SYNTHESIS AND STUDY OF POLYDENTATE LIGANDS THAT CONTAIN

A PYRIMIDINE RING

A. V. Ivashchenko, B. E. Zaitsev, S. V. Krikunova, and R. V. Poponova UDC 547,855.7'772.07

The corresponding hydrazones, azo compounds, and 2,4-bis(lH-pyrazol-l-yl)pyrimidines were synthesized by the reaction of 5-ethyl-2-hydrazino-6-methyl-4(3H)-pyrimidinone, 2-(N-p-butylanilino)-4-hydrazino-6-methylpyrimidine, and 4-hydrazino-<math>2-(lH-pyrazol-l-yl)pyrimidines with salicylaldehyde, isatin, β -naphthoquinone, phenanthrenequinone, and acetylacetone. The structures of the synthesized compounds are discussed on the basis of a study of their electronic, IR, and mass spectra.

We have previously proposed that pyrimidine derivatives be used as nodal links in the directed synthesis of several types of ligands [1-6], including those that are capable of reacting with salts of transition metals to give complexes that are stabilized by additional metal chelate rings that include an intramolecular hydrogen bond [5, 6]. Their complexes have also been studied [7-11]. The published results [1-6] have not by any means exhausted the possibilities of pyrimidine derivatives, particularly hydrazinopyrimidines, in the construction of various types of multidentate ligands with a fixed stereochemistry. In the present research we investigated the possibility of the synthesis of new ligands, viz., several pyrimidine hydrazones, arylazopyrimidines, and 2,4-bis(1H-pyrazol-1-yl)pyrimidines, which are of interest as tri- and quadridentate ligands.

We used our previously synthesized 5-ethyl-2-hydrazino-6-methyl-4(3H)-pyrimidinone (I) [1-3], 2-(N-p-butylanilino)-4-hydrazino-6-methylpyrimidine (II) [5], and 4-hydrazino-6-methyl-2-(1H-pyrazol-1-yl)pyrimidines (III) [1-3] as the starting compounds in the reaction with salicylaldehyde, isatin, β -naphthoquinone, phenanthrenequinone, and β -diketones. The condensation of hydrazinopyrimidines I-III with carbonyl compounds was carried out by mixing equimolar alcohol solutions of the components with heating. As a result, we obtained the corresponding hydrazones (IV, VII, and VIII), azo compounds (V, VI, and IX), and 2,4-bis(1H-pyrazol-1-yl)pyrimidines (X and XI).

The structures of the compounds obtained were confirmed by the results of elementary analysis and the UV, IR, and mass spectra (Tables 1-3).

Com-	mp, °C	Found. %			Empirical	Calc., %			Yield,
pound		С	Н	N	formula	С	Н	N	9/0
IV VI VII VIII IX XI	$\begin{array}{c} 304 \ (\text{dec.})^{a} \\ 237 \ (\text{dec.})^{b} \\ 252 \ (\text{dec.})^{b} \\ 242 \\ 265.5 - 266.5 \\ a \\ 249.0 - 250.0 \\ b \\ 66.5 - 67.5 \\ 95.4 - 96.4 \end{array}$	57,4 66,3 70,6 68,5 69,1 71,3 69,7 65,9	5,8 5,6 5,3 6,1 6,2 7,2 8,5 7,0	22,2 18,0 15,6 17,6 20,4 17,7 21,6 27,3	$\begin{array}{c} C_{15}H_{15}N_5O_2\cdot H_2O\\ C_{17}H_{16}N_4O_2\\ C_{21}H_{16}N_4O_2\\ C_{21}H_{16}N_4O_2\\ C_{23}H_{24}N_6O\\ C_{28}H_{34}N_6O\\ C_{23}H_{34}N_6\\ C_{23}H_{34}N_6\\ C_{17}H_{22}N_6 \end{array}$	57,1 66,0 70,4 68,7 69,0 71,5 70,0 65,8	5,4 5,5 5,1 6,4 6,0 7,3 8,7 7,1	22,2 18,1 15,6 17,3 20,0 17,9 21,3 27,1	71,5 65,0 67,0 32,0 75,0 85,0 82,0 90,0

TABLE 1. Melting Points, Results of Elementary Analysis, and Yields of the Synthesized Compounds

^aFrom acetic acid. ^bFrom ethanol. ^cFrom heptane.

