Synthesis and electrochemical study of complexes of 2-methylthio-5-(pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-ones with transition metals (Co, Ni, and Cu). Molecular structures of $Cu^{II}L^1Cl_2$ (L^1 is (5*Z*)-2-methylthio-3-phenyl-5-(α-pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-one) and $Co^{II}L^2Cl_2$ (L^2 is (5*Z*)-3-methyl-2-methylthio-5-(α-pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-one)

E. K. Beloglazkina,★ *S. Z. Vatsadze, A. G. Majouga, N. A. Frolova, R. B. Romashkina,*
N. V. Zyk, A. A. Moiseeva, and K. P. Butin†

Department of Chemistry, M. V. Lomonosov Moscow State University,
1 Leninskie Gory, 119992 Moscow, Russian Federation.
E-mail: bel@org.chem.msu.su

New transition metal (Ni^{II}, Co^{II}, and Cu^{II}) complexes with 2-methylthio-5-(pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-ones were synthesized by the reaction of 5-(α-, β-, or γ-)pyridyl-substituted 2-methylthio-3,5-dihydro-4*H*-imidazol-4-ones with $MCl_2 \cdot nH_2O$. In the complexes with α-Py-substituted ligands, the metal atom has a tetrahedral coordination environment and is coordinated by the nitrogen atoms of the pyridine and thiohydantoin rings and two chloride anions. The results of electronic spectroscopy and magnetic susceptibility measurements suggest that the complexes with the β- and γ-Py-substituted ligands have polymeric structures, and the metal atoms in these complexes are in an octahedral environment. The molecular and crystal structures of $Cu^{II}L^1Cl_2$ (L^1 is (5*Z*)-2-methylthio-3-phenyl-5-(α-pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-one) and $Co^{II}L^2Cl_2$ (L^2 is (5*Z*)-3-methyl-2-methylthio-5-(α-pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-one) were established by X-ray diffraction. Semiempirical quantum-chemical calculations were performed for 2-methylthio-5-(pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-ones. The complexes, starting ligands, and metal chlorides were studied electrochemically. The mechanism of electrooxidation and electroreduction of 2-methylthio-5-(pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-ones and their cobalt, nickel, and copper complexes was proposed.

Key words: 2-alkylthio-3,5-dihydro-4*H*-imidazol-4-ones, nickel(II), cobalt(II), copper(II), transition metal complexes, electrochemistry, molecular structure.

In recent years, 2-thiohydantoins (4-oxoimidazolidine-2-thiones) and their *S*-alkylated derivatives (2-alkylthio-3,5-dihydro-4*H*-imidazol-4-ones) have been extensively studied because these compounds have a broad spectrum of biological activities. The hydantoin and thiohydantoin fragments in organic molecules are responsible for antiarrhythmic[1] and antihypertensive[2,3] activities. In addition, thiohydantoins possess fungicidal and herbicidal properties.[4] 5-Substituted 3-aryl- and 3-hetarylthiohydantoins have considerable or moderate activity against herpes viruses,[5] HIV,[6,7] and leukemia cells,[8] exhibit anticonvulsant[9,10] and antithrombotic[11] activities, and have moderate antitumor activity.[7] *S*-Alkylated 5-arylidenethiohydantoins[12] possess antidepressant and analgetic properties. *S*-Alkylation products of thiohydantoins were examined also for antiviral and antitumor activities.[13]

2-Thiohydantoins and their *S*-alkylated derivatives containing donor N and S atoms can be coordinated to metals as neutral molecules or (for example, in the case of thiohydantoins containing the NH—C=S fragment) monoanions, which are formed upon deprotonation of the N atom.[14—18] These compounds are of interest as ligands for the preparation of chelate complexes because coordination to transition metal ions often increases antiviral and antitumor activities of drugs.[19] The introduction of substituents containing electron-donating atoms at position 5 of the thiohydantoin ring enhances the coordination ability of these classes of compounds.[20—22] However, the known complexes of hydantoins and thiohydantoins with the Cu^{II},[15,16,20,22] Fe^{III},[15,16] Co^{II},[15,16] Ni^{II},[15,16,22]

---

† Deceased.

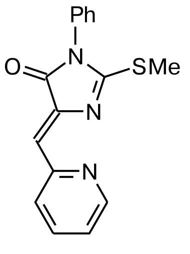
Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2679—2689, December, 2005.

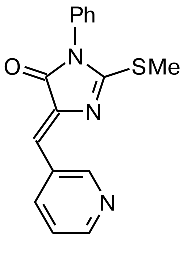
Mn^{II},[16] Cs^{I},[14] Tl^{III},[21] Zn^{II}, Cd^{II}, and Hg^{II},[17] V^{III}, V^{IV}, and V^{V} ions[18] are few in number, whereas data on complexes of *S*-alkylated thiohydantoins are, to our knowledge, lacking.

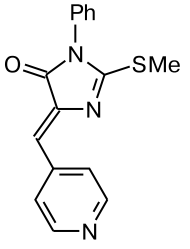
The aim of the present study was to synthesize complexes of divalent Co, Ni, and Cu ions with isomeric α-, β-, and γ-pyridyl-(5*Z*)-2-methylthio-3-phenyl-5-(pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-ones and the Co complex with (5*Z*)-3-methyl-2-methylthio-5-(α-pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-one and investigate these complexes by electrochemical methods. Recently, we have developed a convenient procedure for the synthesis of such complexes.[23—25]

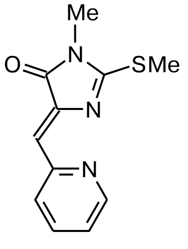
Results and Discussion

Complexes of 3,5-dihydro-4*H*-imidazol-4-ones **1**—**4** with Co (**a**), Ni (**b**) and Cu (**c**) salts were synthesized using two methods depending on the solubility of the ligand in organic solvents.


1

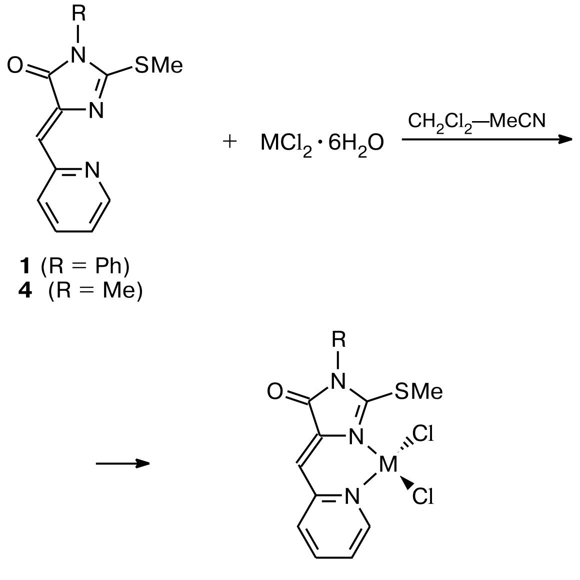

2


3


4

In the case of readily soluble (5*Z*)-2-methylthio-3-phenyl-(or -3-methyl)-5-(α-pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-ones **1** and **4**, it is most convenient to use slow diffusion of a solution of the ligand in CH_2Cl_2 into a solution of $MCl_2 \cdot 6H_2O$ (M = Co, Ni, or Cu) in MeCN (Scheme 1). In the reactions with the cobalt and copper salts, crystals of the target complexes deposited on the walls of the reaction flask after 6—7 days. In the reaction with nickel chloride, the crystalline complex was not isolated. However, the formation of the latter in a solution of a mixture of **1** and $NiCl_2 \cdot 6H_2O$ in MeCN was detected electrochemically (see below).

