REACTION OF 2-VINYLPYRIDINE AND 2-(1-METHOXYVINYL)PYRIDINE WITH ACRYLIC ACID DERIVATIVES

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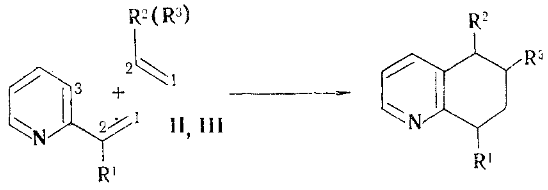
The regiospecificity of the reaction of 2-vinylpyridine and 2-(1-methoxyvinyl)-pyridine with acrylonitrile and methyl acrylate was predicted on the basis of MO perturbation theory and was confirmed experimentally. The regioisomeric compositions of the reaction mixtures were studied by means of chromatographic mass spectrometry.

We recently described the cyclodimerization, via the scheme of the diene synthesis, of vinylpyridines, in which one of the molecules acts as a diene, while a second acts as a dienophile [1]. We found good agreement between the theoretically calculated and experimentally observed regiospecificity of the process.

Using the known quantum-chemical parameters of 2-vinylpyridine (Ia) [1] and the parameters that we found for 2-(1-methoxyvinyl)pyridine (Ib), acrylonitrile (II), and methyl acrylate (III) (see Table 1),† we calculated‡ the π-electron stabilization energies (ΔE_π) of various regioisomers, the formation of which can be expected in the reaction of vinylpyridines Ia, b with dienophiles II and III.



I a,b IV-V a-d, VI

I a $R^1=H$, b $R^1=OCH_3$; IV $R^1=H$; V $R^1=OCH_3$; VI $R^1=R^3=H$, $R^2=$ 2-pyridyl; IV, V a $R^2=CN$, $R^3=H$, b $R^2=H$, $R^3=CN$, c $R^2=COOCH_3$, $R^3=H$, d $R^2=H$, $R^3=COOCH_3$

It follows from the data in Table 2 that in the reaction of Ia and II one should expect the preferred formation of regioisomer IVa, while in the reaction of Ia and III the probabilities of the formation of both regioisomers (IVc and IVd) are appreciably close. It is apparent from a comparison of the relative orientation of the energy levels of the upper occupied molecular orbitals (UOMO) and the lower vacant molecular orbitals (LVMO) of Ia, b, II, and III (Fig. 1) that the LVMO level of vinylpyridine Ia lies lower (0.376 eV lower) than in the case of acrylonitrile (II) and only slightly higher (0.126 eV higher) than in the case of methyl acrylate (III). This makes it possible to also assume the possibility of the simultaneous occurrence of processes involving the dimerization of vinylpyridine Ia (VI) along with its reaction with dienophile II or III. At the same time, one should apparently not fear processes involving the dimerization of dienophile II, since its UOMO level lies considerably lower (1.19 eV lower) than in the case of "dienes" Ia and Ib. The side dimerization of vinylpyridine Ib is also possible from an energetic point of view; however, steric factors (because we are dealing with a 1,1-disubstituted dienophile) may hinder it.

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*Deceased.

†The calculation was made with a BÉSM-6 computer by the MINDO/3 method with a TOPEAMOP program [2]. A. V. Gorelov participated in the calculation.

‡The ΔE_π values were calculated from a known formula [3, 4].

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TABLE 1. Coefficients of the AO and Energies of the Boundary Orbitals of Ib, II, and III

Compound	Empirical orbital	Coefficients of the AO of the atoms[a]			E, eV
		1	2	3	
Ib[b]	LVMO	0,38040	−0,27834	0,14865	0,6657
	UOMO	−0,56965	−0,34681	0,33925	−8,5361
II[c]	LVMO	0,66712	−0,56077	—	1,1820
	UOMO	0,66123	0,54870	—	−9,7948
III	LVMO	0,69434	−0,50898	—	0,5810
	UOMO	0,62822	0,65510	—	−10,5860

[a] The numbers of the atoms are indicated in the reaction scheme.
[b] In the configuration depicted in the reaction scheme. [c] The calculated coefficients are close to those previously described by the CNDO/2 method [5].

