of Ib (mp 245°C) or form aqueous ethanol in the case of Ic (mp 235-237°C)]. The alcohol solution (in the preparation of Ia) was cooled to 0°C, 3 ml of a 30% solution of sodium hydroxide was added, and coupling with p-toluenediazonium chloride (from 4.2 mmole of p-toluidine in 10 ml of 2 N HCl and 4.5 mmole of sodium nitrite) was carried out while maintaining the pH of the medium at 9-10. At the end of the addition of the diazonium salt, the reaction mixture was maintained at 0°C for 1 h, after which it was carefully neutralized with hydrochloric acid solution, and the precipitate was removed by filtration. Compounds Ib, c were similarly obtained. Coupling was carried out at 0°C, and the reaction mixture was allowed to stand for 24 h. In the case of Ib DMF was used as the solvent. Formazans Ia-c were crystallized from ethanol or ethanol—water (Table 3).

1,5-Bis(1-aryl-2-benzimidazolyl)-3-methylformazans. These compounds were obtained as dark crystals with a metallic luster by autooxidation in ethanol in the presence of sodium acetate (Table 3).

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TAUTOMERISM OF AZINE DERIVATIVES. 4.* KETO-ENOL TAUTOMERISM OF β-KETO ESTERS OF THE AZINE SERIES

S. A. Stekhova, O. A. Zagulyaeva, V. V. Lapachev, and V. P. Mamaeva

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The structures of pyrazinoyl-, 3-pyridazinoyl-, 4-pyrimidoyl-, and 2-, 3-, and 4-pyridoylacetic esters were studied by means of IR, NMR, and ^1H and ^{13}C NMR spectroscopy and quantum-chemical calculations (Pariser—Parr—Pople and CNDO/2). The effect of solvents (including strongly and weakly basic solvents) on the position of the tautomeric equilibria of these β-keto esters was studied. The σ^+ constants for the keto and enol fragments were estimated by means of quantum-chemical calculations and ^{13}C NMR spectroscopy.

Little study has been devoted to the tautomerism of azine analogs of β-dicarbonyl compounds of the benzene series [2-4], although the presence of a heteroatom that is capable of forming a hydrogen bond and undergoing protonation may have a substantial effect on the structures of the tautomeric forms and on the position of the equilibrium between them.

In the present research we studied the tautomerism of aza analogs of benzoylacetic esters (I-VI) in various solvents.

Compounds I-VI, together with the previously described 2-pyrimidoyl [2] and 4-pyridazinoylacetic [3] esters, represent a series of azinoylacetic esters that contain most of the possible combinations of one or two nitrogen atoms in the ring with respect to the tautomeric

*See [1] for communication No. 3.

Novosibirsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Novosibirsk 6300090.

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TABLE 1. Parameters of the PMR Spectra of the β-Keto Esters (for 3-5% Solutions at −35°C)

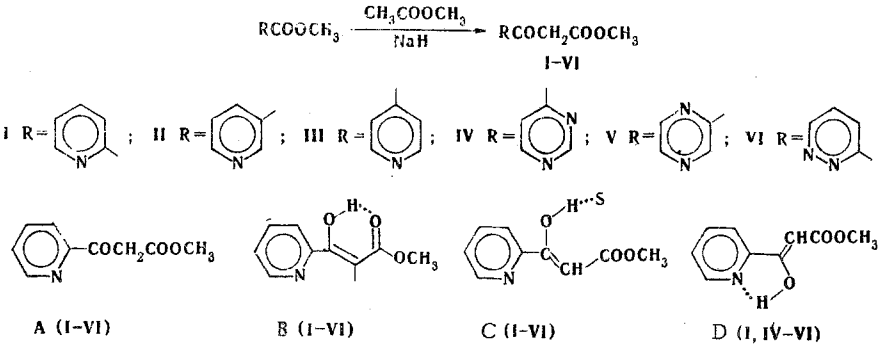
Compound	Solvent	Chemical shifts, δ, ppm					Enol content, * %
		=CH	CH_2	OCH_3 k	OCH_3 e	OH	
I	$CDCl_3$	6,33	4.21	3,73	3,81	12,5	25
	CCl_4	6,29	4,16	3,66	3,76		34
	CF_3COOH						61
II	$CDCl_3$	5,70	3,90	3.74	3,80		35
	CCl_4	5,69	3,96	3,76	3,80	12,46	63
	CF_3COOH						48
III	$CDCl_3$	5,80	4.02	3,76	3.82		57
	CCl_4	5,70	3,92	3,72	3,85	12,32	82
	CF_3COOH						85
IV	$CDCl_3$	6,43	4,16	3,71	3,83		55
	CCl_4	6,47	4,07	3,73	3,83	12,2	80
	CF_3COOH						82
V	$CDCl_3$	6,34	4,20	3,76	3,84		35
	CF_3COOH						84
VI	$CDCl_3$	6,66	4.38	3,74	3,80		21