Scheme 1



1a (R = Ph, M = Co)
1c (R = Ph, M = Cu)
4a (R = Me, M = Co)

Complexes with poorly soluble compounds, *viz*., β- and γ-Py-substituted (5*Z*)-2-methylthio-3-phenyl-5-(pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-ones **2** and **3**, were synthesized by prolonged refluxing in a CH_2Cl_2—MeCN mixture. The complexes were isolated as powdered amorphous compounds. The compositions of the complexes are given in Table 1. Analysis of the results (see Table 1) revealed some characteristic features of the complexes based on the ligands of the series under consideration. In the case of α-Py-substituted ligands **1** and **4**, chelate tetrahedral complexes of composition $L \cdot MCl_2$ were obtained. The structures of cobalt derivatives **1a**[24] and **4a** and copper complex **1c** were established by X-ray diffraction in the present study and in the earlier publication.[24]

Apparently, the coordination environment of the central metal ion in the complexes of composition $2L \cdot MCl_2$ with β- and γ-Py-substituted ligands **2** and **3** differs from that in the above-described complexes. The measured specific magnetic susceptibility χ_r of cobalt complex **3a** is $13.36 \cdot 10^{-6}$ cm^3 g^{-1} at 293.8 K. The effective magnetic moment of complex **3a** calculated from this value is 5.09 μ_B, which agrees well with the published data[26] for the octahedral Co^{II} complexes (4.7—5.2 μ_B).

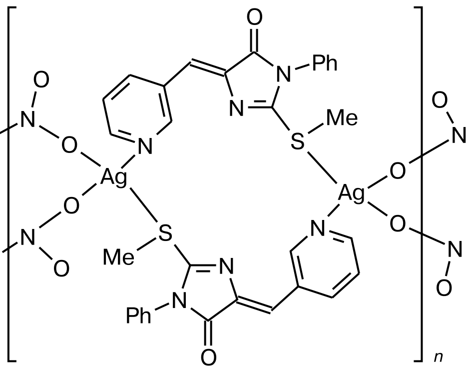
Earlier,[25] we have studied the complex of ligand **3** with $AgNO_3$ by X-ray diffraction and demonstrated that this complex exists as a polymer in the crystalline state, the donor sulfur and nitrogen atoms of the pyridine ring being involved in complexation.

Apparently, the complexes with ligands **2** and **3** with the empirical formula $2L \cdot CoCl_2$ also have polymeric structures, as evidenced by their magnetic moments. Un-

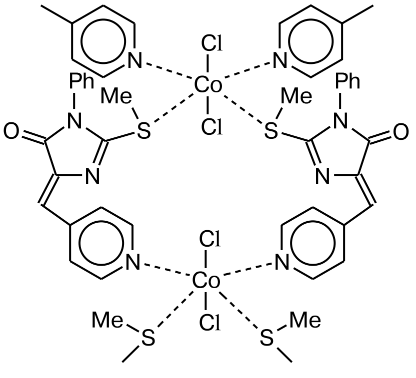
Table 1. Compositions, color, and melting points of the complexes with ligands **1—4**

Ligand L	Metal (M)	Complex	Color of the complex	M.p./°C	Composition of the complex
1	Co	**1a**	Dark green	228	$L \cdot CoCl_2 \cdot 1/2MeCN$
	Ni	**1b**	*		
	Cu	**1c**	Dark cherry	276	$L \cdot CuCl_2 \cdot 2H_2O$
2	Co	**2a**	Gray-green	281	$2L \cdot CoCl_2 \cdot H_2O$
	Ni	**2b**	Yellow	295 (decomp.)	$2L \cdot NiCl_2$
	Cu	**2c**	Green	270	$2L \cdot CuCl_2$
3	Co	**3a**	Pale green	263	$2L \cdot CoCl_2 \cdot CH_2Cl_2$
4	Co	**4a**	Dark green	246	$L \cdot CoCl_2 \cdot 2H_2O$

* The complex was not isolated; its formation was detected electrochemically.



like the metal atom in the above-considered complex, the central metal ion in the latter complexes is in an octahedral environment. The structure of complex **3a** is shown below as an example.



3a

The polymeric structures of the complexes with ligands **2** and **3** are consistent with their very poor solubility in most organic solvents.

Molecular structures of compounds 1c and 4a. The structures of complexes **1c** and **4a** were established by X-ray diffraction (Figs 1 and 2, respectively). The crystallographic data, details of X-ray diffraction study, and characteristics of the structure refinement for compounds **1c** and **4a** are given in Table 2. In both complexes, the copper and cobalt atoms have a distorted tetrahedral ligand environment and are coordinated by two nitrogen atoms of the pyridine and thiohydantoin rings and two chloride anions. The thiohydantoin and pyridine rings in molecules **1c** and **4a** are planar and are virtually coplanar. In molecule **1c**, the carbon atoms of the benzene ring at the N(2) atom deviate from the plane of the five-membered ring of the ligand; the angle of deviation is ~90°.

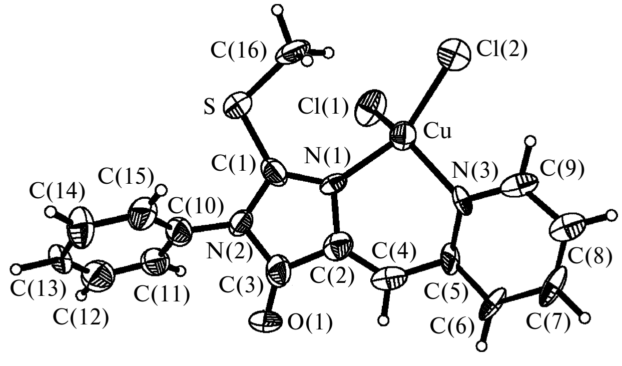


Fig. 1. Molecular structure of compound **1c**. Selected bond lengths/Å: Cu—N(1), 1.967(5); Cu—N(3), 2.032(5); Cu—Cl(1), 2.228(2); Cu—Cl(2), 2.202(2). Selected bond angles/deg: N(1)—Cu—N(3), 93.5(3); N(1)—Cu—Cl(2), 141.39(17); N(3)—Cu—Cl(2), 99.8(2); N(1)—Cu—Cl(1), 96.89(16); N(3)—Cu—Cl(1), 132.02(18); Cl(2)—Cu—Cl(1), 100.46(9).

In the crystal structures of the complexes with ligands **1** and **4**, the tetrahedral geometry of the coordination environment about the cobalt atom, which has a rather small valence shell consisting of 15 electrons, is strongly distorted. The coordination polyhedron can be approximately described as a trigonal bipyramid with one axial ligand removed. As a result, dissolution of these complexes can, apparently, lead to coordination by an additional donor molecule (for example, by a solvent molecule or molecular oxygen) to form a compound, in which the Co atom has a 17-electron valence shell. In coordinating solvents, coordination of the second solvent molecule giving rise to a six-coordinate 19-electron complex is probable.

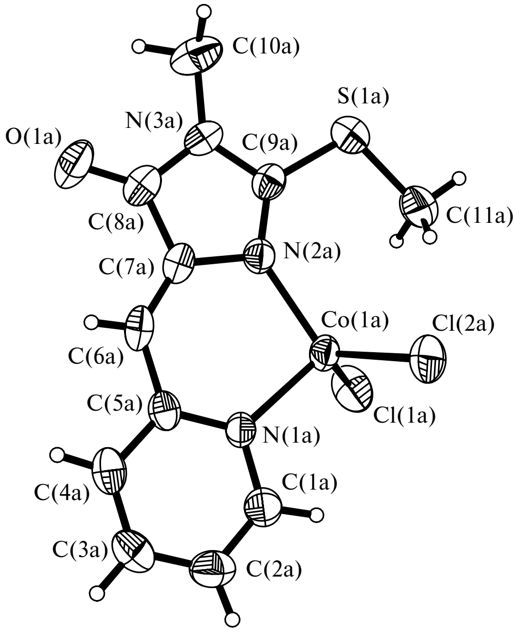
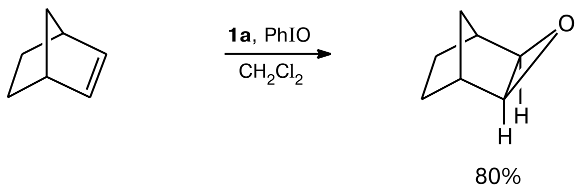


Fig. 2. Molecular structure of compound **4a** (one of three crystallographically independent molecules is shown). Selected bond lengths/Å: Co—N(1), 2.031(3) [2.041(3), 2.024(4)]; Co—N(2), 2.010(3) [2.005(3), 2.005(3)]; Co—Cl(1), 2.2413(14) [2.2353(15), 2.2311(14)]; Co—Cl(2), 2.2462(15) [2.2381(15), 2.2339(15)]. Selected bond angles/deg: N(2)—Co—N(1), 96.80(14) [97.56(14), 96.59(14)]; N(2)—Co—Cl(1), 115.29(11) [114.21(11), 118.60(12)]; N(1)—Co—Cl(1), 106.24(11) [109.35(11), 104.28(11)]; N(2)—Co—Cl(2), 114.44(11) [113.95(12), 112.48(11)]; N(1)—Co—Cl(2), 105.98(11) [103.85(11), 106.31(11)]; Cl(2)—Co—Cl(1), 115.41(6) [115.61(6), 115.44(6)]. Data for two other crystallographically independent molecules are given in square brackets.

