NEW RECYCLIZATIONS AND TRANSFORMATIONS OF AZINES

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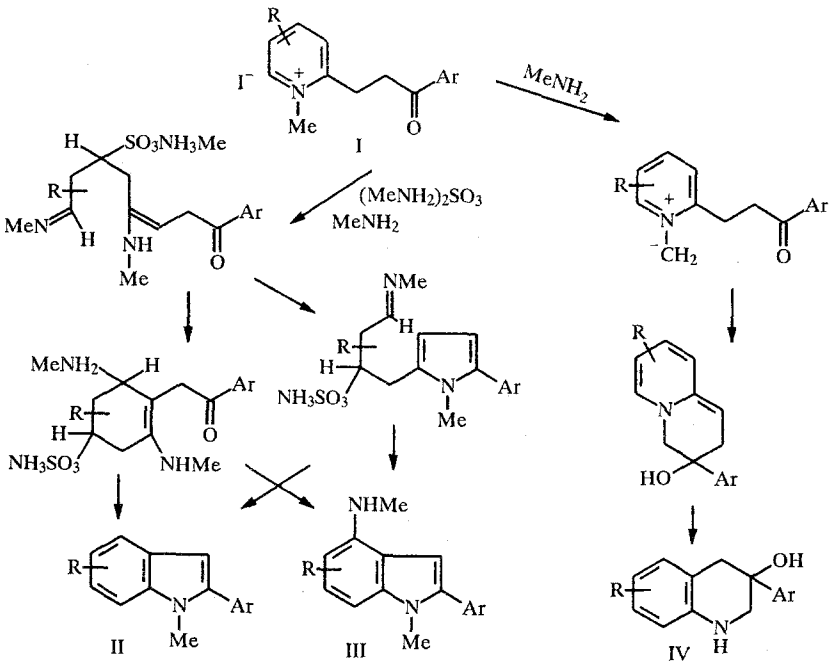
The review correlates new data on the isomerizational recyclization and transformation of azines in the last ten years.

The phenomenon of isomerizational recyclization of nitrogen heterocycles was discovered in the nineteen seventies in the laboratory of biologically active organic compounds in the chemistry department of Moscow State University under the supervision of Professor A. N. Kost. This review is devoted to the development of this research in the chemistry of azines in recent years.

It is known that activated azines (for example, α-alkylnitropyridinium salts) generally enter into this rearrangement under the influence of aqueous or alcoholic alkali [1]. Unactivated substrates require the sulfite anion as the recyclizing agent, which considerably expands the limits of applicability of this reaction [2].

We have extended the rearrangement to azinium systems that contain a functional group in the side chain and have shown that the recyclization of pyridinium salts I with a carbonyl group in the γ position of the α-alkyl substituent leads to indole derivatives [3, 4].



R = H, Me; Ar = Ph, 2-thienyl

Both alkylindoles II and aminoindoles III are formed as a result of the reaction. The pyridine ring of starting salt I is opened under the influence of methylammonium sulfite. The formation of either a six-membered carbocycle or a five-membered pyrrole ring may then occur. Oxidation with the introduction of a methylamino group, which leads to aminoindole

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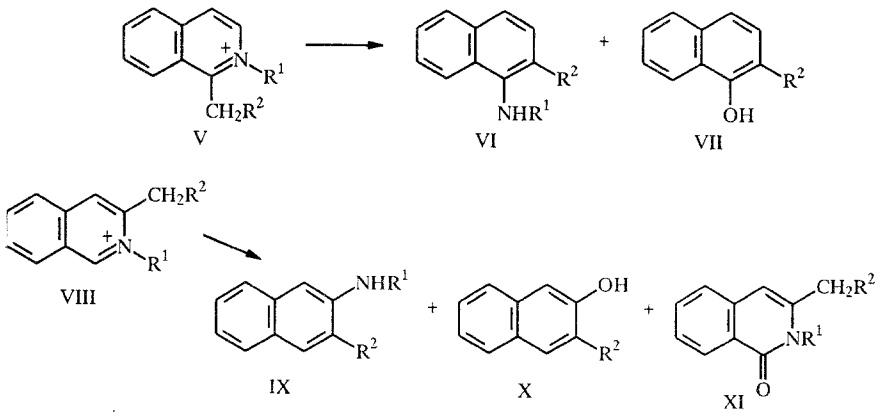
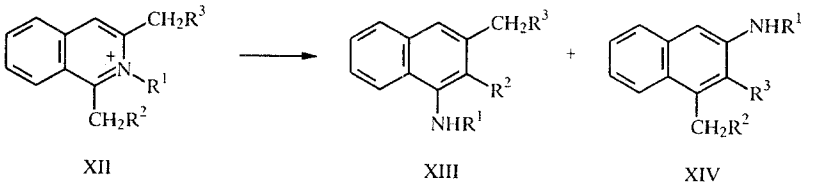
III, evidently occurs after the formation of a pyrrole ring with simultaneous splitting out of the sulfite reagent and restoration of the aromatic character. It should be noted that this process is a new pathway of transformations in the recyclization of pyridinium salts that differs from the classical enamine rearrangement. In addition to indoles II and III, 3-hydroxy-1,2,3,4-tetrahydroquinoline derivatives IV are formed as a result of this reaction. Deprotonation of the N-methyl group occurs under the influence of a base in this case, and this is followed by intramolecular condensation with the participation of the resulting anionic center and the carbonyl group present in the molecule. The next step is isomerizational recyclization of the tetrahydroquinolizine ring to a tetrahydroquinoline ring, which proceeds in the same way as the rearrangement of nitroindolizines to nitroindoles [5].

Whereas pyridinium salts that do not contain acceptor substituents undergo recyclization under the influence of an alkylammonium sulfite, alcohol solutions of alkylamines were used as the nucleophiles for the rearrangement of isoquinolinium salts; 1-alkylisoquinolinium salts V undergo rearrangement to 1-alkylaminonaphthalenes VI in 70-90% yields, and 3-alkylisoquinolinium salts VIII undergo rearrangement to 2-alkylaminonaphthalenes IX in 30-60% yields [6, 7]. The corresponding α-naphthols VII or β-naphthols X are formed in addition to aminonaphthalenes when an aqueous solution of an alkylamine is used as the recyclizing reagent.



