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SYNTHESIS AND PROPERTIES OF 2-SUBSTITUTED 1-ARYL-7,8-DIHYDRO-6H-PYRIMIDO[4,5-*b*]PYRINDINE-4-ONES

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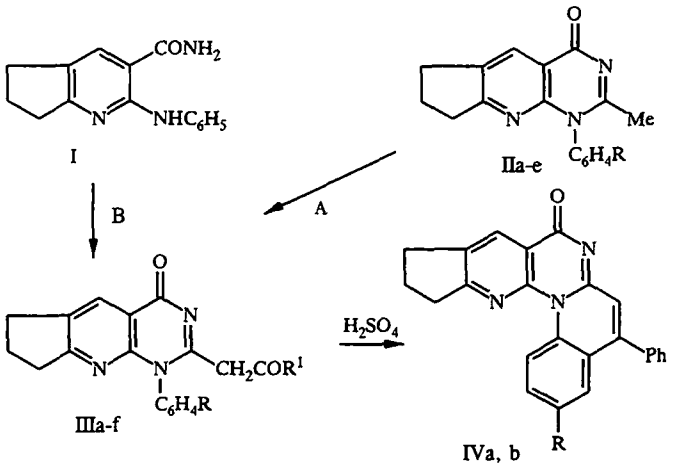
In reaction with acylating agents, 2-aryl-2-methyl-7,8-dihydro-6H-pyrimido[4,5-b]pyrindin-4-ones are acylated at the methyl group and also enter into reaction with diethyl oxalate. 1-Aryl-2-phenacyl-7,8-dihydro-6H-pyrimido[4,5-b]pyrindin-4-ones undergo dehydration under the influence of concentrated sulfuric acid. On the basis of the PMR and UV spectra, it was concluded that 1-aryl-2-acetonyl(phenacyl)-7,8-dihydro-6H-pyrimido[4,5-b]pyrindin-4-ones exist in two tautomeric forms with strong intramolecular hydrogen bonds of the chelate type — enaminocarbonyl and enol.

In one of our previous communications [1], we described the synthesis of 1-aryl-2-methyl-7,8-dihydro-6H-pyrimido[4,5-*b*]pyrindin-4-ones, which readily undergo condensation with aldehydes at the active methylene group at position 2. In order to investigate the reactivity of the methyl group in these compounds further, we carried out acylation and studied the properties of the obtained substances.

The investigations showed that compound (I) underwent acetylation when heated with an excess of acetic anhydride (method A) and was converted into 1-phenyl-2-acetonyl-7,8-dihydro-6H-pyrimido[4,5-*b*]pyrindin-4-one (IIIa) (Table 1). Compound (IIIa) was formed with a smaller yield by boiling 2-anilino-6,7-dihydro-5H-pyridine-3-carboxamide (I) [2] with acetic anhydride in the presence of anhydrous sodium acetate (method B).



II, III a,b R = H, c R = *p*-OMe, d R = *p*-Br, e R = *p*-Me, f R = *m*-Me; III a R^1 = Me, b,c,d R^1 = Ph, e R^1 = NHPh, f R^1 = COOEt; IVa R = H, b R = Br

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TABLE 1. Characteristics of the Synthesized Compounds (IIIa-f, IVa, b)

Compound	Molecular formula	Found, %			Calculated, %			mp, °C	UV spectrum, λ_{max} (log ε)†	R_f	Yield, %
		C	H	N	C	H	N				
IIIa	$C_{19}H_{17}N_3O_2$	71,21	5,56	13,29	71,49	5,32	13,16	292...293	—	0,86	72
IIIb	$C_{24}H_{19}N_3O_2$	75,51	4,68	11,28	75,21	4,98	11,01	199...201	—	0,51	46
IIIc	$C_{25}H_{21}N_3O_3$	73,27	4,90	10,02	73,02	5,11	10,21	226...228	271(4,03), 330 (4,34), 372 (4,18)	0,82	72
IIId*	$C_{24}H_{18}BrN_3O_2$	—	—	8,81	—	—	8,57	284...285	—	0,43	61
IIIe	$C_{25}H_{22}N_4O_2$	71,65	5,01	13,03	71,45	5,23	13,32	171...173	255 (3,91), 319 (4,02), 355 pl (3,53)	0,76	86
IIIf	$C_{22}H_{21}N_3O_4$	67,29	5,68	10,98	67,54	5,37	10,73	157...159	255 (3,79), 318 (4,05), 356 (3,70)	0,73	85
IVa	$C_{24}H_{17}N_3O$	79,67	4,35	11,78	79,35	4,68	11,56	242...243	227 (4,45), 293 (3,90), 384 (4,33)	0,94	62
IVb	$C_{24}H_{16}BrN_3O$	—	—	9,16	—	—	9,49	271...273	228(4,51), 288 (3,94), 386 (4,31)	—	68

