

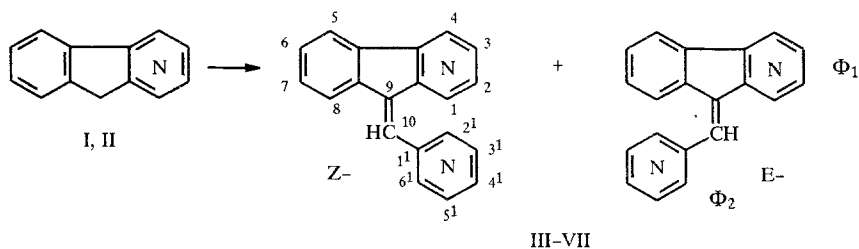
GEOMETRIC ISOMERS OF 9-PICOLYLIDENEAZAFLUORENES

N. M. Kolyadina, A. T. Soldatenkov, L. A. Murugova,
A. A. Ustenko, E. A. Ageev, and N. S. Prostakov

By condensation of 1- and 4-azafluorenes with $\alpha(\beta, \gamma)$ -formylpyridines, we have synthesized 9-picolidene-1- and 4-azafluorenes, which we have isolated as pure Z and E isomers. Using PMR spectroscopy we have established their configuration. We discuss hypotheses concerning the dependence of the physical properties of the Z and E isomers of 9-picolylideneazafluorenes on their structure.

In [1], synthesis of geometric isomers of 9-arylideneazafluorenes is described, whose configuration has been established by PMR spectroscopy. These heterocyclic compounds are of interest because they exhibit neurotropic and growth-regulating activity [1, 2].

In this paper, we describe condensation of 1-azafluorene (I) with α -, β -, and γ -formylpyridine, and also 4-azafluorene (II) with α - and γ -formylpyridine in the presence of sodium methylate 9- $\{\alpha(\text{III})[\beta(\text{IV}), \gamma(\text{V})]$ -picolylidene}-1-azafluorenes are obtained in close to theoretical yields from azafluorene I, while 9- $\{\alpha(\text{VI})[\gamma(\text{VII})]$ -picolylidene}-4-azafluorenes are obtained from azafluorene II.



I, III—V 1-aza; II, VI, VII 4-aza; III, VI pyridyl-2; IV pyridyl-3; V, VII pyridyl-4

All the compounds except for III are obtained as a mixture of Z and E isomers.

The pure isomers were isolated using column chromatography. Their configuration was established by PMR spectroscopy (Table 1). The Z and E configurations were established on the basis of the characteristic values of the chemical shifts of the vinyl proton (in Table 1, called 10-H), the protons of the pyridyl radical, and in some cases the protons of the azafluorene fragment. In the PMR spectra of the E isomers of 9-arylidene-1-azafluorenes [3], the signal from the vinyl proton undergoes a downfield shift (0.6 ppm) compared with the Z isomers, due to the anisotropic effect of the unshared electron pair of the nitrogen atom of the pyridylidene ring. Thus, the Z configuration is assigned to the isomer of compound V with T_{mp} 136-138°C, while the E configuration is assigned to the isomer with T_{mp} 82°C, since the vinyl proton in the Z isomer case appears more upfield (at 7.50 ppm) than in the E isomer case (at 8.09 ppm) (Table 1). Under the influence of the unshared electron pair of the nitrogen atom of the pyridine nucleus of the azafluorene, the protons in the 3'- and 5'-positions of the pyridyl radical of the Z isomer undergo a downfield shift by 0.76 ppm compared to the E isomer. Such an effect was observed earlier for the Z and E isomers of 9-benzylidene-1-azafluorenes [3]. Based on measurements of the integrated intensities of the signals from the 10-H, 3'-H, and 5'-H protons, it was established that the ratio of Z and E isomers of compound V in the reaction mixture is 1.0:1.3.