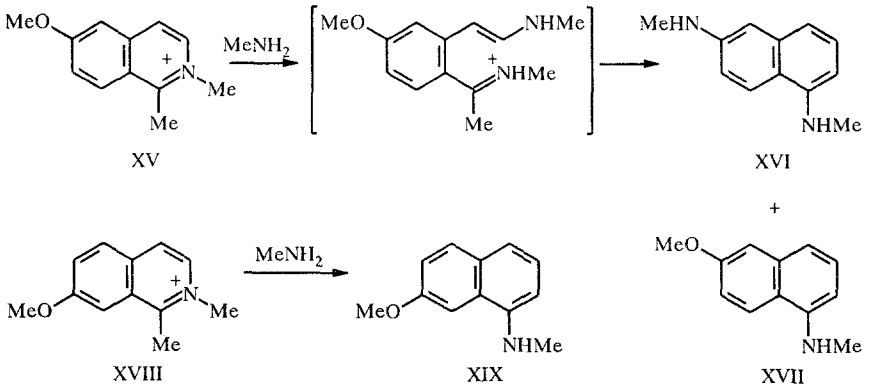
R^1 = Me, Et, $CHMe_2$; R^2 = H, Me, Ph

The rearrangement of 1,3-dialkylisoquinolinium salts XII proceeds via two pathways, leading to both 1-aminonaphthalene derivatives XIII in 30-68% yields and 2-aminonaphthalene derivatives XIV (in 7-40% yields). The predominant formation of 1-aminonaphthalenes is in agreement with the results of quantum-chemical calculations [8].



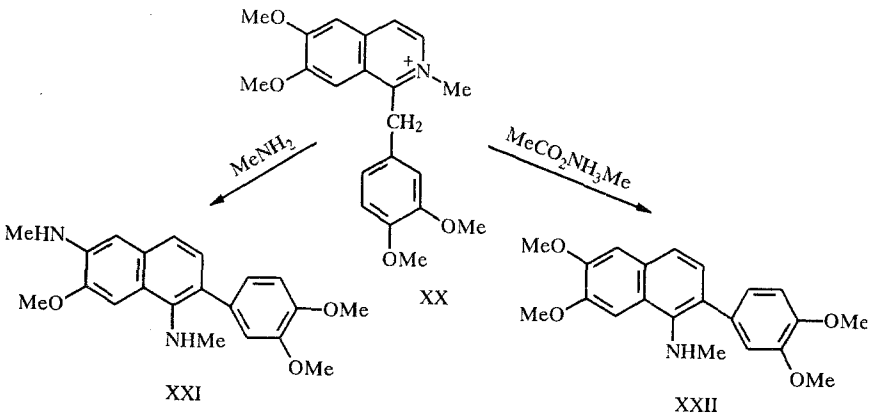
R^1 = Me, Ph; R^2 = H, Ph

The introduction of donor substituents into the benzene ring of the isoquinolinium salt decreases the electrophilicity of the pyridine ring and hinders rearrangement of the isoquinoline ring to a naphthalene ring. The presence of two methoxy groups in the 6 and 7 positions of the 1-methylisoquinoline molecule leads to impossibility of recyclization of the corresponding salt under the influence of methylamine [9]. The introduction of one donor substituent into the 6 and 7 position does not hinder rearrangement of the 1,2-dimethylisoquinolinium salt [10]; during the reaction the methoxy group in the 6 position of the isoquinoline undergoes virtually complete replacement by a methylamino group, as a result of which the principal product of the rearrangement of salt XV is aminonaphthalene XVI, while aminonaphthalene XIX is formed in the recyclization of salt XVIII.

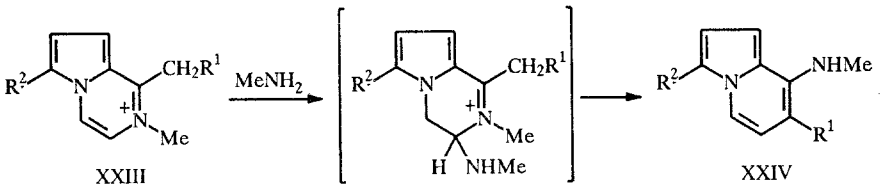


Replacement of the methoxy group by a methylamino group may occur both in the starting salt, in which the electron density of the isoquinoline ring is decreased because of quaternization, and in a step involving an acyclic intermediate, in which, during the reaction, the iminium group activates nucleophilic substitution of the methoxy group in the para position [11]. The fact that replacement of the methoxy group in both 6- and 7-methoxyquinoline cannot be realized under the influence of an alcohol solution of methylamine in the presence of ammonium chloride at the rearrangement temperature constitutes evidence that substitution takes place in a step involving an acyclic intermediate.

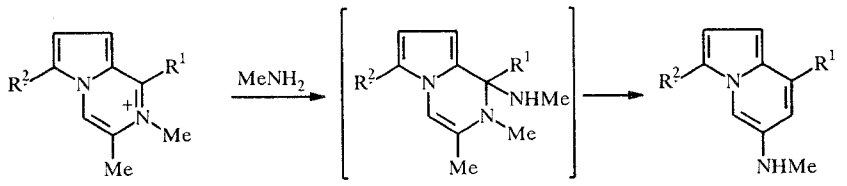
It has been shown that the rearrangement of papaverine methiodide (XX) under the influence of an alcohol solution of methylamine also proceeds with replacement of the methoxy group in the 6 position by a methylamino group [9, 12]. Rearrangement product XXII, with retention of the methoxy group in the 6 position, was obtained when methylammonium acetate, which has a smaller degree of nucleophilicity than methylamine, was used as the recyclizing agent.



