REACTION OF SUBSTITUTED 2-VINYLPYRIDINES WITH AZO DIENOPHILES

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The reaction of 2-(1-alkoxyvinyl)pyridines with dimethyl azodicarboxylate proceeds primarily via a scheme involving addition to the vinyl substituent to give a mixture of cis- and trans-2-[1-alkoxy-2-(N,N'-dicarbomethoxyhydrazino)-vinyl]pyridines, which undergo partial reaction with a second molecule of azodicarboxylic acid ester via a 1,4-cycloaddition scheme to give substituted 1,2,3,4-tetrahydro-5-azacinnolines. 2-(1-Bromovinyl)pyridine does not react with dimethyl azodicarboxylate. 1-Phenyl-1,3,4-triazoline-2,5-dione reacts with 2-(1-alkoxyvinyl)pyridines also via a scheme involving addition to the vinyl substituent, and its reaction with 2-(1-bromovinyl)pyridine gives 1,2-bis(carbomethoxy)-1,2-dihydro-5-azacinnoline.

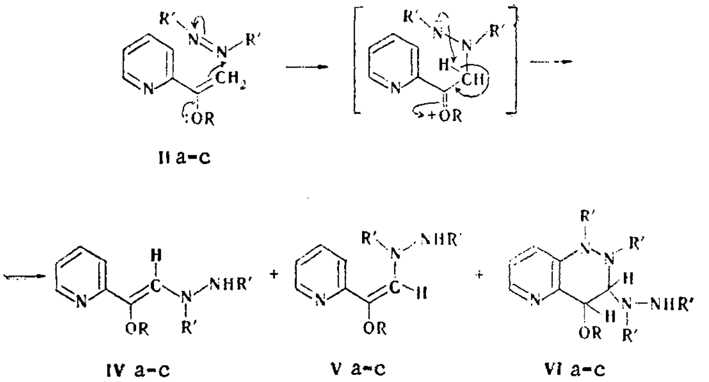
We have recently shown [1, 2] that the pseudodiene system of vinylpyridines is capable of reacting with azodicarboxylic acid esters and 1-phenyl-1,3,4-triazoline-2,5-dione (I) via a scheme involving 1,4-cycloaddition to give 1,2,3,4-tetrahydro-5-azacinnoline derivatives.

In the present research we examined the effect of a substituent in the vinyl group on the direction of the reaction, for which we investigated the reaction of 2-(1-alkoxyvinyl)-pyridines (IIa-c) and 2-(1-bromovinyl)pyridine (IId) with dimethyl azodicarboxylate (III) and triazolinedione I.

As in the case of unsubstituted vinylpyridines, ester III reacts with IIa-c only in the case of refluxing in benzene for many hours; the overall yields of reaction products do not exceed 35-40%, regardless of the size of the alkoxy group. Compound Id does not react with ester III even when the components are heated in benzene for 30 h; when the temperature is raised (140°C in xylene), polymerization is observed.

The reactions of ester III with vinylpyridines IIa-c proceed identically to give three reaction products — IVa-c, Va-c, and VIa-c. The yields of the last two products are considerably lower than the yields of the first products (see Table 1).

It was found that cis and trans isomers IVa-c and Va-c have different R_f values but very similar UV spectra (see Table 1). The same two absorption bands at 1720 and 1760 cm^{-1} of the stretching vibrations of ester C=O groups and an absorption band at 3290-3300 cm^{-1} corresponding to the stretching vibrations of the N-H bond are observed in the IR spectra.



$R' = COOCH_3$; II, IV-VI a $R = CH_3$; b $R = C_2H_5$; c $R = i\text{-}C_3H_7$

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TABLE 1. Yields, Constants, and Spectral Properties of IVa-c and Va-c