*For compound (IIId), found, %: Br 16.56, calculated, %: Br 16.30. For compound (IVb), found, %: Br 17.79, calculated, %: Br 18.07.
†UV spectrum of compound (IIa), λ_{max} (log ε): 220 (4.45), 315 (3.90).

TABLE 2. PMR Spectra of the Synthesized Compounds (IIIa-f, IVa, b) in $CDCl_3$

Compound	Chemical shifts, δ, ppm†						
	CH_2 (6,8), m (4H)	CH_2 (7), m (2H)	CH_3, s	=CH, s	H_{arom}, m	$H_{\gamma\text{-pyrid}}$, s	$H_{chelate\ ring}$, s
IIIa	2,62...2,99	1,99...2,29	1,84	4,37	7,09...7,64	8,14	14,09
IIIb	2,59...2,97	1,85...2,15	—	4,89	7,24...7,89	8,15	14,67
IIIc	2,65...2,93	1,85...2,30	3,87	5,12	7,00...7,60	8,09	14,57
IIId	2,62...2,98	1,92...2,33	—	5,11	7,06...7,57	8,26	12,94
IIIe†	2,60...3,07	1,85...2,18	2,24	3,76	6,84...7,60	8,33	13,17
IIIf	2,64...2,97	1,88...2,18	2,26; 1,21 t	3,83	6,64...7,58	7,92	10,39
IVa	2,45...2,82	1,58...1,84	—	5,07	7,02...7,58	8,04	—
IVb	2,28...2,62	1,64...1,89	—	4,91	7,06...7,69	8,27	—

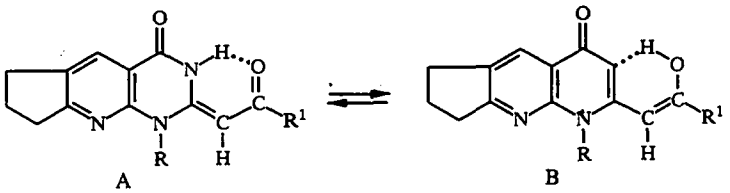
*The signal of the NH group is observed at 7.98-8.18 ppm.
†The spectrum of compound (IIIb) was recorded in DMSO-d_6.

When heated with benzoyl chloride and triethylamine in dry benzene, compounds (IIb-d) give 1-aryl-2-phenacyl-7,8-dihydro-6H-pyrimido[4,5-*b*]pyridin-4-ones (IIIb-d). The reaction of compound (IIe) with phenyl isocyanate in benzene gives 1-tolyl-2-(N-phenylcarbamoylmethyl)-7,8-dihydro-6H-pyrimido[4,5-*b*]pyrindin-4-one (IIIe). In ester condensation with diethyl oxalate in the presence of sodium ethoxide in anhydrous ethanol, compound (IIf) is converted into 1-(3-tolyl)-2-ethoxalylmethyl-7,8-dihydro-6H-pyrimido[4,5-*b*]pyrindin-4-one (IIIf).

The ease with which the reactions occur is due to the high mobility of the hydrogen atoms of the methyl group at position 2 of compounds (IIa-e), and this results from the hyperconjugation in the O=C−N=C−CH_3 system. The methylene group at position 8 has significantly lower CH acidity and does not react either with acylating agents or with aldehydes [1].

The structure of the synthesized compounds was studied by means of the UV, IR, and PMR spectra. In the UV spectra of (IIIb, f), in contrast to those of (IIa) (Table 1), there is a bathochromic shift, and an additional long-wave band appears due to the increase in the length of the conjugation chain.

The presence of signals at 3.83-5.12 ppm, due to the ethylene proton, and at 10.39-14.67 ppm, due to the protons of the chelate ring, indicates that they exist in the form of the enaminocarbonyl (A) and iminoenol (B) tautomers with an intramolecular hydrogen bond.