*The relative percentages of the keto (k) and enol (e) forms were determined from the ratio of the integral intensities of the signals of the protons of the methoxy groups.

fragment. On the bssis of this series it is convenient to discuss the effect of the nitrogen atom in various positions of the heteroaromatic ring on the keto-enol equilibrium.

β-Keto esters I-VI were synthesized by ester condensation of methyl esters of heterocyclic acids with methyl acetate. The structures of the tautomeric forms of the β-keto esters were studied by means of IR and ^{13}C and ^{1}H NMR spectrocopy.

On the basis of the literature data [2, 5] we examined the possibility of the existence of the β-keto esters in tautomeric forms of the A-D types:



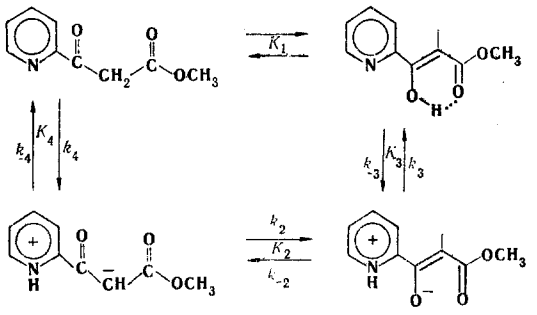
It is known [6] that bases that are capable of forming a strong intermolecular hydrogen bond favor the development of tautomer C. One of the peculiarities of β-keto esters of the azine series may be the development of tautomer C even in the absence of strongly basic additives, in which case the heterocyclic ring, particularly the pyridine ring, may act as the base. In fact, the transition from dilute solutions of I in $CHCl_3$, for which cleavage of the intramolecular hydrogen bond is unlikely, to pure liquids is accompanied by a change in the position of the δ_{OH} signal in the PMR spectra (12.5 and 12.0 ppm, respectively); this is usually associated with cleavage of the intramolecular hydrogen bond and the formation of an intermolecular hydrogen bond [6, 7]. At the same time, in the case of benzoylacetic ester the position of the signal is virtually independent of the concentration (12.6 ppm for $CHCl_3$ as compared with 12.7 ppm for the pure liquid). Judging from the invariability of the position of the δ_{OH} signal in the 1-10% concentration range, the presence of form C in dilute solutions of I-VI in $CHCl_3$ is not characteristic. An analysis of the IR spectra of solutions of the compounds in CCl_4 and $CHCl_3$, in which absorption of the OH group, which participates in intermolecular hydrogen bonding [8] (3200-3450 cm^{-1}), is absent, leads to the same conclusion. The data from the IR spectra also simultaneously constitute evidence for the absence of tautomer D, for the five-membered chelate ring of which the characteristic frequencies

of the vibrations of the OH groups are found in the same region [2, 9]. Thus, the formation of a five-membered chelate ring for the β-dicarbonyl compounds of the azine series is evidently not characteristic, and the conclusions in [4] regarding the existence of a tautomer of the D type for the β-diketones of the pyridine series require more rigorous evidence.

The presence of vibrations of ketone (1720-1730 cm^{-1}) and ester (1730-1750 cm^{-1}) carbonyl groups, as well as vibrations at 1615-1670 cm^{-1} due to the absorption of a carbonyl group that is conjugated with a double bond and participates in the formation of an intramolecular hydrogen bond [8], indicates the presence of keto form A and enol form B in neutral solvents. The increase in the percentage of the A form in the tautomeric mixture (the increase in the intensity of the bands of the carbonyl groups of keto form A) on passing from CCl_4 to the more polar $CHCl_3$, which is in good agreement with the well-known concepts of the effect of polarity of the medium on keto-enol equilibria [5], is a confirmation of the fact that the β-keto esters exist in solutions in the form of a mixture of two tautomeric forms A and B. The existence of a tautomeric equilibrium with the participation of forms A and B is also confirmed by the PMR spectroscopic data (Table 1).

