PROPERTIES OF A MULTIPLE BOND CONJUGATED WITH THE PYRIDINE RING

X.* CHANGE IN THE ORIENTATION OF THE ADDITION OF DIAZOMETHANE TO THE POLARIZED MULTIPLE BOND OF SUBSTITUTED VINYLPYRIDINES

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The products of the addition of diazomethane to the double bond of α-, β-, and γ-vinylpyridines, 2-propenyl-, 2-styryl-, and 2-(p-nitrostyryl)pyridines, and β-(2-pyridyl)acrylic acid were obtained. When a hydrogen atom or alkyl or phenyl group is present in the β-position of the vinyl group, 3-pyridyl-Δ^2- pyrazolines are formed (they are isolated as the acetyl derivatives). Electron-acceptor substituents ($COOCH_3$ and $C_6H_4NO_2$) in this position disrupt the polarization, and this leads to the formation of a mixture of two isomeric pyrazolines. The primary formation of Δ^1-pyrazolines was proved by means of IR and UV spectroscopy.

The ease and direction of 1,3-dipolar addition of diazoalkanes to activated olefins is determined by both electronic and steric factors [2, 3]. However, in the case of unsubstituted diazomethane, the direction of addition is determined only by electronic effects, and steric factors affect only the reaction rate [4-6]. When the polarity of the multiple bond is ambiguous, one should expect the formation of a mixture of isomeric addition products also in the case of diazomethane, as, for example, has been observed for substituted vinyl sulfones [7].

Both unsubstituted [8] and side-chain substituted [9] vinylpyridines add nucleophilic agents (amines, alcohols, etc.), and the terminal carbon atom of the multiple bond is electrophilic. If one disregards the communication [10] (published while the present paper was being put into final form) regarding the possibility of the addition of diazomethane to 2- and 4-vinylpyridines, very little study has been devoted to the cycloaddition of diazomethane to vinylpyridines. However, Steward and co-workers [10] were unable to isolate the reaction products in their individual states and prove their structures.

In order to study the effect of the degree of conjugation of the multiple bond with the pyridine ring and the effect of substituents in the β-position of the double bond on the character of its polarization, we investigated the reaction of diazomethane with compounds of the general formula $Py-CH=CH-R$ (I-VII).† The reaction was carried out in the dark at 5-7° in ether solution, under which conditions it gives high yields and is practically complete in 2-5 days.

Investigation of the reaction mass (after removal of the ether and excess diazomethane) in the case of I-III, VI, and VII demonstrated that the primary products of the reaction are Δ^1-pyrazolines, since absorption bands at 3300-3400 cm^{-1} (N−H) were absent in the IR spectra, and there was a weak absorption band at 1550 ±5 cm^{-1} (N=N). In addition to an absorption maximum at 260 ± 5 nm, which corresponds to the π, π^* transition of the pyridine ring, the UV spectra contained a maximum at 320± 5 mm, which is characteristic for the n, π^* transition typical for an azo group [11]. A chromatographic-mass spectral investi-

*See [1] for communication IX.

† In all cases where R ≠ H, we worked with the trans isomers.