In recent years, mono- (see Refs 26 and 27) and dinuclear[28,29] Co^{II} complexes with chelate nitrogen-containing ligands have been proposed as molecular oxygen carriers. We examined the possibility of absorption of O_2 with cobalt-containing complex **1a**. During bubbling of air through a 0.1 *M* solution of **1a** in MeCN for several hours, the solution gradually turned colorless, which was accompanied by the corresponding changes in the electronic spectrum; more particularly, the intensities of the d—d transition bands at λ ~600 nm decreased (see below). Analogous changes in the spectrum were observed upon the addition of an excess of H_2O_2. It should be noted that the colorless solution of **1a** obtained after purging with air instantaneously returned to the initial green color upon the addition of an equal volume of oxygen-free MeCN.

In addition, it was found that complex **1a** exhibits catalytic activity in alkene epoxidation with iodobenzene (Scheme 2). The addition of 5—10 mol. % of this complex to a solution of an equimolar mixture of alkene and PhIO in CH_2Cl_2 afforded the corresponding epoxide in 80% yield. It should be noted that neither ligand **1** nor $CoCl_2 \cdot 6H_2O$ exhibited catalytic activity.

Scheme 2



According to the above-considered data, complex **1a** can reversibly absorb molecular oxygen. We are now examining the possibility of the use of this complex for catalysis of various types of oxidation reactions, in particular, of alkene epoxidation.

Electronic spectroscopy. Ligands **1**, **2**, and **4** and the complexes synthesized with the use of these ligands were studied by UV—Vis spectroscopy. The spectroscopic data are given in Table 3. The UV—Vis spectra of ligand **1**, its cobalt complex **1a**, and the $CoCl_2 \cdot 6H_2O$ compound are shown in Fig. 3. Ligand **1** is characterized only by absorption bands in the UV region corresponding to p—p* and n—p* transitions in the organic molecule. The $CoCl_2 \cdot 6H_2O$ compound is characterized by three medium-intensity d—d-transition bands in the visible region (550—700 nm). Complexation leads to small shifts and a decrease in the intensity of the absorption bands of the ligand in the UV region and shifts of the d—d-transition bands of the metal atom to lower wavelengths.

The electronic spectra of the complexes with β- and γ-Py-substituted ligands **2** and **3** differ substantially from the above-described spectra. These spectra show an absorption band at ~370 nm (its frequency is equal to that

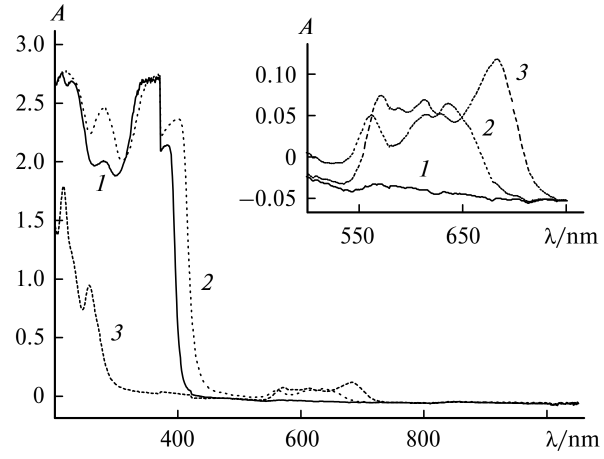


Fig. 3. Electronic spectra of ligand **1** (*1*), complex **1a** (*2*), and $CoCl_2 \cdot 6H_2O$ (*3*) (MeCN, 10^{-3} mol L^{-1}). An enlarged fragment is shown in the inset.

Table 2. Crystallographic data, details of X-ray diffraction study, and characteristics of the structure refinement for compounds **1c** and **4a**

Parameter	**1c**	**4a**
Molecular formula	$C_{16}H_{17}Cl_2CuN_3O_3S$	$C_{11}H_{11}Cl_2CoN_3OS$
Molecular weight	465.83	363.12
Color, crystal shape	Dark cherry platelets	Dark green prisms
Crystal dimensions/mm	0.45×0.18×0.10	0.38×0.14×0.14
Crystal system	Monoclinic	Monoclinic
Space group	*P*2(1)/*c*	*P*2(1)/*n*
a/Å	10.668(2)	15.038(3)
b/Å	27.135(5)	10.360(2)
c/Å	6.850(1)	27.451(5)
α/deg	90	90
β/deg	91.28(3)	94.57(4)
γ/deg	90	90
V/Å^3	1982.4(6)	4274.0(14)
Z	4	12
ρ_{calc}/g cm^{-3}	1.561	1.693
Linear absorption coefficient/cm^{-1}	1.497	1.719
F(000)	948	2196
θ Angle range/deg	2.05—24.98	1.52—22.97
Ranges of reflection indices	$-12 \leq h \leq 12$	$0 \leq h \leq 16$
	$0 \leq k \leq 32$	$-9 \leq k \leq 0$
	$0 \leq l \leq 8$	$-30 \leq l \leq 30$
Number of measured reflections	3775	5185
Number of independent reflections	3469 (R_{int} = 0.1012)	4968 (R_{int} = 0.0455)
Number of reflections with $I > 2\sigma(I)$	755	2856
Number of parameters in refinement	233	646
Goodness-of-fit on F^2	0.650	0.772
R Factors based on reflections with $I > 2\sigma(I)$		
R_1	0.0492	0.0264
wR_2	0.0847	0.0601
R Factors based on all data		
R_1	0.3300	0.0848
wR_2	0.0963	0.0646
Residual electron density (min/max)/e Å^{-3}	0.545/–0.307	0.258/–0.288

* The crystal under examination slowly decomposed in the course of X-ray diffraction study.

Table 3. Electronic spectra of the ligands, the starting inorganic salts, and the complexes (~$2 \cdot 10^{-3}$ mol L^{-1}) in solutions in MeCN or DMF

Compound	Solvent	λ/nm ($\varepsilon \cdot 10^{-4}$/L mol^{-1} cm^{-1})
1	MeCN	277 (1.59), 353 (1.99), 369 (2.00)
2	DMF	369 (2.00)
4	MeCN	273 (2.58), 361 (1.70)
1a	MeCN	280 (1.59), 388 (1.60), 400 (1.26), 562 (0.32), 616 (0.32), 636 (0.40)
2a	DMF	367 (2.94), 608 (0.02), 679 (0.03)
3a	DMF	297 (1.49), 369 (3.02), 607 (0.03), 665 (0.03)
4a	MeCN	268 (3.51), 378 (3.31), 560 (0.37), 629 (0.16)
$CoCl_2 \cdot 6H_2O$	MeCN	570 (0.33), 613 (0.32), 682 (0.35)
$CuCl_2 \cdot 2H_2O$	MeCN	329 (0.14), 426 (0.01)

observed for the free ligand but the intensity of the band is higher) and two very weak d—d-transition bands at λ = 600—700 nm (see Table 3). This agrees well with the proposed octahedral structures of the complexes with ligands **2** and **3**.

Electrochemistry. Free ligands **1—4** and their complexes with MCl_2 were studied also by cyclic voltammetry (CV) and rotating disk electrode (RDE) voltammetry in anhydrous DMF in the presence of 0.05 *M* Bu_4NClO_4 as the supporting electrolyte. The complexes, which were synthesized and characterized, as well as the complexes, which prepared *in situ* in an electrochemical cell by mixing ligand **1** with an equimolar amount of a metal salt, were studied. The reaction of ligand **1** with MCl_2 in DMF is fast, which is evidenced by an instantaneous change in the color of the solution observed upon mixing of the reagents. As a rule, the electrochemical characteristics of the complexes prepared *in situ* differ only slightly from those of the presynthesized complexes. The electrochemical results and the experimental conditions are given in Table 4.