TABLE 2. π-Electron Stabilization Energies (ΔE_π) of IVa-d and Va-d

	IV				V			
	a	b	c	d	a	b	c	d
ΔE_π kJ/mole	93,8	89,3	96,8	96,2	101,6	92,7	107,0	96,0

We carried out the reaction of Ia, b with II and III by heating the components in a ratio of 1:10 in sealed ampuls in an argon atmosphere in the presence of hydroquinone at 150°C for 30 h. Many unchanged components remain in the reaction medium at lower temperatures, and the yields of polymeric products increase at higher temperatures. Nevertheless, even under the selected optimum conditions the overall yield of the sum of the nitrogenous bases of nonpolymeric character does not exceed 15-16%. This indicates that the rate of polymerizztion exceeds the rate of the diene synthesis appreciably.*

An analysis of the isolated mixtures of bases by chromatographic mass spectrometry showed that, in agreement with the calculation, regioisomers IVa and IVc are actually formed in large amounts (IVa:IVb and IVc:IVd ≈ 9:1), whereas in addition to the adducts, the reaction mixture also contained dimerization product VI, which was identical to the previously described compound [1] with respect to its physical and spectral properties. The structures of IVa-d follow from both an analysis of the character of their mass-spectral fragmentation and from data from the PMR spectrum of IVa. Thus a molecule of ethylene is eliminated in the retrodiene fragmentation (RDF) of the molecular ion of adduct IVa, while a molecule of acrylonitrile is eliminated from the molecular ion of IVb. Retrodiene fragmentation is less characteristic for the molecular ions of IVc and IVd. However, IVd eliminates a methyl acrylate radical (the ion with m/e 106†) under the influence of electron impact, which is not characteristic for the molecular ion of isomer IVc.

The reaction of vinylpyridine Ib with the same dienophiles is also complicated significantly by polymerization processes. Chromatographic mass-spectral analysis of the isolated sums of the bases demonstrated the absence in them of dimers of vinylpyridine Ib. Two compounds (in approximately equal ratios) that have close chromatographic characteristics and virtually identical mass spectra are detected in the products of the reaction of "diene" Ib with both nitrile II (Va) and ester III (Vc). An analysis of the scheme of their mass-spectral fragmentation makes it possible to assert that in each case we are dealing with a mixture of two geometrical isomers (cis and trans) of the corresponding regioisomers Va and Vc. Intense $(M-CH_3)$ ion peaks that subsequently lose CHCN (Va, 134), and respectively, CH_2COOCH_3 (Vf, 133) fragments are characteristic for the mass spectra of both Va and Vc (Table 3) subsequent elimination of H_2CN or HCN by these fragments leads to an ion with m/e 106.

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*Attempts to raise the yields of the adducts by carrying out the process at 10,000 atm were unsuccessful.
†Here and subsequently, the m/e values of the ions are given.

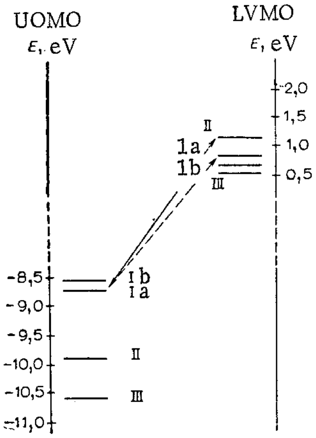

Fig. 1. Relative orientation of the levels of the UOMO and LVMO of Ia, b, II, and III.

TABLE 3. Mass Spectra^a of IVa-d and Va, c

Compound	m/e (relative intensity, %)
IVa	158 (78), 157 (100), 143 (20), 131 (25), 130 (80), 118 (32), 103 (19), 79 (20), 77 (20), 65 (18), 51 (22)
IVb	158 (17), 157 (20), 130 (19), 118 (21), 106 (18), 105 (80), 104 (38), 79 (100), 78 (23), 52 (38), 51 (42)
IVc	191 (22), 159 (12), 132 (100), 131 (23), 130 (20), 117 (41), 103 (12), 78 (12), 77 (8), 65 (11), 51 (10)
IVd	191 (6), 190 (5), 176 (7), 160 (10), 132 (100), 131 (18), 130 (30), 117 (36), 106 (40), 93 (26), 79 (40)
Va^b	188 (4), 173 (68), 134 (52), 131 (38), 130 (40), 117 (37), 106 (66), 105 (88), 104 (80), 79 (95), 78 (100)
Vc^b	221 (6), 206 (28), 174 (49), 148 (28), 146 (26), 133 (16), 130 (20), 117 (38), 106 (78), 79 (22), 78 (100)

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[a] The molecular ion peak and the 10 most intense peaks are presented. [b] One of the geometrical isomers.