The recyclization of the pyrrolo[1,2-*a*]pyrazine molecule has been investigated [13-15]. This heterocyclic system is of interest in connection with the fact that it contains two nitrogen atoms, each of which can participate in recyclization. Rearrangement with the participation of the $N_{(2)}$ atom should proceed in the same way as the rearrangement of isoquinolinium salts and requires the presence of a methyl or methylene group in the α position relative to this nitrogen atom. Depending on whether the alkyl substituent is located in the 1 or 3 position, the products of rearrangement of pyrrolo[1,2-*a*]pyrazine will be the corresponding 8- or 6-aminoindolizines. Quaternization of the pyrazine ring should promote this recyclization pathway. The $N_{(4)}$ atom is a bridge atom, and rearrangement with its participation may proceed in the same way as the recyclization of indolizines and lead to 6-azaindoles. However, this latter recyclization pathway is not realized in practice. We have found that 1-alkylpyrrolo[1,2-*a*]pyrazine salts XXIII undergo recyclization under the influence of an alcohol solution of methylamine to give 8-aminoindolizine derivatives XXIV. The reaction proceeds with attack by the nucleophile at the 3 position of the pyrrolo[1,2-*a*]pyrazine position with subsequent cleavage of the $C_{(3)}$—$N_{(2)}$ bond and cyclization of the resulting acyclic intermediate. The fact that a mixture of two 8-alkylaminoindolizines is always formed as a result of the reaction when an amine with an alkyl substituent that differs from the radical in the starting salt is used as the reagent constitutes evidence that the rearrangement proceeds with cleavage of the $C_{(3)}$—$N_{(2)}$ bond rather than the $C_{(1)}$—$N_{(2)}$ bond.



XXIII XXIV



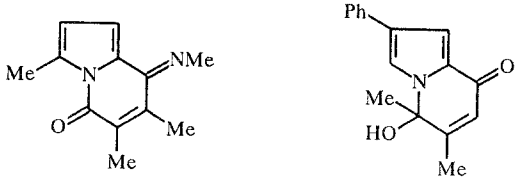
XXV XXVI

XXIII, XXIV R^1=H, Me, Ph; R^2=H, Me; XXV, XXVI R^1=H, Ph; R^2=H, Me

Under the rearrangement conditions, 3-alkylpyrrolo[1,2-*a*]pyrazinium salts XXV undergo attack by the nucleophile at the 1 position with cleavage of the pyrazine ring at the $C_{(1)}$—$N_{(2)}$ bond, which leads to 6-alkylaminoindolizines XXVI. The yields of 6- and 8-aminoindolizines reach 59-80%.

When alkyl substituents are present simultaneously in the 1 and 3 positions, the rearrangement of pyrrolo[1,2-*a*]pyrazinium salts proceeds via two pathways with the primary formation of 8-aminoindolizines; the overall yields of the indolizines range from 65% to 85%.

When the resulting aminoindolizines contain alkyl groups in the pyridine ring, these compound are readily oxidized during isolation to give quinoid structures of the XXVII and XXVIII type.



XXVII XXVIII

In turn, the indolizines themselves are capable of undergoing recyclization to the isomeric indoles. This reaction, which was discovered in 1976 in the research of Kost and coworkers [5, 16, 17] in the case of the rearrangement of 2-methyl(phenyl)-6(8)-nitroindolizines to 3-methyl(phenyl)-5(7)-nitroindoles, opened up a new page in the chemistry of indolizines, which previously had had extremely limited application. The accessibility of indolizines (which are easily obtained by the Chichibabin method from α-alkylpyridines), as well as the possibility of extensive variation of the substituents in the pyrrole fragment of the indolizine ring due to electrophilic-substitution reactions, opened up new prospects in the synthesis of indoles with a predesignated orientation of the functional groups. It was also previously established [5] that in the absence of a 6(8)-nitro group, which activates the pyridine fragment of the molecule to undergo opening under the influence of a nucleophile (for example, in the case of 2-methylindolizine), the rearrangement is not realized. The chief tasks in the further development of this pathway were therefore an analysis of the effect of substituents on the electron structure and reactivity of the indolizine ring and the establishment of the limits of applicability of the reaction.

Thorough quantum-chemical CNDO/2 analysis [18, 19] of the effect of a nitro group from various positions of 2-methylindolizine on the electron-density distribution and the structures of the boundary orbitals showed a serious decrease in both the total charge and π charge on the $C_{(5)}$ atom and an increase in the coefficient of the contribution of this atom to the lowest vacant molecular orbital (LVMO) when a nitro group was introduced into the 6 or 8 position. However, in the case of 1- and 3-nitroindolizines (which are distinctive vinylogs of the 6- and 8-nitro isomers) transmission of the effect of the nitro group along the conjugation chain attenuates, and the population of the $C_{(5)}$ atom remains virtually unchanged (see Fig. 1); this made it possible to regard the possibility of recyclization of these compounds as unlikely.