Cobalt, nickel, and copper chlorides. The $CoCl_2 \cdot 6H_2O$ compound undergoes two-electron reduction on a rotating disk electrode to give metallic Co^0, which is oxidized at +0.35 V during the reverse scan to the anodic region with the formation of a triangular (without a diffusion tail) steeple-like peak characteristic of oxidative desorption from the electrode surface. At the same time, two cathodic peaks are observed in the CV curve (see Table 4). Anodic oxidation on a rotating disk electrode gives two one-electron waves. One of them is, apparently, associated with the $Co^{II} \rightarrow Co^{III}$ transition, and another wave corresponds to oxidation of one of the ligands, for example, of the water molecule

$$[Cl_2Co^{III}—OH_2]^+ - e \rightarrow 1/2\ [Cl_2Co^{III}—O]_2 + 2\ H^+$$

or chloride ligands

$$3\ [CoCl_2]^+ - 2\ e^- \rightarrow 3\ Co^+ + 2\ Cl_3^-.$$

The $NiCl_2 \cdot 6H_2O$ compound undergoes one-step two-electron reduction under cathodic polarization with an anodic desorption peak of Ni^0 in the reverse scan of the CV curve at +0.16 V. Under anodic polarization, oxidation of this compound also occurs as a one-step two-electron process.

Table 4. Electrochemical reduction potentials (E^{Red}) and oxidation potentials (E^{Ox}) of the ligands and complexes measured relative to Ag|AgCl|KCl(sat.) by the CV (E_p is the peak potential) and RDE ($E_{1/2}$ is the half-wave potential) methods at a glassy-carbon electrode[a]

Compound	E_p^{Red}	$E_{1/2}^{Red}$	E_p^{Ox}	$E_{1/2}^{Ox}$
	V			
1[b]	−1.29/−1.23[c]	−1.28(1)	1.66	1.66(2)
	−1.77	−1.77(1)	2.16	
	−1.99	−2.47(1)		
1a	−0.63	−0.58(1)	1.76	1.72(2)
	−1.24	−1.19(1)	2.10	2.03(>2)
	−1.79	−1.65(1)		
	−1.99			
1b[d]	−0.64	−0.61(1)	1.37	1.31(2)
	−1.35	−1.27(1)	1.96	1.52(2)
	−1.79	−2.13(1)		
	−2.49			
1c	+0.45/+0.52[c,e]		0.58[d]	0.50(1)[f]
	−0.51[g]		1.32	1.35(1)
	−1.32	−1.28(1)[h]		
	−1.94	−1.96(1)		
2	−1.28/−1.23[c]	−1.33(1)	1.64	1.58(2)
	−1.89			
	−2.46			
2a	−1.29	−1.24(1)	1.25	1.16(2)
	−1.97	−2.03(1)	1.60	1.61(2)
2b	−1.26	−1.22(1)	1.14	1.16(1)
	−1.96			1.60(1)
	−2.30			
2c	+0.45/+0.51[c]		0.56/0.45[c]	0.44
	−1.32/−1.26	−1.28(1)[h]	1.21(2)	1.13(1)
	−1.94/−1.84	−1.96(1)	1.63	1.60
3	−1.16/−1.10[c]	−1.17(1)	0.64	0.77
	−1.64	−1.70(1)	1.13	1.16[i]
	−2.32	−2.26		
3a	−1.14	−1.00(1)	1.24	1.14(2)
4	−1.29	−1.20(1)	1.62	1.52(2)
	−1.46	−1.86(1)		
	−2.02	−2.04(1)		
	−2.36	−2.40(1)		
4a	−0.68	−0.64[j]	1.33	1.27(2)
	−1.30	−1.14		
	−1.84			
$CoCl_2 \cdot 6H_2O$	−0.86	−1.30	1.53	1.50(1)
	−1.21/+0.35[c]		1.70	1.70(1)
$NiCl_2 \cdot 6H_2O$	−1.32/+0.16[c]	−1.30(2)	1.20	1.00(2)
$CuCl_2 \cdot 2H_2O$	+0.45/+0.58[c,e]	+0.50(1)[h]		
	−0.51/−0.16[c]			

[a] Experimental conditions: DMF, 0.05 *M* Bu_4NClO_4; CV, 200 mV s^{-1}; RDE, 20 mV s^{-1}; 2800 min^{-1} (the number of electrons transferred in the step, which was determined on a rotating disk electrode by comparing with the one-electron oxidation wave of ferrocene, is given in parentheses).

[b] In MeCN.

[c] The peak potentials in the reverse scans of the CV curves.

[d] The complex was prepared *in situ* in DMF from equimolar amounts of the ligand and $MCl_2 \cdot nH_2O$.

[e] The initial potential was +0.7 V.

[f] The resulting complex on Pt.

[g] The peak at −0.51 V is poorly pronounced and is not always reproduced.

[h] The initial potential was 0 V.

[i] The height of the second wave is half as large as that of the first wave.

[j] The height of the peak corresponds to the transfer of 0.5—0.7 electrons.

Reduction of $CuCl_2 \cdot 2H_2O$ is characterized by two cathodic peaks in the CV curve at +0.45 and –0.51 V, which correspond to two one-electron steps ($Cu^{II} \rightarrow Cu^{I} \rightarrow Cu^{0}$). Each peaks corresponds to a reoxidation peak in the reverse scan. However, only the first one-electron peak (+0.50 V) is observed for a stirred solution by the RDE method during a slow cathodic potential scan from +0.7 V, whereas the second peak does not appear. Apparently, this is associated with the formation of a nonconducting film of an insoluble one-electron reduction product of copper on the electrode surface, which blocks electron transfer. No peaks or oxidation waves of $CuCl_2 \cdot 2H_2O$, which could correspond to the formation of trivalent copper, were observed in the anodic region up to +1.7 V.

Ligands. Ligands **1—4** are successively reduced in several one-electron steps and are oxidized to give a two-electron wave. The exception is ligand **3**, for which a large prewave was observed at potentials from +0.64 to +0.77 V by both the CV and RDE methods (see Table 4).

We performed semiempirical quantum-chemical calculations by the PM3 method.[31] These calculations demonstrated that both the highest occupied molecular orbitals (HOMO) and the lowest unoccupied molecular orbitals (LUMO) in molecules **1—4** have a π symmetry and are localized predominantly on the thiohydantoin fragment (Fig. 4). The orbital of the sulfur lone pair makes the major contribution to HOMO, whereas the cross-conjugated methylidenehydantoin π-system O=CC(=C)N=C makes the major contribution to LUMO. These results suggest that both oxidation and reduction occur primarily at the thiohydantoin moiety of the ligands.

The degree of involvement of the *N*-phenyl and Py groups in the redox orbitals depends on the degree of their coplanarity with the thiohydantoin ring. The geometry optimization of the ligands by the PM3 method demonstrated that at least four stereoisomers can exist. Their heats of formation differ by 3.7 kcal mol^{-1}. These isomers, which differ in the configuration of the substituents at the double bond (*E, Z*) and the orientation of the dipole of the MeS group relative to the C=N bond of the thiohydantoin ring (*syn* or *anti*), are shown below. The calculated heats of formation, the torsion angles between the planes of the hydantoin and 2-pyridine substituents (Py/Hyd), and the torsion angles between the hydantoin and *N*-phenyl substituents (Ph/Hyd) for ligand **1** are also presented. The results of calculations are consistent with the X-ray diffraction data on stability of the (*Z*)-*syn* form.[24]

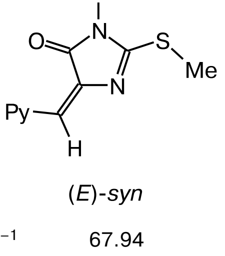
In all conformations of compounds **1—3**, the torsion angles between the planes of the thiohydantoin ring and the *N*-phenyl group are close to 90°, whereas the torsion angle between the planes of the thiohydantoin and pyridine rings is strongly related to the geometric isomerism (see above) and, to a lesser extent, to the isomerism of the pyridyl fragment (for the (*E*)-*syn* conformations: **1** and **4**, 87°; **3**, 75°; and **2**, 61°). Therefore, the orbitals of the *N*-phenyl group are almost not involved in the redox orbitals of the ligand, whereas the orbitals of the Py groups have a particular effect on the redox orbitals, the degree of their influence depending on the geometry of the ligand.