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Considering the fact that hydrazones IV, VII, and VIII may have both hydrazone (IV, VII, and VIII) and azine forms, while azo compounds V, VI, and IX may have azo, azine, or quinone-hydrazone forms, we investigated their IR, UV, and mass spectra. To simplify the interpretation



111, 1X, X, X11, X111 $R = C_3 H_7$, $R' = C_2 H_5$; X1 $R = C H_3$, $R' - H_3$

of the spectra of VI-VIII we obtained and studied the spectra of the previously described [2, 3] hydrazones XII and XIII.

The IR spectrum of a polycrystalline sample of IV in the region of stretching vibrations of N-H bonds contains a $v_{\rm NH}$ band at 3468 cm⁻¹ and a broad band with a fine structure at 3400-3400 cm⁻¹ [sic], which is characteristic for associated N-H bonds. There is also an intense band in the region of stretching vibrations of C=C, C=N, and C=O bonds with a number of maxima at 1710, 1666, 1650, 1640, and 1625 cm⁻¹. A comparison of the spectrum of IV with the spectra of a polycrystalline sample and a dilute solution of hydrazone XII and the spectra of substituted 4(3H)-pyrimidinones, which we synthesized in [3], makes it possible to assign the $v_{\rm NH}$ band at 3468 cm⁻¹ and the $v_{\rm C=O}$ band at 1710 cm⁻¹ to the isatin part of the molecule and the $v_{\rm C=O}$ band at 1666 cm⁻¹ to the pyrimidine part of the molecule. The series of bands at 1650, 1640, and 1625 cm⁻¹ is evidently due to stretching vibrations of C=C and C=N bonds. The molecular-ion peaks with m/e 297* have the maximum intensity in the mass spectrum of IV.

*Here and subsequently, the numbers that characterize the ions specify the mass to charge ratios.

TABLE 2. Electronic Spectra of $5\cdot 10^{-4}$ M Solutions of the Synthesized Compounds in Ethanol

Com- pound	λ_{\max} (ig ε), cm ⁻¹
IV	48880 (4,38), 40000 (4,17), 35000 ^a (3,70), 26000 (4,31)
V	(4,00) (4,28), 39600 (4,31), 38000 (4,28), 36900 (4,25), 24000 ^a (3,97), 21600 (4,07)
VI	49000(4.38), 42000(4.35), 34480(4.10), 21360(4.09)
VII	48000 (4,42), 41440 (4,22), 34650 (4,46), 29160 (4,39)
VIII	48640 (4,48), 38560 (4,37), 37600 (4,34) ^a , 35600 (4,23) ^a , 28000 (4,32)
IX	42200 (4,47), 38640 (4,51), 33600 (3,92), 25000 (4,42) ^a , 24320 (4,47), 23360
	(4,38)
Х	36800 (4,42)
XI	37760 (4,43), 34800 (3,96)
XII	49000 (4,36), 38640 (4,38), 36800 (4,29) ^a , 26800 (4,24), 22000 (3,85) ^a , 21000
	(3,68) ^a
XIII	48500 (4,36), 40500 (4,31), 37000 (4,25), 34720 (4,17), 33300 (4,18), 32000
	(4,24), 29460 (4,39), 28400 (4,36)

aShoulder.

