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Synthesis, Structure, and Biological Properties of Mixed Cobalt(III) Dioximates with Guanidine Derivatives

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Abstract—Two Co(III) dioximates, cyanoguanidine complex $\{[Na_2(\mu\text{-}H_2O)_2(L^1)_2(H_2O)_2][Co^{III}(DmgH)_2(N_3)_2]\}_n[Co^{III}(DmgH)_2(N_3)_2]_n$ ($L^1 = (H_2N)_2C{=}N{-}C{\equiv}N$) (**I**) and aminoguanidine complex $[H_3L^2][Co(DmgH)_2(N_3)_2]$ ($H_2L^2 = H_2N{-}C({=}NH){-}NH{-}NH_2$) (**II**), were synthesized from the $[CoCl(DmgH)_2(H_2O)]$ structural unit ($DmgH^-$ is the dimethylglyoxime monoanion). The implementation of the synthesis was confirmed by chemical analysis, IR spectroscopy, and X-ray diffraction (CIF files CCDC 1531845 (**I**), 1531846 (**II**)). Both compounds are ionic. Compound **I** consists of cations representing centrosymmetrical 2D coordination polymers, $\{[Na_2(\mu\text{-}H_2O)_2(L^1)_2(H_2O)_2][Co^{III}(DmgH)_2(N_3)_2]\}_n^{n+}$, and monomeric $[Co(DmgH)_2(N_3)_2]^-$ anions, while in **II**, the charge of the $[Co(DmgH)_2(N_3)_2]^-$ complex anion is counterbalanced by the organic $[H_3L^2]^+$ cation. In **I**, L^1 is coordinated to the metal as a monodentate neutral ligand, while in **II**, H_2L^2 occurs in the complex as a protonated uncoordinated component. Since L^1 in **I** and H_2L^2 in **II** contain functional amine groups able to form intermolecular hydrogen bonds acting as proton donors, the component packing mode in the crystals was analyzed assuming various types of interactions, apart from electrostatic ones. The biological properties of the complexes were tested considering their effect on the biosynthesis of proteases by the micromycete *Fusarium gibbosum* CNMN FD 12 strain. Culturing the producer on a culture medium containing complex **I** in the selected optimal concentrations of 5–10 mg/L was found to increase the acid protease activity by 140–150%.

Keywords: cobalt coordination compounds, dimethylglyoxime, guanidine derivatives, X-ray diffraction, biological activity

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INTRODUCTION

As a continuation of studies of substitution reactions using the $[CoCl(DmgH)_2(H_2O)]$ structural unit ($DmgH^-$ is the dimethylglyoxime monoanion) [1, 2] and to prepare polynuclear structures, including polymers, we synthesized two Co(III) glyoximates with different guanidine derivatives as polydentate ligands. The Cambridge Crystallographic Data Centre (CCDC) [3] includes data on a large number of transition metal complexes with guanidine $NH_2{-}C({=}NH){-}NH_2$ (more than 400), in which guanidine is mainly present as a protonated uncoordinated organic cation. Only in a few complexes (formed by Cu(II) and Os(III) [4, 5]), is this ligand coordinated in the monodentate fashion via the imine nitrogen atom. According to CCDC analysis [3], cyanoguanidine can be coordinated in transition metal complexes as a monodentate ligand (e.g., Ni(II) complex [6]) or as a bidentate ligand to give binuclear associates (Cu(II) complex [7]) or coordination polymers (Cu(II), Cd(II), Zn(II), and Hg(II) complexes [8–11]). Analysis of the CCDC data [3] indicated that both aminoguanidine in Pd(II), Pt(II), or Cu(II) complexes containing one or two ligands [12, 13] and aminoguanidine derivatives with a nitro group in Cu(II), Ni(II), Co(II), and other transition metal complexes [14, 15], or $-NH_3$ (diaminoguanidinium) in Cu(II) complex [16] are coordinated in the chelating bidentate fashion.

Proceeding from the $[CoCl(DmgH)_2(H_2O)]$ structural unit, we obtained two Co(III) dioximates incorporating the $[Co(DmgH)_2(N_3)_2]^-$ complex anion: a polymeric complex with cyanoguanidine, $\{[Na_2(\mu\text{-}H_2O)_2(L^1)_2(H_2O)_2][Co^{III}(DmgH)_2(N_3)_2]\}_n[Co^{III}(Dmg-$

[†] Deceased.

