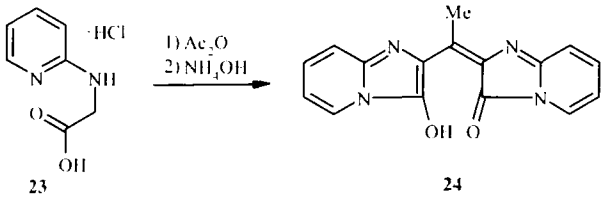
In 2- and 3-oxoimidazopyridines acylation takes place both at the oxygen atom and at position 2 or 3 respectively. During the benzoylation of 2-oxoimidazopyridine **15** compounds **19-21** (R = Ph) are formed, depending on the reaction conditions. Thus, the O-benzoyl derivative **19**was obtained after heating with benzoyl chloride in pyridine, while compounds **20** and **21** were obtained in the Schotten–Baumann reaction [63-65]. When heated with the respective anhydrides 2-oxoimidazopyridinium chloride gave the diacetyl and distearyl derivatives **21**, which were easily hydrolyzed to compound **20** [57].



19 20 21 22

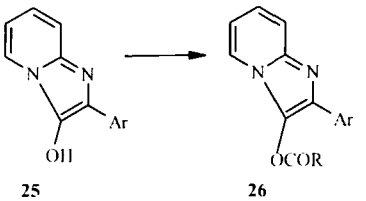
The diacetyl derivative was also obtained without isolation of imidazopyridine **15** by heating 2-iminopyridine **22** in acetic anhydride [66].

3-Oxoimidazopyridines **C** also react like the 2-oxo derivative **B**. It is clear that the intermediates in the reaction of hydrochloride of N-(2-pyridyl)aminoacetic acid **23** with acetic anhydride, leading to compound **24**, are the products from O- and C-acetylation of the 3-oxoimidazopyridine that forms [6].



23 24

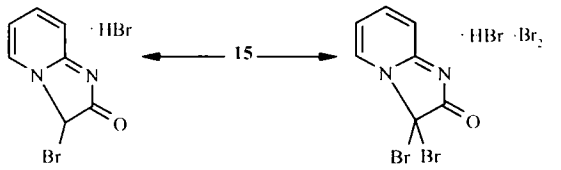
Treatment of compounds **25** with a small excess of acetic anhydride in the presence of triethylamine gave the O-acetyl derivatives **26** (R = Me); the more stable O-benzoyl derivatives **26** (R = Ph) were obtained during benzoylation in the Schotten–Baumann reaction [7, 19].



25 26

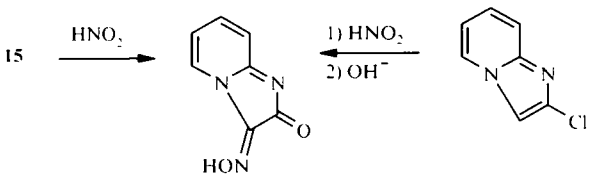
2.1.3. Halogenation, Nitrosation, Nitration, and Sulfonation. Electrophilic reactions in the series of 2,3-dihydroimidazo[1,2-*a*]pyridines **A** take place in the pyridine ring – bromination and chlorination give the 6- or 8-halogen derivatives (depending on which of the β-positions of the pyridine ring is unsubstituted) [38, 59].

During the halogenation of 2-oxoimidazopyridines substitution takes place in the imidazole ring. For example, The synthesis of the 3-bromo derivative **27** was realized by bromination of hydrochloride of 2-oxoimidazopyridine **15** with a twofold excess of bromine, but with a tenfold excess of bromine compound **28** was obtained [67].



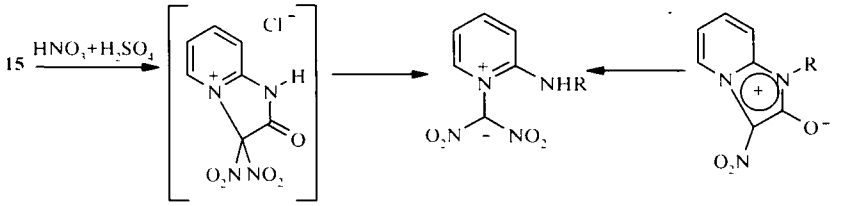
27 **28**

The nitrosation of 2-oxoimidazo[1,2-*a*]pyridine **15** with nitrous acid [63, 64, 66] gives imidazopyridine **29**, which is also produced during the nitrosation and subsequent hydrolysis of 2-chloroimidazopyridine **30** [68]. An attempt at the nitrosation of a compound of type **C** led to cleavage of the imidazole ring [19] (see 2.2.1).