Compound	mp, °C	Found, %			Empirical formula	Calc. %			R_f band during isolation[a]	UV spectrum,[b] λ_{max}, nm (log ε)	PMR spectrum, δ, ppm	Mass spectrum,[c] m/e (intensity in percent relative to the maximum peak)	Yield, %
		C	H	N		C	H	N					
IVa	142—143	51,3	5,51	14,8	$C_{12}H_{15}N_3O_5$	51,2	5,34	14,9	0,5—0.7	280 (3,84)	6,26	281 (54), 266 (100), 222 (20), 207 (22), 148 (54), 147 (82), 134 (36), 133 (14), 119 (40), 106 (60)	20
IVb	136—138	52,8	5,70	14,3	$C_{13}H_{17}N_3O_5$	53,0	5,77	14,2	0,5—0,6	280 (3,82)	6,20	295 (10), 266 (100), 222 (10), 207 (10), 148 (60), 147 (72), 134 (12), 133 (48), 119 (30), 106 (17)	22
IVc	128—130	54,5	6,23	13,7	$C_{14}H_{19}N_3O_5$	54,4	6,17	13,6	0,5—0,6	275 (3,80)	6,32	309 (6), 266 (100), 222 (5), 207 (40), 148 (40), 147 (53), 134 (15), 133 (30), 119 (42), 106 (20)	18
Va	27—29	51,2	5,42	14,9	$C_{12}H_{15}N_3O_5$	51,2	5,34	14,9	0,3—0,5	280 (3,80)	4,89	281 (52), 266 (100), 222 (24), 207 (46), 148 (52), 147 (80), 134 (39), 133 (70), 119 (38), 106 (18)	5
Vb	28—31	53,1	5,84	14,3	$C_{13}H_{17}N_3O_5$	53,0	5,77	14,2	0,3—0,5	280 (3,82)	4,96	295 (11), 266 (100), 222 (15), 207 (12), 148 (65), 147 (70), 134 (16), 133 (38); 119 (35), 106 (13)	7
Vc	35—37	54,2	6,10	13,5	$C_{14}H_{19}N_3O_5$	54,4	6,17	13,6	0,3—0,4	275 (3,82)	5,00	309 (4), 266 (100), 222 (3), 207 (46), 148 (35), 147 (44), 134 (18), 133 (36), 119 (26), 106 (12)	8

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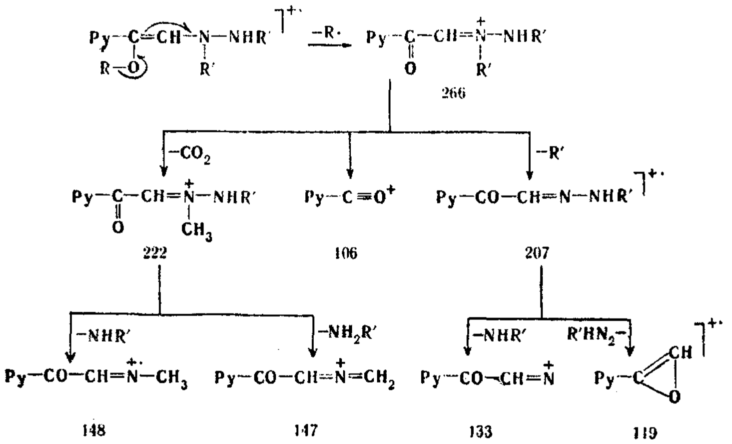
a) Benzene—methanol—chloroform system (9:1:1). b) In methanol. c) Here and subsequently, the ten most intense peaks are presented.

TABLE 2. Yields, Constants, and Spectral Properties of VIa-c

Compound	mp, °C	Found, %		Empirical formula	Calc., %		UV spectrum,[a] λ_{max}, nm (log ε)	Mass spectrum, m/e (intensity in percent relative to the maximum peak)	Yield, %
		C	H		C	H			
VIa	98—100	45,1	4,70	$C_{16}H_{21}N_5O_9$	45,0	4,63	210 (4,1), 250 (3,98), 300 (3,70)	427 (10), 281 (68), 266 (100), 222 (20), 202 (32), 193 (20), 149 (70), 148 (60), 133 (50)	10
VIb	84—86	46,2	5,23	$C_{17}H_{23}N_5O_9$	46,3	5,31	205 (4,0), 250 (3,93), 300 (3,70)	441 (16), 294 (60), 266 (100), 222 (20), 207 (30), 193 (50), 149 (50), 148 (13), 133 (80)	9
VIc	80—82	47,5	5,50	$C_{18}H_{25}N_5O_9$	47,4	5,42	210 (4,03), 250 (3,90), 305 (3,72)	455 (7), 440 (18), 425 (60), 266 (100), 222 (10), 207 (10), 193 (20), 149 (60), 148 (70), 133 (74)	9



Py = 2-pyridyl

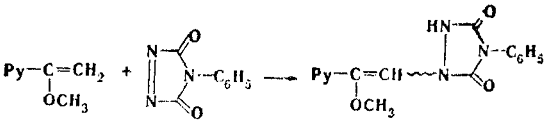
The character of their mass-spectral fragmentation is virtually identical, since the first process in the fragmentation of the molecular ions of IVa-c and Va-c is the loss of an alkyl radical from the alkoxy group to give an ion with m/e 266,* the peak of which has the maximum intensity.

The PMR spectra of isomeric enehydrazines IV and V are also almost identical (except for the signals of the protons of the alkoxy groups); however, the signal of the olefin proton of IVa-c lies at 6.2-6.3 ppm, whereas it is observed at stronger field (δ 4.9-5.0 ppm) in the spectra of Va-c (see Table 1). Finally, enehydrazines IVa-c have higher melting points. All of this enabled us to assign a structure with a trans orientation of the hydrogen atom with respect to the alkoxy group to IVa-c and a cis structure to Va-c. Thus, owing to the increased nucleophilicity of the terminal methylene group, IIa-c, like α-methoxystyrene [3], probably react with ester III primarily via a scheme involving vinyl substitution.