$H)_2(N_3)_2]_n$ ($L^1 = (H_2N)_2C{=}N{-}C{\equiv}N$) (**I**) and a monomeric complex with aminoguanidine, $[H_3L^2][Co(DmgH)_2(N_3)_2]$ ($H_2L^2 = H_2N{-}C({=}NH){-}NH{-}NH_2$) (**II**). The implementation of the synthesis was confirmed by the results of chemical, spectral, and X-ray diffraction analyses.

The enhanced interest in the transition metal complexes is also due to the fact that many of them possess various types of biological activity, in particular, stimulate the biosynthetic processes in microorganisms [17, 18]. This opens up broad prospects for using these compounds to enhance and control the synthesis of secondary metabolites in microorganisms producing valuable biologically active products such as enzymes, vitamins, antibiotics, lipids, and so on.

EXPERIMENTAL

Synthesis of complex I. A solution of $[CoCl(DmgH)_2H_2O]$ (0.34 g, 0.001 mol) in ethanol (10 mL) and a solution of cyanoguanidine (0.08 g, 0.001 mol) in ethanol (10 mL) were added successively to a stirred solution of sodium azide (0.13 g, 0.002 mol) in water (5 mL). The reaction mixture was heated on a water bath at 50°C for 30 min, then the solution was filtered and left at room temperature for crystallization. After 3 days, a red-colored crystals were formed, out of which plate-like single crystals suitable for X-ray diffraction were selected, and the rest of the product was washed with ethanol and diethyl ether and dried in air.

For $C_{20}H_{44}N_{28}O_{12}Na_2Co_2$

Anal. calcd., %:	C, 23.26;	H, 4.30;	N, 37.98;	Co, 11.41.
Found, %:	C, 23.45;	H, 4.60;	N, 37.56;	Co, 11.05.

Synthesis of complex II. A solution of $[CoCl(DmgH)_2(H_2O)]$ (0.34 g, 0.001 mol) in ethanol (10 mL) and a solution of aminoguanidine nitrate (0.14 g, 0.001 mol) in ethanol (10 mL) were added successively to a continuously stirred solution of NaN_3 (0.13 g, 0.002 mol) in water (5 mL). The reaction mixture was heated on a water bath at 50°C for 20 min, then the solution was filtered and left at room temperature for crystallization. After 3 days, dark brown plates were formed, out of which single crystals suitable for X-ray diffraction were selected. The rest of the product was washed with ethanol and diethyl ether and dried in air.

For $C_9H_{21}N_{14}O_4Co$

Anal. calcd., %:	C, 24.11;	H, 4.72;	N, 43.74;	Co, 13.15.
Found, %:	C, 24.45;	H, 4.65;	N, 43.18;	Co, 13.01.

The IR spectra for ligands and metal complexes were recorded on an FT-IR Perkin-Elmer Spectrum 100 spectrophotometer in mineral oil in the 4000–400 cm^{-1} range and in the ATR mode in the 4000–650 cm^{-1} range.

X-ray diffraction. Experimental data for **I** and **II** were collected at room temperature (293(2) K) on an Xcalibur E diffractometer (MoK_α radiation, graphite monochromator). The unit cell parameters refined for the whole array and other experimental data were obtained using the CrysAlis Oxford Diffraction program package [19]. The crystal structures were solved by direct methods and refined by the least-squares method in the full-matrix anisotropic approximation for non-hydrogen atoms (SHELX-97) [20]. The positions of hydrogen atoms of the solvation water molecules were found from difference Fourier maps, those for the other H atoms were calculated geometrically. All atoms were refined isotropically in the "rigid body" model with $U_{ef} = 1.2\ U_{equiv}$ or $1.5\ U_{equiv}$ of the corresponding O, N, and C atoms. The X-ray experiment and structure refinement details for **I** and **II** are summarized in Table 1, selected interatomic distances and bond angles are in Table. 2, and the geometric parameters of hydrogen bonds are given in Table 3. The positional and thermal parameters of the atoms for compounds **I** and **II** are deposited with the Cambridge Crystallographic Data Centre (nos. 1531845 and 1531846, respectively; deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk/data_request/cif).

Biological assay. The producer was cultured by the submerged culture method in a medium with the previously selected composition [21] with the initial pH of 6.25 at 28–30°C with continuous stirring on a shaker (rotation rate of 180–200 rpm). The duration of culturing was 6 days. The test complexes were inserted into the sterile culture medium in concentrations of 5, 10, and 15 mg/L simultaneously with the seed material. The medium with no complex added served as the control.