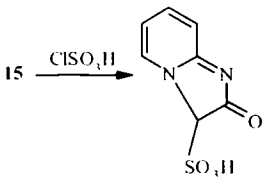
29 **30**

During the nitration of hydrochloride of 2-oxoimidazo[1,2-*a*]pyridine **15** with a nitrating mixture the five-membered ring is opened with the formation of 2-aminopyridinium dinitromethylide **31** (R = H). Ylides **31** were also obtained by the nitration of the mesoionic derivatives **32** (R = H, Me) [28]. An attempt at the nitration of 3-hydroxy-2-phenylimidazo[1,2-*a*]pyridine with a nitrating mixture led to oxidation products [19].



31 **32**

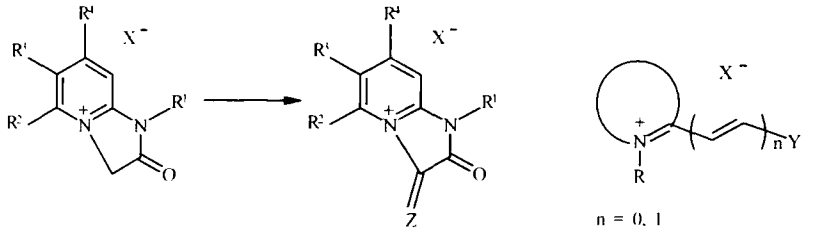
The sulfonation of 2-oxoimidazopyridine **15** with chlorosulfonic acid takes place in the imidazole ring with the formation of sulfonic acid **33** [69].



33

2.1.4. Condensation, Azo Coupling, and Addition. These reactions are characteristic of 2- and 3-oxoimidazopyridines **B** and **C**. Since they have been described in detail [2], here we give only the general scheme, supplemented by more recent data. 2-Oxoimidazopyridines **34** (usually in the form of salts) [3, 5, 20, 23,

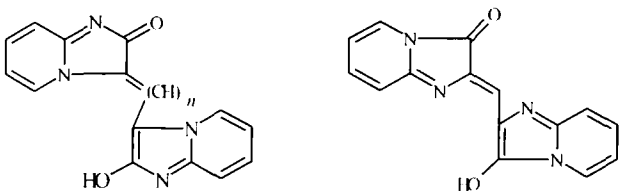
50, 51, 58, 67, 70-77] and their 1-alkyl derivatives [23, 57] enter into the reaction at the methylene group of the imidazole ring. With aromatic aldehydes [3, 20, 58, 71-74, 77], arenediazonium salts [50, 51], *p*-nitrosodialkylanilines [57, 67, 70], and derivatives of cyclic quaternary ammonium compounds (**35**) [3, 5, 23, 75-77] compounds **36**, used as dyes, were obtained.



34 **36** **35**

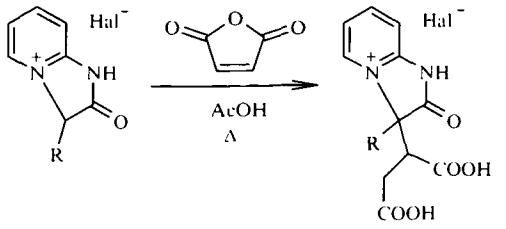
Similarly, with the above-mentioned reagents in pyridine and in the presence of triethylamine 3-oxoimidazo[1,2-*a*]pyridinium chloride also reacts at the methylene group [6]..

In the reaction of 2-oxoimidazopyridine salts **15** with ethylisoformanilide [4] or orthoformic ester [3] compound **37** (n = 1) was obtained, while in the reaction with 1,3,3-triethoxypropene (in a ratio of 2:1) compound **37** (n = 3) was obtained [3]. With orthoformic ester 3-oxoimidazo[1,2-*a*]pyridinium forms oxonol **38** [6].



37 **38**

Salts of 2-oxoimidazopyridines **39** add to Michael acceptors, such as maleic anhydride, with the formation of compounds **40** which are intermediates in the synthesis of 2,3-disubstituted maleic anhydrides (see 2.2.1) [21, 27, 31, 78].



39 **40**

The Michael reaction takes place with 3-penten-2-one, methyl crotonate, and crotononitrile in an alkaline medium and with α,β-unsaturated carbonyl compounds in a neutral medium [31].

