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CYCLOPENTA- AND INDENOPYRIDINE ANHYDROBASES. A REVIEW

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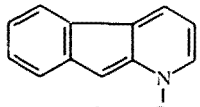
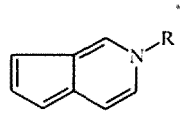
The preparation, structure, spectral characteristics, and chemical transformations of cyclopenta- and indenopyridine anhydrobases are reviewed.

1(2)H-Indenopyridines such as I and 1(2)H-cyclopentapyridines such as II are anhydrobases containing a pyridine fragment, which along with other pseudoazulenes (thialenes and oxalenes), is an isoelectronic aza analog of azulene, i.e., has a nonbenzoid aromatic 10π-electron system similar to azulene [1-8].



I

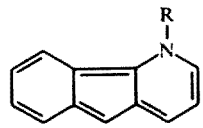


II

The chemistry of azulenes [1, 9-11] and polycyclic azulenoid systems [11] has undergone extensive development. In light of their broad range of biological activity, nitrogen analogs of azulene, namely, azaazulenes, and pseudoazulenes have been subjected to quantum chemical, spectral, and chemical investigation [2, 12, 13]. Some natural products such as the alkaloids, semperverin [14], flavopereirin [15], and other derivatives [12, 16], have pseudoazulene indolopyridine fragments.

However, the reactivity, spectral properties, and biological action of such azulene analogs and carboline anhydrobases such as 1(2)H-indenopyridines have hardly been examined. This failure is attributed to the inavailability and instability of this pseudoazulene group.

Unsubstituted 1(2)H-cyclopenta- and 1(1)H-indenopyridines and their derivatives with electron-donor substituents are extremely labile. In contrast to azulene, these compounds undergo rapid oxidation and polymerization. Quantum chemical calculations show that the more stable 1H-pyridines have greater electron density in the five-membered ring than their 2H analogs [2, 3]. Their fusion to a five-membered ring leads to some increase in stability [17-19]. 1(2)H-Indenopyridines I [20-22] have proven sufficiently stable for the study of their spectral, chemical, and biological properties [23-26]. 1(2)H-Indenopyridines III, which have *ortho*-quinoid benzene ring fragments, are less stable [27, 28].



III

Pyridine IV, which, as expected, should be more stable due to fusion at the pyridine ring, has not been characterized as a pure compound. Upon contact with air, this compound forms polymers, which are nonvolatile under mass spectrometric conditions [29].

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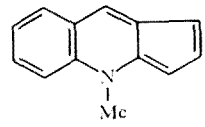


IV

Phenyl and, especially, picryl substituents have a significant stabilizing effect. Such polyarylpyridines are stable for several months under ordinary storage conditions [2, 25]. Further fusion of NH-indenopyridines [19, 31] or the introduction of aryl [18, 32] and electron-withdrawing substituents [21, 24, 27, 30] additionally enhances the stability of these pseudoazulenes. Stable N-phenacylindenopyridines [21] have been isolated but analogous anhydrobases with an N-acyl fragment are unstable and rearrange to give C-acylazafluorenes [33].

1(2)H-Indenopyridines are highly colored, crystalline compounds with moderate solubility in benzene and limited solubility in most other organic solvents. These compounds are insoluble in water. The solubility of phenyl-substituted 1H-indeno[2,1-*c*]pyridines decreases in the series: benzene, ethyl acetate, acetone, ether, cyclohexane, ethanol, methanol, petroleum ether [32]. Solutions of 1(2)H-indenopyridines in benzene are rather stable but these compounds rapidly decompose in alcohols and other protic solvents. Thus, they are difficult to purify by crystallization. Only a few such anhydrobases have chromatographic mobility, do not decompose on alumina and silica gel, and may be purified by adsorption chromatography.

SPECTRAL CHARACTERISTICS

There has yet been no systematic study of the spectral characteristics of 1(2)H-cyclopentapyridine and 1(2)H-indenopyridine anhydrobases. The UV spectra of anhydrobases derived from azafluorenes and cyclopentapyridines have characteristic long-wavelength maxima at 500-700 nm [22, 34-39] (azulene absorbs at 580 nm [9]). Observation of this band may be used for proving the formation of these often unstable systems during a reaction [20, 21, 30, 34, 40-43]. Electron-withdrawing substituents such a nitro and acyl groups in the five-membered ring cause a hypsochromic shift [24] of the major long-wavelength anhydrobase band, while electron-donor groups such as methyl, methoxy, phenyl, and halo substituents lead to a bathochromic shift [38]. Such a substituent effect has been noted in the case of azulene [9]. The emission spectra of 2H-indeno[2,1-*c*]pyridines have a fluorescence maximum at 440 nm [18]. The IR spectra of 1H-1-methylindeno[2,1-*b*]pyridines and 2H-2-methylindeno[1,2-*c*]pyridine [20, 21] have bands at 1635-1645 cm^{-1} for the C=C bonds of the five-membered ring and 1525-1580 cm^{-1} for the pyridine fragment in addition to the benzene ring bands at ~1600 and 1500 cm^{-1}. The C=C band in the IR spectrum of azulene is also shifted toward lower frequencies (1570 cm^{-1}) [9], while the bands for noncondensed methylene pyridine anhydrobases are as indicated above for 1(2)H-indenopyridines [44].

The bands are usually shifted toward lower frequencies for acyl substituents in the five-membered ring. Thus, the carbonyl stretching band in the case of formyl-substituted NH-indenoquinoline and benzene-substituted 1(2)H-indenopyridines is found at 1640-1560 cm^{-1} [24, 45]. The experimental IR spectra of 1(2H)-pyridines and cyclopentaquinolines have been given by various workers [29, 30, 37, 39, 46, 47].

The mass spectra of N-methylpseudoazulenes obtained from 1- and 3-azafluorenes have maximum-intensity molecular ion peaks and well as peaks for $[M-CH_3]^+$ ions (27%) and doubly charged M^{+2} peaks (18%) [20, 21]. The decomposition of these condensed compounds featuring a small number of fragmentation ion peaks and their low intensity, maximum-intensity or strong molecular ion peaks, and rather strong doubly charged M^{+2} peaks reflects the aromatic nature of the anhydrobases. However, a weak M^+ peak is found in some cases [39, 47, 48]. The fragmentation of substituted 1H-indenopyridines and the analogous anhydrobases upon electron impact is a function of the skeletal structure and nature of the substituents [21, 24, 28-30, 37, 39, 47, 48]. In contrast to the case of other nitrogen heterocycles, there is no loss of HCN or only a weak HCN peak (~1% intensity) in the fragmentation of pseudoazulenes [2, 49, 50].