The activities of three types of proteases, that is, acid (pH 3.6), neutral (pH 7.4), and alkaline (pH 9.0) proteses, were assayed by the Anson method modified according to [22] over time on the 4th, 5th, and 6th days of culturing, which is the period of maximum biosynthesis for the given enzymes upon the classic culturing of the producer.

RESULTS AND DISCUSSION

The reaction of the $[CoCl(DmgH)_2(H_2O)]$ structural unit with cyano- and aminoguanidine gave two dimethylglyoximate complexes incorporating different guanidine derivatives.

The IR spectra of **I** and **II** exhibit the following bands (cm^{-1}): 2980–2930 $\nu(CH_3)$; 1480–1360 $\delta(CH_3)$; 2065–2022 $\nu(C{\equiv}N)$; ~1230 and ~1084 $\nu(NO^-)$, and a broad weak band at ~1750 cm^{-1} characteristic of the intramolecular O–H···O hydrogen bond between the dimethylglyoxime monoanions in

Table 1. Crystallographic data and X-ray experiment details for compounds **I** and **II**

Parameter	Value	
	I	**II**
M	1032.67	448.33
System	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/c$
Unit cell parameters:		
a, Å	7.6954(4)	8.7385(7)
b, Å	8.1426(4)	22.034(2)
c, Å	17.4282(7)	10.4174(7)
α, deg	95.910(3)	90
β, deg	94.428(4)	108.704(8)
γ, deg	94.037(4)	90
V, Å^3	1079.62(9)	1899.9(3)
Z	1	4
ρ(calcd.), g/cm^3	1.588	1.567
μ, mm^{-1}	0.875	0.954
F(000)	532	928
Crystal size, mm	0.36 × 0.16 × 0.03	0.45 × 0.25 × 0.09
Range of θ, deg	3.00–25.50	3.08–25.50
Ranges of reflection indices	$-9 \leq h \leq 9$, $-9 \leq k \leq 9$, $-21 \leq l \leq 13$	$-9 \leq h \leq 10$, $-26 \leq k \leq 12$, $-12 \leq l \leq 12$
Number of measured / unique reflections ($R_{\rm int}$)	6382/3984 (0.0252)	6356/3506 (0.0429)
Number of reflections with $I > 2\sigma(I)$	3107	2331
Number of refined parameters	310	285
Filling, % (θ = 25.50°)	99.2	99.0
GOOF	1.014	1.015
R factor ($I > 2\sigma(I)$)	$R_1 = 0.0403$, $wR_2 = 0.0913$	$R_1 = 0.0508$, $wR_2 = 0.0841$
R factor (for the whole array)	$R_1 = 0.0573$, $wR_2 = 0.1010$	$R_1 = 0.0846$, $wR_2 = 0.1017$
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$, e Å^{-3}	0.345, –0.277	0.516, –0.456

the $[Co(DmgH)_2(N_3)_2]^-$ complex anions. The IR spectra of **I** and **II** show absorption bands at 3400–3200 cm^{-1} ν(NH$_2$) and ν(NH) and at 1650–1590 cm^{-1} δ(NH$_2$), as well as at 2024 cm^{-1} ν(C≡N) (**I**).

According to X-ray diffraction data, **I** is an ionic type compound consisting of cations representing centrosymmetrical 2D coordination polymers, $\{[Na_2(\mu\text{-}H_2O)_2(L^1)_2(H_2O)_2][Co^{III}(DmgH)_2(N_3)_2]\}_n^{n+}$, and centrosymmetrical complex anions, $[Co(DmgH_2)_2(N_3)_2]^-$. The CCDC [3] includes one structure with this type of anion and Mn(II) hexaaqua complex as the cation [23]. Figure 1 shows a fragment of the coordination polymer cation and the complex anion of **I**. The polymeric cation contains $[Co^{III}(DmgH)_2(N_3)_2]^-$ complex anions linked by Co(III)-coordinated N_3^- anions to four different Na$^+$ cations to form a 1D chain. These structures are linked through the $[Na_2(\mu\text{-}H_2O)_2L_2(H_2O)_2]^{2+}$ cations to form a more complex 2D-layered centrosymmetrical $\{[Na_2(\mu\text{-}H_2O)_2(L^1)_2(H_2O)_2][Co^{III}(DmgH)_2(N_3)_2]\}_n^{n+}$ system (Fig. 2). The Na$^+$ cations in $[Na_2(\mu\text{-}H_2O)_2(L^1)_2(H_2O)_2]^{2+}$ are bridged by two water molecules. The coordination number of sodium is 6, the coordination polyhedron is formed by the N_3O_3 set of donor atoms of one monodentate water molecule, one monodentate L^1 ligand, two N_3^- ions of neighboring $[Co^{III}(DmgH)_2(N_3)_2]^-$ anions (the latter are linked by different nitrogen atoms), and two bridging water molecules. In