TABLE 3. Mass Spectra of the Synthesized Compounds

C o m- pound	М	m/e Values (relative intensities of the ion peaks in percent relative to the maximum peak ^a)
IV	297	76 (10,9), 77 (12,1), 90 (18,2), 91 (10,1), 96 (27,3), 102 (10,9), 110 (12,7), 117 (21,8), 118 (26,5), 138 (27,3), 144 (12,7), 145 (26,6), 152 (29,1)
V	308	253 (100), 254 (82,8), 268 (69,1), 269 (42,6), 282 (54,5), 297 (100) 77 (10,2), 96 (12,5), 101 (13,1), 102 (11,0), 114 (20,5), 115 (44,1), 128 (21,6), 130 (10,8), 138 (187), 142 (10,8), 143 (45,9), 152 (10,2), 156 (21,6), 130 (10,8), 138 (187), 142 (10,8), 143 (45,9), 152 (10,2), 156
VI	358	$ \begin{array}{c} (19,9), \ 169 \ (17,0), \ 263 \ (14,0), \ 265 \ (23,9), \ 279 \ (20,1), \ 280 \ (16,8), \ 293 \\ (17,0), \ 308 \ (100) \\ 96 \ (13,0), \ 137 \ (10,9), \ 138 \ (16,6), \ 151 \ (28,3), \ 152 \ (30,2), \ 163 \ (19,6), \ 164 \\ (44,1), \ 165 \ (85,7), \ 177 \ (21,7), \ 178 \ (33,0), \ 179 \ (21,3), \ 180 \ (15,7), \ 193 \\ (13,0), \ 206 \ (23,9), \ 315 \ (43,4), \ 329 \ (23,9), \ 330 \ (37,7), \ 343 \ (13,0), \ 358 \end{array} $
VII	375	(100) 106 (13,8), 131 (24,3), 211 (14,6), 212 (15,0), 213 (94,9), 214 (12,9), 255 (13,6), 256 (23,1), 332 (21,0), 358 (49,8), 359 (12,4), 374 (14,6), 375
XIII	434	(100), 376 (23,1) 181 (10,2), 254 (23,1), 312 (28,0), 313 (12,4), 314 (46,8), 315 (29,6), 417 (11,3), 419 (27,4), 433 (10,2), 434 (100), 435 (32,3)

^aThe peaks with relative intensities greater than 10% are presented.

Peaks of $[M-CH_3]^+$ (282), $[M-CO]^+$ (269), $[M-CHO]^+$ (268), and $[M-CONH]^+$ (254) ions, which are formed as a result of splitting out of substituents from the molecular ions, are also observed in the spectrum; this constitutes evidence for the relative strength of the hydrazone bridge. The formation of ions a and b is associated with the characteristic (for hydrazones) cleavage of the N-N bridge bond, during which the charge is localized on one of the fragments of the molecule.



The IR spectrum of a dilute solution of V in CCl₄ contains a series of intense bands in the region of stretching vibrations at 1706, 1682, 1647, and 1630 cm⁻¹, as well as a broad band with a fine structure at 2800-3300 cm⁻¹ with a broad maximum at \sim 3120 cm⁻¹ and a narrow band at 3400 cm⁻¹. The $v_{C=0}$ band at 1682 cm⁻¹ and the v_{NH} band at 3400 cm⁻¹ are characteristic for the amide grouping of the pyrimidinone ring [3], while the bands at 1647 and 1630 cm⁻¹ are due to the stretching vibrations of C=0 and C=N bonds, and the band at 1706 cm⁻¹ is due to the stretching vibrations of yet another C=0 bond, the presence of which is possible only in the case of realization of a quinonehydrazone structure (V*). The broad band with a maximum at \sim 3120 cm⁻¹ characterizes an N...H...0 intramolecular bond.



The IR spectrum of VI is similar to the spectrum of V.