TABLE 1. Parameters* of PMR Spectra of Compounds III-VII (δ , ppm)

Com- pound	Iso- mer	1-H	2-H	3-H	4-H	8-H	10-H	2'-H	3'-H	4'-H	5'-H	6'-H
III	<i>E</i>		8,52	7,25	7,94	9,10	8,18		*	*	*	8,86
IV	<i>Z</i>		8,50	7,25	7,96	**	7,58	9,25		9,16	7,39	8,60
	<i>E</i>		8,54	7,30	7,98	**	8,16	8,94		7,95	*	8,67
V	<i>Z</i>		8,50	7,25	7,96	**	7,50	8,74	8,28		8,28	8,74
	<i>E</i>		8,52	7,28	7,97	**	8,09	8,74	7,52		7,52	8,74
VI	<i>Z</i>	9,02	7,15	8,54		**	7,66		*	*	*	8,82
	<i>E</i>	7,98	7,13	8,55		8,48	7,53		*	*	*	8,80
VII	<i>Z</i>	7,66	6,98	8,52		**	7,63	8,74	7,44		7,44	8,74
	<i>E</i>	7,99	7,23	8,60		**	7,45	8,74	7,47		7,47	8,74

*Spin-spin coupling constants (J, Hz) for the pyridine fragments: III-VII- $J_{\alpha-\beta}$ = 4.8-4.9; $J_{\alpha-\gamma}$ = 1.6; $J_{\beta-\gamma}$ = 8.0.

**Chemical shifts were not determined due to overlap of signals from other protons.

TABLE 2. Electronic Absorption Spectra of 9-Picolylideneazafluorenes III-VII (in 96% ethanol)

Com- pound	Config- uration	λ_{\max} , nm (lg ϵ)		
		β - band	ρ - band	α - band
III	<i>E</i>	212 (4,40)	258 (4,52)	325 sh (4,24)
		230 (4,57)	296 (4,43)	
IV	<i>Z, E</i>	210 (4,51)	265 (4,37)	333 sh (4,34)
		230 (4,55)	298 (4,36)	347 (4,40)
			300 (4,42)	360 sh (4,29)
V	<i>Z</i>	210 (4,62)	270 (4,61)	328 sh (4,54)
		230 (4,72)	295 (4,60)	340 (4,61)
	<i>E</i>	210 (4,73)	258 (4,87)	355 sh (4,13)
		230 (4,88)	295 (4,77)	320 sh (4,60)
VI	<i>Z, E</i>	214 (4,76)	276 (4,57)	330 sh (4,60)
		233 (4,95)	316 (4,63)	345 (4,66)
VII	<i>Z</i>	214 (4,55)	257 (4,61)	360 sh (4,54)
		230 (4,73)	316 (4,47)	330 sh (4,29)

The *Z* and *E* isomers of compounds IV were identified analogously from the signals of the 10-H, 2'-H, and 4'-H protons. The *E* configuration was assigned to compound III on the basis of the magnitude of the chemical shift of the 10-H proton (8.18 ppm) and the 8-H proton (9.10 ppm), the significant downfield shift of which is probably due to the effect of the nitrogen atom of the α -pyridyl radical.

For compounds VI, characteristic signals come from protons 1-H and 8-H. Their signals experience a significant deshielding effect from the unshared electron pair of the nitrogen atom of the α -pyridyl radical and have chemical shifts of 9.02 ppm (1-H, *Z* isomer) and 8.48 ppm (8-H, *E* isomer).

The configuration of the isomers of compounds VII and their ratio in the reaction mixture were established on the basis of the upfield shifts of the signals from the 1-H, 2-H, and 3-H protons for the *Z* isomer, experiencing the effect of the magnetic anisotropy of the γ -pyridyl substituent. The ratio of the isomers in this case is $\sim 1.0:2.5$.

In the mass spectra of compounds III-VII, there are intense peaks for the M^+ and $[M-H]^+$ ions.

In the UV spectra of compounds III-VII (Table 2), we observe β -, ρ -, and α -bands with λ_{\max} 210-233, 257-316, and 320-360 nm, respectively. In the spectra of the *Z* isomers of compounds IV-VII (derivatives of 1-azafluorene), the long-wavelength absorption band consists of three components with a major maximum at 340-347 nm (log ϵ 4.61-4.40), and the