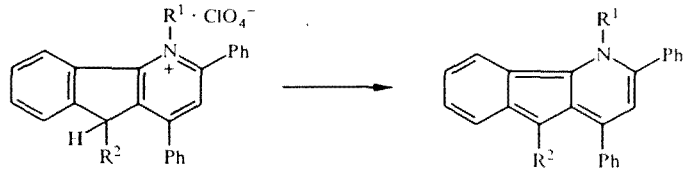
A study of the ^{13}C and ^1H NMR spectra of the anhydrobases indicated aromaticity for the five-membered ring [20, 21, 24, 39, 46-48]. The protons of this ring appear at 5.5-5.7, while the protons of the pyridine ring appear at 6.3-7.5 (β-H) and 7.5-8.9 ppm (α-H and γ-H). The 5- and 7-H protons are most shielded in the five-membered ring and have the greatest

π-electron density as indicated by a quantum chemical calculation [35]. The signals for the methine protons of the five-membered ring in 1(2)H-indenopyridines appear at 5.8-6.4 ppm [20, 21, 24]. The assignment of all the aromatic proton signals was theoretically calculated in some cases [24]. The 2- and 3-H protons of the pyridine ring in 1H-1-methylindeno[2,1-*b*]pyridine give signals at 7.2 and 6.3 ppm, respectively, which are shifted upfield by about 1 ppm in comparison with the signals of the same protons in starting 1-azafluorene. The ^{13}C NMR spectra of these two compounds show a similar pattern with an upfield shift of $C_{(2)}$ and $C_{(3)}$ by 14-18 ppm [24, 51]. The signal for $C_{(9)}$ is found at 86 ppm but with a coupling constant of -140 Hz, which indicates its sp^2-hybridization. The α-H proton in this anhydrobase is found upfield relative to γ-H. These data indicate some loss of aromaticity of the pyridine fragment upon going from 1-azafluorene to 1(2)H-indenopyridine.

METHODS OF PREPARATION

The major method for the synthesis of indenopyridine anhydrobases involves deprotonation of quaternary azafluorenium salts by alkaline agents [2]. Such salts should contain a methylene group in the five-membered ring with high CH-acidity sufficient for proton loss upon the action of dilute alkali, sodium acetate, and other such basic reagents.

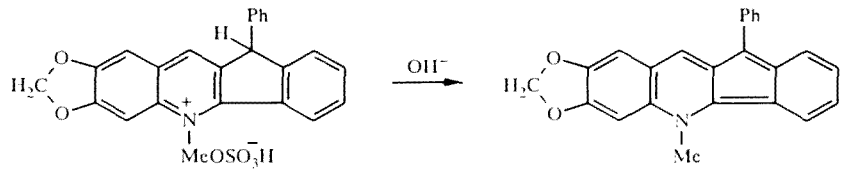
This method has been used for the synthesis of a variety of pseudoazulenes and pyridine anhydrobases [2, 44, 53]. The first 1(2)H-indenopyridines Vb were rather recently obtained by the treatment of 1,3-diphenyl-4-azafluorenium perchlorates Va with 10% ethanolic alkali or 30% aqueous methylamine [19].



Va Vb

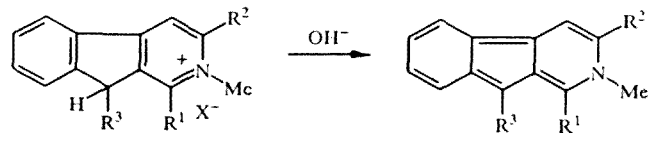
R^1 = Me, Ph; R^2 = H, Ph

Methyl sulfates VIa are also readily converted to 1(2)H-indenopyridine anhydrobases VIb [54].



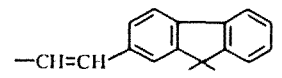
VIa VIb

A series of substituted 2H-indeno[2,1-*c*]pyridines VIIb was synthesized by the action of alkali on the corresponding 2-azafluorenium iodomethylates or methosulfates VIIa [18, 43].



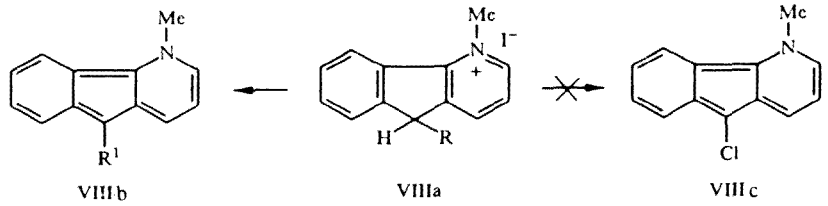
VIIa VIIb

R^1 = H, Me; R^2 = H, Me, Ph,
R^3 = H, Ph, α-naphthyl

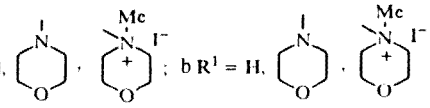


Only those pseudoazulenes having aryl or arylethyl substituents proved stable in all the cases presented.

A series of anhydrobases serving as precursors for indenopyridine pseudoazulenes was obtained from 1-, 3-, and 4-azafluorenes [20-22, 27, 34, 55-57]. It is interesting to note that 1H-1-methylindeno[1,2-*b*]pyridine is formed upon the alkaline treatment of 9-chloro-4-azafluorenium salt VIIIb [55].