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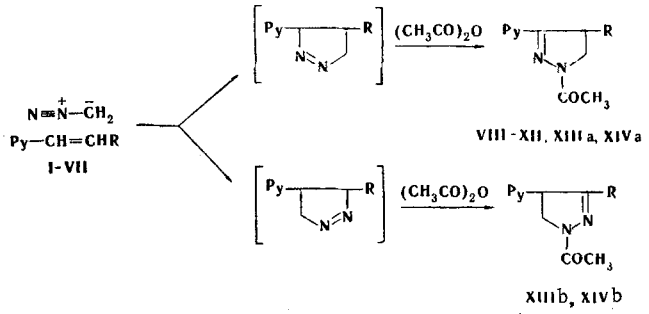
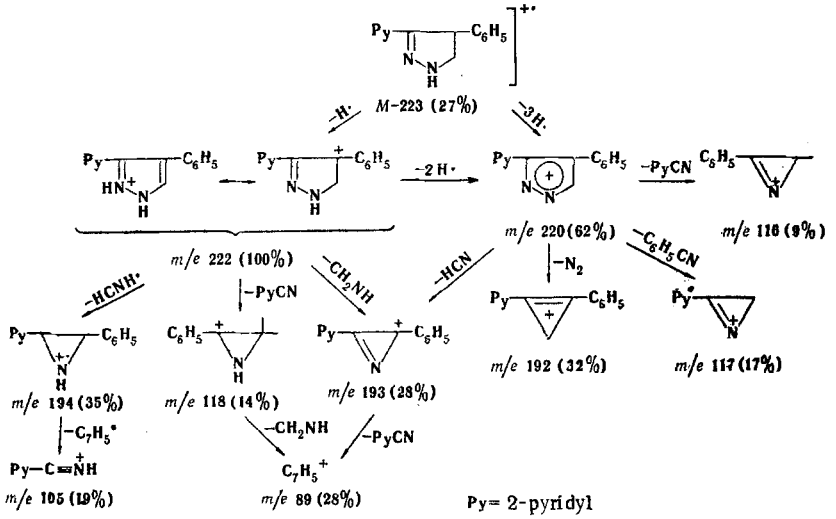


I, VIII Py=2-pyridyl, R=H; II, IX Py=2-pyridyl, R=CH_3; III, X Py=2-pyridyl, R=C_6H_5; IV, XIIIa,b Py=2-pyridyl, R=$C_6H_4NO_2$-*p*; V, XIVa,b Py=2-pyridyl, R=$COOCH_3$; VI, XI Py=2-methyl-5-pyridyl, R=H; VII, XII Py=4-pyridyl, R=H.

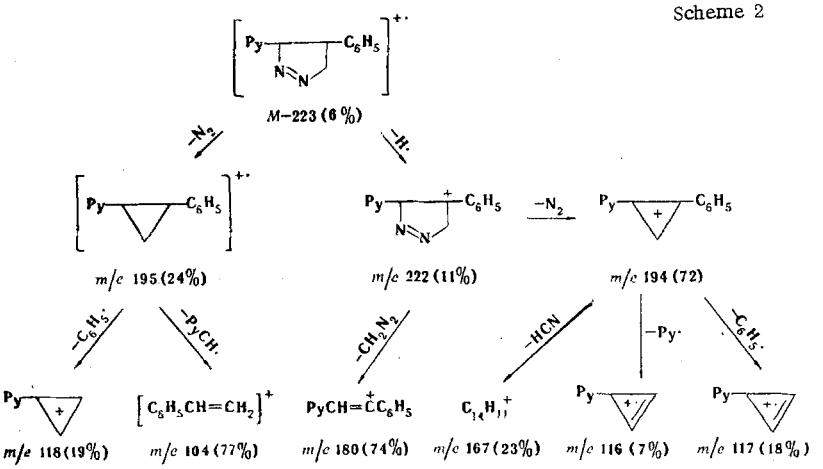
pyridine ring, the UV spectra contained a maximum at 320 ±5 nm, which is characteristic for the n, π^* transition typical for an azo group [11]. A chromatographic-mass spectral investigation of the reaction mass obtained from III gave two principal peaks on the chromatogram. The appearance of a second Δ^2-pyrazoline peak is due to partial isomerization of the Δ^1-pyrazoline to a Δ^2-pyrazoline under the chromatographic conditions. The fragmentation of the isomeric pyrazolines is presented in Schemes 1 and 2.