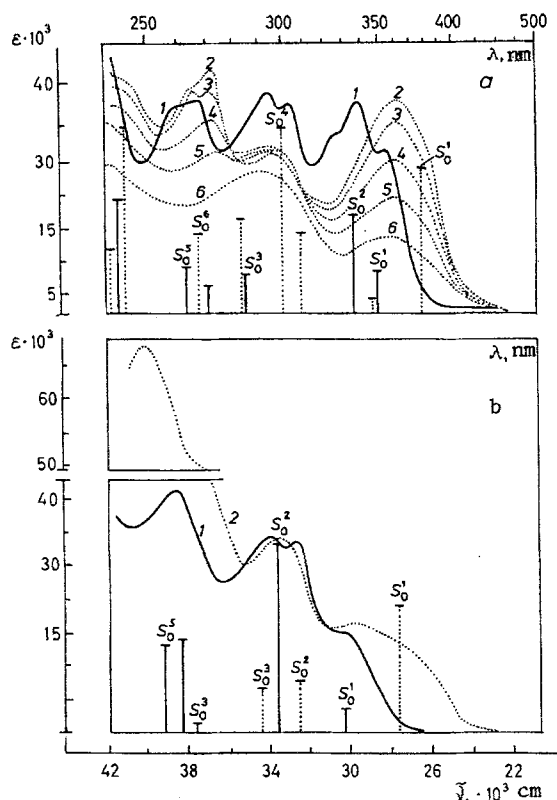


Fig. 1. Experimental and theoretical electronic absorption spectra of 9-(γ -picolyldiene)-1-azafluorene: a) Z isomer (in 96% ethanol — 1); 2-6) absorption curves upon acidification of the ethanol solution with a 2 N H_2SO_4 solution up to pH 2); b) E isomer (in 96% ethanol — 1; absorption curve in ethanol + H_2SO_4 — 2); S_0^n — singlet-singlet $\pi\pi^*$ transitions in theoretical spectra of basic (solid line) and cationic (dotted line) forms.

longest wavelength component of this band (Fig. 1a) is located at 355-360 nm ($\log \epsilon$ 4.13-4.29). In the spectra of the E isomers of these compounds, the long-wavelength band (the α -band) undergoes a hypsochromic shift of ~ 30 -40 nm relative to the longest wavelength component of the Z isomers and, overlapping with the ρ -band (λ_{max} 258-316 nm), appears as a shoulder on its long-wavelength slope (Fig. 1b, Table 2). Analogous spectral differences were obtained in the UV spectra of the E and Z isomers of 9-benzylidene-1-azafluorene [3], which indicates a similarity in their spatial and π -electron structure. Therefore, we may assume that the hypsochromic shift of the long-wavelength band of all the E isomers is explained by steric hindrances created by the spatially close 8-H and 2'-H (5'-H) atoms of the azafluorene and pyridyl fragments Φ_1 and Φ_2 , respectively, leading to deviation of the Ar(Py) residue from the plane of the molecule and disruption of the π -conjugation in it (Θ 60-75°). Weakening of the intensity of the long-wavelength absorption band its broadening are due to the increase in the contribution from strong twisting vibrations about the $\text{C}_{(10)}-\text{Ar}(\text{Py})$ bond (Table 2).

In the Z isomers of derivatives of 1-azafluorene IV-VI, steric strain is lessened to the absence of the 1'-H proton (in the free bases). The electron-acceptor interaction of the unshared electron pair of the $\text{N}_{(1)}$ nitrogen atom with the 2'-H, 3'-H protons of the Φ_2 fragment rigidly fixes the latter in a flattened form suitable for π -conjugation. This is confirmed by quantum chemical calculations of the electronic absorption spectra and the π -electron structure of compound V (Z, E), taken as a model. This compound was selected because in its molecule the maximum degree of conjugation between the Φ_1 and Φ_2 fragments can be achieved (Θ 0-25°). The calculations were done taking into account their noncoplanarity with respect to the $\text{C}_{(10)}-\Phi_2$ bond by the Pariser-Parr-Pople method with configuration interaction (PPP with CI) [4-6] within a unified calculation scheme using the same parameters for the C, N, and O atoms as in [3].