A B

In the IR spectrum of compound (IIIa) there is a band at 1685 cm^{-1}, due to the absorption of the keto group at position 4. The IR spectra of the other compounds also correspond to the structures assigned to them. The vibrations of the N−H bonds, which could be expected in the case of the nonchelate NH tautomers, are not observed. Thus, the data from the PMR and IR spectra make it possible to conclude that the nonchelate OH and NH tautomers are practically absent for compounds (IIIa-f).

Under the influence of concentrated sulfuric acid at 20°C, compounds (IIIb, d) undergo cyclization with the formation of 5-aryl-8-oxo-8,14-dihydrocyclopentano[2,3]pyrido[2,3-*a*]-4,11-phenanthrolines (IVa, b), the PMR spectra of which, unlike the initial substances, do not contain the signals of the protons of the chelate ring, while the signal of the proton of the =CH− group is shifted downfield. The UV spectra of these compounds have a bathochromic shift compared with the spectra of compounds (IIa) and (III) and also of 1-phenyl-2-styryl-6,7,8,9-tetrahydropyrimido[4,5-*b*]quinolin-4-one [3], due to the annellation of the two six-membered aromatic rings.

EXPERIMENTAL

The IR spectra were recorded in Vaseline oil on UR-20 and Specord M-80 instruments. The UV spectra were obtained in ethanol on an SF-16 instrument ($C = 1 \cdot 10^{-5}$ M). The PMR spectra were obtained on a Tesla B5-587 A instrument (80.023 MHz) at 20°C for 5% solutions of the compounds with HMDS as internal standard. Thin-layer chromatography was conducted on Silufol UV-254 plates (1:1 butanol−benzene).

1-Phenyl-2-acetonyl-7,8-dihydro-6H-pyrimido[4,5-*b*]pyrindin-4-one (IIIa). A. A solution of 2.77 g (0.01 mole) of 1-phenyl-2-methyl-7,8-dihydro-6H-pyrimido[4,5-*b*]pyrindin-4-one in 10 ml of acetic anhydride was heated at 140°C for 4 h. The mixture was poured into water, and the precipitate was filtered off and crystallized from ethanol.

B. A mixture of 2.53 g (0.01 mole) of 2-anilino-6,7-dihydro-5H-pyrindine-3-carboxamide, 0.8 g (0.01 mole) of anhydrous sodium acetate, and 10 ml of acetic anhydride was boiled for 9 h. The mixture was then poured into water, and the precipitate that separated was crystallized. We obtained 1.53 g (48%) of compound (IIIa); mp 292-293°C. A mixed melting test with compound (IIIa) obtained under the conditions of expt. A did not give a melting point depression.

1-Aryl-2-phenacyl-7,8-dihydro-6H-pyrimido[4,5-*b*]pyrindin-4-ones (IIIb-d). A 0.01-mole sample of the compound (IIb-d) was dissolved in 50 ml of dry benzene, and 0.2 ml of triethylamine and a solution of 0.01 mole of benzoyl chloride in 3 ml of dry benzene were added. The mixture was boiled for 10 h. The precipitated triethylamine hydrochloride was filtered off, the benzene was evaporated, and the residue was crystallized from ethanol.

1-(4-Tolyl)-2-(N-phenylcarbamoylmethyl)-7,8-6H-pyrimido[4,5-*b*]pyrindin-4-one (IIIe). A solution of 2.91 g (0.01 mole) of (IIe) and 1.2 g (0.01 mole) of phenyl isocyanate in 20 ml of dry benzene was boiled for 2 h. The solvent was distilled, and the residue was crystallized from ethanol.

1-(3-Tolyl)-2-ethoxalylmethyl-7,8-dihydro-6H-pyrimido[4,5-*b*]pyrindin-4-one (IIIf). A solution of 2.91 g (0.01 mole) of compound (IIf), 1.46 g (0.01 mole) of diethyl oxalate, and 0.68 g (0.01 mole) of sodium ethoxide in 20 ml of anhydrous ethanol was boiled for 5 h, cooled, and treated with 10% hydrochloric acid solution. The precipitate was filtered off, dried, washed with ether, and crystallized from ethanol.

5-Aryl-8-oxo-8,14-dihydrocyclopentano[2,3]pyrido[2,3-*a*]-4,11-phenanthrolines (IVa, b). We dissolved 0.01 mole of the compound (IIIb, d) in 2 ml of acetic acid and added 10 ml of concentrated sulfuric acid. After standing for 72 h at 20°C, the mixture was diluted with water. The precipitate was filtered off, treated with a 10% solution of sodium carbonate and with water, dried, and crystallized from dimethylformamide.

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