Table 2. Interatomic distances (*d*) and bond angles (ω) in structures **I** and **II** *

Bond	Co(III) coordination polyhedra			
	I		**II**	
	d, Å			
	A, Co(1)	B, Co(2)	A, Co(1)	B, Co(1)
Co–N(1)	1.884(2)	1.894(2)	1.911(3)	1.878(3)
Co–N(2)	1.890(2)	1.893(2)	1.909(3)	1.882(3)
Co–N(3)	1.953(2)	1.963(2)	1.967(3)	1.942(3)
Angle	ω, deg			
	A, Co(1)	B, Co(2)	A, Co(1)	B, Co(1)
N(1*A*)CoN(2*A*)	80.82(9)	81.07(11)	79.8(1)	82.4(1)
N(1*A*)CoN(2*A*)	99.18(9)$^{\#1}$	98.93(11)$^{\#2}$	99.4(1)	98.5(1)
N(1*A*)CoN(3*A*)	86.07(9)	88.67(10)	91.2(1)	92.0(1)
N(1*A*)CoN(3*A*)	93.93(9)$^{\#1}$	91.33(10)$^{\#2}$	89.8(1)	87.2(1)
N(2*A*)CoN(3*A*)	90.46(10)	91.28(10)	93.0(1)	87.3(1)
N(2*A*)CoN(3*A*)	89.54(10)$^{\#1}$	88.72(10)$^{\#2}$	93.0(1)	86.8(1)

* $^{\#1}$ $-x + 2, -y, -z + 1$; $^{\#2}$ $-x + 1, -y + 1, -z + 2$.

Na coordination polyhedron					
I					
Bond	*d*, Å	Angle	ω, deg	Angle	ω, deg
Na–O(1*w*)	2.510(2)	O(1*w*)NaO(1*w*)$^{\#2}$	85.01(9)	O(1*w*)$^{\#2}$NaN(3)	162.74(9)
Na–O(1*w*)$^{\#2}$	2.460(3)	O(1*w*)NaO(2*w*)	80.71(9)	O(2*w*)NaN(3*A*)$^{\#1}$	126.74(9)
Na–O(2*w*)	2.375(3)	O(1*w*)NaN(3*A*)$^{\#1}$	152.48(9)	O(2*w*)NaN(5*A*)	155.42(10)
Na–N(3*A*)$^{\#1}$	2.697(2)	O(1*w*)NaN(5*A*)	78.69(9)	O(2*w*)NaN(3)	86.84(9)
Na–N(5*A*)	2.373(3)	O(1*w*)NaN(3)	104.37(9)	N(3*A*)$^{\#1}$NaN(5*A*)	75.01(8)
Na–N(3)	2.651(3)	O(1*w*)$^{\#2}$NaO(2*w*)	109.22(10)	N(3*A*)$^{\#1}$NaN(3)	81.64(8)
		O(1*w*)$^{\#2}$NaN(3*A*)$^{\#1}$	83.54(8)	N(5*A*)NaN(3)	85.4(1)
		O(1*w*)$^{\#2}$NaN(5*A*)	82.23(10)		

* Symmetry codes: $^{\#1}$ $-x + 2, -y + 1, -z + 1$; $^{\#2}$ $-x + 1, -y + 1, -z + 1$.

