SYNTHESIS AND STRUCTURE OF AZOMETHINES OF 1-METHYL-2-KETO-3-FORMYLINDOLINE[*]

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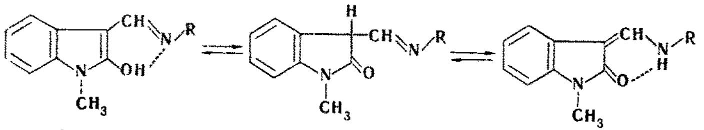
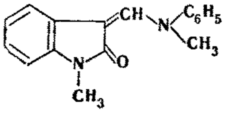
Azomethines of 1-methyl-2-keto-3-formylindoline, to which a ketoamine structure was assigned on the basis of their UV, IR, and PMR spectra, were synthesized. The stability of tautomers of this type is explained by means of quantum-chemical calculations.

A prototropic benzoid-quinoid equilibrium was previously observed in anils of 3-hydroxy-2-formylbenzofurans and 2-formylbenzothiophenes [2-4]. In analogy, the existence of three tautomeric forms (Ia-c) can be assumed for imines of 1-methyl-2-keto-3-formylindoline in solution.



Ia Ib Ic



II

Azomethines and model structure II were obtained by reaction of 1-methyl-2-keto-3-formylindoline with amines or of 1-methyl-2-ketoindoline with diarylformamidines (Table 1). 1-Methyl-2-methoxy-3-formylindole imines, which model the fixed benzoid form, could not be obtained by these methods.

The electronic absorption spectra of azomethines I contain a characteristic band at 370-390 nm, which is shifted hypsochromically by 30-40 nm in the spectrum of the benzylimine (Table 2). This band is practically insensitive to changes in the structure of substituent R, the solvent polarity, and the temperature (Fig. 1), and this constitutes evidence for predominance of only one of the possible tautomeric forms. The spectra of anils I are similar to the spectrum of II, which models fixed quinoid form Ic (Fig. 1). They are in good agreement with the spectral paramenters calculated by the Pariser—Parr—Pople (PPP) self-consistent field (SCF) MO method for tautomer Ic and differ from the calculated spectrum of benzoid structure Ia (Table 3).

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[*] Communication XXII from the series "Benzoid-Quinoid Tautomerism of Azomethines and Their Structural Analogs." See [1] for communication XXI.

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TABLE 1. Azomethines

No.	R	mp, °C	Preparative method	Empirical formula	Found, %			Calc., %		
					C	H	N	C	H	N
1	C_6H_5	142—143	2	$C_{16}H_{14}N_2O$	76,8	5,7	11,1	76,8	5,6	11,3
2	p-$CH_3OC_6H_4$	144	2	$C_{17}H_{16}N_2O_2$	72,7	5,7	9,9	72,8	5,8	10,0
3	p-ClC_6H_4	165	2	$C_{16}H_{13}N_2OCl$[*]	67,8	4,7	9,5	67,5	4,6	9,8
4	p-$NO_2C_6H_4$	275	1	$C_{16}H_{13}N_3O_3$	65,1	4,3	14,0	65,1	4,4	14,2
5	$CH_2C_6H_5$	177	1	$C_{17}H_{16}N_2O$	77,4	6,1	10,3	77,2	6,1	10,6
6[†]	C_6H_5	138	1	$C_{16}H_{14}N_2O$	76,9	5,9	11,4	76,5	5,6	11,6
7	H	146—147	1	$C_{17}H_{16}N_2O$	76,8	6,1	10,8	77,2	6,1	10,6

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[*] Found: Cl 12.7%. Calculated: Cl 12.4%.

[†] The ^{15}N isotope in the amine residue.