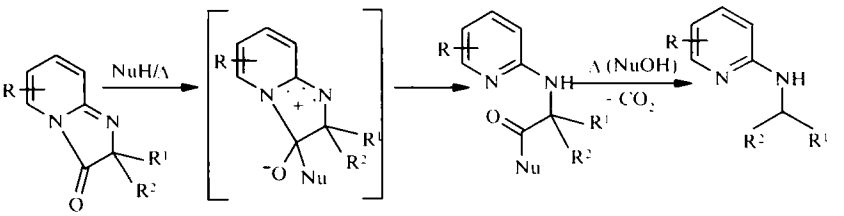
2-Oxoimidazopyridines also react at the carbonyl group. During an attempt to realize the Pschorr reaction with imidazopyridine **41** in glacial acetic acid condensation occurred, and the tetracyclic system **42** was formed with a 24% yield [58].

41 42

2.2. Nucleophilic Reactions

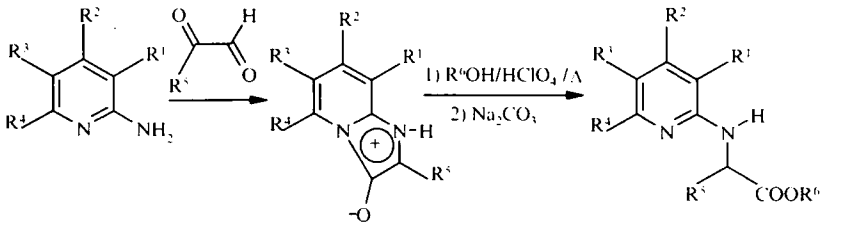
2,3-Dihydroimidazo[1,2-*a*]pyridines enter into reaction with various nucleophiles. The imidazole ring is usually cleaved with the formation of 2-alkylaminopyridines or 1-alkyl-2-iminopyridines. Such reactions take place particularly easily with oxoimidazopyridines [79]. The cleavage of the six-membered ring in 2,3-dihydroimidazo[1,2-*a*]pyridines has not been described in the literature, although recyclizations with opening of the pyridine ring have been predicted [80]. Imidazopyridines **A** can also add nucleophiles with the formation of pseudobases – the addition of nucleophiles at the $C_{(8a)}=N_{(1)}$ double bond [59] and at the conjugated system $C_{(7)}=C_{(8)}-C_{(8a)}=N_{(1)}$ [38] is well known.

2.2.1. Hydrolysis and Solvolysis. 3-Oxoimidazopyridines **43** and the corresponding mesoionic compounds are in the opinion of certain authors [6, 10, 20] very unstable. Others consider that they are fairly stable but readily enter into reactions with various nucleophiles – water [6, 10-12, 15, 17], primary alcohols [6, 11, 12, 15], primary amines [11, 12], hydrazine [11, 12], alkali [12, 81] – with cleavage of the imidazoline ring and the formation of pyridines **44** or **45**. The motivating force of these reactions is the regeneration of the aromaticity of the pyridine ring. With secondary and tertiary alcohols and amines and also with the presence of electron-donating groups (R = Me, OH, OMe) at position 8 cleavage of the five-membered ring does not occur even after prolonged heating [12].



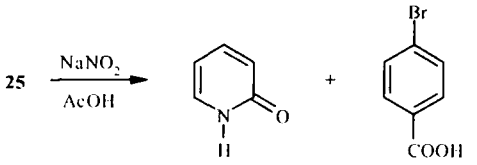
43 44 45

Cleavage of the five-membered ring in imidazopyridines **46** formed the basis of the method for the synthesis of esters of N-(2-pyridyl)-α-amino acids **47** from 2-aminopyridines **48** and α-keto aldehydes [12, 14, 16].



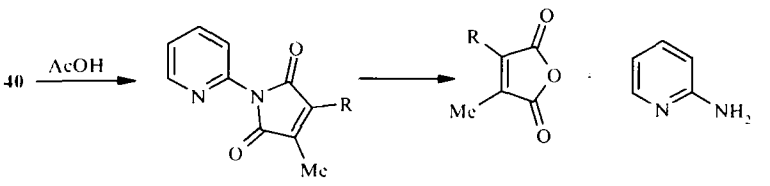
48 46 47

Decomposition of the bicyclic system with the formation of pyridone **49** occurs during the treatment of imidazopyridine **25** (Ar = *p*-BrC_6H_4) with nitrous acid [19].



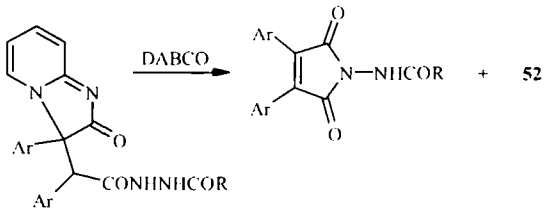
49

Opening of the ring in 2-oxoimidazopyridines by the action of acetic acid has been used in the synthesis of 2,3-disubstituted maleic anhydrides [21, 27, 31, 78]. Hydrolysis of the obtained pyridine **50** gives anhydride **51** and 2-aminopyridine **52**.