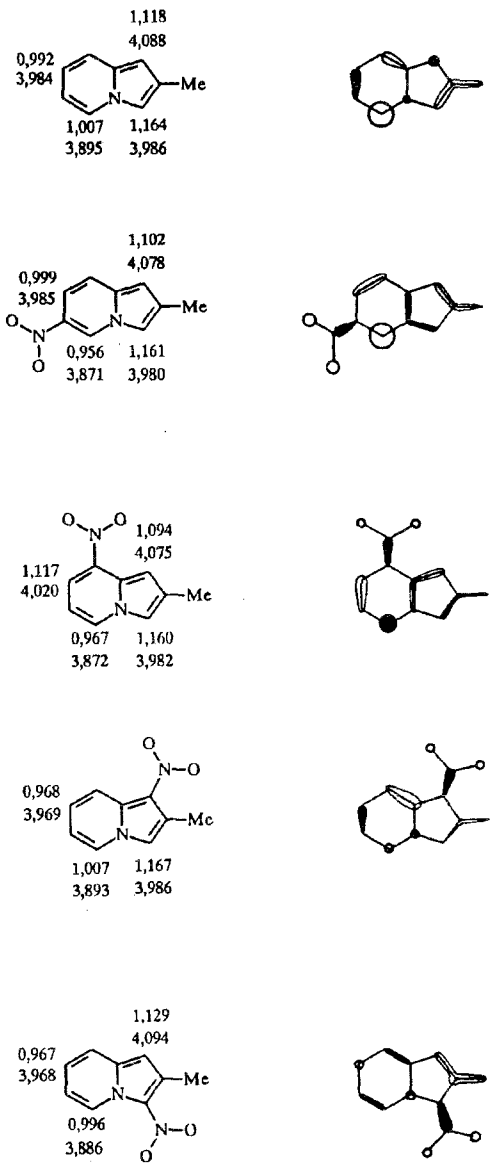


Fig. 1. Electron structures of 2-methylindolizine and its 6-, 8-, 1-, and 3-nitro derivatives according to the results of quantum-chemical CNDO/2 calculations. The π and (π + σ) populations of the 1, 3, 5, and 7 positions of the indolizine ring, as well as the corresponding diagrams of the LVMO of the indolizines (the dimensions are proportional to the coefficients of the contribution of the p_z orbitals of the atoms to the boundary orbital), are presented.

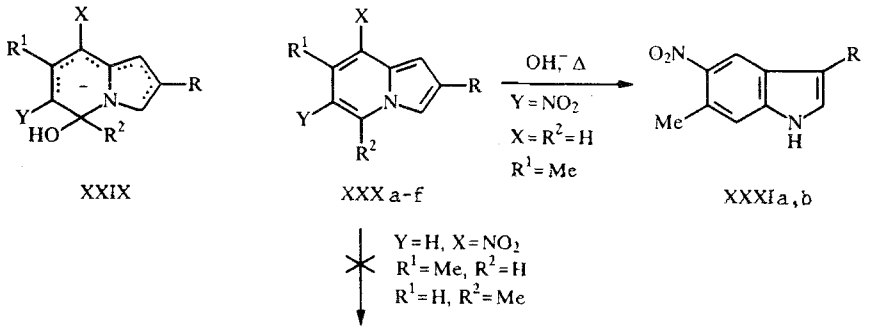
Experimental verification actually showed [19] that, even under the severe conditions of refluxing with alkali, the isomeric 1- and 3-nitroindolizines do not undergo ring transformation. (It has been previously noted that indolizines with the acceptor substituent COR, COOR, and CN in the 1 or 3 positions react with nucleophiles at the functional group [20]; alkaline deacylation was observed in the case of 3-trifluoroacetylindolizines [19, 21].)

Other compounds that are potentially capable of undergoing recyclization could be indolizines that contain acceptor substituents, other than nitro groups, in the 6 or 8 positions. However, experiments showed that 6(8)-cyano- and acetylindolizines are also incapable of undergoing rearrangement [22]; only the usual saponification was previously noted in the reaction of 6- and 8-ethoxycarbonylindolizines with alkali [23].

On the basis of the results obtained it may be asserted that a necessary condition for the recyclization of indolizines to indoles is the presence in the 6(8) position of the indolizine of a substituent, the electron-acceptor character of which would be no less pronounced than that of the nitro group.

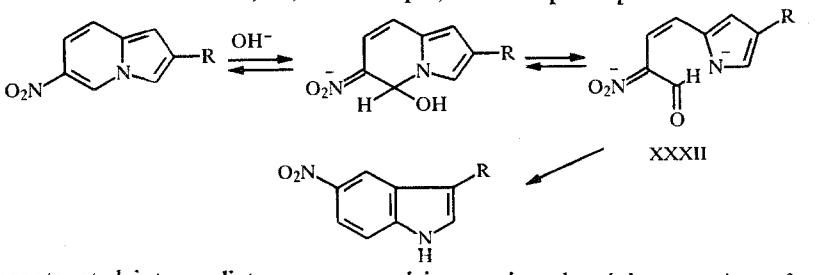
The readily accessible homologs of 6- and 8-nitroindolizines [19, 24] reacted with alkali or sodium methoxide to give anionic σ complexes XXIX, which were detected by electronic and PMR spectroscopy; the nucleophile attacked the 5 position. The reaction with alkali at high temperatures in the case of 7-methyl-6-nitro derivatives XXXa, b led to the expected 6-methyl-5-nitroindoles XXXIa, b [25], while the isomeric 7-methyl-8-nitroindolizines XXXc, d (as well as 5-methyl-8-nitro isomers XXXe, f) were saponified completely under these conditions.

This is evidently associated with the increased CH acidity of the 7-CH_3 groups, which are in direct conjugation with the 8-NO_2 group (but not with the 6-NO_2 group), the deprotonation of which may lead to side processes [19, 25]. This sort of nonequivalence of the mutual effect of groups that are separated by an essentially single bond or essentially double bond of the tetraene skeleton of indolizine has found convincing confirmation in an analysis of the regularities of the electronic and ^{13}C and ^1H NMR spectra [19, 24, 26] and mass spectra [27] in the methylnitroindolizine series.



XXX, XXXI	Compound	X	Y	R	R^1	R^2
	a	H	NO_2	Me	Me	H
	b	H	NO_2	Ph	Me	H
	c	NO_2	H	Me	Me	H
	d	NO_2	H	Ph	Me	H
	e	NO_2	H	Me	H	Me
	f	NO_2	H	Ph	H	Me

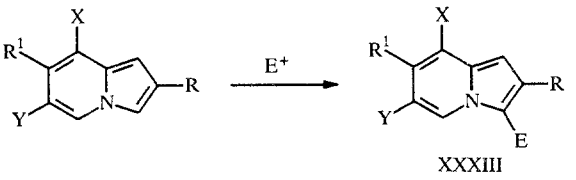
The presence of a substituent in the 1 position in 6-nitroindolizines should hinder the development of the open form during recyclization. It was found that 1,2-dimethyl-6-nitro- and 2-methyl-1,6-dinitroindolizines, in contrast to the cases examined above, are recovered unchanged even after refluxing for many hours in a solution of alkali (under conditions that lead to opening of the ring of other 6-nitroindolizines); this is associated [28, 29] with the possibility of the reversible cyclization of the open form of nitroindolizines, i.e., the reverse formation of a pyridine ring (similar to the reversible Dimroth rearrangement in the 1-aza-6(8)-nitroindolizine series [30]). A study of the recyclization of 2-methyl-6- and 8-nitroindolizines in D_2O—MeOD showed that a deuterium label develops only at the nitrogen atom but is not associated with the carbon atoms of the indole ring [19]. This makes it possible to exclude forms that contain deuterium in the meta position relative to the 6(8)-NO_2 group from the number of possible open intermediates and to propose a more precisely defined mechanism for the recyclization of nitroindolizines to nitroindoles, as, for example, with the participation of dianionic intermediate XXXII:



(The participation of deprotonated intermediates was proved in reactions involving opening of pyridinium salts under the influence of bases [31].) It has been previously noted that the recyclization of 6(8)-nitroindolizines under the influence of

sodium methoxide in methanol does not take place [5]; it was established that in CD_3ONa/CD_3OD 2-methyl-6-nitroindolizine undergoes selective deuterium exchange in the 5 position [32].

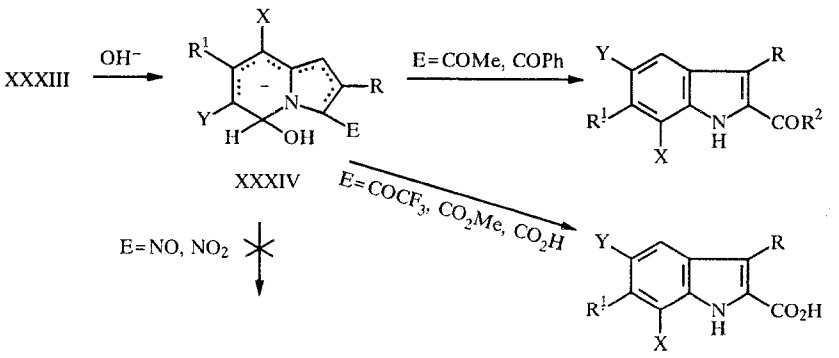
A further expansion of the series of compounds that are capable of undergoing recyclization was realized through electrophilic-substitution reactions in the 6- and 8-nitroindolizine series; the results of CNDO/2 calculations provided evidence for the insignificant effect of the 6(8)-NO_2 group on the electron density of the pyrrole fragment of indolizine [19] (see Fig. 1). The corresponding 3-substituted 6(8)-nitroindolizines XXXIII were isolated in high (in some cases quantitative) yields in acylation, nitration, nitrosation, and methoxycarbonylation reactions [19, 28, 29, 33, 34]; a mixture of 1- and 3-nitro derivatives was formed in the nitration of 2-methyl-6-nitroindolizine with acetyl nitrate [29].



XXXIII

E = NO, NO_2, COMe, COPh, $COCF_3$, CO_2Me; X, Y = H, NO_2; R^1 = H, Me; R = Me, Ph

According to the results of electronic spectroscopy, all of the 3-substituted 6(8)-nitroindolizines XXXIII are converted reversibly to bright-orange σ complexes XXXIV under the influence of alkali [19, 28, 29] (the indicator effect; see [29]); attack by the nucleophile at the 5 position was proved for the 3-benzoyl derivative by the data from the PMR spectra obtained in CD_3ONa/CD_3OD. The subsequent pathway of the reaction with alkali is determined by the nature of the electron-acceptor substituent in the 3 position. On standing in a solution of alkali or on brief heating, 3-nitro- and nitroso derivatives XXXIII (E = NO, NO_2) underwent complete saponification [19, 29], while 3-acetyl(benzoyl)-6(8)-nitroindolizines after brief heating with alkali were converted to the expected 2-acetyl(benzoyl)-5(7)-nitroindoles XXXV in good yields [22, 31, 37]. It is important that the recyclization of 3-acyl derivatives of 6(8)-nitroindolizines XXXIII (E = COMe, COPh) proceeded more readily than in the case of 6(8)-nitroindolizines XXX, i.e., the presence of a 3-COR group facilitates opening of the pyridine fragment without hindering the ring closing of the open form, in contrast to the 3-nitroso(nitro) group, which evidently hinders both the formation of a benzene ring and the reverse formation of a pyridine ring. (The absence of rearrangement in the case of 2-tert-butyl-6-nitroindolizine was previously associated with steric hindrance to ring closing of the open form [5].)