The molecular-iou peaks have the maximum intensity in the mass spectra of V and VI, and two groups of ions are also recorded. The first group corresponds to splitting out of substituents and their fragments from the molecular ions, as in the case of IV. The second group of ions is associated with cleavage of the N-C bridge bond, which is characteristic for the fragmentation of azo compounds in the azo form. Formally speaking, four types of ions can be formed in the case of direct cleavage:



The intensity ratios of the peaks of ions c-f depend on the probability of charge localization on the F^1 or F^2 fragments and on the nitrogen atoms of the azo group. Primarily ions of the d and f type are recorded in the spectra of V and VI, while the peaks of the c and e ions have low intensities (5-8%). The peaks of ions with m/e 169 (g, V) and 219 (h, VI), which are formed as a result of the loss of two hydrogen atoms from the F^2 fragment, have high relative intensities. However, their formation is more likely due to the quinonehydrazone form, with which the formation of rearranged ions with m/e 138 is evidently also associated. The cleavage of the N-N bond that is characteristic for this form leads to the formation of common ions with m/e 156 (i) and 206 (j), respectively.



The IR spectra of dilute solutions of hydrazones VII and VIII in CCl₄ contain a band of stretching vibrations of the N-H bond, which is characteristic for the secondary amino group in 2-arylaminopyrimidines [5] ($v_{\rm NH}$ = 3440 and 3448 cm⁻¹, respectively). In addition, the spectrum of VII contains a $v_{\rm NH}$ band at 3461 cm⁻¹, which is due to the hydrazone form, and a broad band with a maximum at \sim 3060 cm⁻¹, which is characteristic for the stretching vibrations of an O-H bond that participates in the formation of an intramolecular hydrogen bond. The spectrum of VIII contains a $v_{\rm NH}$ band at 3466 cm⁻¹ and a $v_{\rm C=O}$ band at 1716 cm⁻¹ from the isatin part of the molecule and a broad band with a maximum at 3230 cm⁻¹, which is evidently due to the N-H bond of a hydrazone grouping that participates in the formation of an intramolecular hydrogen bond.

The principal pathway of fragmentation of hydrazone VII under electron impact involves cleavage of the NH-N bond (the ion with m/e 255); this process is accompanied by hydrogen migration to the charged part of the molecule (the ion with m/e 256). This is followed by splitting out of a $C_{3}H_{7}$ particle (m/e 213). Splitting out of a $C_{3}H_{7}$ radical from the molecular ion gives a fragment with m/e 332; however, the most probable process is ejection of a C0 particle from the molecular ion. The second fragmentation pathway involves cleavage of the bond between the CH group and the phenolic residue with the formation of ions with m/e 282. However, this fragmentation pathway is considerably less probable than the principal pathway.

It must be noted that the principal fragmentation pathway in the mass spectrum of hydrazone XII also involves cleavage of the NH-N bond. The charge in this case is localized almost completely on the pyrimidine part of the molecule — witness the ion with m/e 314 and the rearranged ion with m/e 315. The next process is evidently cyclization with the loss of two hydrogen atoms (the ion with m/e 312). However, the loss of substituents also takes place $-C_3H_6$ from the fragment with m/e 312. For example, $312 \longrightarrow 270$.

Three bands at 1682, 1662, and 1636 cm⁻¹, which, with respect to their position and overall integral intensity (A = $12.1 \cdot 10^4$ liters/mole-cm²) correspond to the bands in the spectrum of quinolone [12], are observed in the IR spectrum of a dilute solution of IX in CC14 in the region of the stretching vibrations. A band at 3361 cm⁻¹ with an intensity of 3.93.10⁴ liters/mole-cm² is observed in the region of the stretching vibrations of N-H bonds. Thus IX has a quinonehydrazone structure (IX*).



As expected, bands characteristic for the stretching vibrations of C=O and N-H bonds are absent in the IR spectra of X and XI; this is in agreement with their structures.

The electronic spectra of the synthesized compounds (see Table 2) are in complete agreement with the data from the IR and mass spectra, according to which IV, VII, VIII, XI, and XIII exist in the hydrazone form, whereas an equilibrium between the azo and quinonehydrazone forms exists for V, VI, and IX.