the crystal of **I**, one can distinguish chains formed by different centrosymmetrical metallacycles involving Na^+ cations. One of the metallacycles is four-membered and is composed of two Na(1) atoms and two O(1*w*) atoms (Na(1)···Na(1)* 3.664 Å), while the other one is eight-membered, being composed of two Na(1) atoms and two N_3^- anions (Na(1)···Na(1)* 6.198 Å) (Fig. 2). The Co(III) atoms in both the cation and the anion are chelated by two dimethylglyoxime monoanions (DmgH⁻); their environment is completed by two N_3^- anions. The Co(III) coordination octahedra in **I** are formed by the N_6 sets of donor atoms, four of which belong to two DmgH⁻ anions located in the equatorial plane of the octahedron and two of which refer to two monodentate N_3^- anions in the axial positions. The Co–N(oxime) interatomic distances in the cation of **I** are 1.884(2) and 1.890(2) Å, while the Co–N(N_3^-) distance is 1.953(2) Å; in the complex anion of **I**, the Co–N(oxime) distances are 1.893(2) and 1.894(2) Å, while the Co–N(N_3^-) distance is 1.963(2) Å (Table 2). This is in line with the data for complexes with a similar N_3^- anion [1, 2, 24]. Like in all Co(III) complexes with dioximes (e.g., those reported in [1, 2, 24]), the equatorial [Co(DmgH)$_2$] moiety is stabilized by intramolecular O–H···O hydrogen bond between two DmgH⁻ ligands (O···O 2.485(3) Å in the cation and 2.505(3) Å in the anion (Table 3)). The coordination polymer cation is additionally stabilized by intramolecular hydrogen bonds: N(2)–H···O(2*w*),

Table 3. Geometric parameters of intra- and intermolecular hydrogen bonds in structures **I** and **II**

D–H···A contact	Distance, Å			DHA angle	Coordinates of A atoms, deg
	D–H	H···A	D···A		
			I		
O(1*A*)–H(1)···O(2*A*)	1.07	1.43	2.485(3)	168	−*x* + 2, −*y*, −*z* + 1
O(1*B*)–H(1)···O(2*B*)	0.99	1.52	2.505(3)	170	−*x* + 1, −*y* + 1, −*z*
N(1)–H(1)···O(2*B*)	0.86	2.42	3.141(4)	142	−*x* + 2, −*y* + 1, −*z* + 1
N(1)–H(2)···N(3*B*)	0.86	2.37	3.148(4)	151	*x*, *y*, *z* + 1
N(2)–H(1)···N(3*B*)	0.86	2.55	3.292(4)	145	*x*, *y*, *z* + 1
N(2)–H(1)···O(2*B*)	0.86	2.54	3.176(3)	131	−*x* + 1, −*y* + 1, −*z* + 1
N(2)–H(2)···O(2*w*)	0.86	2.08	2.920(4)	167	*x*, *y*, *z*
O(1*w*)–H(1)···N(4)	0.85	2.22	3.059(4)	168	*x* − 1, *y*, *z*
O(1*w*)–H(2)···O(2*A*)	0.85	2.32	2.997(3)	137	−*x* + 1, −*y*, −*z* + 1
O(2*w*)–H(1)···O(2*A*)	0.85	1.98	2.822(3)	171	−*x* + 1, −*y* + 1, −*z* + 1
O(2*w*)–H(2)···N(4)	0.85	2.07	2.923(4)	179	*x* − 1, *y*, *z*
			II		
O(1*A*)–H(1)···O(2*B*)	0.82	1.76	2.543(4)	160	*x*, *y*, *z*
O(2*A*)–H(1)···O(1*B*)	0.82	1.70	2.487(4)	161	*x*, *y*, *z*
N(1)–H(1)···N(5*A*)	0.82	2.34	3.085(6)	152	*x*, *y*, *z*
N(1)–H(2)···O(2*A*)	0.94	2.28	3.128(6)	150	*x* − 1, −*y* + 3/2, *z* − 1/2
N(2)–H(1)···O(1*B*)	0.84	2.03	2.857(4)	171	*x* − 1, *y*, *z*
N(3)–H(1)···N(3*B*)	0.91	2.13	2.978(5)	154	*x* − 1, *y*, *z* − 1
N(3)–H(2)···O(2*B*)	0.81	2.12	2.918(5)	172	−*x*, −*y* + 2, −*z*
N(4)–H(1)···N(3*A*)	0.78	2.35	3.065(5)	154	*x* − 1, *y*, *z*
N(4)–H(2)···O(2*B*)	0.78	2.63	3.289(5)	143	−*x*, −*y* + 2, −*z*

O(1*w*)–H···N(4), O(2*w*)–H···N(4), O(1*w*)–H···O(2*A*), and O(2*w*)–H···O(2*A*) (Table 3, Fig. 2). The polymeric cations are linked to the complex anions by intermolecular hydrogen bonds: N(1)–H···O(2*B*), N(1)–H···N(3*B*), N(2)–H···O(2*B*), and N(2)–H···N(3*B*) (Table 3, Fig. 3), in which the coordinated cyanoguanidine L^1 molecule of the cation is the proton donor and the O and N atoms of the coordinated $DmgH^-$ and N_3^- ligands of the complex anion are proton acceptors.