The identification of oxidation and reduction products of the ligands by preparative electrolysis was beyond the scope of the present study. Nevertheless, taking into account the types of orbitals (see Fig. 4), it can be hypothesized that oxidation occurs predominantly at the sulfur atoms.

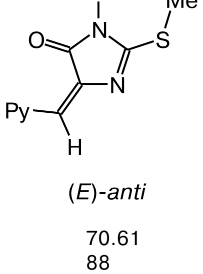
The probable four-step (see Table 4) mechanism of electroreduction of these compounds is presented in Scheme 3. Four one-electron waves will be observed, for example, if the primary radical anion accepts an electron followed by protonation of the dianion with water at the imine double bond. Then stepwise reduction occurs at the 1,2 and 1,4 positions of the Michael system O=C—C=C of thiohydantoin.

Complexes. The cyclic voltammograms of the complexes, the free ligands, and Ni and Co chlorides (see above) are shown in Fig. 5. As compared to free ligand **1**, tetrahedral cobalt complex **1a** is characterized by an additional cathodic peak at less negative potentials (see Fig. 5, *a*) than the first peak of the free ligand. This peak appears rather early for Co^{II} complexes (–0.63 V) and corresponds, more likely, to the $Co^{III} \rightarrow Co^{II}$ transition rather than to the $Co^{II} \rightarrow Co^{I}$ transition.

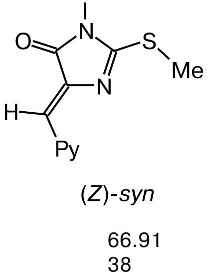
These results can be explained as follows. The structures of compounds **1a—c** and **4a** (based on their empiri-



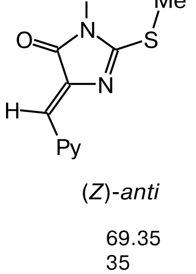
(*E*)-*syn*



(*E*)-*anti*



(*Z*)-*syn*



(*Z*)-*anti*

ΔH_f/kcal mol^{-1}	67.94	70.61	66.91	69.35
Py/Hyd Angle/deg	87	88	38	35
Ph/Hyd Angle/deg	86	87	87	87

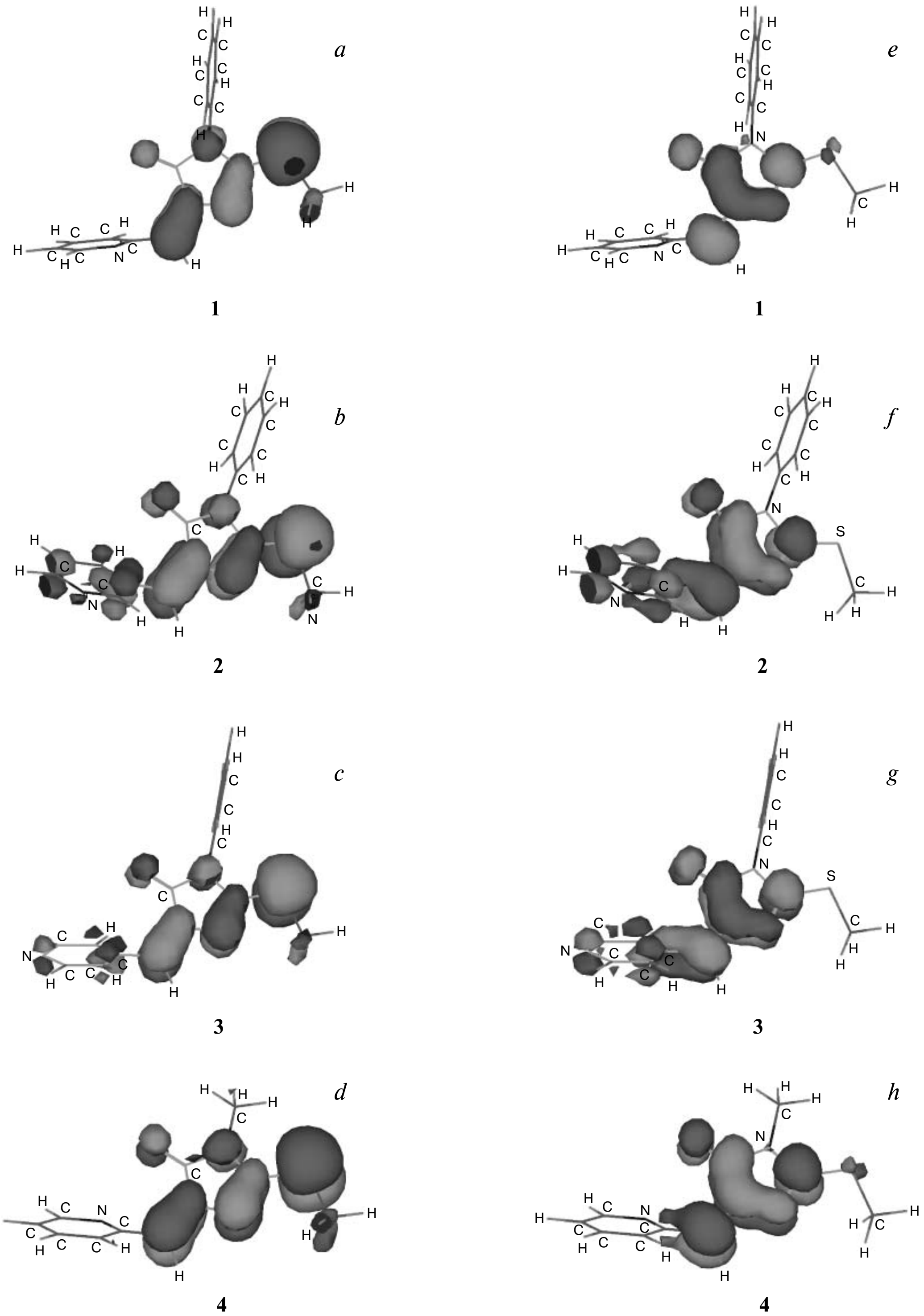
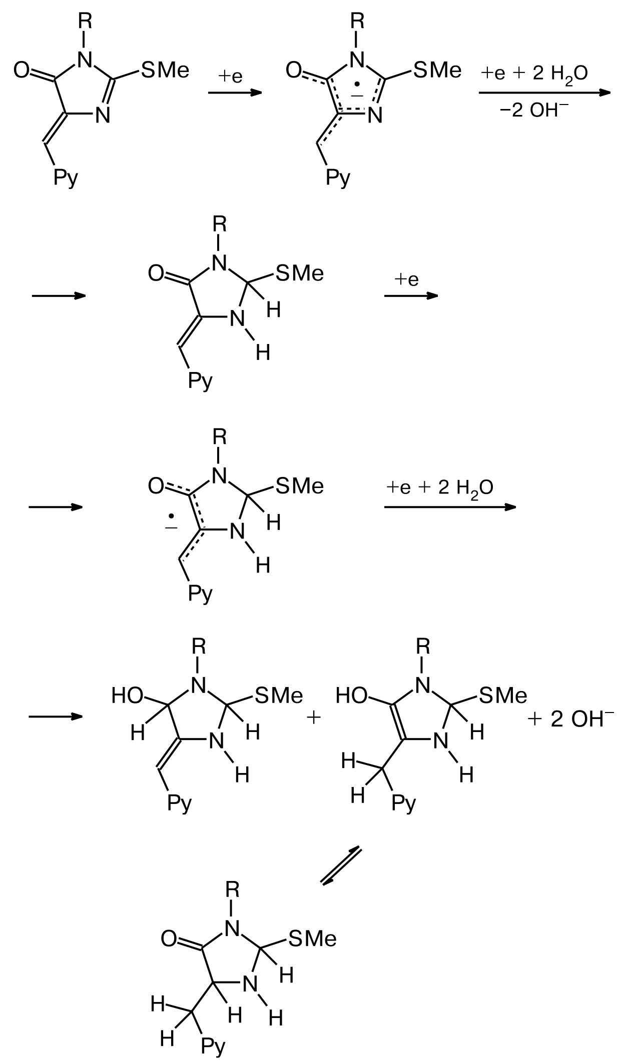