50 51 52

Cleavage of imidazopyridines **53** with diazobicyclooctane (DABCO) formed the basis of a method for the synthesis of N-aminomaleimides **54** [82].

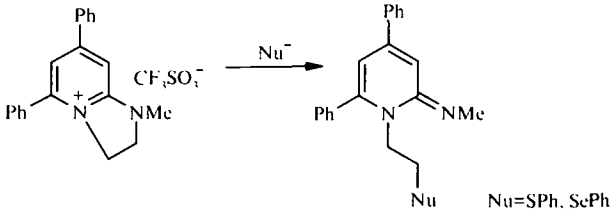


53 54

The action of heat on 2,3-dihydroimidazopyridine **55** in 1 N sulfuric acid for 10 min at 100°C also leads to a reaction with decomposition of the five-membered ring [83].

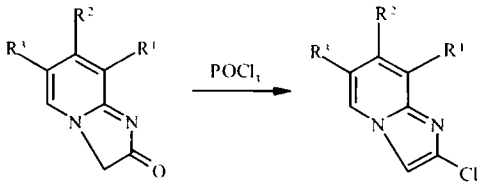
55

Only one case [60] of opening of the imidazoline ring by the action of nucleophiles in an imidazopyridine not containing an oxo group has been mentioned. This is the reaction of 2,3-dihydro-4,6-diphenylimidazo[1,2-*a*]pyridinium triflate (**56**) with thiophenolate or selenophenolate with the formation of 1-alkyl-2-iminopyridines **57**.



56 57

2.2.2 Substitution. The reaction of 2-oxoimidazo[1,2-*a*]pyridines **58** in the form of sodium salts [29] or hydrochlorides [84] with phosphorus oxychloride leads to nucleophilic substitution of the hydroxy group, and 2-chloroimidazo[1,2-*a*]pyridines **59** are formed. In the case of imidazopyridinium bromides difficultly separated mixtures of 2-bromo- and 2-chloroimidazo[1,2-*a*]pyridines were obtained [84].

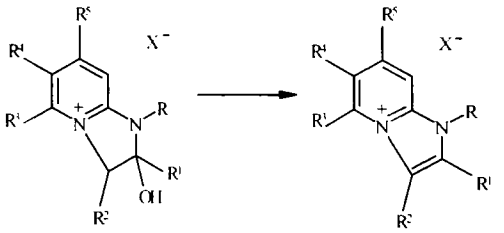


58 **59**

2.3. Dehydration of 2- and 3-Hydroxy Derivatives

2,3-Dihydroimidazopyridines containing a hydroxy group in the imidazole ring undergo dehydration. The reaction is assisted by the formation of the aromatic imidazopyridinium system.

When compounds **60** are heated in ethanol [85], polyphosphoric acid [52, 86], acetic acid [43], or acetic anhydride [45, 86] and also when they are treated with hydrobromic or perchloric acids [44], dehydration occurs with the formation of imidazo[1,2-*a*]pyridinium derivatives **61**.

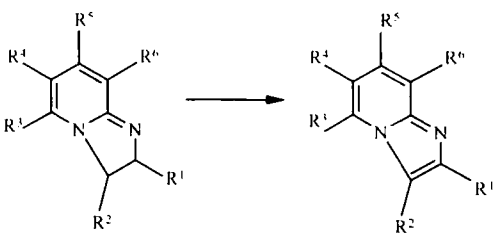


60 **61**

In a similar way N-(3-carboxy-2-pyridyl)aminoacetaldehyde, which is a tautomeric form of 2,3-dihydro-3-hydroxy-8-carboxyimidazo[1,2-*a*]pyridine, was dehydrated when heated in acetic anhydride [40].

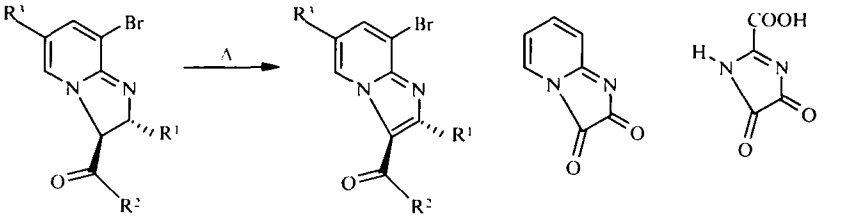
2.4. Oxidation

The action of dichlorodicyanobenzoquinone [24], potassium permanganate [87], potassium ferricyanide [22, 88, 89], and lead tetraacetate [89] on 2,3-dihydroimidazopyridines **62** leads to oxidation of the imidazoline ring to imidazole with the formation of imidazopyridines **63**. The catalytic dehydrogenation (Pd/C) of imidazopyridines **62** (R^1–R^4 = R^6 = H; R^5 = H, $CONH_2$, Ph) gave yields of 52-80% [88].