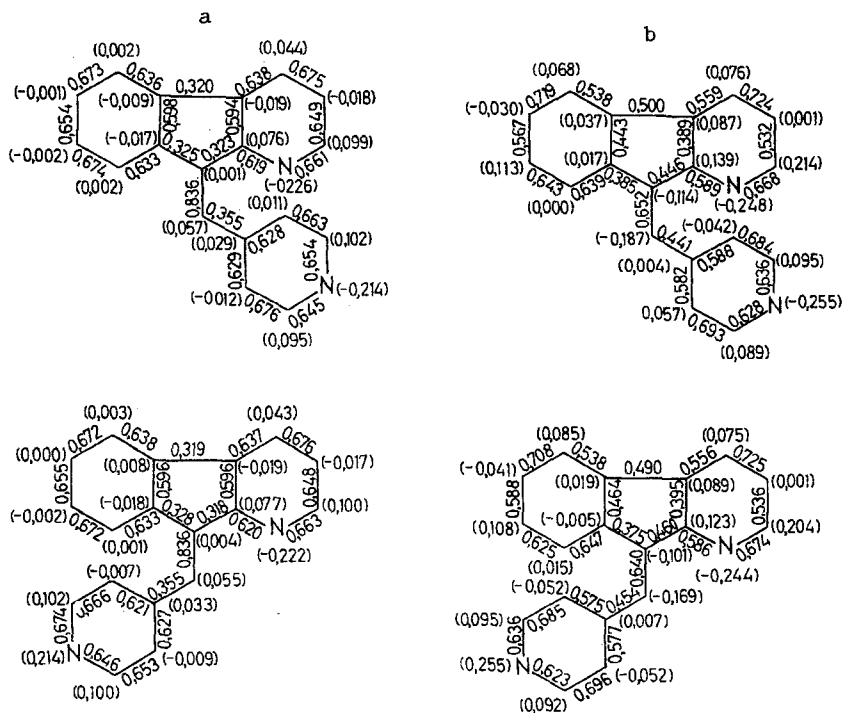


Fig. 2. Molecular diagrams of Z and E isomers of 9-(γ -picolyldene)-1-azafluorene: a) in ground-state (S_0) and b) in first excited state ($S^1\pi\pi^*$).

Comparative analysis of the experimental and theoretically calculated electronic absorption spectra of compound V (Fig. 1) showed that the long-wavelength band of the Z isomer for $\Theta = 0^\circ$ is formed by two one-electron transitions ($S_0 \rightarrow S\pi\pi^{*1}$ and $S_0 \rightarrow S\pi\pi^{*2}$) [λ_{\max}^1 351 nm ($f_{\text{osc}} = 0.11$) and λ_{\max}^2 341 nm ($f_{\text{osc}} = 0.30$)], which agrees well with experimental data (Fig. 1a). In the case of the E isomer, the corresponding calculated data for the long-wavelength absorption band, formed by two analogous transitions with close parameters (Fig. 1a), agree better with the experimental data (Table 2) for $\Theta = 60^\circ$. In this case, the effective disruption of conjugation leads to lessening of the intensity (probability) of the first of the transitions $S_0 \rightarrow S\pi\pi^{*1}$ and $S_0 \rightarrow S_0 \rightarrow S\pi\pi^{*2}$ [λ_{\max}^1 328 nm ($f_{\text{osc}} = 0.068$) and λ_{\max}^2 297 nm ($f_{\text{osc}} = 0.56$)] and their hypsochromic shift relative to the transitions and corresponding bands in the spectra of the Z isomer.

Analysis of the energy levels of the highest occupied and lowest unoccupied molecular orbitals showed that the HOMO and LUMO in the molecule of the Z isomer are relatively closer together compared with the orbitals in the E isomer (Table 3), which also serves as a reason for their spectral differences.

Analysis of the distribution of π -electron density in the molecule of the Z isomer in the ground state (S_0) (Fig. 2a) indicates an overall π -excess of the heterocycle of the Φ_1 ($\Sigma_{qi} = -0.044$ eu) and π -deficiency of Φ_2 ($\Sigma_{qi} = 0.011$ eu), while in the case of the E isomer these quantities are about half as much (Fig. 2b). In the $S_0 \rightarrow S\pi\pi^{*1}$ transition, interfragment transfer of π -electrons from the heterocycle of the Φ_1 fragment to the atom $C_{(9)} = C_{(10)} - \Phi_2$, which reveals the electron-acceptor character of the pyridine fragment Φ_2 , slightly enhanced compared with the aryl fragment of 9-benzylidene-1-azafluorene [3] due to the presence of the nitrogen atom. Taking into account the spatial closeness of the unshared electron pair of the $N_{(1)}$ atom to the Φ_2 fragment in the molecule of the Z isomer of compound V, we can hypothesize that it is possible to form a charge-transfer complex of the $n \rightarrow \pi^*$ type. This hypothesis has also been confirmed by the experimental data and by a theoretical study of the UV spectrum of the protonated forms of compound V (Fig. 1). Upon protonation of the E and Z isomers, we observe approximately identical bathochromic shifts of the long-wavelength band ($\Delta\lambda_{\max}$ 15-20 nm) (both experimental and theoretical), just as in the spectra of 9-benzylidene-1-azafluorenes [3]. Therefore, we can assume that in both cases, protonation occurs at the atom of the fragment Φ_1 (monoprotonated form). A distinguishing feature of the spectrum of the cation of the Z isomer of compound V is the fact that with an increase in the acid concentration (Fig. 1a, curves 2-6), the intensity of the long-wavelength band gradually decreases (in this case, we observe an isosbestic point in the spectrum), compared with the intensity of the corresponding band in the spectra of the cation of the E isomer (Fig. 1b, curve 2). This may be explained by the disappearance