TABLE 2. UV and IR Spectra of Azomethines

Compound No[*]	Solvent	UV spectra λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	IR spectra, cm^{-1} (in mineral oil)
1	CCl_4	$\left.\begin{matrix}289\\293\end{matrix}\right\}$ (10,1) $\left.\begin{matrix}373\\382\end{matrix}\right\}$ (16,5)	
	Benzene	292 (13,5), 372 (20,2), 382 (19,8)	1600, 1630, 1680, 2960, 3310
	Methanol	287 (13,2), $\left.\begin{matrix}370\\376\end{matrix}\right\}$ (23,1)	[†]1600, 1630, 1680, 3080, 3300
	DMFA	290 (12,6) $\left.\begin{matrix}372\\380\end{matrix}\right\}$ (22,6)	
2	CCl_4	288 (9,5) 396 (19,0)	
	Benzene	288 (10,0) 384 (19,9)	1610, 1630, 1680, 3100, 3300
	DMFA	286 (11,4) 387 (23,2)	
	Methanol	285 (10,5) 373 (22,2) 384 (22,4)	
3	CCl_4	$\left.\begin{matrix}286\\292\end{matrix}\right\}$ (9,9) 373 (18,2) 385 (18,6)	1610, 1630, 1680, 3100, 3260
	Benzene	$\left.\begin{matrix}285\\292\end{matrix}\right\}$ (9,8) 374 (18,2) 383 (18,5)	
	Methanol	282 (12,5) 287 (11,8) 375 (24,0)	
	DMFA	$\left.\begin{matrix}285\\290\end{matrix}\right\}$ (11,6) 380 (21,8)	
4	Benzene	290 (9,0) 410 (25,4)	1600 1645 1680 3200—3300
	DMFA	276 (8,2) 415 (28,0)	
5	Benzene	285 (22,7) 320 (17,3) 352 (12,0)	
	Methanol	280 (19,6) 322 (15,7) 340 (13,1)	1595 1620 1670 3250
	DMSO	283 (22,2) 321 (16,0) 350 (14,6)	
6			1600 1630 1680 2250 2400
7	Benzene	288 (13,1) 380 (22,0)	1570 1610 1680
	Methanol	280 (12,1) 368 (22,2)	

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[*] See Table 1.

[†] In carbon tetrachloride.

The results of redistribution of the π-electron charges on the atoms during electron transitions caused by long-wave ($S_0 \rightarrow S_1$) and short-wave ($S_0 \rightarrow S_2$) excitation in molecules of the Ic type are shown in the molecular diagram. An analysis of the magnitudes of the increase in the π charges on the atoms makes it possible to draw the following conclusions. (See scheme on following page.)

1) The long-wave $S_0 \rightarrow S_1$ transition is determined by charge transfer from the C, O, and N atoms of the ketoamine fragment to the methylidyne carbon atom: 2) redistribution of the π-electron density from the annelated system and the heterocyclic nitrogen atom to the methylidyne carbon atom without participation of the electrons of the oxygen atom is responsible for the short-wave $S_0 \rightarrow S_2$ transition. In both cases, the π-electron system of the amine

TABLE 3. Calculated and Experimental Characteristics of Azomethines

Compound	Theoretical spectrum		Solvent	Exptl. spectrum	
	λ, nm	f*		λ, nm	f
1-Methyl-3-(N-phenylaminomethylene)-2-ketoindoline	298 356	0,11 0,57	Benzene	289 293	0,16
				373 382	0,53
			Alcohol	287	0,17
				370 376	0,56
			DMFA	290	0,15
				372 380	0,56
1-Methyl-2-methoxy-3-formyl indole	274 340	0,07 0,88			

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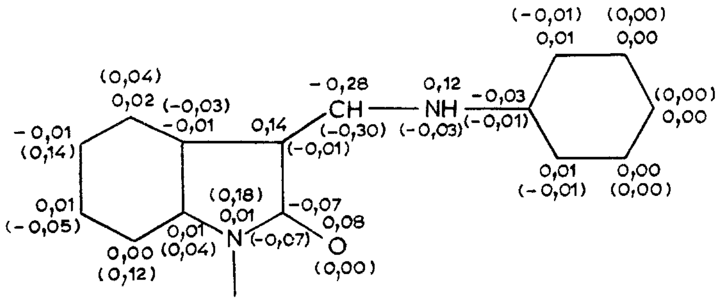
*The symbol f indicates the oscillator force.

TABLE 4. Differences in the Heats of Atomization with Allowance for the Differences in the Solvation Energies of Tautomers Ic and Ia

R	$\Delta\Delta H_a$, kcal/mole		
	gas	ε=2,2	ε=48,9
H	8,72	18,96	27,12
C_6H_5	6,32	16,78	25,10



benzene ring remains practically unperturbed by the indicated transitions.

Thus an analysis of the data from the electronic absorption spectra leads to the conclusion that 1-methyl-2-keto-3-formylindoline azomethines exist primarily in quinoid form Ic. The PMR spectra of anils I contain the signal of the proton of an NH group with J = 13.5 Hz, which disappears upon deuteration, at weak field at δ ∿ 10.6 ppm. It is characteristic for the $>$CH–NH– AB system (Fig. 2). A comparison of the chemical shifts of the protons of the NH group with the analogous shifts in the spectra of the anils of formylbenzofurans and formylbenzothiophenes [2-4] confirms that this value does not depend on the nature of the ring heteroatom.