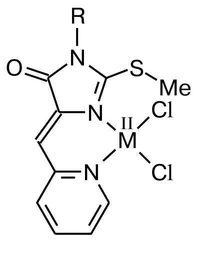
Fig. 4. Frontier (redox) orbitals of ligands **1—4** in (*E*)-*syn* conformations calculated by the PM3 method: HOMO (*a—d*) and LUMO (*e—h*).

cal formula $LMCl_2$) can be represented either as an M^{II} complex with the uncharged organic ligand (**A**) or as an M^{III} complex with the radical-anionic ligand (**B**). Consequently, complexes with ligands **1** and **4** should be assigned to metal complexes with non-innocent ligands,[30] for which neither the oxidation state of the central metal ion nor the bond orders in the ligand cannot *a priori* be determined. The fact that complex **1a** is reduced 580 mV

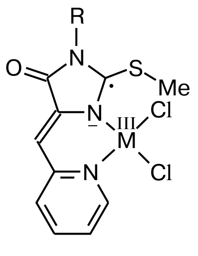
Scheme 3



more easily than $CoCl_2 \cdot 6H_2O$ (see Table 4), even though coordination by donor ligands should hinder reduction of metal ions, suggests that the true structure of complex **1a** (and, probably, of **4a**) is similar to **B**.



A



B

It should also be noted that the first peak in the anodic branch of the polarization curves of complexes **1a** and **4a** is shifted to more positive potentials by 100 mV compared to that of the ligand and by 230 mV compared to $CoCl_2 \cdot 6H_2O$. It is unlikely that this peak corresponds to the $Co^{II} \rightarrow Co^{III}$ transition because complexation with donor ligands should facilitate oxidation if it occurs at the metal atom. The shift of the potential to the anodic region upon complexation of the ligand with Lewis acids signifies that oxidation occurs most likely at the ligand.

The structure **B** for compound **1a** is additionally confirmed by the structural data.[24,25] The N(1)—C(1) bond in the thiohydantoin ring of this compound is substantially longer than that in the free ligand, *i.e.*, this formally double bond in the complex better corresponds to a single bond. The exocyclic C(1)—S bond length in complex **1a** is virtually equal to that in the free ligand and corresponds to the single C—S bond.[24] In the β-Py-containing complex of ligand **2** with $AgNO_3$, the N(1)—C(1) and C(1)—S bond lengths are similar to the corresponding bond lengths in the free ligand.[25]

Therefore, the electrochemical and structural data suggest that complex **1a** can be represented as a Co^{III} complex with the radical-anionic ligand, *i.e.*, the structure of the ligand in the complex differs from that of the free ligand, and ligand **1** should be considered as non-innocent.[30]

A similar situation is observed for nickel complex **1b**, which was prepared *in situ* by mixing $2 \cdot 10^{-5}$ *M* $NiCl_2 \cdot 6H_2O$ solutions in DMF (see Fig. 5, *b*). The first reduction potential is 680 mV less negative than the reduction potential of $NiCl_2 \cdot 6H_2O$, whereas the first oxidation potential is 170 mV more positive than the oxidation potential of the salt. The potential of the first reduction step of the complex is also unusually low (−0.64 V). Consequently, compound **1b** can also be represented as a Ni^{III} complex with the radical-anionic ligand.

The possible mechanism of reduction of the non-innocent complexes (taking into account the fact that reduction of the complexes, unlike reduction of the salts, is not accompanied by metal deposition on an electrode) is presented in Scheme 4.

Therefore, the first reduction step occurs, presumably, at the trivalent metal atom (and then at the ligand).

Copper complex **1c** undergoes a reversible redox transition at the same potential as $CuCl_2 \cdot 2H_2O$ (+0.45 V; $Cu^{II} \rightarrow Cu^{I}$). However, unlike the salt, the copper complex gives the poorly pronounced and sometimes irreproducible second reduction peak at −0.50 V ($Cu^{I} \rightarrow Cu^{0}$) (see Fig. 5, *c*). Suppression of the peak at −0.5 V may be a consequence of the coverage of the electrode surface by the adsorbed electrolysis product. During the anodic potential scan from the initial value of 0 V (at which Cu exists in a monovalent state), the first oxidation peak is observed at +0.58 V ($Cu^{I} \rightarrow Cu^{II}$), whereas no oxidation peaks are observed for $CuCl_2 \cdot 2H_2O$ in DMF at potentials up to +1.7 V. The potential of the second oxidation peak of complex **1c** is 340 mV more positive than the

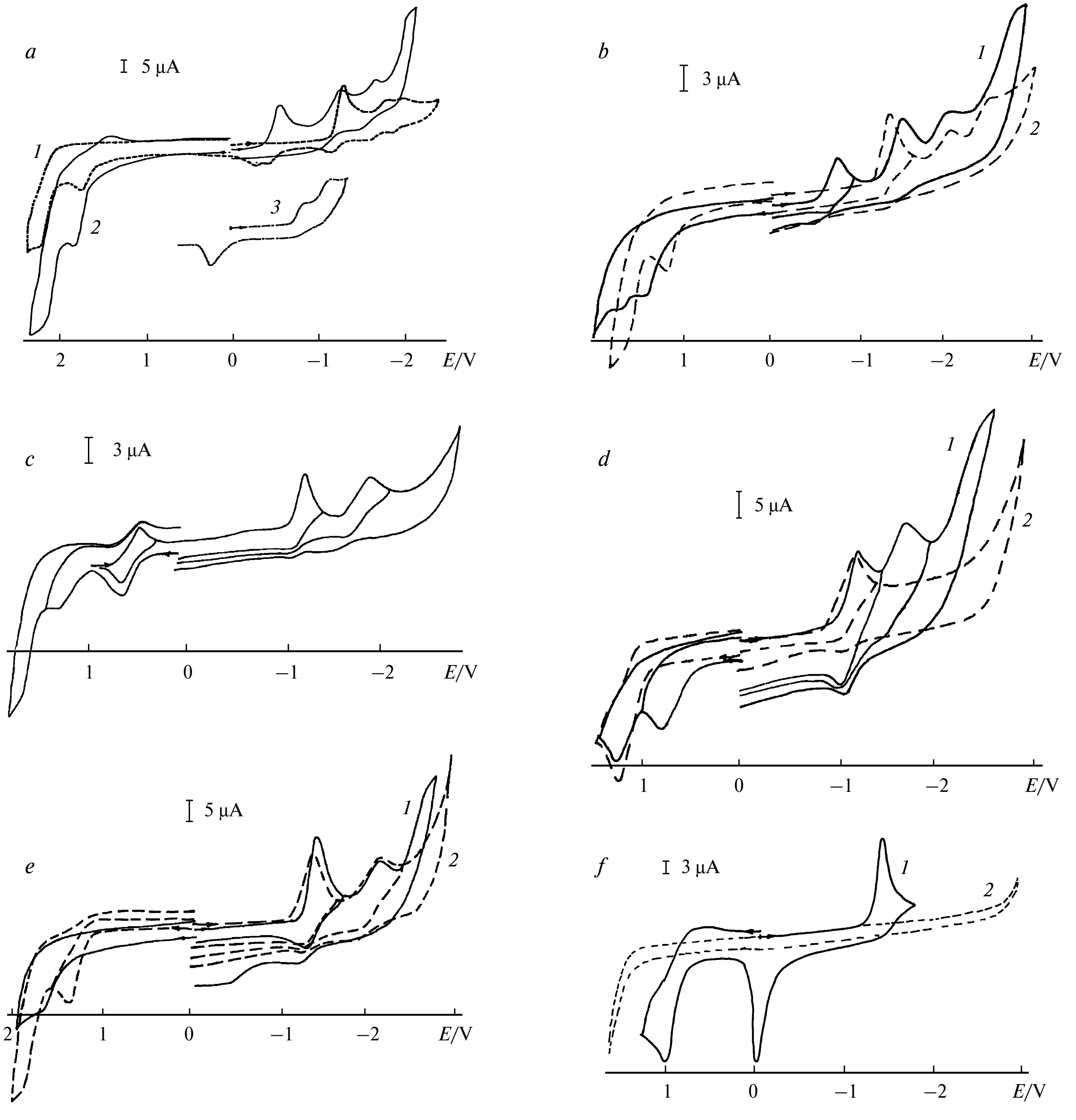
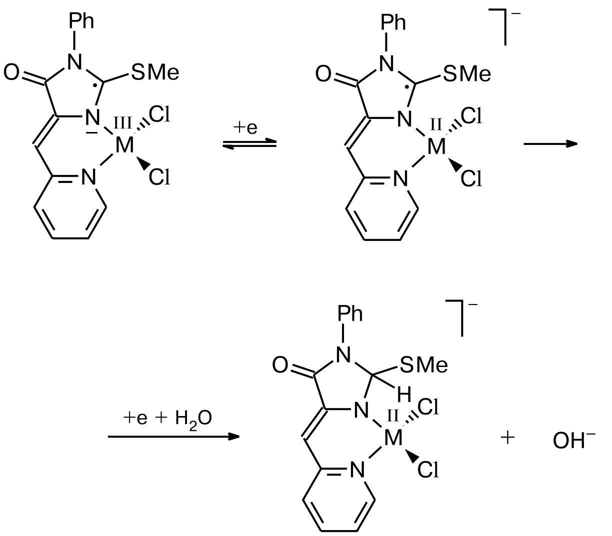