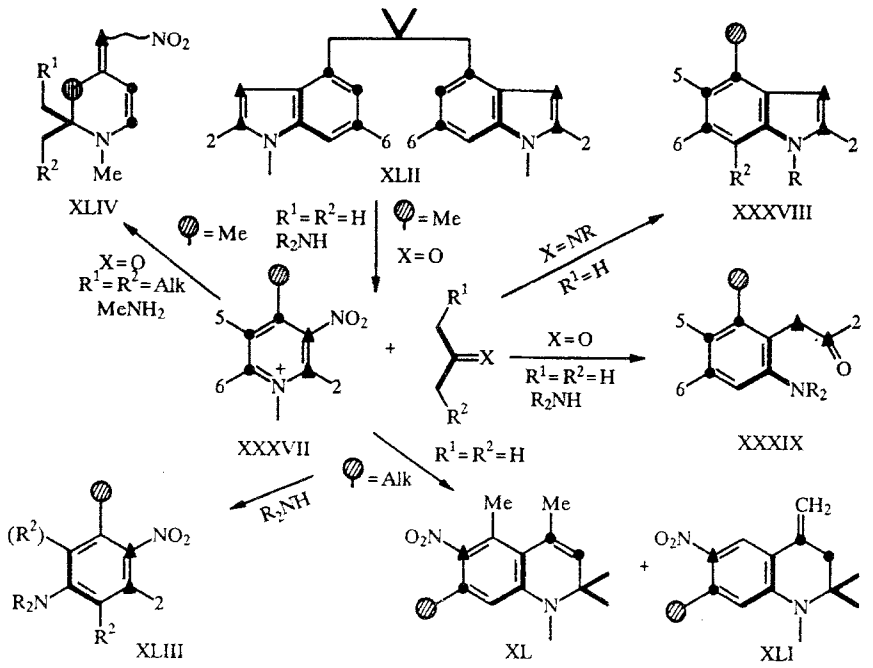


On reaction with alkali 3-trifluoroacetyl-6(8)-nitroindolizines undergo recyclization even at room temperature; in this case the transformation of the pyridine fragment is accompanied by a haloform reaction: the isolated reaction products are the corresponding 5(7)-nitroindole-2-carboxylic acids XXXVI [19, 33, 35]. It was established that the intermediates of this "haloform recyclization" are extremely unstable 6(8)-nitroindolizine-3-carboxylic acids, which are also preparatively isolatable by the action of a solution of sodium methoxide in methanol on 3-trifluoroacetyl-6(8)-nitroindolizines, i.e., under conditions that hinder ring opening. The resulting indolizines undergo isomerization unusually readily (even at 0°C) to the corresponding nitroindolecarboxylic acids. The recyclization of 3-methoxycarbonyl-6-nitroindolizine to 5-nitroindole-2-carboxylic acid proceeds at room temperature through the formation of a similar intermediate [19]. Thus the presence of groups of the COX type (X = CH_3, Ph, CF_3, OMe, OH) in the 3 position of the 6- and 8-nitroindolizine molecules significantly facilitates rearrangement of the indolizine ring to an indole ring.

The data obtained are of practical interest first and foremost as a new convenient method for the synthesis of 2-acyl-5-nitroindoles and 5-nitroindole-2-carboxylic acids — important intermediates in the synthesis of tranquilizers of the benzodiazepine series (nitrazepam, hypnone) [36-38].

The examined examples of the transformation of the six-membered ring in both azolo azines and azinium salts were realized by the action of N- or O-nucleophiles.

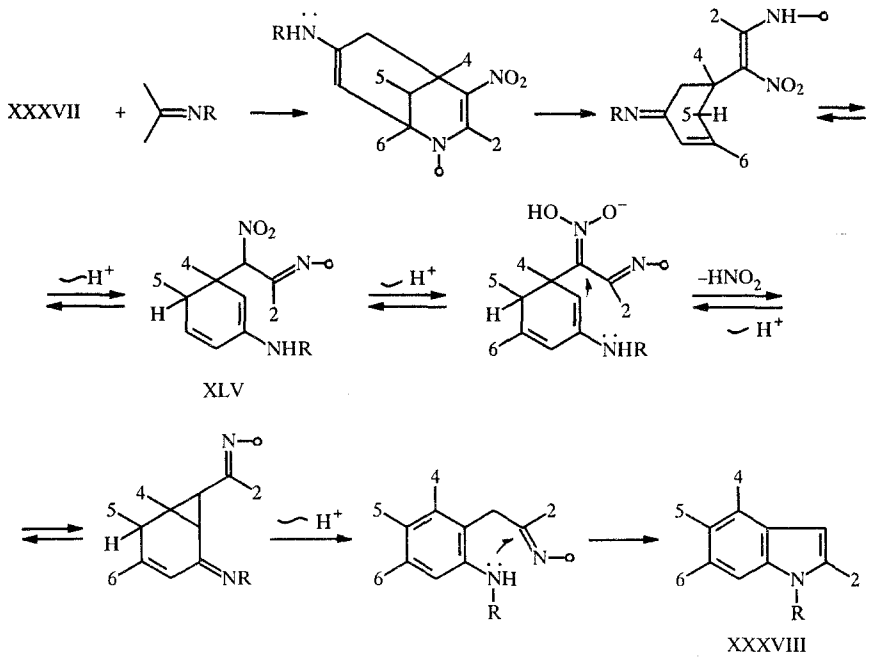
The use of 1,3-bis-C,C-nucleophiles (enamine forms of N-alkylketimines) in reactions with N-alkyl-3-nitropyridinium salts XXXVII opens up new synthetic possibilities. Thus it was found that the latter are unique synthones that are capable of undergoing transformation to a number of new carbo- and heterocycles. We were able to uncover a family of transformations of 3-nitropyridinium cations XXXVII under the influence of ketimines (or mixtures of ketones with amines) that can be represented by the following scheme:



This multifaceted character of the transformations is due, first, to the high reactivity of the α and γ positions of the XXXVII cations with respect to nucleophiles, in addition to the possibility of reactions of the CH-acidic α- and γ-alkyl substituents with electrophiles, and, second, to the fact that the aliphatic ketone—amine reaction system may act as a C-nucleophile (the enamine form of the ketimine) and as a C-electrophile (the free ketone).

As we will show, the pathway of the processes is determined to a considerable extent by the structures of the starting compounds and the conditions under which the reactions are carried out.

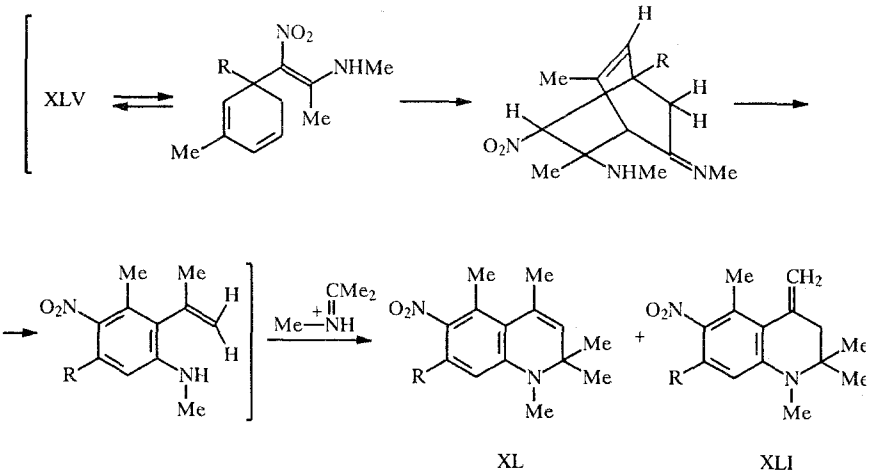
One of the most interesting transformations is the transformation of polyalkyl-substituted cations XXXVII to polyalkylindoles XXXVIII [39-44]. As proved using chemical (salts XXXVII, which contain alkyl radicals with different structures in various positions of the ring [39, 44, 48]) and isotope (the reaction of salts XXXVII with a mixture of deuteroacetone and methylamine) labels, the XXXVII cation in this process undergoes cleavage of the $C_{(3)}$—$C_{(4)}$ bond and is the source of a five-carbon (3 + 2) fragment; the $C_{(4)}$—$C_{(5)}$—$C_{(6)}$ atoms participate in the construction of the benzene ring of indole, while the $C_{(2)}$—$C_{(3)}$ atoms participate in the construction of a pyrrole ring. The three-carbon fragment of the ketimine, inasmuch as it is "built in" between the fragments of the pyridinium cation, participates in the construction of both parts of the indole molecule, being simultaneously also a source of the indole nitrogen atom [42]. The nitro group of the starting XXXVII cation is eliminated during the formation of the indoles in the form of the NO_2^- ion. The scheme of this process, which does not have literature analogies, can be represented in the following way [48]:



XXXVIII

Since ketimines (in the enamine form) are the source of the nitrogen atom in the molecules of the resulting indoles XXXVIII [42], the use of secondary amines in a mixture with the ketones enabled us to avoid the formation of a pyrrole ring in the XLV → XXXVIII step and to isolate stable analogs of intermediates of the process, viz., o-N,N-dialkylaminobenzyl ketones XXXIX [50], which is one of the confirmations of the proposed scheme.

It should be noted that the developed method for obtaining polyalkylindoles is distinguished by its simplicity, the mild conditions under which the reaction is carried out (20°C, 1-3 days, in DMF in the case of the preprepared ketimine or in excess ketone when mixtures of ketones with the amines are used), the preparative yields (the maximum yields reach ~80%), and the possibility of the purposeful synthesis of indoles with virtually any number, location, and structure of the alkyl substituents.



XL XLI

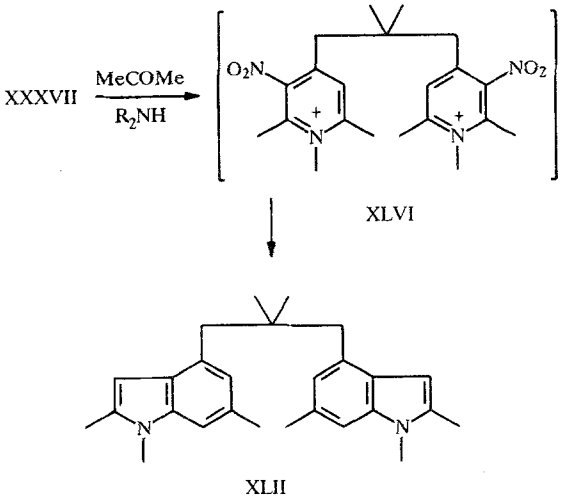
R=Me, XL (4%), XLI (2%); R=CH_2-*t*-Bu XL (18%), XLI (6%)

However, under the indicated conditions the formation of indoles is not the only pathway of the process. Thus 1,2,2-trimethyl-6-nitrodi- XL and -tetrahydroquinolines XLI can also be isolated from the reaction mixture in the reaction of 2,4,6-trialkyl-3-nitropyridinium cations XXXVII with N-methylacetoneimine [51]. Another pathway leading to XL and XLI is evidently also possible in addition to the indicated (in the scheme) formation of indoles via the transformation of intermediate XLV.

In this case two molecules of the imine participate in the construction of the quinoline ring; one acts as an electrophile, while the other acts as a 1,1,3-trisnucleophile, bonding with the $C_{(2)}$, $C_{(4)}$, and $C_{(6)}$ atoms of the XXXVII cation. An idiosyncrasy of this process is cleavage of the $C_{(4)}$—$C_{(5)}$ bond of the pyridine ring.

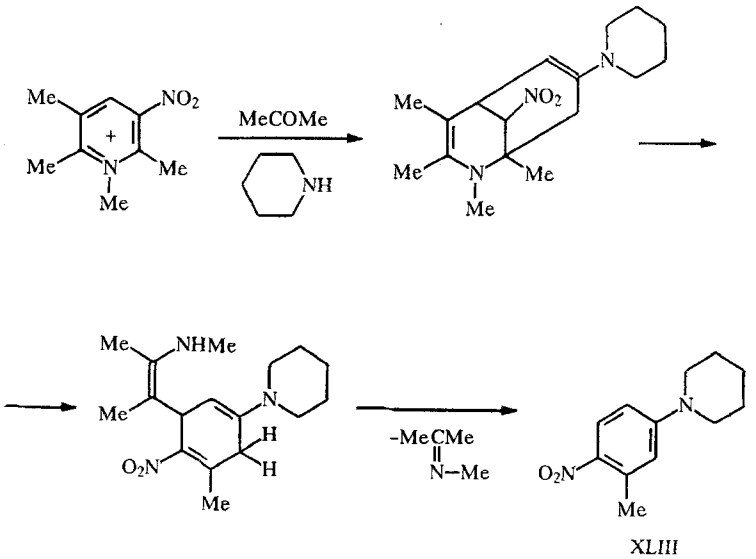
When secondary amines (in mixtures with ketones), which are more basic than primary amines, are used in the reactions with 4-methyl-substituted cations XXXVII, 1,3-bisindolylpropanes XLII can also be isolated in addition to the above

-indicated o-aminobenzyl ketones XXXIX. The formation of these compounds can be conceived as being the preliminary condensation of the 4-CH_3 groups with the free ketone due to the presence in the medium of a strong base, viz., the secondary amine, with subsequent transformation of the resulting bis salt XLVI via an already known scheme [50]:



In contrast to the formation of indoles XXXVIII, three fragments of the ketone, two of which display the properties of a 1,3-bis-C,C-nucleophile, and one of which displays the properties of an electrophile, participate in the construction of the molecules of XLII.