Scheme 1

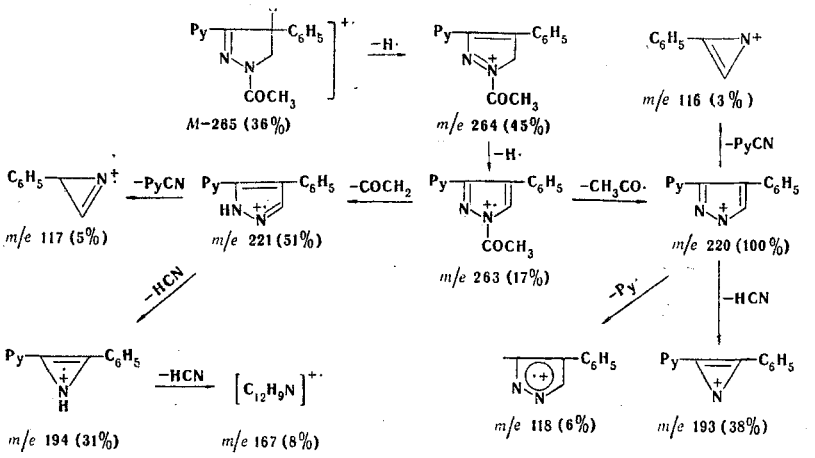


The free base products are extremely unstable, and we therefore treated the reaction mass with excess acetic anhydride (this resulted in the isomerization of the Δ^1-pyrazolines to Δ^2-pyrazolines) and isolated the Δ^2-pyrazolines as the N-acetyl derivatives (see Table 1).

Scheme 2



Scheme 3



The pattern of signals typical for an ABX system was observed at 3.5-5.5 ppm in the PMR spectrum of XIIIa in chloroform (the quartet of a proton of X in the 4 position and a multiplet of AB protons in the 5 position), and X had δ 5.00 ppm. Replacement of the chloroform by trifluoroacetic acid (protonation of the pyridine nitrogen atom) has practically no effect on the position of the signal of this proton.

Just as in XIIIa, the PMR spectrum of XIIIb in chloroform contained signals of the protons of an ABX system with the center of the quartet of the methylidyne proton of X at 5.07 ppm. However, protonation of the pyridine nitrogen atom (in trifluoroacetic acid) caused a pronounced shift of the quartet of X to weaker field (δ5.6 ppm). This sort of change in the pattern of the PMR spectra in chloroform and trifluoroacetic acid confirmed the structures of XIIIa and XIIIb.

The adsorption properties of XIVa and XIVb proved to be closer, and we therefore were able to isolate only XIVb in the individual state. An absorption maximum at 286 nm, which is characteristic for the $-N=C-COOR$ chromophore [4], was observed in the UV spectrum of XIVb. Two absorption maxima at 1720 and 1680 cm^{-1}, which correspond to the stretching vibrations of a conjugated ester and amide carbonyl groups, were observed in its IR spectrum (in chloroform) in the carbonyl band region. On the other hand, there were four absorption bands in the IR spectrum of the mixture in this region: 1735, 1720, 1680, and 1670 cm^{-1}. This makes it possible to assert that XIVa has the high vibrational frequency of an unconjugated ester carbonyl group at 1735 cm^{-1} and of an amide carbonyl group at 1670 cm^{-1}.

Two signals of methyl groups were also observed in the PMR spectrum (in CCl_4) of a mixture of XIVa and XIVb: an acetyl group (δ 2.26 and 2.30 ppm) and a carbomethoxy group (δ3.61 and 3.67 ppm). Integration of these signals made it possible to establish that these compounds are present in a 3:7 ratio in the mixture, since individual XIVb had two signals of protons of methyl groups at δ2.3 and 3.67 ppm in its PMR spectrum.

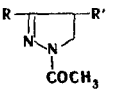
Thus the pyridine ring displays rather strong electron-acceptor properties with respect to the olefin double bond, and these properties are manifested even in the case of derivatives of the 3-vinylpyridine ring. The introduction of electron-acceptor groups into the β-position of the double bond of 2-vinylpyridine makes it possible to markedly change its polarization. In this case, the electron-acceptor effect of the 2-pyridyl group is approximately equal to the effect of the p-nitrophenyl group but less than the effect of the carbomethoxy group.

The change in orientation of the addition of diazomethane in the cases presented above is consequently determined only by the change in bond polarity and not by steric factors.