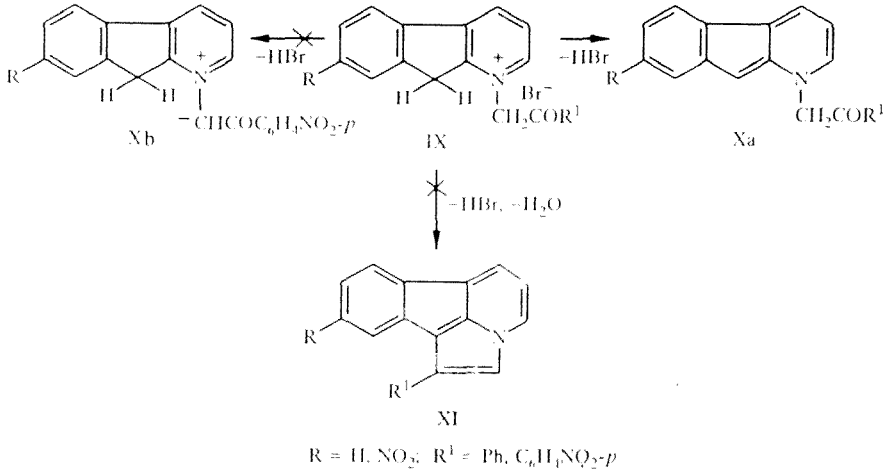


VIIIb VIIIa VIIIc

VIII a R = Cl,  ; b R^1 = H,

The generation of this pseudo azulene occurs as a consequence of the loss not of a hydrogen atom but rather of chlorine from $C_{(9)}$ in salt VIIIa. The expected chloroindeno[1,2-*b*]pyridine VIIIc is not formed under these conditions. Indirect evidence for the ease of elimination of chlorine is found in the mass spectrum of 9-chloro-4-azafluorene with M^+ 201, 203, in which the strongest peak corresponds to $[M-Cl]^+$ with *m/z* 166. On the other hand, fragments of the 9-morpholino derivatives VIIIIa are not lost in the generation of pseudoazulenes although the anhydrobases obtained, VIIIb are very unstable and have been characterized only by their UV spectra in solution (λ_{max} 508) [56].

Since two deprotonation sites are characteristic for N-phenacyl derivatives of azafluorenium salts, the action of alkaline agents may lead to two anhydrobase types, namely, ylids Xb and 1(2)H-benzopyridines Xa. Only stable anhydrobases Xa with a pseudoazulene fragment are formed from 1-azafluorenium salts IX upon the action of sodium acetate or potassium carbonate [21, 22] (conditions for the conversion of pyridinium salts into N^+-C^- ylids [58, 59]).



Xb IX Xa

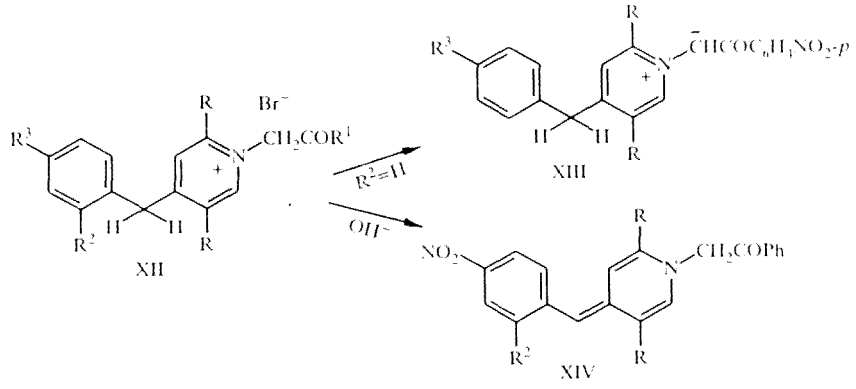
XI

R = H, NO_2; R^1 = Ph, $C_6H_4NO_2$-*p*

The pseudoazulene system also proved more favorable in an attempt to generate stable ylid IX by the introduction of an electron-withdrawing nitro group into the N-phenacyl fragment.

Thus, of the two deprotonation sites in salts VIII, the methylene group of the five-membered ring has greater CH-acidity than the exocyclic CH_2 group at the nitrogen atom. Even under vigorous conditions for the synthesis of indolizines by the Chichibabin reaction (heating at reflux in the presence of potassium carbonate), quaternary salts VIII are not converted into the expected indenoindolizines XI, but rather form stable pseudoazulenes X as in the case examined above [21].

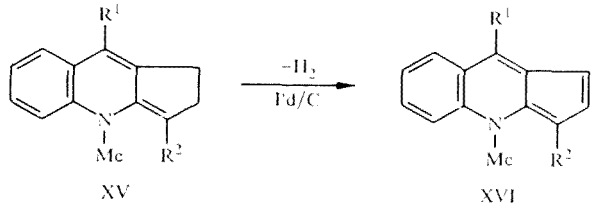
On the other hand, either indolizines (not shown in the scheme) or anhydrobases XIII and XIV may be readily formed from acyclic azafluorene analogs, namely, N-phenacyl-γ-benzylpyridinium bromides XII under analogous conditions [60]. The position of the nitrogen group in the starting pyridinium salts XII determines the type of anhydrobase. The presence of an N-nitrophenacyl group facilitates formation of ylids XIII, while the introduction of a nitrobenzyl group at $C_{(4)}$ in the pyridine ring stabilizes 1,4-dihydropyridine system XIV. The number and position of the nitro groups in the starting salts affects the yields of the indolizines and anhydrobases.



R = Me; R^1 = Ph, $C_6H_4NO_2$-*p*; R^2 = H, NO_2; R^3 = H, NO_2

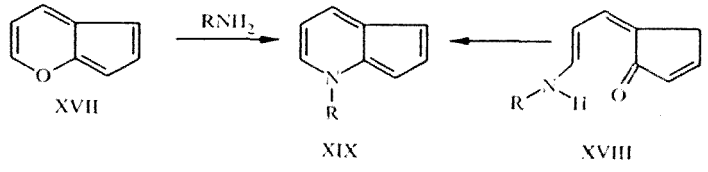
Azafluorenium benzoylmethylides were obtained in the dehydrohalogenation of N-bromo-phenacyl- 3-methyl-2-azafluorenium salts by potassium carbonate [30, 61]. Quaternary 1-azafluorenium salts with acetyl or aroyl substituents at the nitrogen atom do not generate anhydrobases upon treatment with aqueous solutions of alkali or triethylamine, but rather undergo quantitative conversion to azafluorenes [33]. Anhydrobases are generated from these salts upon the action of triethylamine on their suspensions in absolute benzene [33]. However, N-acyl anhydrobases have not been isolated as pure compounds as a result of their instability and have been characterized only by their spectra.