EXPERIMENTAL

The IR spectra were recorded with a UR-20 spectrometer, the electronic spectra were obtained with a Specord UV-vis spectrophotometer, and the mass spectra were recorded with an MS-702 spectrometer with systems for the direct introduction of the samples.

5-Ethyl-2-hydrazino-6-methyl-4(3H)-pyrimidinone (I) was obtained by the method in [1], 2-(N-p-butylanilino)-4-hydrazino-6-methylpyrimidine (II) was obtained by the method in [5], and the 4-hydrazino-6-methyl-5-R-2-(1H-pyrazol-1-yl)pyrimidines (III, R = H, CH₃, C₂H₅, and C₃H₇) and their hydrazones (XII and XIII) were obtained by the methods in [2].

General Method for the Preparation of IV-IX. A 0.01-mole sample of hydrazine I-III was refluxed with 0.01 mole of isatin, salicylaldehyde, β -naphthoquinone, or phenanthrenequinone in 20 ml of ethanol or methanol for 30 min, after which the mixture was cooled to give IV-IX. The yields and the results of analysis are presented in Table 1, the electronic spectra are presented in Table 2, and the mass spectra are presented in Table 3.

<u>General Method for the Preparation of 2,4-Bis(lH-pyrazol-l-yl)pyrimidines X and XI.</u> A mixture of 0.01 mole of hydrazine III and 0.01 mole of the β -diketone in 10 ml of ethanol was refluxed for 2 h, after which the solvent was removed by vacuum distillation, and the residue was recrystallized from heptane.

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SYNTHESIS OF 1-ALKYL-4(5)-HYDROXYMETHYL-1,2,3-TRIAZOLES

A. V. Maksikova, E. S. Serebryakova,

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L. G. Tikhonova, and L. I. Vereshchagin

An in situ method for the synthesis of 1-alky1-4(5)-hydroxymethy1-1,2,3-triazoles by the action of acetylenic alcohols with alky1 azides as the latter are formed from sodium azide and alky1 halides in dimethylformamide is proposed.

1-Alky1-4(5)-hydroxymethy1-1,2,3-triazoles (I) are usually obtained by the reaction of acetylenic carbinols with various alky1 azides [1-4]. However, this reaction does not always give satisfactory results, particularly when lower alky1 azides are used. The cycloaddition of alky1 azides generally takes place during prolonged heating of the reaction mixture at 100-120°C, which is unacceptable for low-boiling azides. When the synthesis is carried out in an autoclave, the yields of lower N-alky1-substituted triazoles do not exceed 20% [5]. The use of dimethylformamide (DMF) as the solvent markedly reduces the reaction time, but a diffucult-to-separate azeotropic mixture of alky1 azide and solvent is formed in this case.

In the present paper we present an in situ method for the synthesis of 1-alky1-4(5)-hydroxymethy1-1,2,3-triazoles by the reaction of acetylenic alcohols with alky1 azides as the latter are formed from sodium azide and alky1 halides.

This method excludes the step involving the isolation and purification of the alkyl azides. The most effective solvents in this reaction are DMF and Carbitol [2-(2-ethoxyethoxy)ethanol]. Various alkyl halides react equally successfully, but alkyl chlorides are to be preferred, since the resulting sodium chloride precipitates. Sodium bromide and iodide are partially soluble in DMF and hinder the isolation of the desired reaction products. The yields of the triazoles depend to a considerable extent on the length of the alkyl substituent in the alkyl halide. The higher alkyl halides give higher yields of triazoles (see Table 1). Of all of the examined acetylenic alcohols, propargyl alcohol reacts more readily. Prolonged heating of the reaction mixture at high temperatures is required for the synthesis with butynediol.

Institute of Petrochemical and Coal-Chemical Synthesis at A. A. Zhdanov Irkutsk State University, Angarsk 665813. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1688-1689, December, 1980. Original article submitted April 21, 1980.