Fig. 5. Cyclic voltammograms: *a*, **1** (*1*), **1a** (*2*), $CoCl_2 \cdot 6H_2O$ (*3*); *b*, **1b** (*1*), **2b** (*2*); *c*, **1c**; *d*, **2** (*1*), **2a** (*2*); *e*, **3** (*1*), **3a** (*2*); *f*, $NiCl_2 \cdot 6H_2O$ (*1*), a background curve (*2*).

potential of the first oxidation peak of ligand **1** (see Table 4).

The polarization curves for complexes **2a** and **2b** are shown in Figs 5, *b*,*d*, and the corresponding curve for **1a** is presented in Fig. 5, *a*. In the cathodic region, the first reduction peaks of **2a,b** and **3a** are very similar to the first reduction peaks of the ligands and are only slightly shifted to more negative potentials compared to $CoCl_2$ and $NiCl_2$ hexahydrates (see Table 4). This may be indicative of reduction of both at the ligand and metal. Like the above-considered complex, copper complex **2c**, is characterized by the presence of a peak at +0.45 V, which coincides with the peak for $CuCl_2 \cdot 2H_2O$ ($Cu^{II} \rightarrow Cu^{I}$), whereas the peak at −0.50 V, which is observed for a $CuCl_2 \cdot 2H_2O$ solution ($Cu^{I} \rightarrow Cu^{0}$), is absent. The first oxidation potentials of complexes **2a,b** and **3a** are less positive than the oxidation potentials of the ligand, *i.e.*, oxidation of the complexes occurs at the metal atom. In addition, the

Scheme 4



oxidation potentials of complexes **2a,b** are less positive than the oxidation potentials of $MCl_2 \cdot 6H_2O$, which is also indicative of oxidation at metal.

Experimental

Ligands **1**—**3** were synthesized according to a known procedure.[24] The IR spectra were measured on a UR-20 instrument in Nujol mulls. The UV-Vis spectra were recorded on Specord M-40 (200—900 nm) and Nicolet Helios-α (200—1100 nm) instruments in 0.1-cm quartz cells at 20—22 °C. The ^1H NMR spectra were measured on a Varian-VXR-400 instrument at 400 MHz. The EI mass spectra were obtained on a JMS-D300 GLC-mass spectrometer equipped with a JMA-2000 computer and an HP-5890 chromatograph. The magnetic susceptibility was measured by the Faraday method at 293.8 K.

X-ray diffraction data sets were collected on a Syntex P21 diffractometer (graphite monochromator, λ(Mo-Kα) = 0.71073 Å, ω scanning technique) at 293 K. Absorption corrections were applied based on the intensities of equivalent reflections (T_{min}/T_{max}). The structures were solved by direct methods (SHELXS-97)[31] and refined by the full-matrix least-squares method against F^2 with anisotropic displacement parameters for all nonhydrogen atoms (SHELXL-97).[32] All hydrogen atoms were located from electron density maps and refined isotropically.

Electrochemical studies were carried out on a PI-50-1.1 potentiostat. A glassy-carbon (GC) disk (2 mm in diameter) was used as the working electrode, a 0.05 *M* Bu_4NClO_4 solution in DMF served as the supporting electrolyte, and Ag/AgCl/KCl(satur.) was used as the reference electrode. All measurements were carried out under argon. The samples were dissolved in the pre-deaerated solvent. Dimethylformamide (high-purity grade) was purified by stirring over freshly calcined K_2CO_3 for 4 days followed by successive vacuum distillation over P_2O_5 and anhydrous $CuSO_4$.

Quantum-chemical calculations were performed with the use of the semiempirical SCF PM3 method,[33] which was extended by including the parameters for all first-row transition metals and selected second- and third-row transition metals. This extended method (PM3(tm)) is implemented in the HyperChem program package (HyperCube Inc., FL, USA). Geometry optimization of the molecules was carried out with a gradient of no higher than 10 kal $Å^{-1}$ mol^{-1} as the convergence criterion.

3-Methyl-2-methylthio-5-((*Z*)-2-pyridylmethylidene)imidazol-4-one (4). A 15% KOH solution (1 mL) was added to a solution of 2-thioxo-5-((*Z*)-2-pyridylmethylidene)imidazol-4-one (0.5 g, 2 mmol) in a 1 : 1 MeOH—water mixture (20 mL). After complete dissolution of 2-thioxo-5-((*Z*)-2-pyridylmethylidene)imidazol-4-one, MeI (0.7 g, 4 mmol) was added, and the reaction mixture was stirred for 1 h. The precipitate that formed was filtered off, washed with water, and dried in air. The yield of compound **4** was 0.3 g (70%), m.p. 206 °C. Found (%): C, 56.48; H, 4.23; N, 18.07. $C_{11}H_{11}N_3OS$. Calculated (%): C, 56.65; H, 4.72; N, 18.03. ^1H NMR ($CDCl_3$), δ: 8.69 (d, 1 H, H_α-Py, *J* = 8.3 Hz); 8.53 (d, 1 H, $H_{\beta'}$-Py, *J* = 4.4 Hz); 8.03 (t, 1 H, H_β-Py, *J* = 4.4 Hz); 7.46 (d, H_γ-Py, *J* = 4.2 Hz); 6.88 (s, 1 H, CH=); 3.18 (s, 3 H, NMe); 2.70 (s, 3 H, SMe). IR, ν/cm^{-1}: 1740 (C=O); 1670 (C=N); 1600 (C=C).

Synthesis of complexes with 2-methylthio-5-(pyridylmethylidene)-3,5-dihydro-4*H*-imidazol-4-ones. ***A*** **(for complexes with ligands 1 and 4).** Acetonitrile (3 mL) was added to a solution of the ligand (0.034 mmol) in CH_2Cl_2 (2—3 mL) until stratification occurred. Then a solution of the salt $CoCl_2 \cdot 6H_2O$ or $CuCl_2 \cdot 6H_2O$ (0.034 mmol) in EtOH (2—3 mL) was slowly added. The reaction mixture was tightly closed and kept until crystals formed. The yield was 75—80%.

B **(for complexes with ligands 2 and 3).** The ligand (0.678 mmol) and the salt $CoCl_2 \cdot 6H_2O$, $CuCl_2 \cdot 6H_2O$, or $NiCl_2 \cdot 6H_2O$ (0.678 mmol) were dissolved in a mixture of CH_2Cl_2 and MeCN (10—15 mL). The reaction mixture was refluxed with vigorous stirring for 2 h (until a precipitate was obtained). The precipitate was filtered off and washed with diethyl ether. The yield was 80—90%.

Complex $Co^{II}(1)Cl_2 \cdot 0.5MeCN$ (1a). Found (%): C, 46.58; H, 3.57; N, 9.26. $(C_{16}H_{13}OSN_3 \cdot CoCl_2)_2 \cdot CH_3CN$. Calculated (%): C, 45.79; H, 3.25; N, 9.54. IR, ν/cm^{-1}: 1756, 1746, 1644, 1594.