The third type of isolated compound (VI) has lower chromatographic mobility and UV spectra that differ from the spectra of IV and V but are similar to the spectra of 1,2,3,4-tetrahydro-5-azacinnolines [1]. According to the results of elementary analysis and the mass spectra (see Table 2), the compounds are the products of the reaction of two molecules of ester III with one molecule of IIa-c. Signals of aromatic protons (8.40-8.46, 7.28-7.35, and 7.52-7.63) and doublets of two protons (3-H and 4-H) at 4.8-5.0 ppm (J = 6 Hz) are observed in the PMR spectra of VIa-c at medium and weak field. Unfortunately, this J value does not make it possible to form a judgment regarding the stereochemistry of the substituents attached to the $C_{(3)}$ and $C_{(4)}$ atoms, although from general considerations one should expect primarily an axial—axial orientation of the hydrogen atoms. The IR spectra of VIa-c contain an absorption band at 3320-3300 cm^{-1}, which indicates the presence of an N-H group; this confirms the proposed structure.

These compounds are secondary reaction products. In fact, a substance identical to VIa with respect to its physical and spectral properties was obtained when a mixture of IVa and Va was refluxed with ester III in benzene.

As one should have expected, the reaction of vinylpyridine IIa with triazolinedione I proceeds more vigorously even in the cold. Adduct VII, which was isolated in high yield (80%), has a UV spectrum that is similar to the spectra of IV and V, and two signals at 4.3 and 5.4 ppm, with an intensity of about 0.5 of a proton unit, are observed at medium field in its PMR spectrum. This makes it possible to assume the presence of a mixture of cis and trans isomers similar to the isomers IV and V. However, attempts to isolate individual components from the mixture were unsuccessful.



VII

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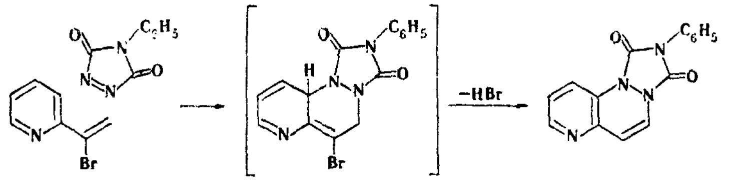
*Here and subsequently, the m/e values of the ions are presented.

In contrast to vinyl ethers, bromovinyl compound IId reacts with triazolidine I considerably more slowly (the solution is decolorized only after 2 h). A halogen-free compound, the UV spectrum of which was similar to the UV spectra of the previously described 5-azacinnoline derivatives [1], was isolated in 73% yield after neutralization of the reaction mixture with sodium carbonate. Absorption bands at 3200-3400 cm^{-1} are not observed in its IR spectrum, and, according to the results of elementary analysis and the mass spectrum, it contains two hydrogen atoms less than the "monoadduct." This makes it possible to assign cyclic structure VIII to it. Analysis of the fragmentation of its molecular ion — intense C_6H_5NCO (119) and $[M - 119]^+$ peaks and the absence of peaks of ions of triazolinedione I (175), etc. — confirms this assumption.



II VIII

Thus activation of the pseudodiene system of vinylpyridines by introduction of electron-donor substituents leads to a sharp change in the specificity of their reaction with aza dienophiles to favor processes involving addition to the vinyl substituent and to suppression of their strictly diene properties.

EXPERIMENTAL

Preparative chromatography was accomplished in a layer of aluminum oxide (1.5-mm thick) in a benzene—methanol—chloroform system (9:1:1) with development with UV light. The UV spectra were obtained with a Cary-15 spectrophotometer. The IR spectra of mineral oil suspensions of the compounds were recorded with an IKS-22 spectrometer. The PMR spectra of solutions of the compounds in deuteromethanol were recorded with a Varian XL-100 spectrometer with hexamethyldisiloxane as the internal standard. The mass spectra were obtained with a Varian MAT-111 (Gnom) spectrometer with direct introduction of the substances into the ion source at 20-80°C and an ionization energy of 80 eV. We described the synthesis of IIa-d in [4]. Dimethyl azodicarboxylate (III) was obtained by a known method [5], and triazolinedione I was obtained by the method in [6].

Reaction of Substituted Vinylpyridines IIa-c with Ester III. A solution of 10 mmole of the appropriate vinylpyridine I and 2.9 g (20 mmole) of ester III in 20 ml of benzene was refluxed for 30 h, after which it was cooled and chromatographed in a thick layer of aluminum oxide, as a result of which the bands with the R_f values indicated in Table 1 were obtained. The yields and constants of IVa-c and Va-c are also presented in Table 1. The yields and constants of VIa-c are given in Table 2.

