SYNTHESIS AND STUDY OF THE PMR SPECTRA OF 1,10,11,20-TETRAHYDRODIPYRAZOLO[3,4-f:3',4'-m]DIPYRIDO[2,3-c:2',3'-j][1,2,5,8,9,12]HEXAAZACYCLOTETRADECENE DERIVATIVES

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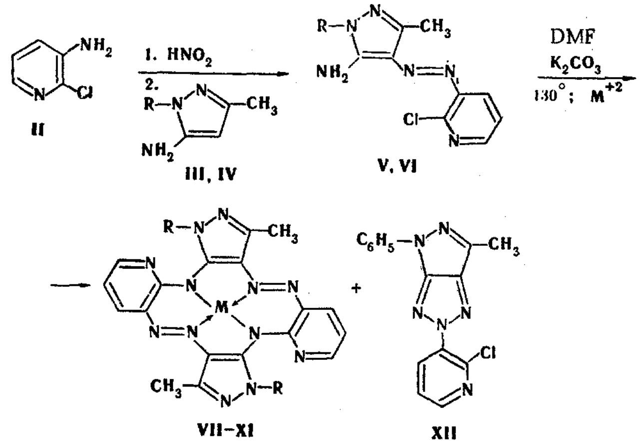
1,10,11,20-Tetrahydropyrazolo[3,4-f:3',4'-m]dipyrido[2,3-c:2',3'-j][1,2,5,8,9,12]hexaazacyclotetradecene derivatives were obtained by the reaction of nickel nitrate, palladium chloride, potassium tetrachloroplatinate, or copper sulfate with 5-amino-3-methyl-4-(2-chloro-3-pyridylazo)-1-R-pyrazoles in dimethylformamide in the presence of potassium carbonate and were characterized by the results of elementary analysis and data from the IR, UV, PMR, and mass spectra.

Many researchers have expressed interest in macrocyclic compounds with a condensed pyridine ring [1]. Among the hexaazacyclotetradecene series, dibenzo[f,j]pyrazolo[5,4-m]pyrido[3,2-c]hexaazacyclotetradecene [2] and dinaphtho[1,2-c:1',2'-j]dipyrido[2,3-f:2',3'-m]hexaazacyclotetradecene [3] derivatives have been described.

In order to synthesize the first representatives of derivatives of tetrahydrodipyrazolodipyrido[1,2,5,8,9,12]hexaazacyclotetradecene systems we used template cyclization of o-chloro-o'-aminoazo compounds V and VI in the presence of potassium carbonate and nickel(II) nitrate hexahydrate, palladium(II) chloride, potassium tetrachloroplatinate, or copper(II) sulfate. The synthesis was carried out by the following scheme:



III, V $R=C_2H_5$; IV, VI, XII $R=C_6H_5$; VII $R=C_2H_5$, M=Ni; VIII $R=C_6H_5$, M=Ni;
IX $R=C_6H_5$, M=Pd; X $R=C_6H_5$, M=Pt; XI $R=C_6H_5$, M=Cu

Compounds V and VI were obtained by diazo coupling of the diazonium salts of 3-amino-2-chloropyridine with pyrazoles III and IV in acetic acid in the presence of sodium acetate. The IR spectra of V and VI contains a doublet of bands of symmetrical and asymmetrical stretching vibrations of the amino troup at 3475 and 3370 cm^{-1}. The signal of an amino group at 6.63-6.70 ppm (in $CDCl_3$), the singlet of a methyl group of pyrazole, the signals of ethyl or phenyl substituents attached to the pyrazole nitrogen atom, and the signals of three pyridine protons are observed in the PMR spectra. These spectroscopic data indicate that V and VI exist in the azo form.

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TABLE 1. Physicochemical Constants of V-XII

Compound	mp, °C	λ_{max}, nm (lg ε)			Found, %				Empirical formula	Calc., %				M	M^{+}*	Yield, %
		1	2	3	C	H	N	Cl		C	H	N	Cl			
V	183—185	390 (3,15)	415 (4,16)		49,8	5,0	31,8	13,1	$C_{11}H_{13}N_6Cl$	49,9	4,9	31,7	13,4	264,7	264	52
VI	165,5—166,5	390 (4,14)	420 (4,21)		57,5	4,1	26,9	11,4	$C_{15}H_{13}N_6Cl$	57,6	4,2	26,9	11,3	312,8	312	53
VII	251—252		470 (3,49)		51,4	4,3	32,8		$C_{22}H_{22}N_{12}Ni$	51,5	4,3	32,7		513,2	512	59
VIII	Above 353		470 (4,61)	620 (3,57)	59,0	3,7	27,5		$C_{30}H_{22}N_{12}Ni$	59,1	3,6	27,6		609,3	608	72
IX†	Above 332		445 (4,84)	560 (3,64)	54,8	3,4	25,5		$C_{30}H_{22}N_{12}Pd$	54,8	3,4	25,6		657,0	652	69
X	Above 332	i 420 (4,24)	440 (4,45) sh 470 (4,04)	620 (3,30)	48,3	3,0	22,6		$C_{30}H_{22}N_{12}Pt$	48,3	3,0	22,5		745,7	740	43
XI	176—178	430 (4,10)	490 (3,78)	570 (2,82)	58,8	3,5	27,4	11,5	$C_{30}H_{22}N_{12}Cu$	58,7	3,6	27,4		614,1	613	41
XII	169—170,5	425 (3,19)	490 (2,86)		57,9	3,5	27,0		$C_{15}H_{11}N_6Cl$	58,0	3,6	27,1	11,4	310,7	310	24,4