Examples have been reported for the synthesis of anhydrobases by the thermal dehydrogenation of XV with a pyrindane fragment in the presence of palladium on charcoal [62-64]. This method has been used to obtain 4H-cyclopentaquinoline XVI.



Chloranil [51, 52], picric acid, picryl chloride [18], and dicyanodichlorobenzoquinone have been used as dehydrogenating agents. UV irradiation has also served for this purpose [2, 44]. The instability of anhydrobases and the ease of their reaction with dehydrogenating agents hinder the use of this synthetic approach.

We should note one-step methods for the preparation of NH-pyridines XIX by the conversion of cyclopentapyrans XVII (or the corresponding pyrilium salts) upon their heating with primary amines [53] as well as by the intramolecular condensation of ketoamines XVIII [48].

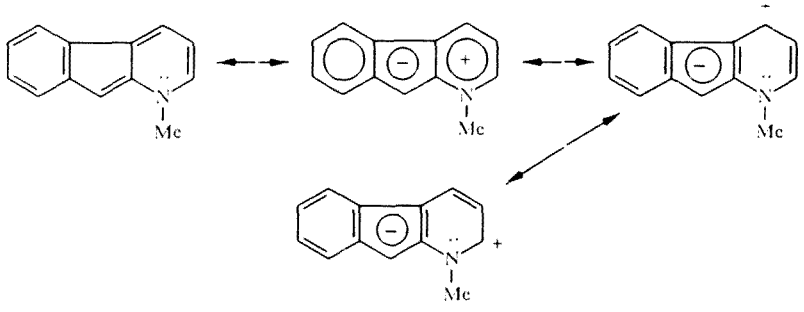


CHEMICAL TRANSFORMATIONS
REACTIVITY

The nonuniform distribution of electron density in pyridines and benzopyridines [35] should lead to significant polarization of these anhydrobases and enhancement in their reactivity. Analysis of the classical formulas of such compounds suggests their high reactivity since they contain a variety of structural elements such as dihydropyridines, enamines, dienes, and fulvenes.

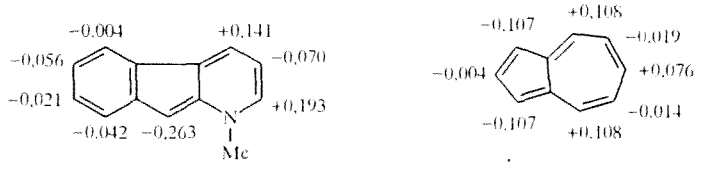
Quantum chemical calculations have shown that the positive charge in 1H-indeno[2,1-*b*]pyridine is localized in the pyridine ring, which has a π-electron deficiency [40]. The negative charge is localized in the five-membered ring with excess π-electron density, mainly on the methine $C_{(9)}$ atom. The existence of these two sites with significant charge separation permits the attack of this pseudoazulene by both electrophilic and nucleophilic reagents.

Examination of the resonance structures of 1H-1-methylindeno[2,1-*b*]pyridine (I) indicates that nucleophilic reagents will attack this molecule at $C_{(2)}$ and $C_{(4)}$ of the pyridine fragment, while electrophilic reagents will attack at $C_{(9)}$ of the five-membered ring.



We cannot exclude the possibility of electrophilic attack at the unshared electron pair of the nitrogen atom conjugated with the π-electron system of the pyridine portion of the molecule. Analogous predictions concerning the π-electron deficiency of the nitrogen-containing ring and π-electron excess of the five-membered ring follow from a quantum chemical calculation of the electron density distribution in this anhydrobase [40].

The calculated data [40] somewhat correlate with the experimental results on the electrophilic and nucleophilic substitution of 1H-1-methylindeno[2,1-*b*]pyridine [24, 33]. The calculated and experimental data on the reactivity of azulene [10, 52] show that electrophilic attack is directed toward $C_{(1)}$ and $C_{(3)}$ of the five-membered ring, while nucleophilic attack is directed toward $C_{(4)}$ and/or $C_{(8)}$ and then $C_{(6)}$. This comparison justifies the analogy between azulene and NH-indenopyridine pseudoazulenes (anhydrobases).

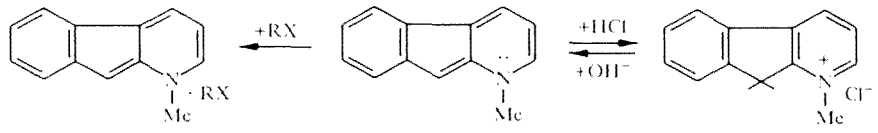


1-Methyl-1H-indeno[2,1-*b*]pyridine (pK_a = 12.5), similar to 1(2)H-pyridines, is a rather strong base [2, 34].

REACTION WITH ACIDS AND ALKYL HALIDES

The protonation of 1(2)H-pyridine anhydrobases proceeds at positions 5 and/or 7, which corresponds to the protonation of azulene at $C_{(1)}$ [67, 68]. Only the nitrogen atom is protonated in the case of 5-azaazulene [69]. Protonated anhydrobases sometimes polymerize and form tars under the experimental conditions and are not regenerated by the action of bases on their acid solutions [67]. 1(2)H-Indenoquinoline is deuterated by deuterosulfuric or deuterophosphoric acid at the anionic site of the five-membered ring [70]. Quantitative protonation at $C_{(9)}$ is found upon the treatment of 1(2)H-indenopyri-

dine by hydrogen chloride in dry ether [21]. The resultant 1-azafluorenium chloromethylate regenerates the anhydrobase upon the action of alkali.

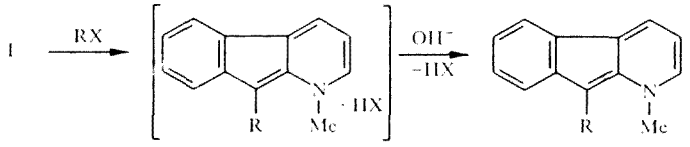


I

RX = $HClO_4$; $C_6H_2(NO_2)_3OH$

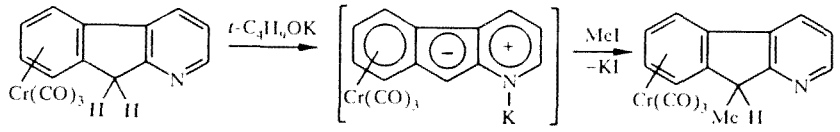
The anhydrobase structure is retained upon the treatment of 1(2)H-indenopyridine by perchloric or picric acid in methanol. A highly colored perchlorate is formed (the color is probably due to intramolecular charge transfer). The picrate formed has the UV band at 580-590 nm characteristic for anhydrobases [21]. Azulene also forms charge transfer complexes with some electron-deficient compounds such as picric acid [10, 71].