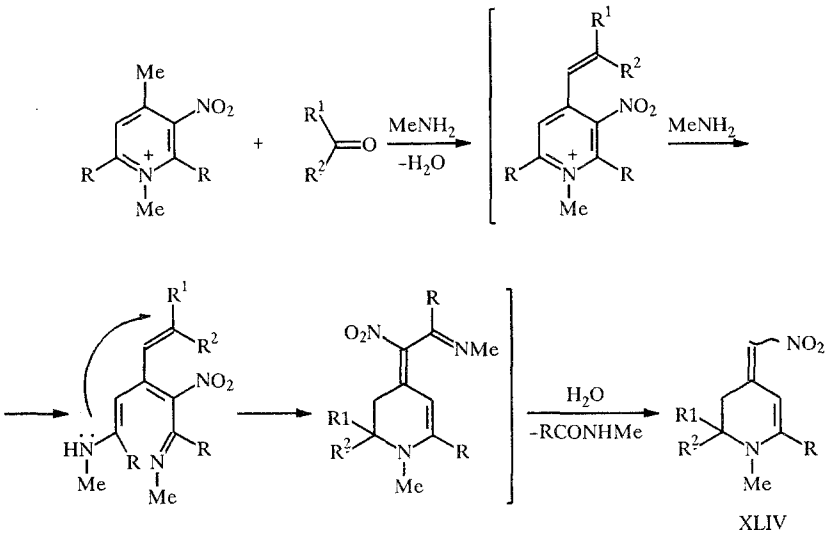
In the proposed scheme for the formation of indoles XXXVIII we assume that the first step in the process is stepwise 4,6-meta-bonding of the electron-deficient XXXVII cation with the enamine form of the ketimine. On the basis of the results of quantum-chemical calculations regarding the greatest electrophilicity of the 6 position in 2,4,6-trialkyl-3-nitropyridinium cations [52], it might be assumed that the initial attack by the nucleophile will take place in the 6 position, which leads only to one possible variation of meta bonding (4,6). The absence of a substituent in the 4 position of salt XXXVII leads to a change in the site of initial attack (the 4 position) and makes both 4,6- and 2,4-meta-bonding virtually equally likely. Whereas the first variation of meta bonding leads to indoles XXXVIII, the result of the second variation is the production of p-nitroanilines XLIII. The formation of XLIII is observed under various conditions of carrying out the reactions of 4-unsubstituted salts XXXVII with both preprepared ketimines and with the free ketones in the presence of secondary amines [50]:



In this case a molecule of the ketone and the $C_{(2)}$—$C_{(3)}$—$C_{(4)}$ fragment of the starting salt participate in the construction of the benzene ring, while the $C_{(5)}$—$C_{(6)}$ fragment is eliminated in the form of the N-methylimine of the corresponding ketone, which is detected in the reaction mixture in the form of the free ketone (by GLC).

Here, just as in the formation of quinolines XL and XLI, the process is accompanied by cleavage of the $C_{(4)}$—$C_{(5)}$ bond of the XXXVII cation. A literature analogy to the formation of p-nitroanilines is their production in the transformation of the ring of 3,5-dinitro-2-pyridones under the influence of ketones and aliphatic amines (secondary or primary), the only difference being that, instead of the ketone imine, a molecule of nitroacetamide is eliminated [53].

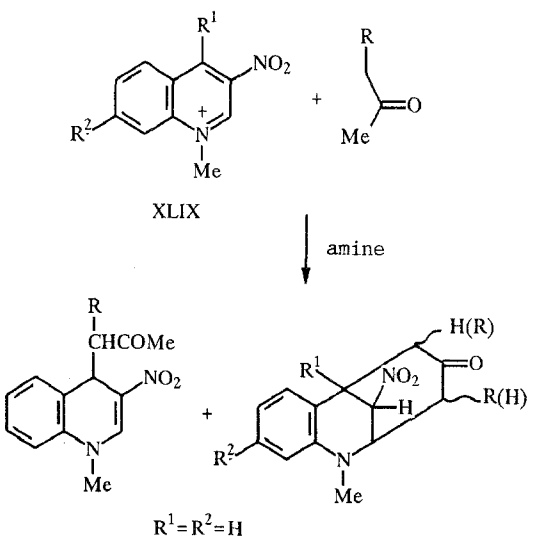
The described changes in the pathways of the transformations were heretofore attributed to idiosyncrasies of the structures of the XXXVII cations and amines. However, it was found that the structure of the ketone component also plays a substantial role. Thus passing from methyl alkyl ketones to dialkyl ketones radically changes the pathway of the transformation of XXXVII cations under the influence of mixtures of these ketones with methylamine, and the principal pathway becomes the formation of 1,2,3,4-tetrahydro-2,2-dialkyl-4-nitromethylenepyridines XLIV [46, 54].



The new pyridine ring of XLIV is constructed through a three-carbon fragment of the starting salt and the carbon atom of the γ-methyl group, while the $C_{(3)}$ atom forms an exocyclic methylene group. The ketone here displays electrophilic properties, and the process begins with condensation of it at the 4-CH_3 group of the starting salt. This is followed by a series of successive transformations: opening of the ring under the influence of the amine, its recyclization, and, finally, splitting out of a fragment of the N-methylamide of the corresponding acid.

Thus, depending on the structures of the starting compounds, various types of transformations of 3-nitropyridinium cations with the inclusion of ketone fragments can be realized.

Annelation with a benzene ring, i.e., transition to 3-nitroquinolinium salts XLIX stabilizes the molecule and prevents cleavage of the nitropyridinium ring under the influence of the amine—ketone reaction system. As one should have expected, the latter, in the reaction with salts XLIX, acts both as a mono- and a 1,3-bis-C,C-nucleophile, forming both monoaddition products and stable 2,4-meta-bonding adducts, viz., benzazabicyclo[3.3.1]nonane derivatives.



Thus a series of detailed investigations of the transformations of 3-nitropyridinium salts XXXVII and 3-nitroquinolinium salts XLIV under the influence of ketimines (or mixtures of ketones with amines) made it possible to discover previously unknown processes involving the transformation of an activated quaternized pyridinium ring and to propose nitro azinium cations as convenient and promising synthones for obtaining diverse arenes and hetarenes.

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