EXPERIMENTAL

The UV spectra of chloroform solutions were recorded with a Cary spectrometer. The IR spectra of mineral oil suspensions were recorded with an IKS-22 spectrometer. The PMR spectra of pyridine solutions were recorded with a Varian T-60 spectrometer with hexamethyldisiloxane as the internal standard. The chromatographic mass-spectral investigation was performed with a Varian Mat CH-8 apparatus: the column was 1 m long, the packing was silicone oil, the column temperature was 200°, and the vaporizer temperature 235°.

TABLE 1



Compound	R	R′	mp, °C	Empirical formula
VIII	2-Pyridyl	H	132—133	$C_{10}H_{11}N_3O$
IX	2-Pyridyl	CH_3	95—96	$C_{11}H_{13}N_3O$
X	2-Pyridyl	C_6H_5	128—129	$C_{16}H_{15}N_3O$
XI	2-Methyl-5-pyridyl	H	115—116	$C_{11}H_{13}N_3O$
XII	4-Pyridyl	H	161—162	$C_{10}H_{10}N_3O$
XIIIa	2-Pyridyl	4-$NO_2C_6H_4$	166—167	$C_{16}H_{14}N_4O_3$**
XIIIб	4-$NO_2C_6H_4$	2-Pyridyl	214—215	$C_{16}H_{14}N_4O_3$
XIVб	CH_3OCO	2-Pyridyl	87—88	$C_{12}H_{13}N_3O_3$

TABLE 1 (continued)

Compound	Found, %			Calc., %			ν_{CO}, cm^{-1}	λ_{max}, nm (lg ε)	Yield, %
	C	H	N	C	H	N			
VIII	63,7	6,0	—	63,5	5,9	—	1650	306 (4,56)	90
IX	65,0	6,8	—	65,0	6,5	—	1640	306 (4,43)	65
X	72,8	5,8	15,7	72,4	5,7	15,8	1650	301 (4,07)	75
XI	—	—	20,8	—	—	20,7	1645	304 (4,34)	70
XII	63,8	5,6	22,2	63,5	5,9	22,2	1660	306 (4,30)	85
XIIIa							1660	297 (4,65)	85*
XIIIb	62,3	4,6	17,6	61,9	4,6	18,0	1660	238 (3,96), 346 (4,15)	—
XIVb	58,6	5,4	17,3	58,3	5,3	17,0	1680 1720	286 (4,40)	65*

* The overall yield for mixtures of XIIIa, b and XIVa, b is presented.
† Found: mol. wt. 310 (mass spectrum). Calculated: mol. wt. 310.

The only reaction products in the reaction of diazomethane with I-III, VI, and VII are 1-acetyl-3-pyridyl-4-R-Δ^2-pyrazolines. The absorption band of the π,π^*-transition of the pyridine ring in their UV spectra undergoes a bathochromic shift due to conjugation with the C=N bond, and all of the compounds obtained had one absorption maximum at 301-306 nm.

The PMR spectra of VIII-XII (in CCl_4) did not contain the signals of the vinyl proton in the 3 position of the pyrazoline at 7 ppm [11] that should have been observed for 1-acetyl-5-pyridyl-4-R-Δ^2-pyrazolines. At the same time, the PMR spectra of VIII, XI, and XII did contain signals from four aliphatic protons (in the 4 and 5 positions), which comprise the typical symmetrical pattern of an A_2B_2 system with a center of symmetry at ~3.5 ppm. The signal from the protons of the 4-CH_3 group (δ 1.08 ppm) in the PMR spectrum of IX is split into a doublet (J 7 Hz), and this corresponded only to structure IX. In the case of X, the PMR spectrum is the pattern typical for an ABX system (the quartet of a proton of X in the 4 position at δ4.9 ppm and a complex multiplet of AB protons in the 5 position at 3.8-4.5 ppm). The integral intensities corresponded to the expected values.

The mass spectral disintegration of X also confirms the structure proposed for it (Scheme 3).

