SYNTHESIS AND STUDY OF 2-(1-PYRAZOLYL)PYRIMIDINE DERIVATIVES

A. V. Ivashchenko and V. M. Dziomko

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Alkyl derivatives of 2-(1-pyrazolyl)-4(3H)-pyrimidinone were synthesized and converted to 4-chloro-, 4-arylamino-, and 4-hydrazino-2-(1-pyrazolyl)pyrimidines. The corresponding hydrazones were obtained by reaction of 5-ethyl-2-hydrazino-6-methyl-2-(4-ethyl-3,5-di-n-propylpyrazolyl)pyrimidine with isatin and salicylaldehyde. The UV and IR spectra of the synthesized compounds were studied. It was established that the hydrazones contain intramolecular hydrogen bonds.

In a continuation of research on the synthesis and study of azaheterocyclic ligands [1, 2] we have obtained, as described in [3-5] (scheme), alkyl derivatives of 2-(1-pyrazolyl)-4(3H)-pyrimidinone (III-V). The structures of the compounds obtained were confirmed by the results of elementary analysis (Table 1), the UV (Table 2) and IR spectra, and chemical transformations.

The IR spectra of dilute solutions of III-V in CCl_4 contain a band of stretching vibrations of an N−H bond (3385 cm^{-1}) and an "amide I" band (1678 cm^{-1}); this indicates that they have an amide structure. A shift of the absorption bands is observed in the UV spectra of I-V in 1 N ethanolic KOH as compared with the UV spectra of solutions in ethanol; this is explained by a change in the conjugation chain in the anions as compared with the neutral molecules.

As in [6, 7], 4-chloro- (VI, VII), 4-(p-n-butylphenylamino)- (VIII) and 4-hydrazino-2-(1-pyrazolyl)pyrimidines (IX, X) were obtained successively from IV and V. The latter were converted to hydrazones (XI, XII) by reaction with isatin and salicylaldehyde in ethanol.

TABLE 1. Synthesized Compounds

Compound	mp, °C[a]	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
II	236 (dec.)	50,1	7,2	33.6	$C_7H_{12}N_4O$	50,0	7,2	33,3	54
III	134,5—135,5	62,4	6,8	24.0	$C_{12}H_{16}N_4O$	62,1	6,9	24,1	75
IV[b]	137—137,4	58,6	5,8	27,1	$C_{10}H_{12}N_4O$	58,8	5,9	27,4	80
V	99,5—100,5	68,1	8,8	18.0	$C_{18}H_{28}N_4O$	68,3	8,9	17,7	55
VI[c]	62,5—63,5	54,2	5,3	25.4	$C_{10}H_{11}N_4Cl$	53,9	5,0	25,2	88
VII	58,4—59,4	64,6	7,8	17,0	$C_{18}H_{27}N_4Cl$	64,4	8.1	16,7	74
VIII	144—145	74,8	9.3	15,6	$C_{28}H_{41}N_5$	75,1	9,2	15,6	58
IX[d]	214—215	55,2	6,8	38,6	$C_{10}H_{14}N_6$	55,0	6,5	38,5	74
X	161,5—162,5	65,3	9,1	25,7	$C_{18}H_{30}N_6$	65.4	9,2	25,4	88
XI	182—184	67,9	7,2	21,6	$C_{26}H_{33}N_7O$	68,0	7,2	21,3	97
XII	192—194	69,4	7,4	19,4	$C_{25}H_{33}N_6O$	69,3	7,7	19,4	88

[a] Compound II was recrystallized from methanol, III-V and VIII-XI were recrystallized from ethanol, VI and VII were recrystallized from hexane, and XII was recrystallized from heptane.

[b] This compound had mp 135-137°C [3].

[c] This compound had mp 57°C and was obtained in 55% yield [6].

[d] This compound had mp 183-184°C and was obtained in 72.5% yield [6].