The crystal structure of **II**, like that of **I**, is ionic and consists of one crystallographically independent $[H_3L^2]^+$ organic cation and the $[Co(DmgH)_2(N_3)_2]^-$ complex anion. In the anion of **II**, as in **I**, the central metal atom is chelated by two dimethylglyoxime monoanions ($DmgH^-$) (Fig. 1), while the metal environment is completed by two coordinated N_3^- anions. The octahedral Co(III) coordination polyhedron is formed by the N_6 set of donor atoms, out of which four atoms belong to two $DmgH^-$ located in the equatorial plane of the octahedron and two atoms belong to the axial N_3^- anions. The $Co–N_{oxime}$ interatomic distances in the equatorial plane of the metal coordination polyhedron are in the 1.878(3)–1.911(3) Å range; the $Co–N(N_3)$ distances are 1.967(3) and 1.942(3) Å (Table 2), which is in line with the data for similar complexes [2, 3]. In the complex anion, the $DmgH^-$ ligands are linked by intramolecular O–H···O bonds (O···O 2.543(4) and 2.487(4) Å (Table 3, Fig. 4)).

Since the organic $[H_3L^2]^+$ cation of **II** contains amide and amine functional groups capable of forming intermolecular hydrogen bonds as proton donors, we analyzed the packing mode of components in the crystal and the probability of hydrogen bonding between components (apart from electrostatic interactions). This type of aminoguanidine crystallization as organic cations was found in complexes of various metals [3] (e.g., in complexes containing $[ZnCl_4]^{2-}$, $[CuCl_6]^{4-}$, bis(N-(1H-tetrazol-5-yl)-1H-tetrazole-5-aminato)zinc(II) [25–27]). In the crystal of **II**, the organic $[H_3L^2]^+$ cation is linked to five $[Co(DmgH)_2(N_3)_2]^-$ anions by intermolecular N–H···N and N–H···O hydrogen bonds (Table 3, Fig. 5), in which the oxime O atoms of $DmgH^-$ or various N atoms of N_3^- act as acceptors.

Recent studies attest to the possibility of using transition metal complexes with various organic

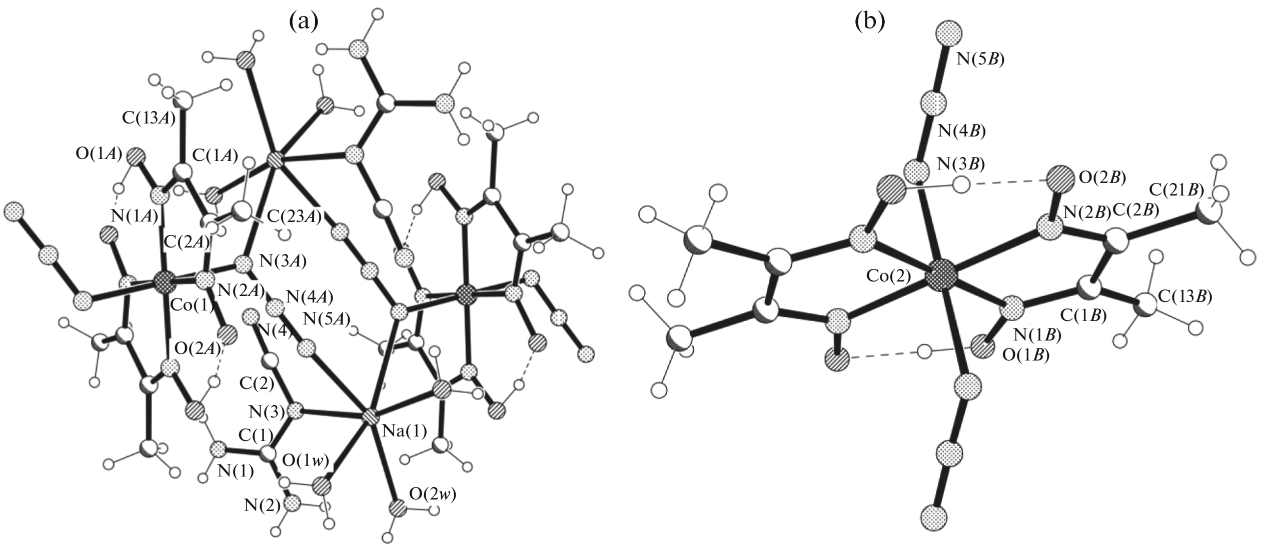

Fig. 1. Structure of (a) complex cations and (b) complex anions in **I**.