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*This is the value for the lightest isotope. †The Pd was determined by emission spectroscopy (with an ISP-30 apparatus) with respect to the lines at 247.6, 302.79, 311.4, 306.53, and 324.22 nm.

TABLE 2. PMR Spectra of V-XII in $CDCl_3$

Compound	Concn., mole	δ, ppm, J, Hz					
		NH_2	CH_3	6-H	5-H	4-H	R
V	0,3	6,63 br s	2,43 s	8,21 dd J=4,75; 1,75	7,26 dd J=4,75; 8,0	7,96 dd J=8,0; 1,75	1,40 м (3H, J=7,3; CH_3—C—); 3,90 q (2H, J=7,3; —CH_2—N)
VI	0,3	6,70 br s	2,52 s	8,24 dd J=4,65; 1,94	7,26 dd J=4,65; 8,0	8,06 dd J=8,0; 1,94	7,54—7,39 m (5H, C_6H_5)
VII	0,1		2,36s	7,81 dd J=4,75, 1,65	6,61 dd J=4,75; 8,0	7,71 dd J=8,0; 1,65	1,31 t (3H, J=7,8; CH_3—C—); 4,27 q (2H, J=7,8; —CH_2—N)
VIII	0,2		2,36 s	7,10 dd J=4,75; 1,7	6,36 dd J=4,75; 8,0	7,60 dd J=8,0; 1,7	7,16 cm (5H, C_6H_5)
IX	0,05		2,38 s	7,11 dd J=4,5; 1,73	6,42 dd J=4,5; 8,0	7,68 dd J=8,0; 1,73	7,18 cm (5H, C_6H_5)
X	0,1		2,41 s	7,12 dd J=4,7; 1,6	6,37 dd J=4,7; 8,0	7,70 dd J=8,0; 1,6	7,28 cm (5H, C_6H_5)
XII	0,2		3,01 s	7,76—8,14 m	7,16 dd J=8,0	8,51 dd	7,76—8,14 m (2H, 2,6-H); 7,29—7,59 m (3H, 3,4,5-H)

Macrocyclic compounds VII-XI were obtained by template self-condensation of o-chloro-o'-aminoazo compounds V and VI with the metal(II) salt in the presence of potassium carbonate in a polar aprotic solvent [dimethylformamide (DMF)]. The structures of these compounds were confirmed by the IR, PMR, mass, and electronic spectra. The IR spectra do not contain the characteristic bands in the region of the stretching vibrations of NH bonds. We selected 5-amino-3-methyl-1-R-pyrazoles (where R = C_2H_5 or C_6H_5) as the azo components. The PMR spectra of the aromatic protons of all of the intermediates and final products had a form convenient for interpretation; in contrast to the macrocyclic compounds of dibenzodipyrazolohexaazacyclotetradecene derivatives [4], the solubility of phenyl derivative VIII in trichloromethane is higher by a factor of three than the solubility of derivative VII. The signals observed in the PMR spectrum confirm the presence in the molecule of three aromatic protons, a methyl group, and, correspondingly, an ethyl or phenyl group attached to a pyrazole nitrogen atom. Compounds VII-X contain a second-order axis of symmetry, and this leads to equivalence of the two groups of pyrazole and pyridine protons in the PMR spectra. The signals of the methyl groups and the substituents attached to the pyrazole nitrogen atom do not experience significant shifts during cyclization and complexing. The 4-H and 5-H signals are shifted 0.5-0.9 ppm to strong field as compared with azo compounds V and VI. The 6-H signal in the spectrum of macrocycle VII is shifted only slightly (a 0.4 ppm shift to strong field), whereas the 6-H signal of VII-X experiences a significant shift (∿1.13 ppm) to strong field as compared with VI. The considerable shift to strong field of the 6-H signal of VIII-X is evidently due to the magnetic anisotropy of the N-phenyl ring, and it may thus be assumed that the phenyl ring deviates from the plane of the macrocycle. This fact probably affects the strength of the intermolecular association of VIII-XI and thereby their solubilities.