An analysis of the effect of solvents (including strongly and weakly basic solvents) on the position of the tautomeric equilibria of I-VI shows that the β-keto esters (I-VI) of the azine series have important features as compared with their benzene analogs [11, 12]. It is known [6] that strongly basic solvents (for example, hexametapol) in many cases cleave the intramolecular hydrogen bond. In our investigation of the structures of the β-keto esters in strongly basic solvents we used the data in [13, 14], according to which cleavage of the intramolecular hydrogen bond in chelates and the formation of an intermolecular hydrogen bond with the solvent is accompanied by a 4-5 ppm shift of the signal of the carbon atom of the carbonyl group in the ^{13}C NMR spectrum to strong field. Judging from our calculations by the CNDO/2 method, this shift is not a random shift and is in agreement with a change in the electron density on the carbon atom of the carbonyl group. The signal of the carbonyl carbon atom of the enol form in the ^{13}C NMR spectra recorded for 4-pyridoylacetic ester is shifted 1.4 ppm to strong field on passing from chloroform (171.2 ppm) to chloroform–hexametapol (1:2) (169.8 ppm). Thus, it may be assumed that, just as in the case of their benzene analogs [15], the equilibria of azinoylacetic esters I-VI in strongly basic solvents are characterized by the presence of appreciable amounts of nonchelate enol form C. As in the case of β-keto esters of the benzene series [5], the equilibrium percentage of the keto form for I-VI increases as the polarity of the solvent increases (Table 1). However, in protonating media (of the CF_3COOH type) the percentage of the keto form decreases markedly as compared with $CHCl_3$; whereas this effect is observed in CF_3COOH for pyrimidoylacetic esters, it is observed in CH_3COOH for more basic pyridoylacetic esters.

The tautomeric equilibrium with the participation of the protonated forms can be depicted by the scheme



The relationship between the acid-base equilibrium and tautomeric equilibrium constants K_1-K_4 can be obtained starting from the properties of the standard chemical potentials [16]: $\Delta\mu_1^0=\Delta\mu_2^0+\Delta\mu_3^0+\Delta\mu_4^0$. After the substitution $\Delta\mu_i=-RT\ln K_i$ and conversion to the antilogarithms we obtain $K_1=K_2\cdot K_3\cdot K_4$ or $K_2=K_1\cdot K_e/K_\kappa$, where K_1 and K_2 are the tautomeric equilibrium constants, and K_e and K_k are the basicity constants of the enol and keto forms, respectively.

We have previously [2] assumed that the basicity of the enol form is greater than that of the keto form and that this is also responsible for the shift of the tautomeric equilibrium to favor the enol form on passing to protonating media. The adjusted data obtained by means of quantum-chemical calculations, the Pariser–Parr–Pople (PPP) method with the usual parametrization, and ^{13}C NMR spectroscopy serve as reliable evidence for this. Thus a calculation

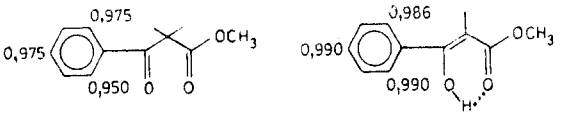


Fig. 1. π-Electron densities in the ortho and para positions of the benzene ring for the tautomers of benzoylacetic ester calculated by the Pariser–Parr–Pople method.

TABLE 2. Characteristics of β-Keto Esters I-VI

Compound	mp, °C	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
I	140 (5)*	60,6	5,1	7,4	$C_9H_9NO_3$	60,3	5,0	7,8	56
II	34—36	60,0	5,1	7,4	$C_9H_9NO_3$	60,3	5,0	7,8	35
III	72—75	60,3	5,0	7,9	$C_9H_9NO_3$	60,3	5,0	7,8	39
IV	82—90	53,3	4,6	15,7	$C_8H_8N_2O_3$	53,3	4,4	15,5	23
V	103—105	53,4	4,6	15,7	$C_8H_8N_2O_3$	53,3	4,4	15,5	33
VI	95—97	53,5	4,5	15,7	$C_8H_8N_2O_3$	53,3	4,4	15,5	35

*This is the boiling point.

of the π-electron densities for the tautomeric forms of benzoylacetic ester clearly indicates a large electron deficit in the ortho and para positions of the benzene ring of the keto form (Fig. 1).