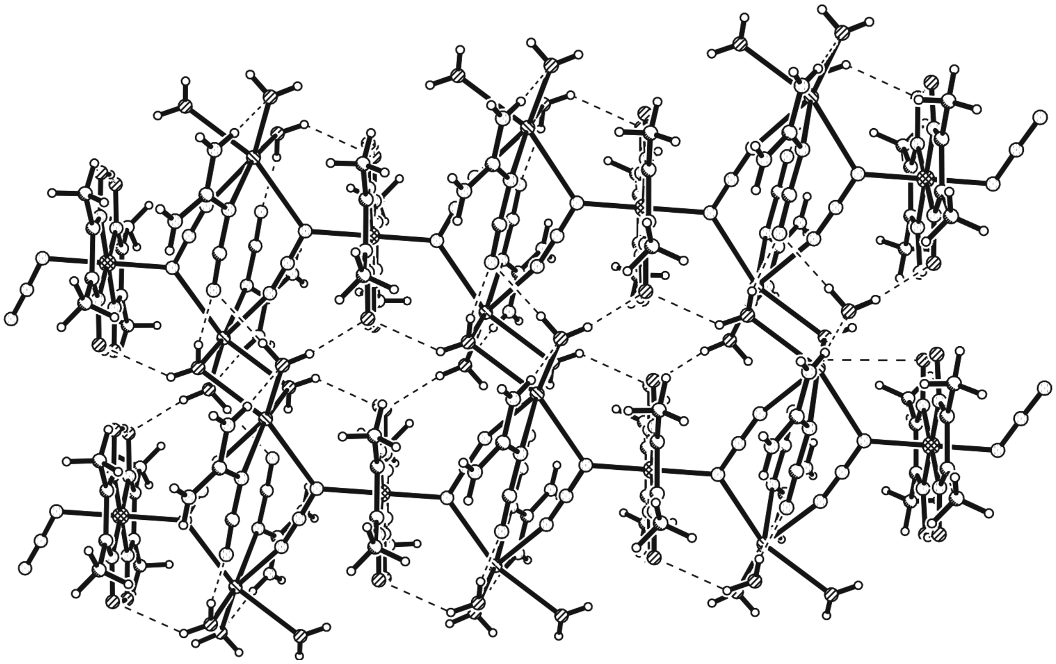

Fig. 2. Fragment of the coordination polymer cation in **I**.

ligands to stimulate the synthesis of secondary metabolites of microorganisms, in particular, extracellular hydrolytic enzymes [28–30]. In the preliminary studies, we detected the stimulating action of some cobalt dioximates on the biosynthesis of extracellular hydrolases (pectinases, amylases, or lipases). Cobalt(III) complexes with dimethylglyoxime, $[Co(DmgH)_2\text{-}(Thio)_2]_3F[SiF_6] \cdot 1.5H_2O$, $[Co(DmgH)_2\text{-}(Thio)_2]_2\text{-}[SiF_6] \cdot 3H_2O$, and $[Co(DmgH)_2\text{-}(Thio)_2][BF_4] \cdot 3H_2O$, were found to efficiently stimulate the pectolytic activity of the *Rhizopus arrhizus* F 67 strain, by increasing the enzyme biosynthesis by 97.1–115.3%. The addition of $[Co(DmgH)_2(An)_2]_2[TiF_6] \cdot 3H_2O$, $[Co(NioxH)_2(Sam)_2]_2[TiF_6] \cdot 3H_2O$, or $[Co(NioxH)_2(An)_2]_2[TiF_6] \cdot 3H_2O$ ($NioxH^-$ is the 1,2-cyclohexanedione dioxime monoanion) in concentrations of 5–10 mg/L to the culture medium of the micromycete *A. niger* 33-19 CNMN FD 02A, amylase producer, reduced the culturing period of micromycetes by 24–48 h and increased the amylo-