A doublet of the CH proton with J = 13.5 Hz, which gives a singlet upon deuteration, appears at 7.9 ppm. The spectrum of the benzylimine contains, in addition to the signals presented above, a doublet of the protons of the benzyl CH_2 group at 5.6 ppm with J = 6 Hz, which is close to the splitting constants of the benzyl protons in anils with a thione–enamine structure [5]. After N-deuteration, the CH_2 protons appear as a singlet. PMR

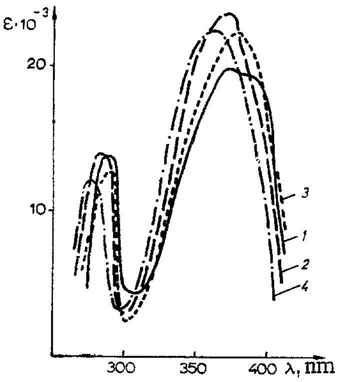


Fig. 1

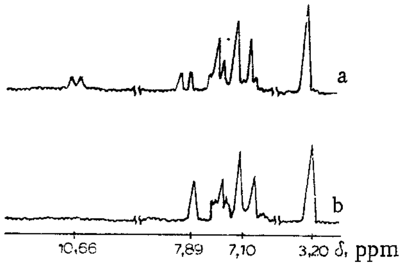


Fig. 2

Fig. 1. Electronic absorption spectra of 1-methyl-3-(N-phenylaminomethylene)-2-ketoindoline in benzene (1), methanol (2), and dimethylformamide (3), and of 1-methyl-3-[N-(methyl)-phenylaminomethylene]-2-ketoindoline in methanol (4).

Fig. 2. PMR spectra of 1-methyl-3-(N-phenylaminomethylene)-2-ketoindoline in methylene chloride: a) undeuterated; b) deuterated.

spectra of this type are characteristic only for structure Ic.

Spin-Spin coupling of the ^{15}N and H nuceli with J_{NH} = 92 Hz is observed in the spectrum of the phenylimine with a ^{15}N isotope. Its magnitude does not change as the temperature is varied, and this constitutes evidence for the absence of proton exchange in the ketoamine fragment. The absence in the PMR spectra of signals corresponding to splitting of the protons in the $>$CHCH=N— group (structure Ib) makes it possible to exclude this tautomer form from consideration.

The IR spectra of the azomethines under consideration also confirm structure Ic (Table 2). They contain a strong band at 1680 cm^{-1}, which is characteristic for the stretching vibrations of the ring carbonyl group, and less intense absorption at 1610-1630 cm^{-1}, which is associated with an exocyclic C=C bond. The same bands are observed in the spectrum of II. Distinctly expressed bands of stretching vibrations of the NH group, which are shifted to 2250-2400 cm^{-1} on deuteration, are present at 3100-3300 cm^{-1}.

The data obtained regarding the relative stability of tautomer Ic (as compared with Ia) are explained by means of calculations by the PPP SCF MO method with the Dewar σ, π parametrization [6, 7]. The differences in the heats of atomization ($\Delta\Delta H_a$) of the quinoid and benzoid forms with allowance for the differences in the solvation energies of tautomers I are presented in Table 4. The calculation predicts the complete preferableness of quinoid form Ic, regardless of the character of radical R and the polarity of the medium; this was previously demonstrated for other heterocyclic systems.

EXPERIMENTAL METHOD

The absorption spectra in the UV and visible regions were recorded with a Specord UV-vis spectrophotometer (German Democratic Republic). The IR spectra were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Tesla BS-407c spectrometer (80 MHz) at 25° and an XL-100/15 spectrometer (100 MHz) at 30, 60, and 90°. The compound concentrations were 10-15 and 3-5% in methylene chloride or dimethyl sulfoxide. The internal standard was hexamethyldisiloxane.

The fundamental details and parameters for the calculation of the relative stabilities of the benzoid and quinoid tautomers and of the electronic absorption spectra and characteristics of the excited states were examined in detail in [8-10].

1-Methyl-2-methoxy-3-formylindole and 1-methyl-3-methoxymethyl-2-ketoindoline [12], which were separated by repeated crystallization from hexane or heptane, were formed simultaneously in the methylation of 1-methyl-2-keto-3-formylindoline [11] with diazomethane.

Anils I and II were prepared by the following two methods.

1. 1-Methyl-2-keto-3-formylindoline was condensed with benzylamine or with aromatic amines by heating equimolecular amounts of them in alcohol for 0.5-1 h. The products were purified by crystallization from ethanol or propanol. The yields were quantitative.

2. A mixture of 1-methyl-2-ketoindoline and the appropriate diarylformamidine in alcohol was refluxed for several hours, and the products were crystallized. The yields were 50-70%. All of the anils were yellow or orange crystalline substances.

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