1(2)H-Indenopyridine is alkylated by methyl iodide and benzyl chloride at $C_{(9)}$ [72].



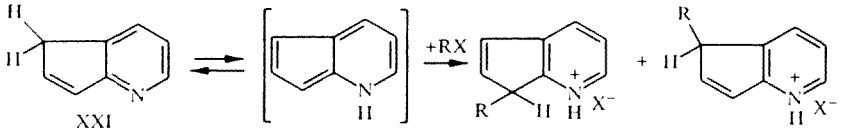
R = Me, $PhCH_2$; X = I, Cl

The chromium tricarbonyl π-complex of 1-azafluorene XX is alkylated in the five-membered ring by methyl iodide in the presence of potassium *tert*-butylate [73, 74]. Initial deprotonation has been proposed followed by alkylation of the anionic site of the intermediate anhydrobase.



XX

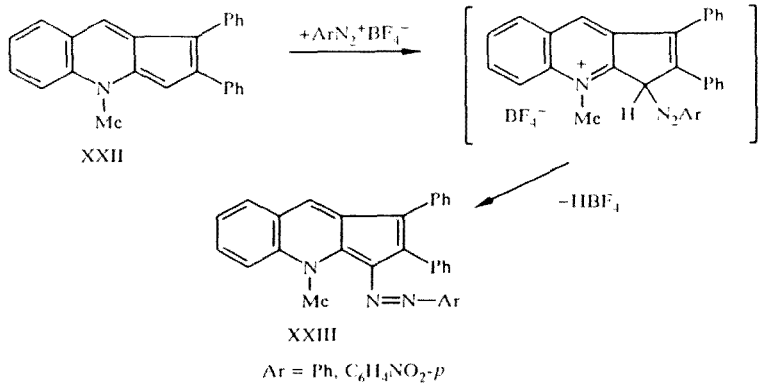
Alkylation of the five-membered ring in 5H-1-pyridine XXI [75-77] and cyclopenta[*b*]quinoline [78] by alkyl halides in the presence of alkali metal amides proceeds through intermediate formation of an anhydrobase [37, 47, 78].



XXI

ELECTROPHILIC SUBSTITUTION

Electrophilic substitution cannot be achieved for anhydrobases in acid media due to their protonation, while the use of Lewis acid catalysts may lead to a reduced yield of the desired products. As a consequence of the high π-electron excess of the five-membered ring, it is readily attacked even by weak electrophilic agents. The azo coupling of N-methyl-1,2-diphenyl-4H-cyclopenta[*b*]quinoline (XXII) with aryldiazonium tetrafluoroborates gave azo dyes XXIII with an azo group in the five-membered ring [53].

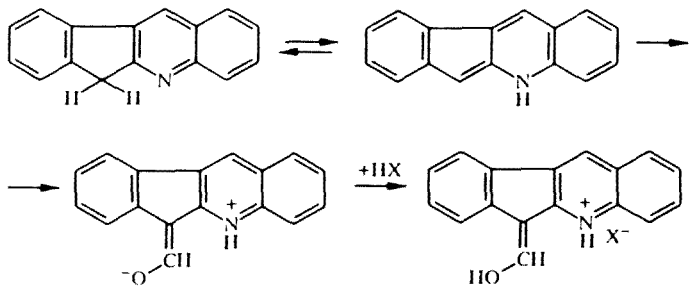


XXII

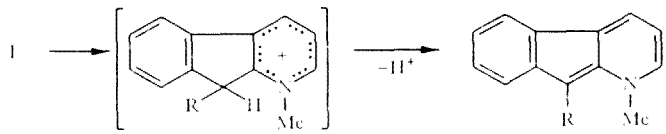
XXIII

Ar = Ph, $C_6H_4NO_2$-*p*

Quite a few studies have been devoted to the acylation of anhydrobases. The formylation of indenoquinoline under Vilsmeier reaction conditions also proceeds at the five-membered ring [45]. An anhydrobase, namely, a tautomeric form of 1(2)H-indenoquinoline, is presumably formed initially upon heating.



Analogous regiospecificity is observed for N-methyl-1(2)H-indenoquinoline [45] and 1(2)H-indenopyridine [24] upon formylation by the Vilsmeier complex, acetylation by acetic anhydride, and benzoylation by benzoyl chloride (with yields of 20, 98, and 56%, respectively). These results are evidence for the theoretical predictions of Borsdorf [40].



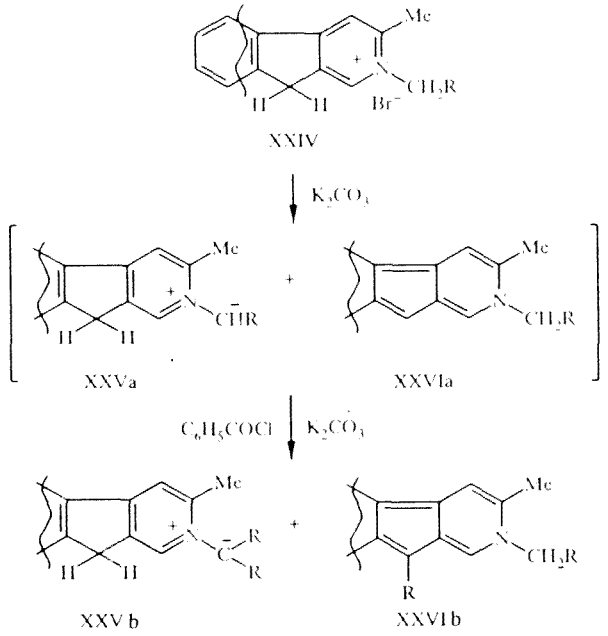
R = CHO, COMe, COPh

The very strong IR bands for the formyl groups shifted to 1620-1544 cm^{-1} disappear upon acidification, which indicates a significant contribution of the zwitter-ionic form with localization of the negative charge on the oxygen atom [45, 79]. Protonation by acid leads to the formation of a quaternary enolic salt.