In a comparison of macrocyclic compounds VIII (M = Ni), IX (M = Pd), and X (M = Pt) it may be noted that, generally speaking, in the case of complexing all of the lines in the PMR spectra are shifted to strong field and that this effect decreases in the order Ni(II) > Pd(II) > Pt(II).

In the preparation of XI, XII, which, according to the NMR and mass spectra, was identified as 2-(2-chloro-3-pyridyl)-6-methyl-4-phenyl-2,4-dihydropyrazolo[4,5-d]-1,2,3-triazole, was isolated from the reaction mixture in 24.4% yield.

TABLE 3. Difference in the Chemical Shifts ($\Delta\delta$, ppm) for VII Relative to V and for VIII, IX, X, and XII Relative to VI

Compound	CH_3	6-H	5-H	4-H	R
VII	−0,07	−0,40	−0,65	−0,25	CH_3— −0,09 CH_2—N— +0,37
VIII	−0,16	−1,14	−0,90	−0,46	−0,305
IX	−0,14	−1,13	−0,84	−0,38	−0,285
X	−0,11	−1,12	−0,89	−0,36	−0,185
XII	+0,49	−0,11	−0,10	+0,27	

TABLE 4. Template Reaction Times (τ) and Yields of the Macrocyclic Compounds

Compound	τ, h	Yield, %	M^{+2}
VII	4	59	$Ni(NO_3)_2 \cdot 6H_2O$
VIII	3^{30}	72	Same
IX	1	69	$PdCl_2$
X	1	43	$K_2[PtCl_4]$
XI	1	40,7	$CuSO_4 \cdot 5H_2O$
XI	1	39,5	$CuSO_4$

Its PMR spectrum (in $CDCl_3$) contains a singlet of a methyl group at 3.01 ppm, signals of three pyridine protons, and an easily interpretable spectrum of a five-spin pyrazole N—C_6H_5 system. The presence of the spectrum of well-resolved signals of a phenyl ring indicates that the pyrazole exists in the quinoid form, such as, for example, 3-methyl-1-phenyl-5-pyrazolone [5]. Molecular-ion peaks with m/e 310-312, which are the maximum peaks in the spectrum, are present in the mass spectrum of XII. The presence of a chlorine atom is identified from the ratio of the intensities of the isotope peaks in the molecular ions, which are in agreement with the calculated values. The fragmentation of XII under the influence of electron impact consists in splitting out of a chlorine atom (m/e 275, 6.5%) and in the formation of chloropyridinium cations (m/e 112-114, 36.4%) and iminopyrazole (m/e 170, 9.1%); this confirms the proposed structure.

Molecular-ion peaks, which are the maximum peaks in the spectra, are observed in the mass spectra of complexes VII-XI. Their intensities amount to 90-95% of the total ion current. The presence of a metal atom is identified unambiguously from the ratio of the intensities of the isotope peaks in the molecular ions, which is in agreement with the calculated value.

It is apparent from the data in Table 4 that the reaction time decreases substantially on passing from Ni(II) to Cu(II) and Pt(II) and that the yields for VIII and IX are higher and do not change when the reaction time is increased; in the case of X and XI the yields decrease substantially when the reaction mixtures are heated for a longer time.

Macrocyclic derivatives were not obtained when a similar reaction was carried out with salts of other metals (Fe^{2+}, Mn^{2+}, La^{3+}, and V^{4+}). The new macrocyclic complexes are characterized by high thermal and chemical stability: They are stable, on the average, up to 400°C and do not liberate nickel, palladium, copper, or platinum ions under the influence of concentrated mineral acids.

EXPERIMENTAL

The IR spectra of solutions of the compounds in trichloromethane were recorded with a UR-20 spectrometer. The PMR spectra of the compounds were recorded with a Varian XL-100-12 spectrometer (100 MHz) at 30°C with tetramethylsilane as the internal standard. The mass spectra were obtained with an AEI MS-702 spectrometer with direct introduction of the samples into the ionization region; the ionizing-electron energy was 70 eV, and the temperature of the sample vaporization system was 120-180°C. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates in an acetone—pentane system (1:5).

3-Amino-2-chloropyridine (II). This compound was obtained by the method in [6] from 3-aminopyridine (I), HCl, and H_2O_2 at 80°C. Its physical constants were in agreement with the literature data [6].

5-Amino-3-methyl-1-R-pyrazoles. These compounds were obtained in analogy with the methods in [7, 8]; III had mp 99-101°C (mp 100-101°C [7]), and IV had mp 114-115°C (mp 116°C [8]).