Thus, in the case of unsubstituted 2-, 3-, and 4-vinylpyridines, and when there is an alkyl or phenyl in the β-position of the double bond of 2-vinylpyridine, the pyridine ring displays a rather strong electron-acceptor effect, and this imparts electrophilic character to the β carbon atom of the olefin bond.

However, chromatographic analysis of the reaction mixtures obtained from both IV and V after acetylation of them demonstrated that they each contain two substances. We were able to isolate isomeric compounds XIIIa and XIIIb in a 1:1 ratio by means of preparative thin-layer chromatography. Compound XIIIa was obtained as cream-colored crystals, the UV spectrum of which had an absorption maximum at 297 nm (similar to the pyrazolines described above). At the same time, two absorption maxima at 238 and 346 nm were observed in the UV spectrum of XIIIb, which was obtained as bright-yellow crystals; this indicated the presence of an unconjugated pyridine ring and a p-nitrophenylazomethine grouping, since a similar maximum (λ 347 nm) was also observed in the case of p-nitrobenzaldehyde hydrazone [12].

The 2- and 4-vinyl- and 2-methyl-5-vinylpyridines were purified by distillation of the technical-grade products, and the degree of purity (95-99%) was monitored by gas-liquid chromatography (GLC) [Tswett-1 chromatograph, column 3 m long and 0.4 cm in diameter, TND-TS-M diatomaceous brick (40-50 mesh) +8% polypropylene glycol adipate, carrier gas (helium) flow rate 10 ml/min]. 2-Propenylpyridine was obtained by a known method [13, 14], and the purity was monitored by GLC (98%). 2-Styryl- and 2-(p-nitrostyryl)pyridines [15] were obtained from picoline, and the purity was monitored by thin-layer chromatography on Al_2O_3 with a benzene–methanol (10:1) system. β-(2-Pyridyl)acrylic acid was obtained from 2-formylpyridine [16].

1-Acetyl-3-pyridyl-4-R-Δ^2-pyrazolines (VIII-XII). A fivefold excess of diazomethane [17] in ether was added to an ether solution of 0.01 mole of the appropriate vinylpyridine, and the mixture was allowed to stand in the cold (5-7°) in the dark for several days. The ether and excess diazomethane were vacuum evaporated, the residual oil was treated immediately with acetic anhydride (a threefold excess), and the mixture was allowed to stand at room temperature for 1 h, after which it was heated on a water bath for 2 h. The excess acetic anhydride was vacuum evaporated; the residue was treated with sodium carbonate solution until it was alkaline. The resulting precipitate was removed by filtration and recrystallized from a nonpolar solvent. The physical constants and yields of the acetylpyrazolines are presented in Table 1.

Reaction of Diazomethane with 2-(p-Nitrostyryl)pyridine. This reaction was accomplished as described above. The precipitate that formed when the mixture was made alkaline was dissolved in chloroform, the solution was filtered through a layer of aluminum oxide, and the filtrate was vacuum evaporated to give a mixture of acetylpyrazolines XIIIa and XIIIb in 85% yield. The isomers were separated preparatively in a thin layer of aluminum oxide (activity II) with a benzene–methanol (10:1) system. A 1.3-g sample of the mixture of isomers was used for the separation. A 500-mg sample of XIIIa was isolated from the band with R_f 0.7, and 500 mg of XIIIb was isolated from the band with R_f 0.55. The physical constants of the substances are presented in Table 1.

Reaction of Diazomethane with β-(2-Pyridyl)acrylic Acid. This reaction was accomplished by the general method with a tenfold excess of diazomethane. The resinous precipitate that was obtained after alkalization was dissolved in benzene, and the solution was filtered through a layer of aluminum oxide. The filtrate was evaporated to dryness to give a mixture of acetylpyrazolines XIVa and XIVb in an overall yield of 65%. To isolate XIVb, the mixture was recrystallized from hexane with the addition of methanol and then from hexane–cyclohexane (2:1). The yield was 200 mg. The physical constants are presented in Table 1.

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