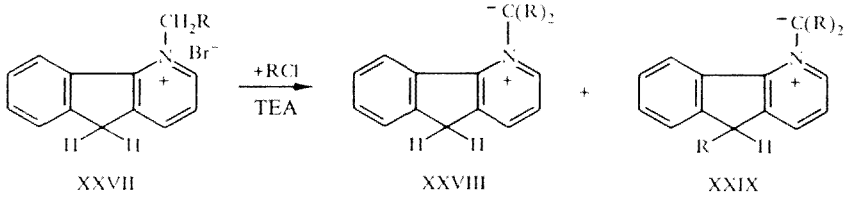
A weak band at 1730 cm^{-1} is found for the benzoyl derivative and it has medium intensity (at 1725 cm^{-1}) only for the acetyl group [24]. The preparation of 5-acylpseudoazulenes in very low yield upon formylation and acetylation of 4-azafluorenium iodomethylate in the presence of triethylamine is attributed to the intermediate formation of an unstable anhydrobase.

The reaction of benzoyl chloride with 2-phenacyl-3-methyl-2-azafluorenium bromide XXIV in the presence of potassium carbonate proceeds is more complicated [30]. A mixture of two tautomeric anhydrobases, namely, ylid XXVb and pseudoazulene XXVIa, is formed initially by the action of potassium carbonate. These intermediates are then benzoylated at

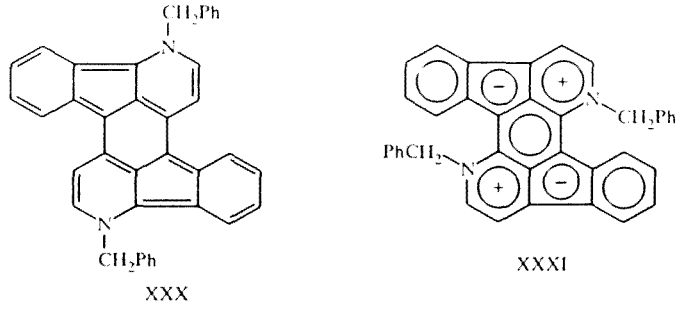
different positions to give two stable products, namely, yellow azafluorenium dibenzoylmethylide XXVb and violet 2-phenacyl-9-benzoyl-2H-indenopyridine XXVIb.



The analogous reaction of benzoyl chloride with 4-azafluorenium salt XXVII leads to dibenzoylmethylide derivatives XXVIII and XXIX [30].



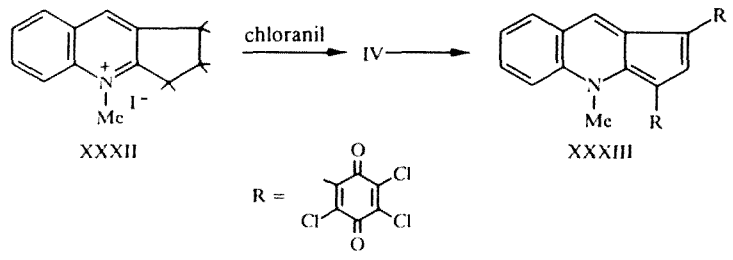
This reaction becomes even more complicated when the N-phenacyl group in the quaternary salts is replaced by a benzyl group and condensed polynuclear heterocycles with pseudoazulene fragments, namely, 1(2)H-diazafluorenofluoranthrenes XXX and XXXI, are formed in addition to the indicated anhydrobases [30].



These dark blue crystalline compounds may be formed upon the intermolecular 1,3-dipolar cycloaddition of the intermediate pyridinium indenides.

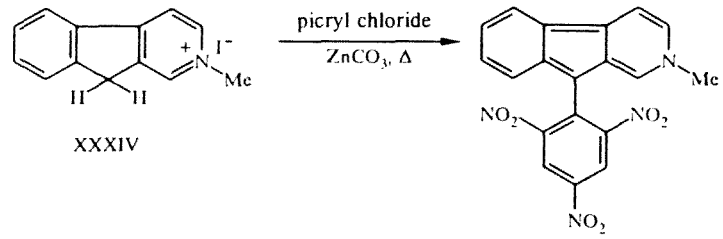
Acylation [53, 65, 66] and azo coupling [37] were also carried out for 1(2)H-pyridines [37, 53] and 1(2)H-cyclopentaquinolines [47, 65, 66].

Anhydrobases IV obtained by the heating of cyclopentaquinoline iodomethylates XXXII in the presence of excess chloranil readily add a chloranil residue as the result of electrophilic attack [65, 66]. Thus, quinidines XXXIII with two chloranil substituents in the five-membered ring were obtained.



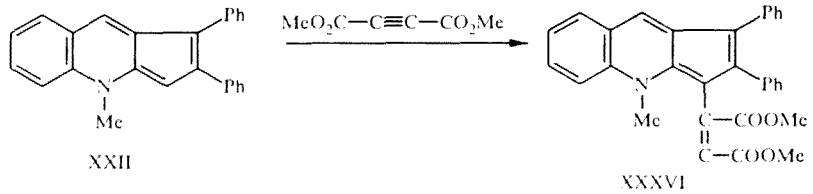
XXXII XXXIII

Analogously, stable 2-methyl-9-picryl-2H-indenopyridine XXXV is obtained upon the dehydrogenation of 2-aza-fluorenium iodomethylate XXXIV by heating with picryl chloride in the presence of zinc carbonate or silver carbonate [18].



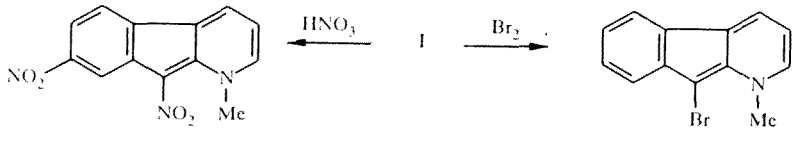
XXXIV XXXV

1,2-Diphenyl-4-methyl-4H-cyclopentaquinoline XXII and NH-indenopyridines react with dimethyl acetyl-enedicarb-oxylate not through a Diels–Alder reaction but rather through electrophilic addition to give anhydrobases with a dicarbomethoxyvinyl substituent XXVI [27, 80].