5-Amino-1-ethyl-3-methyl-4-(2-chloro-3-pyridylazo)pyrazole (V). A diazonium solution prepared from 1.8 g (14 mmole) of amine II in 10 ml of concentrated HCl, 20 ml of water, and 0.98 g (14 mmole) of sodium nitrite in 10 ml of water was added with cooling to 1.67 g (0.013 mole) of aminopyrazole III and 1 g of sodium acetate in 25 ml of acetic acid and 75 ml of water. The precipitate that formed at pH 4-5 was removed by filtration, washed with water, dried, and recrystallized from trichloromethane to give 1.93 g of a yellow crystalline substance that was quite soluble in acetone, dimethylformamide (DMF), and dimethyl sulfoxide (DMSO) but only slightly soluble in trichloromethane and hexane.

5-Amino-3-methyl-1-phenyl-4-(2-chloro-3-pyridylazo)pyrazole (VI). This compound was similarly obtained and was recrystallized from acetone to give a yellow crystalline substance that was quite soluble in DMF and DMSO.

[1,10,11,20-Tetrahydro-1,11-diethyl-3,13-dimethyldipyrazolo[3,4-f:3',4'-m]dipyrido[2,3-c:2',3'-f][1,2,5,8,9,12]hexaazacyclotetradecenato(2-)-$N^{4(5)}$,N^{10},$N^{14(15)}$,N^{20}]nickel (VII). A mixture of 1.34 g (5 mmole) of V, 4 g of potassium carbonate, and 0.725 g (25 mmole) of nickel(II) nitrate hexahydrate in 350 ml of DMF was heated with stirring for 4 h at 130°C (until starting V vanished according to TLC), after which the reaction mixture was cooled and treated with 250 ml of water. The precipitate was removed by filtration and washed successively with water, 50 ml of a 5% solution of HCl, water, 100 ml of a mixture of DMF and water (2:3), and water, dried, and recrystallized from DMF to give 0.76 g of a black finely crystalline powder that was quite soluble in trichloromethane, trifluoroacetic acid but insoluble in acetone, water, hexane, and benzene.

Compounds VIII and IX were similarly obtained. Macrocyclic chelate VIII was recrystallized from DMF to give a black finely crystalline powder that was quite soluble in trichloromethane and trichloroacetic acid but insoluble in acetone, benzene, and water. Chelate IX was recrystallized from DMF to give a light-brown finely crystalline powder that was only slightly soluble in trichloromethane but insoluble in benzene and hexane.

[1,10,11,20-Tetrahydro-3,13-dimethyl-1,11-diphenyldipyrazolo[3,4-f:3',4'-m]dipyrido-[2,3-c:2',3'-j][1,2,5,8,9,12]hexaazacyclotetradecenato(2-)-$N^{4(5)}$,N^{10},$N^{14(15)}$,N^{20}]platinum (X). A mixture of 0.625 g (2 mmole) of VI, 2 g of potassium carbonate, and 0.415 g (1 mmole) of potassium tetrachloroplatinate in 150 ml of DMF was heated at 130°C for 1 h (the course of the reaction was monitored by TLC), after which it was cooled and poured into 100 ml of water. The resulting precipitate was removed by filtration, washed successively with water, 50 ml of 5% HCl, water, a mixture of DMF and H_2O (1:1), and water, and dried. Complex X was isolated by repeated column chromatography on 100/200 silica gel (elution with trichloromethane) to give 0.32 g of X as a black finely crystalline substance that was soluble in trichloromethane but only slightly soluble in acetone and insoluble in water and hexane; it was recrystallized from DMF.

[1,10,11,20-Tetrahydro-3,13-dimethyl-1,11-diphenyldipyrazolo[3,4-f:3',4'-m]dipyrido-[2,3-c:2',3'-j][1,2,5,8,9,12]hexaazacyclotetradecanato(2-)-$N^{4(5)}$,N^{10},$N^{14(15)}$,N^{20}]copper (XI). A mixture of 0.625 g (2 mmole) of VI, 2.0 g of potassium carbonate, and 0.16 g (1 mmole) of anhydrous copper sulfate in 120 ml of DMF was heated with stirring at 130°C for 1 h (until the starting azo compound vanished according to TLC), after which the mixture was cooled and poured into 80 ml of water. The precipitate was removed by filtration, washed successively with water, 50 ml of 5% HCl, and water, and air dried. It was purified by repeated column chromatography with a column filled with 100/200 silica gel (elution with trichloromethane) to give 0.25 g of a dark-brown finely crystalline powder that was soluble in trichloromethane, acetone, DMF, and DMSO but insoluble in water.

2-(2-Chloro-3-pyridyl)-6-methyl-4-phenyl-2,4-dihydropyrazolo[4,5-d]-1,2,3-triazole (XII). This compound was obtained from the first fraction of the first purification of XI with a column filled with 100/200 silica gel (elution with trichloromethane) in the form of a grayish-brown finely crystalline powder that was quite soluble in trichloromethane and acetone but insoluble in water.

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