In addition, loss of a molecule of methanol (174) by the (M–CH_3) ion is characteristic for Vc; this is typical for the methyl esters of acrylic acids [6].

Thus, the observed regiospecificity of processes involving the cycloaddition of acrylic acid derivatives to vinylpyridines Ia, b is in complete agreement with the theoretically predicted regiospecificity.

EXPERIMENTAL

The chromatographic mass spectra were obtained with a Varian MAT-111 spectrometer with a 1.5-m long column containing 3% SE-30 on Chromosorb under programmed thermostatic heating from 170 to 250°C at 20 deg/min. The mass spectra were obtained at an ionization energy of 80 eV. The PMR spectra of solutions of the compounds in CCl_4 were recorded with a Varian T-60 spectrometer with tetramethylsilane as the standard. The IR spectra of liquid films of the compounds were obtained with a UR-20 spectrometer.

Compound Ia was purified by vacuum distillation up to a purity [by gas–liquid chromatography (GLC)] of 99%. Compound Ib was obtained by the method in [7] and had a purity of 99%. Chromatography was carried out on silica gel (5-40 μm) or Silufol UV-254 in chloroform–methanol systems (15:1 and 20:1, respectively).

Reaction of Vinylpyridines Ia, b with Acrylic Acid Derivatives II and III. A mixture of 20 mmole of the corresponding vinylpyridine, 200 mmole of the dienophile (II or III), and 10 mg of hydroquinone was heated in a sealed ampul in an argon atmosphere at 170°C for 30 h, after which it was poured into ether. The resulting mixture was filtered, and the filtrate was concentrated to two-thirds of its original volume and extracted repeatedly with 1 N HCl solution. The aqueous solution was made alkaline to pH 9-10 and extracted with ether to remove the sum of the bases. The extract was dried with anhydrous potassium carbonate and evaporated.

A 108-mg sample of adduct IVa was isolated in the preparative separation of 318 mg of the mixture of bases obtained in the reaction of vinylpyridine Ia with nitrile II. IR spectrum: 2250 cm^{-1}. PMR spectrum, δ: 1.9-2.4 (broad m, 4H, 6,7-CH_2), 2.9 (broad t, 2H, 8-CH_2), 3.95 (broad t, 1H, 5-CH), 7.1 (q, 1H, 3-H), 7.7 (broad d, 1H, 4-H), and 8.5 (broad d, 1H, 2-H). The picrate had mp 144-146°C (from methanol). Found: C 49.9; H 3.7; N 17.6%. $C_{16}H_{13}N_5O_7$. Calculated: C 50.1; H 3.4; N 17.9%. The mass spectrum coincided with the mass spectrum of IVa (Table 3). In addition, 23 mg of VI, with mp 43-45°C [1], was isolated.

The mass spectra of IVa-d, Va, and Vc are presented in Table 3. We were unable to isolate these compounds in individual form (except for IVa).

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MASS SPECTRA OF STEREOISOMERIC cis- AND trans-2-ALKYL-3-ARYL(HETARYL)-4-(METHOXYCARBONYL)-3,4-DIHYDRO-1H-ISOQUINOL-1-ONES AND 1,2,3,4-TETRAHYDROISOQUINOLINES

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The molecular ions of the trans isomers of the investigated compounds are more stable than those of the cis isomers. Their principal fragmentation pathways involve retrodiene fragmentation of the molecular ions, which proceeds with greater probability in the case of the cis isomers, or loss of substituents from the 4 or 3 position. The latter process is characteristic only for tetrahydroisoquinoline derivatives, is not observed for 3,4-dihydro-1H-isoquinol-1-one derivatives, and proceeds more readily in the case of the trans isomers.

We recently described the synthesis and stereochemistry of 3,4-disubstituted derivatives of 1,2,3,4-tetrahydroisoquinoline and 3,4-dihydro-1H-isoquinol-1-one [1-5].

Since difficulties were encountered in the establishment of the stereochemistry of these compounds by NMR methods in a number of cases, to establish the dependence of the mass-spectral fragmentation on the stereochemistry of compounds of this type we studied the behavior of a series of cis and trans isomers of Ia-g and IIa-e, as well as the isomeric trans-III and E-IV, under the influence of electron impact.

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