XXII XXVI

The action of bromine on 1(2)H-indenopyridine I in carbon tetrachloride gives the 9-bromo derivative of this anhydrobase XXXVII in high yield. The nitration of this indenopyridine in acetic anhydride gives only 7,9-dinitro-1(2)H-indenopyridine XXXVIII [24].

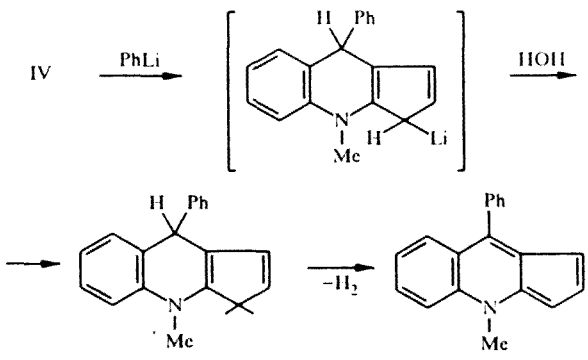


XXXVIII XXXVII

NUCLEOPHILIC SUBSTITUTION

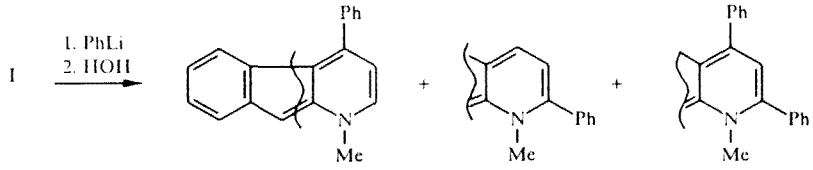
Of the reactions with nucleophiles, only two examples involve the reaction of anhydrobases with phenyllithium [29, 47, 72]. Thus, the reaction of phenyllithium with 4H-cyclopenta[*b*]quinoline IV results in the addition of the carbanion to the

carbon atom at the γ-position of the heterocycle [29, 47]. Subsequent hydrolysis and dehydrogenation lead to phenyl-substituted anhydrobase XXXIX.



XXXIX

Arylation of indenopyridine I [58] proceeds at both free α- and γ-positions of the pyridine fragment with the isolation of diphenylindenopyridine XL in low yield.

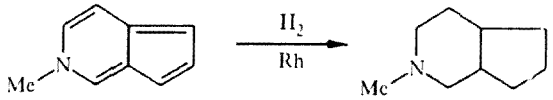


XL

Nucleophilic arylation of pyridine itself or alkylpyridines, in contrast to anhydrobases, proceeds only at the α-position [81-83].

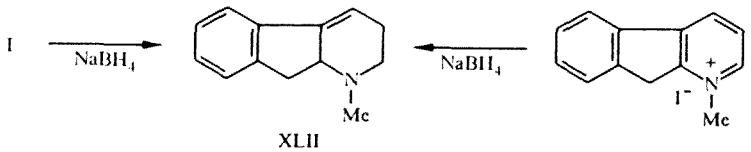
REDUCTION AND OXIDATION

1(2)H-Pyridine XLI was completely hydrogenated on a rhodium catalyst [46].



XLI

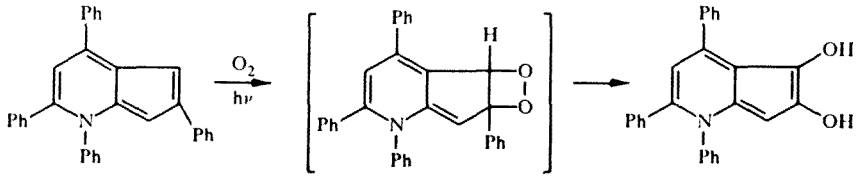
1(2)H-Indenopyridine I is reduced to 1,2,3,9a-tetrahydroazafluorene XLII using sodium borohydride [58]. The same partially hydrogenated compound was obtained under analogous conditions from 1-azafluorenium iodomethylate [84]:



XLII

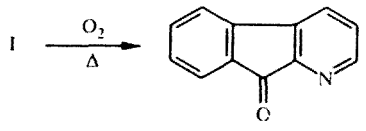
The reduction of this salt probably proceeds through formation of an intermediate anhydrobase. Similar cases of reduction to the tetrahydro derivatives were noted for carboline [85, 86] and pyridine anhydrobases [87] although some pyridoindole anhydrobases could not be reduced by sodium borohydride.

1(2)H-Tetraphenylpyridine LXIIIa (and 1(2)H-cyclopentaquinoline) is converted in the presence of oxygen upon heating or irradiation to dioxetane XLIIIb [88], which could not be isolated due to its high lability. Only 1,2-dihydroxypyridine XLIV could be isolated from the decomposition products.



XLIIIa XLIII b XLIV

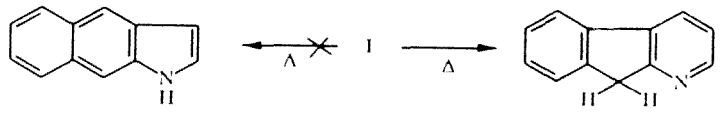
Heating 1(2)H-indenopyridine in the presence of air leads to demethylation and rearrangement to give 9H-indenopyridine, which is oxidized to ketone XLV in yields up to 30% [72].



XLV

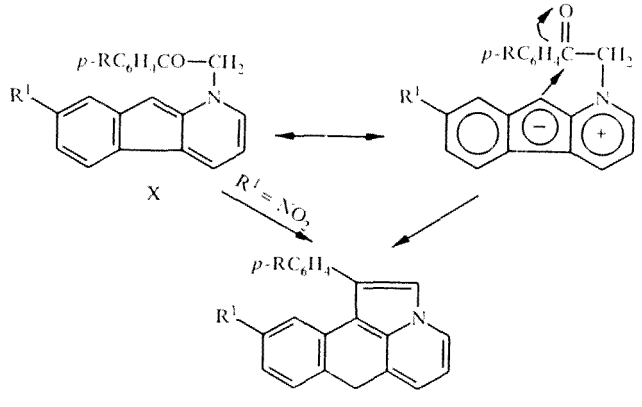
THERMAL TRANSFORMATIONS

Azulene is converted at 500°C to naphthalene [19], while its thio analog, namely, cyclopentathiapyran, is isomerized to thionaphthene [2]. 1(2)H-Indenopyridine I is transformed into 1-azafluorene XLVIa (instead of the expected benzindole XLVIb [72]) upon passage through a quartz tube at 650°C.