The signals of the ring =C—H carbon atoms of the keto form are located at weaker field in the ^{13}C NMR spectra of the 4-pyridoylacetic and benzoylacetic esters as compared with the analogous signals of the enol form. Using the well-known dependence of the ^{13}C NMR chemical shifts of the para carbon atoms in monosubstituted benzenes on the σ^+ constants of the substituents [17], one can quantitatively determine the acceptor capacities of the ketone and enol fragments. The chemical shifts of the para carbon atoms in the keto form of benzoylactic ester and the enol form are, respectively, 133.3 and 130.8 ppm and correspond to $\sigma_k^+ =$ 0.61 for the ketone fragment and $\sigma_e^+ = 0.34$ for the enol fragment. The σ_k^+ and σ_e^+ values presented above make it possible to explain the increase in the percentage of the enol for the benzoylacetic esters and their aza analogs that occurs when acceptor substituents [11, 12] or a heteroatom (III and IV) are introduced in the para position of the aromatic ring. Taking the σ_k^+ and σ_e^+ values into account, one should except a substantial effect of electron-donor and electron-acceptor substituents on the thermodynamic stabilities of both the ketone and enol forms (compare with [11]). However, the ratio of the σ^+ values is responsible for the fact that electron-donor substituents favor the keto form (since $\sigma_k^+ < \sigma_e^+$), whereas electron-acceptor substituents and a heteroatom favor the enol form.

Thus, our study shows that the presence of a heteroatom leads to the development of specific properties of azinoylacetic esters as compared with benzoylacetic esters, viz., association in concentrated solutions (I) and an increase in the degree of enolization in protonating media (I-V).

The latter property is a characteristic feature of β-keto esters of the azine series and possibly of other β-dicarbonyl derivatives of azines.

EXPERIMENTAL

The IR spectra were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Varian A56/60A spectrometer with hexamethyldisiloxane as the external standard. The ^{13}C NMR spectra of 10-20% solutions of the compounds were recorded with a Bruker WP-80 spectrometer. In the case of the benzoylacetic ester the ^{13}C NMR signals of the carbon atoms in the para position relative to the tautomeric fragment were assigned on the basis of the literature data for substituted benzenes [17]. The choice between the signals of the para carbon atoms of the keto and enol forms was made by an analysis of the change in the intensities of the two signals of the para carbon atoms in various solvents that have a slight effect on the position of the signals but substantially change the tautomeric equilibrium constant. The direction of the change in the equilibrium was monitored by PMR spectroscopy. The chemical shifts of the ring carbon atoms of benzoylacetic ester relative to the signal of tetramethylsilane were as follows: enol form 130.8 (p-C), keto form 133.3 ppm (p-C); the ortho and meta carbon atoms of both tautomers resonated at 128.3 ppm; 4-pyri-

doylacetic ester: keto form 149.3 (C_2) and 119.0 ppm (C_3), enol form 148.7 (C_2) and 118.0 ppm (C_3).

Protonation. The spectra of 5% solutions of I-VI in trifluoroacetic and acetic acids were recorded. The percentage of the enol was determined from the integral intensities of the signals of the methoxy groups of the keto and enol forms.

The methyl esters of pyridinecarboxylic, pyrazinecarboxylic, pyridazine-3-carboxylic, and pyrimidine-4-carboxylic acids were synthesized by the methods in [21-24].

Azinoylacetic Esters (I-VI). A 0.02-mole sample of sodium hydride and two to three drops of methanol (as the catalyst) were added to a solution of 0.01 mole of the methyl ester of the corresponding carboxylic acid in 20-50 ml of monoglyme, and a solution of 0.02 mole of methyl acetate in 5 ml of monoglyme was added with thorough stirring in a stream of argon to the resulting suspension. The mixture was refluxed for 3-6 h. The end of the reaction was determined by means of thin-layer chromatography (TLC) on silufol UV-254 (elution with ethyl acetate). After removal of the solvent by distillation, the sodium salt of the keto ester was dissolved in a small amount of ice water, and the solution was washed with petroleum ether. The aqueous layer was acidified with stirring under a layer of diethyl ether, and the aqueous layer was separated and extracted three times with methylene chloride. The extracts were combined and dried over magnesium sulfate, and the solvent was removed by distillation. Compound I was purified by vacuum distillation, II-V were purified by recrystallization from petroleum ether (70-100°C), and VI was purified by sublimation [at 90°C and 20 mm (mercury column)]. The characteristics of I-VI are presented in Table 2.

Programs provided by I. I. Zakharov were used in the quantum-chemical calculations, which were performed in the GP Computer Center of the Siberian Branch of the Academy of Sciences of the USSR. The formamide molecule was used as the solvent molecule in the calculations. The geometry of the molecules was selected in accordance with [18-20].

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