TABLE 3. Energies of Frontier MOs of Z and E Isomers of 4-Picolidene-1-azafluorene (PPP method with CI)

Frontier orbital	Energy* (E), eV			
	Base		Monocation	
	E-	Z-	E-	Z-
HOMO	9,28	9,24	9,39	9,30
LUMO	2,96	2,93	3,28	3,20

*Values of the energy E with a minus sign (-).

TABLE 4. Physical Characteristics of Compounds III-VII

Compound	Overall yield, %	Isomer	Yield, %	T_{mp} , °C	M^+	R_f
III	86	E	86	99...100	256	0,73
IV	96	Z	51	136...138	256	0,45
		E	13	82	256	0,3
V	60	Z	15	101...102	256	0,57
		E	20	87...88	256	0,45
VI	72	Z	22	110...112	256	0,46
		E	5	102...104	256	0,60
VII	96	Z	41	175...176	256	0,36
		E	42	156...157	256	0,41

of the contribution from the $n \rightarrow \pi^*$ transition to this band when the unshared electron pair of the $N_{(1)}$ atom of fragment Φ_1 is blocked due to equilibrium breakdown of the charge-transfer complex.

The experimental similarity of the spectra of the Z isomers of compounds IV and VI with the spectrum of the Z isomer of compound V (Table 2) allows us to also hypothesize that the existence of a charge-transfer complex of the $n \rightarrow \pi^*$ type is also possible for them (in the case of compound VI, the nitrogen atom of fragment Φ_2 probably serves as the electron donor, while the fragment Φ_1 probably serves as the acceptor). In the spectra of compounds III and VII, such a steric interaction is impossible and there are practically no configurational differences in the spectra. This is explained by the mutual repulsion of the unshared electron pairs of both nitrogen atoms in compound III.

Thus, our study of the electronic absorption spectra, the π -electron and spatial structure of 9- $[\alpha(\beta,\gamma)$ -picolyldene]-1(4)-azafluorenes has shown that their Z isomers generally form charge-transfer complexes of the $n \rightarrow \pi^*$ type. This makes it possible to sufficiently reliably identify the isomers from the spectra and in particular from the position in the spectrum of the long-wavelength band, its intensity and structure.

For the Z and E isomers of compounds V and VII, using the PPP method we also calculated the values of the π -dipole moments, which for the Z isomers are 1.32 and 1.17 D, and for the E isomers they are 0.72 and 1.12 D, respectively. Probably the order and ratio of the dipole moments will be analogous for the Z and E isomers of compounds VI, and the different chromatographic mobility of these isomers will be determined by the value of the dipole moment.

EXPERIMENTAL

The PMR spectra were measured on the Bruker WP-80 instrument in $CDCl_3$ solution, internal standard TMS. Column chromatography was done on silica gel L 40/100; eluting agent, ethylacetate-hexane, 20:1. The R_f values were determined by TLC on Silufol UV-254 plates (ethylacetate-hexane, 2:1). The mass spectra were obtained on the MKh-1303 instrument with direct injection of the sample into the ion source with ionizing potential 70 eV. The UV spectra were taken on the Specord UV-VIS spectrophotometer in ethanol.

The elemental analysis data for C, H, and N correspond to the calculated values.

9- $\alpha(\beta,\gamma)$ -Picolylidene-1(4)-azafluorenes (III-VII, C₁₈H₁₂N₂). Four millimoles of finely cut metallic sodium were added to a solution of 1.7 millimoles azafluorene in 30 ml methanol. This was heated to boiling and cooled down to 20°C. A solution of 2 millimoles formylpyridine in 20 ml methanol was added and this was allowed to stand for one day. 30 ml water was added and the methanol was driven off. The reaction products were extracted with ether and then benzene, and then dried with sodium sulfate. The solvents were evaporated and the residue was chromatographed on a column. The isomers of compounds III, IV, V, and VI were crystallized from hexane, while compound VII was crystallized from a mixture of hexane with benzene. All the substances obtained were yellow of different intensities. Their characteristics are presented in Table 4.

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