62 **63**

Sometimes oxidation takes place very readily – when heated in dioxane compound **64** ($R^1 = R^2 = Ph$; $R^3 = Br$) is converted completely into imidazopyridine **65**. The ease of dehydrogenation of compounds **64** on heating in acetic acid in the presence of bromine depends on the mobility of the hydrogen atom at $C_{(3)}$. The oxidation is not so good in the presence of an electron-donating substituent R^2 [90].



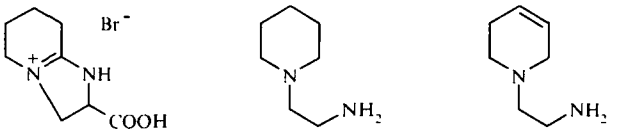
64 **65** **66** **67**

It was observed that of 2-oxoimidazopyridine salts **15** are oxidized by atmospheric oxygen in alkaline and ammonia solutions [62-64] or by potassium ferricyanide in ammonia solution [20, 64, 91, 92] with the formation of the dimer **17**. (For greater detail about the structure of the oxidation product, see [2].) Further oxidation of the dimer of imidazopyridine **17** with hydrogen peroxide [93] of potassium ferricyanide [94] gives the dioxo derivative **66**, which in turn is oxidized with cleavage of the five-membered ring and the formation of 2-aminopyridine **52** [93]. The latter is also formed during the oxidation of compound **15** with a sulfuric acid solution of potassium bichromate. The reaction of this compound with potassium permanganate both in alkaline and in acidic media leads to opening of the pyridine ring and the formation of imidazole **57** [94].

The photooxidation of the mesoionic compound by atmospheric oxygen leads to decomposition of the five-membered ring; in a neutral medium a mixture of various oxidation products with N-(2-pyridyl)benzamide as the main component is formed; in an alkaline medium N-(2-pyridyl)benzamide and benzoic acid are formed [13, 18].

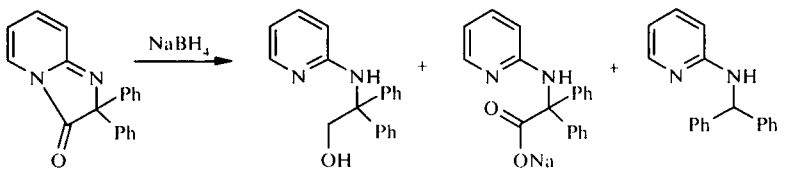
2.5. Reduction

During the reduction of imidazopyridines both hydrogenation of the pyridine ring or opening of the imidazoline ring and simultaneous cleavage of the five-membered ring and the formation of hydrogenated compounds are possible. By catalytic hydrogenation of salts of imidazopyridines A over platinum oxide in alcohol solutions it was possible to reduce the pyridine ring or even to realize the hydrogenolysis of the $C_{(8a)}=N_{(1)}$ bond. Imidazopyridine hydrobromide **2** was reduced in this way to the hexahydro derivative **68** [25], but hydrochloride of compound **12** was reduced to N-(1-aminoethyl)piperidine **69** [95]. The use of sodium borohydride in the case of imidazopyridine **12** led to tetrahydropyridine **70** [95].



68 **69** **70**

During the reduction of 3-oxoimidazopyridine **71** with sodium borohydride cleavage of the imidazoline ring takes place at the $C_{(3)}$–$N_{(4)}$ bond with the formation of a mixture of 2-aminopyridines **72-74**, in which the main product (~70%) is amino alcohol **72**. The use of lithium aluminum hydride in this reaction leads to partial hydrogenation of the pyridine ring and reduction of the carbonyl group with the formation of the bicyclic amidine **75a**, which is easily transformed into the more stable isomer **75b** [12].



71 72 73 74

Catalytic hydrogenation of 3-oxoimidazo[1,2-*a*]pyridines **43** in the presence of palladium on charcoal led to selective reduction of the pyridine ring, since the N-acylamidines formed here are inert to further catalytic hydrogenation [12, 13].

The present review shows that 2,3-dihydroimidazo[1,2-*a*]pyridines are extremely reactive substances. However, their transformations have been studied comparatively little. They will probably open up wide-ranging prospects for solution of the theoretical aspects of this heterocyclic system and also for the synthesis of compounds valuable that will be of value for practical purposes.

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