Complex $Cu^{II}(1)Cl_2 \cdot 2H_2O$ (1c). Found (%): C, 41.53; H, 3.50; N, 9.20. $C_{16}H_{13}OSN_3 \cdot CuCl_2 \cdot 2H_2O$. Calculated (%): C, 41.25; H, 3.68; N, 9.02.

Complex $Co^{II}(2)_2Cl_2 \cdot H_2O$ (2a). Found (%): C, 52.51; H, 3.45; N, 11.01. $(C_{16}H_{13}OSN_3)_2 \cdot CoCl_2 \cdot H_2O$. Calculated (%): C, 52.04; H, 3.82; N, 11.38. IR, ν/cm^{-1}: 1745, 1650, 1609.

Complex $Ni^{II}(2)_2Cl_2$ (2b). Found (%): C, 53.00; H, 3.95; N, 12.43. $(C_{16}H_{13}OSN_3)_2 \cdot NiCl_2$. Calculated (%): C, 53.36; H, 3.61; N, 11,67.

Complex $Cu^{II}(2)_2Cl_2$ (2c). Found (%): C, 52.50; H, 3.43; N, 11.05. $(C_{16}H_{13}OSN_3)_2 \cdot CuCl_2$. Calculated (%): C, 53.00; H, 3.61; N, 11,59.

Complex $Co^{II}(3)_2Cl_2 \cdot CH_2Cl_2$ (3a). Found (%): C, 49.02; H, 3.26; N, 9.42. $(C_{16}H_{13}OSN_3)_2 \cdot CoCl_2 \cdot CH_2Cl_2$. Calculated (%): C, 49.19; H, 3.74; N, 9.94. IR, ν/cm^{-1}: 1725, 1620, 1610.

Complex $Co^{II}(4)Cl_2 \cdot 2H_2O$ (4a). Found (%): C, 33.40; H, 3.58; N, 10.13. $C_{11}H_{11}OSN_3 \cdot CoCl_2 \cdot 2H_2O$. Calculated (%): C, 33.10; H, 3.79; N, 10.53.

Synthesis of *exo*-epoxynorbornene. Compound **1a** (0.0425 g, 0.1 mmol) was added to a solution of norbornene (0.47 g, 5 mmol) and iodobenzene (0.2 g, 1 mmol) in MeCN (5 mL). The reaction mixture was stirred at room temperature for 5 h, passed through a silica gel filter column (h = 3 cm), and concentrated. *exo*-Epoxynorbornene was obtained in a yield of 0.09 g (80%). ^{1}H NMR ($CDCl_3$), δ: 3.03 (br.s, 2 H, HC(2), HC(3)); 2.42 (br.s, 2 H, HC(1), HC(4)); 1.46 (d, 1 H, *syn*-HC(7), J = 9.0 Hz); 1.30 (ddd, 2 H, HC(5), *endo*-HC(6), J_1 = 2.1 Hz, J_2 = 4.5 Hz, J_3 = 8.0 Hz); 1.19 (ddd, 2 H, HC(5), *exo*-HC(6), J_1 = 2.2 Hz, J_2 = 4.5 Hz, J_3 = 8.0 Hz); 0.68 (d, 1 H, *anti*-HC(7), J = 9.0 Hz). MS, m/z: 110 $[M]^+$.

This study was financially supported by the Russian Foundation for Basic Research (Projects Nos 03-03-32401 and 04-03-32845), the Program "Russian Universities" (Grant 05.03.046), and the Presidium of the Russian Academy of Sciences (Program "Theoretical and Experimental Studies of the Nature of Chemical Bonding and Mechanisms of Chemical Reactions and Processes").

References

1. US Pat. 3994904, 1976; *Chem. Abstr.*, 1997, **86**, 10658m.
2. Czech. Pat. 151744, 1974; *Chem. Abstr.*, 1974, **81**, 63633b.
3. US Pat. 4452798A, 1984; *Chem. Abstr.*, 1985, **101**, 38476b.
4. Brit. Pat. 166967, 1964; *Chem. Abstr.*, 1965, **62**, 7768g.
5. A. A. El-Barbary, A. I. Khodair, E. B. Pedersen, and C. Nielsen, *J. Med. Chem.*, 1994, **37**, 73.
6. A. I. Khodair, H. I. El-Subbagh, and A. A. El-Emam, *Bull. Chim. Farm.*, 1997, **136**, 561.
7. S. Suzen, B. T. Demircigil, E. Buyukbingol, and S. A. Ozkam, *New. J. Chem.*, 2003, **27**, 1007.
8. A. A. Al-Obaid, H. I. El-Subbagh, A. I. Khodair, and M. M. A. El-Mazar, *Anti-Cancer Drugs*, 1996, **7**, 873.
9. H. H. Merritt, T. J. Putnam, and W. B. Bywater, *J. Pharmacol.*, 1945, **84**, 67.
10. S. Cortes, Z. K. Liao, D. Watson, and H. Kohn, *J. Med. Chem.*, 1985, **28**, 601.
11. S. M. M. Zaidi, R. K. Satsangi, P. Nasir, R. Argawal, and S. S. Tiwari, *Pharmazie*, 1980, **35**, 755.
12. K. Kiec-Kononowicz and J. Karolak-Wojciechowska, *Phosphorus, Sulfur, Silicon*, 1992, **73**, 235.
13. A. I. Khodair, *Carbohydrate Research*, 2001, **331**, 445.
14. M. Arca, F. Demartin, F. A. Devillanova, A. Garau, F. Ifaia, V. Lippolis, and G. Verani, *Inorg. Chem.*, 1998, **37**, 4164.
15. A. M. A. Hassaan, *Sulfur Lett.*, 1991, **13**, 1.
16. R. S. Srivastava, R. R. Srivastava, and H. N. Bhargava, *Bull. Soc. Chim. Fr.*, 1991, **128**, 671.
17. S. Sharma, M. Kumar, and T. Sharma, *J. Ind. Chem. Soc.*, 1985, **62**, 781.
18. M. Kumar, A. Chaudhary, and S. Sharma, *Ind. J. Chem., Sect. A*, 1986, **25A**, 281.
19. J. A. Grim and H. G. Petring, *Cancer Res.*, 1967, **27**, 1278.
20. M. M. Chowdhry, D. M. Mingos, A. J. White, and D. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 2001, **20**, 3495.
21. J. S. Casas, E. E. Castellano, A. Macfas, N. Playa, A. Sanchez, J. Sordo, J. M. Varela, and J. Zukerman-Schpector, *Inorg. Chim. Acta*, 1995, **238**, 129.
22. M. M. Chowdhry, A. Burrows, D. M. Mingos, A. J. White, and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1995, 1521.
23. A. G. Majouga, E. K. Beloglazkina, S. Z. Vatsadze, A. A. Moiseeva, K. P. Butin, and N. V. Zyk, *Mendeleev Commun.*, 2004, **14**, 115.
24. A. G. Majouga, E. K. Beloglazkina, S. Z. Vatsadze, N. A. Frolova, and N. V. Zyk, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 2734 [*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 2850].
25. A. G. Majouga, Ph. D. (Chem.) Thesis, M. V. Lomonosov Moscow State University, Moscow, 2005, 137 pp. (in Russian).
26. R. D. Jones, D. A. Summervile, and F. Barsolo, *Chem. Rev.*, 1979, **79**, 139.
27. S. Park, V. K. Mathur, and R. P. Planalp, *Polyhedron*, 1998, **17**, 325.
28. J. Gao, R. A. Zingaro, and M. Z. Gao, *Polyhedron*, 2004, **23**, 59.
29. F. A. Cotton and G. Wilkinson, *Advanced Inorganic Chemistry*, J. Wiley and Sons, New York—London—Sydney, 1966.
30. K. P. Butin, E. K. Beloglazkina, and N. V. Zyk, *Usp. Khim.*, 2005, **74**, 531 [*Russ. Chem. Rev.*, 2005, **74** (Engl. Transl.)].
31. G. M. Sheldrick, *Acta. Crystallogr., Sect. A*, 1990, **46**, 467.
32. G. M. Sheldrick, *SHELXL-97. Program for the Refinement of Crystal Structures*, University of Göttingen, Göttingen, Germany, 1997.
33. J. J. P. Stewart, *J. Comput. Chem.*, 1989, **10**, 209.

Received February 28, 2005