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TABLE 2. UV Spectra of 10^{-4}-10^{-5} M Solutions of the Synthesized Compounds

Compound	λ_{max}, nm(lg ε)	
	ethanol	1 N KOH in ethanol
II	236 (3,36), 294 (3,22)	242 (3,62), 282 (3,85)
III	250 (3,88), 278 (3,64)	250 (4,15), 280 (4,02)
IV	247 (3,64), 270 (3,35)[a]	245 (3,91), 277 (3,76)
V	256 (4,11), 300 (4,22)	238 (4,13), 258 (4,19), 281 (4,13)
VI	260 (4,20), 270 (4,16)[a]	265 (4,25)
VII	275 (4,20)	275 (4,20)
VIII	260 (4,02)	250 (4,25), 265 (4,15)[a]
X	260 (4,10), 280 (3,92)[a]	269 (4,38)
XI	250 (3,58), 268 (3,52), 280 (3,48)[a], 296 (3,45), 310 (3,46), 336 (3,65), 395 (3,60)[a]	260 (3,52), 315 (3,20), 370 (3,18)
XII	260 (4,10), 384 (3,95), 464 (3,80), 494 (3,90)	260 (4,51), 385 (4,41), 460 (4,00)

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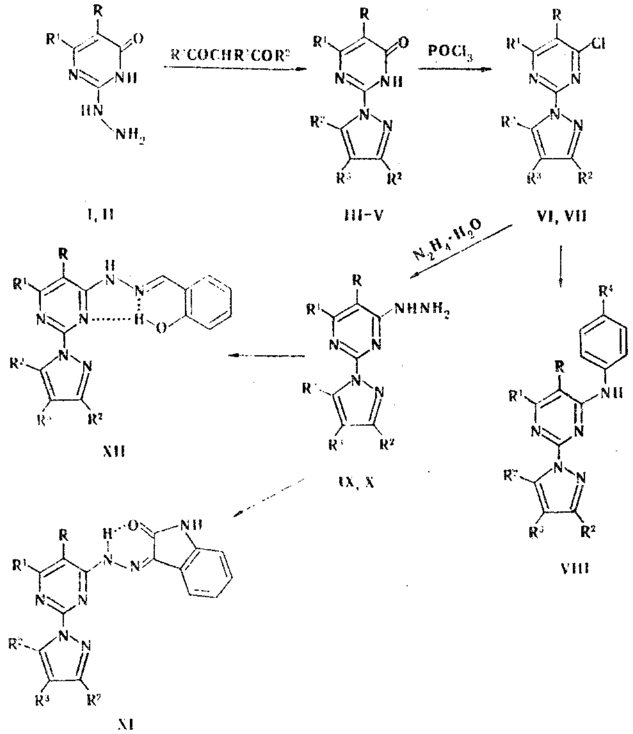
[a] Shoulder.

The IR spectrum of a dilute solution of VIII in CCl_4 contains a band at 3465 cm^{-1}, which is characteristic for the stretching vibrations of a nonassociated N—H bond. The IR spectrum of a solution of hydrazone XI in chloroform contains an intense band of stretching vibrations of a C=O bond at 1720 cm^{-1}, which is shifted to the long-wave region as compared with the absorption band of the C=O bond in the 2 position of isatin (1772-1775 cm^{-1}) [8]. The spectrum of a dilute solution in CCl_4 contains a band at 3450 cm^{-1}, which corresponds to the N—H bond of the isatin ring [8], and a broad band with a fine structure at 3000-3270 cm^{-1}. The latter is due to superimposition of the bands of the stretching vibrations of aromatic C—H bonds and the N—H bond of the hydrazone grouping, which is broadened and shifted to the long-wave region of the spectrum. The shift of the absorption bands of the stretching vibrations of C=O and N—H bonds is evidently associated with the presence of an intramolecular hydrogen bond in the XI molecule.