XLVIb XLVIa

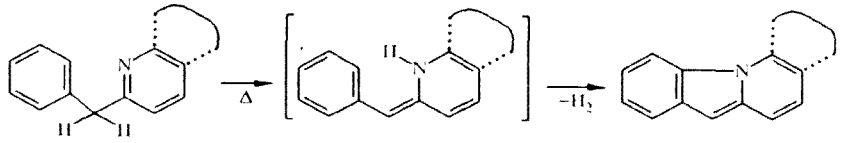
As noted above, N-phenacyl derivatives of 1H-indeno[2,1-*b*]pyridines X are unstable and cyclize under Chichibabin reaction conditions to give indolizine derivatives. Localization of significant negative charge on methine carbon atom $C_{(9)}$ leads to its solvation, which sharply hinders intramolecular electrophilic attack at this position and, thus, cyclization of the anhydrobase. A study of the thermal stability of these anhydrobases in the absence of solvent showed that they are converted to 1-aryl-2aH-benz[5,6]pyrido[1,2,3,-*c*,*d*]azapentalenes XLVII in yields up to 53% upon heating at 140°C and 20 mm Hg for 4 h. These pentalenes are the first representatives of heterocyclic systems containing two pseudoazulene fragments, namely, the pyridine and indolizine fragments [23, 89].



X XLVII R, R^1 = H, NO_2

Cyclization of indenopyridines X proceeds through intramolecular electrophilic attack at $C_{(9)}$ by the carbonyl group carbon atom. Evidence for this hypothesis is found in the increase in yield of benzpyridoazapentalenes XLVII with increasing electrophilicity of the carbonyl group carbon atom by introducing a nitro group into the phenacyl fragment. On the other hand, the introduction of a nitro group at $C_{(7)}$ ($R^1 = NO_2$) reduces the nucleophilicity of $C_{(9)}$ and cyclization does not occur even upon heating for 18 h.

An interesting example of thermal dehydroheterocyclization was found for α-benzylpyridines and α-benzylquinolines, in which noncondensed pyridine anhydrobases probably serve as intermediates [90-92]. The pyrolysis of α-benzylazines in the presence of dehydrogenation catalysts at 590-640°C [90, 93] or without catalyst at 600-700°C [91, 92] leads to indenopyridines and indenoquinolines XLIX (analogs of benzopyridines with an angular nitrogen atom), which were previously difficult to obtain.

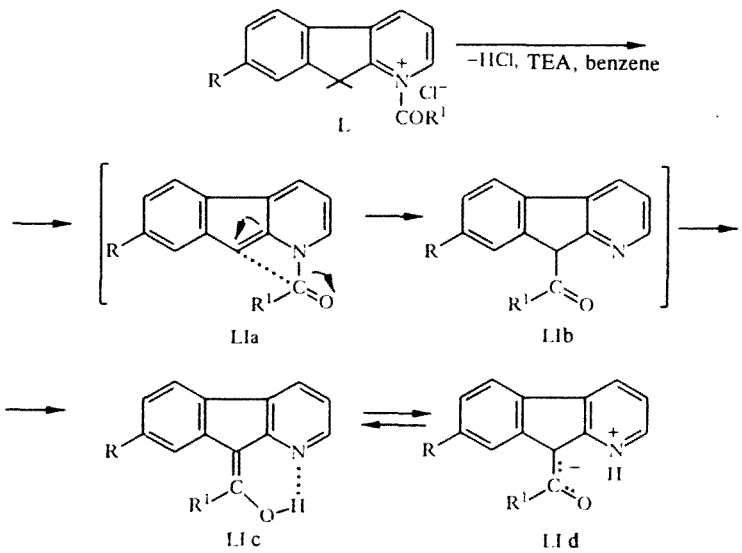


XLIII XLIX

REARRANGEMENT OF N-ALLYL ANHYDROBASES

The spontaneous acyl shift from $N_{(1)}$ to $C_{(9)}$ in N-acyl-1H-indeno[2,1-*b*]pyridines LIa in an attempt to generate these compounds from salts L indicates the high nucleophilicity of $C_{(9)}$ in 1H-indenopyridines I [33]. This rearrangement probably occurs through a four-membered cyclic complex and proceeds to completion in the presence of catalytic amounts of boron trifluoride etherate.

9-Acyl-1-azafluorenes LIb exist in enol form LIc, which is stabilized by formation of an intramolecular hydrogen bond, or as zwitter-ion LId. Complexes of 9-acyl-1-azafluorene LIb with boron trifluoride are formed when an equimolar amount of BF_3 is added.



L LIa LIb

LIc LId

The introduction of an electron-withdrawing nitro group to $C_{(7)}$ of the benzylidene fragment of the azafluorene in order to reduce the electron density in the five-membered ring is not sufficient to stabilize N-acyl anhydrobase LIa. The extent of conversion of the anhydrobases into 9-azafluorenes LIc depends on the structure of the acyl substituent. Thus, complete conversion of the anhydrobase to azafluorene derivative when there is a nitro group in the N-aroyl moiety is observed even in the absence of catalyst.

BIOLOGICAL ACTIVITY

There is hardly any information in the literature on the biological activity or other useful properties of 1(2)H-pyridine and 1(2)H-indenopyridine anhydrobases. This failure should be attributed primarily to the instability of these derivatives. There have been reports of fungicidal, herbicidal, and growth-regulation properties for a few 1(2)H-indenopyridines. Thus, 1-methyl-1H-indeno[2,1-*b*]pyridine upon deposition in the soil during the vegetation stage hinders the growth of garden radish and displays medium toxicity for beet and mustard [25, 26]. This anhydrobase was found acutely toxic when tested on mice (LD_{50} = 50 mg/kg) [22].

This review indicates that pyridine and indenopyridine anhydrobases are highly reactive compounds and may hold considerable interest in organic synthesis as starting reagents and intermediates in the preparation of various heterocyclic systems.

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