3-[2-Methoxy-2-(2'-pyridyl)vinyl]-1-phenylfurazole (VII). A solution of 350 mg (2 mmole) of triazolinedione I in 40 ml of absolute ether was added to a solution of 130 mg (1 mmole) of Ia in 15 ml of absolute ether, and the precipitate that formed in the course of 2 h was removed by filtration, washed with ether, and recrystallized from chloroform to give 245 mg (80%) of a product with mp 152-154°C. UV spectrum, λ_{max} (log ε): 201 (4.0), 240 (3.9), and 284 nm (3.7). Mass spectrum, m/e (intensity in percent relative to the maximum peak): 310 (54), 191 (54), 177 (45), 176 (20), 135 (25), 134 (14), 120 (58), 119 (100), 105 (40), 78 (18). Found, %: C 62.2; H 4.4; N 18.1. $C_{16}H_{14}N_4O_3$. Calculated, %: C 62.0; H 4.5; N 18.1.

1,3,12,13-Tetrahydro-2-phenyl-1,3-dioxo-triazolo[3,4-a]-5-azacinnoline (VIII). A solution of 350 mg (2 mmole) of triazolinedione I in 40 ml of absolute ether was added to a solution of 184 mg (1 mmole) of bromovinyl compound IId in 15 ml of absolute ether, and the precipitate that formed in the course of 2 h was removed by filtration, washed with ether and 10% sodium carbonate solution, dried, and recrystallized from chloroform to give 200 mg (72%) of a product with mp 166-168°C. UV spectrum, λ_{max} (log ε): 201 (3.9), 242 (3.8), and 285 nm (sh). Mass spectrum, m/e (intensity in percent relative to the maximum peak): 278 (9), 201 (6), 173 (58), 159 (10), 145 (30), 131 (12), 119 (100), 117 (6), 103 (26), 91 (86). Found, %: C 64.8; H 3.6; N 20.3. $C_{15}H_{10}N_4O_2$. Calculated, %: C 64.7; H 3.6; N 20.1.

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SYNTHESIS AND CHIRAL-OPTICAL PROPERTIES OF SOME BENZOLACTAMS*

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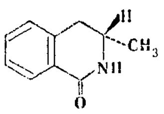
Five- and seven-membered benzolactams — (—)-S-2,3-dimethyl-2,3-dihydroisoindolone and (+)-S-5-methyl-2,3,4,5-tetrahydrobenz[c]azepin-1-one — were synthesized. A study of their chiral-optical properties and comparison with the previously studied six-membered lactam (—)-S-4-methyl-3,4-dihydroisoquinol-1-one showed that their circular dichroism spectra are similar: The spectra contain dichroic absorption bands due to $\pi \to \pi^*$ transitions in the aromatic chromophore (~270 and ~220 nm) and a band of charge transfer in the benzamide chromophore at 240-250 nm. The magnitude of the Cotton effect due to the charge-transfer band increases as the lactam ring becomes larger (five-membered < six-membered < seven-membered benzolactam). The change in the magnitude of the Cotton effect is explained by the development of a strictly dissymetric chromophore.

The spectral and chiral-optical properties of simple cyclic amides have been studied quite thoroughly. A strong transition ($\log \varepsilon$ 4.0), which masks the weaker long-wave $n \to \pi^*$ transition, is observed in the UV spectra of lactams at ~190 nm [2]. However, Chen and Swenson [2] were able to establish the position of the $n \to \pi^*$ transition — 233 nm for cis-lactams and 227-230 nm for trans-lactams — by breaking down the observed absorption band into its Gaussian components.

Cotton effects (CE) due to the $n \to \pi^*$ transition at 230-225 nm and the $\pi \to \pi^*$ transition at ~190 nm are observed in the circular dichroism (CD) spectra of a number of one-ring and two-ring lactams in conformity with their UV spectra (for example, see [3-5]).

Much less study has been devoted to benzolactams containing an aromatic chromophore fixed in a ring and conjugated with the amide grouping. Thus a study of the chiral-optical properties of the previously synthesized (+)-S-3-methyl- (I) [6] and (—)-S-4-methyl-3,4-dihydroisoquinol-1-one (II) [7] showed that they differ from aliphatic lactams with respect to their spectropolarimetric behavior.



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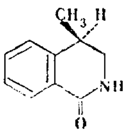

II

In the present research we synthesized and studied five- and seven-membered lactams — (—)-S-2,3-dimethyl-2,3-dihydroisoindolone (III) and (+)-S-5-methyl-2,3,4,5-tetrahydrobenz-

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*Communication XLVI from the series "Stereochemical studies." See [1] for communication XLV.

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