I R=H, $R^1=CH_3$; II $R=C_2H_5$, $R^1=CH_3$; III $R=C_2H_5$, $R^1=R^2=CH_3$, $R^3=H$; IV, VI, IX R=H, $R^1=R^2=CH_3$, $R^3=H$; VII, X—XII $R=C_2H_5$, $R^1=CH_3$, $R^2=n\text{-}C_3H_7$, $R^3=C_2H_5$; VIII $R=C_2H_5$, $R^1=CH_3$, $R^2=n\text{-}C_3H_7$, $R^3=C_2H_5$, $R^4=n\text{-}C_4H_9$

The IR spectrum of a solution of hydrazone XII in CCl_4 contains intense absorption bands of aliphatic C—H bonds at 2952, 2925, and 2870 cm^{-1} and of an N—H bond at 3335 cm^{-1} and a broad band with a fine structure at 3000-3200 cm^{-1}, which is evidently the superimposition of the absorption bands of aromatic C—H bonds and the O—H bond, which are shifted markedly to the long-wave region and broadened due to the formation of an intramolecular hydrogen bond.

The UV spectra of solutions of VIII-XII in 1 N ethanolic KOH differ markedly from the UV spectra of their ethanol solutions (Table 2); this is explained by the change in the conjugation chain during the formation of the anions of these compounds.

2-(1-Pyrazolyl)-4(3H)-pyrimidinone derivatives (III-V, VIII) are of interest as bidentate ligands, and hydrazones XI and XII are of interest as tetradentate ligands [9]. A special communication will be devoted to the study of the complexing ability of the ligands obtained in the present research.

EXPERIMENTAL

The IR spectra of $5 \cdot 10^{-3}$ M solutions in CCl_4 and $1 \cdot 10^{-2}$ M solutions in chloroform of III-V, VIII, XI, and XII in NaCl cuvettes (d = 1 mm) were recorded with a UR-20 spectrometer. The spectra of $1 \cdot 10^{-4}$ M solutions in CCl_4 at 2800-3600 cm^{-1} in NaCl cuvettes (d = 50 mm) were also investigated.

The UV spectra of $1 \cdot 10^{-4}$-$1 \cdot 10^{-5}$ M solutions of the synthesized compounds in ethanol and 1 N ethanolic KOH were recorded with a Hitachi EPS-3T spectrophotometer in quartz cuvettes (d = 10 mm). The maxima of the absorption bands are presented in Table 2.

2-Hydrazino-6-methyl-4(3H)-pyrimidinone (I) and 5-ethyl-2-hydrazino-6-methyl-4(3H)-pyrimidinone (II) were obtained by the method in [10], and the alkyl derivatives of 2-(1-pyrazolyl)-4(3H)-pyrimidinone (III-V) were obtained by condensation of the appropriate β-diketones with I and II in ethanol [3-5].

The alkyl derivatives of 4-chloro-2-(1-pyrazolyl)pyrimidine (VI, VII) were obtained by the method in [6, 7] by the action of phosphorus oxychloride on IV and V but in the presence of triethylamine (1 mole of triethylamine per mole of IV or V was used).

4-(p-n-Butylphenylamino)-5-ethyl-6-methyl-2-(4-ethyl-3,5-di-n-propyl-1-pyrazolyl)pyrimidine (VIII). A mixture of 13.0 mmole of p-n-butylaniline, 6.6 mmole of VII, and 5 ml of dimethylformamide (DMF) was refluxed for 6 h, after which 100 ml of water was added, and the excess p-n-butylaniline and DMF were removed by steam distillation. The residual mixture was cooled, and the precipitated VIII was removed by filtration and recrystallized from ethanol.

4-Hydrazino-2-(1-pyrazolyl)pyrimidines (IX, X). These compounds were obtained by the method in [6].

2-(1-Pyrazolyl)pyrimidin-4-ylhydrazones (XI, XII). A mixture of 8.8 mmole of X, 8.8 mmole of isatin or salicylaldehyde, and 20 ml of ethanol was refluxed for 1 h, after which the ethanol was removed by vacuum distillation, and the residue was crystallized from an appropriate solvent.

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