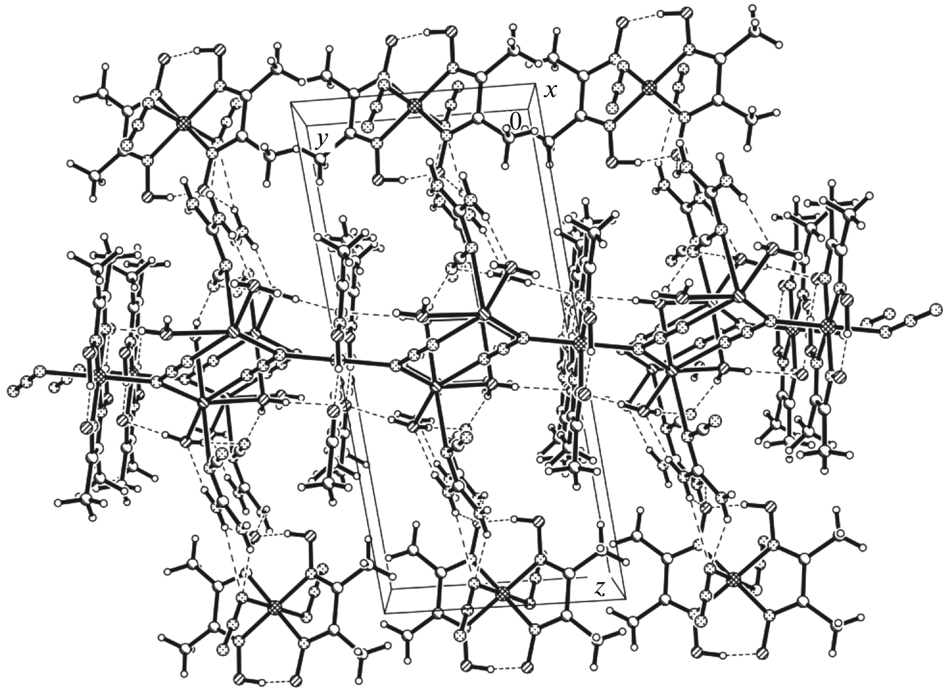

Fig. 3. Fragment of the crystal structure of **I**: linking of the coordination polymer cation and the complex anion via intermolecular hydrogen bonds.

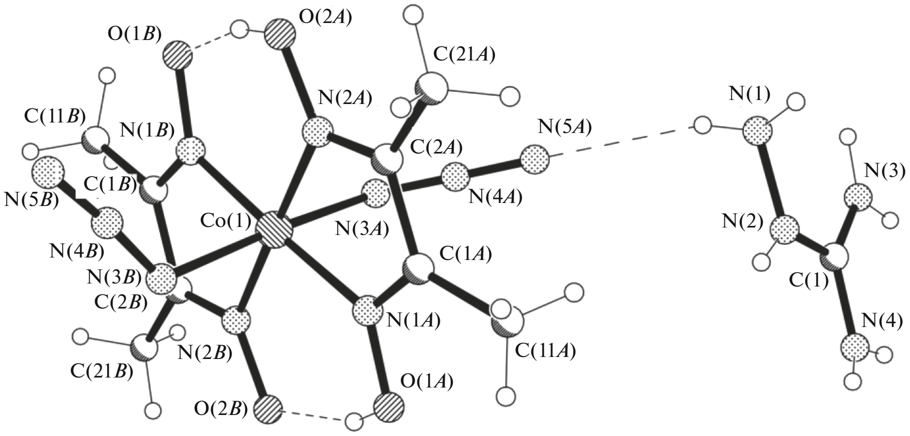

Fig. 4. Structure of the complex $[H_3L^2][Co(DmgH)_2(N_3)_2]$ in **II**.

lytic activity by 23–64% [31–33]. Hydroxy acid germanium complexes were found to exhibit pharmacological, biological, and catalytic activities [34, 35]. Complexes formed by minor nutrient elements are of considerable interest for biotechnology.

Compounds **I** and **II** were tested for the degree of their influence on the protease biosynthesis by the micromycete *Fusarium gibbosum* CNMN FD 12 strain. The insertion of cobalt(III) complex into the culture medium of the strain induced considerable changes in the production of all extracellular proteases considered, depending on the composition and concentration of the complex (Table 4). In the control runs, the maximum proteolytic activity was observed on the 5th day and amounted to 1.26 U/mL for acid, 3.10 U/mL for neutral, and 3.28 U/mL for alkaline proteases. The biosynthesis of acid proteases under optimized conditions is less intense than in the control run and reaches a maximum on the 6th day of culturing. This may be due to the need for the culture acclimatization to new medium conditions, which elongates the lag phase, or may be induced by a more pronounced change in the pH of the medium caused by the dissociation products of the complexes. For this culturing time, the maximum enzy-

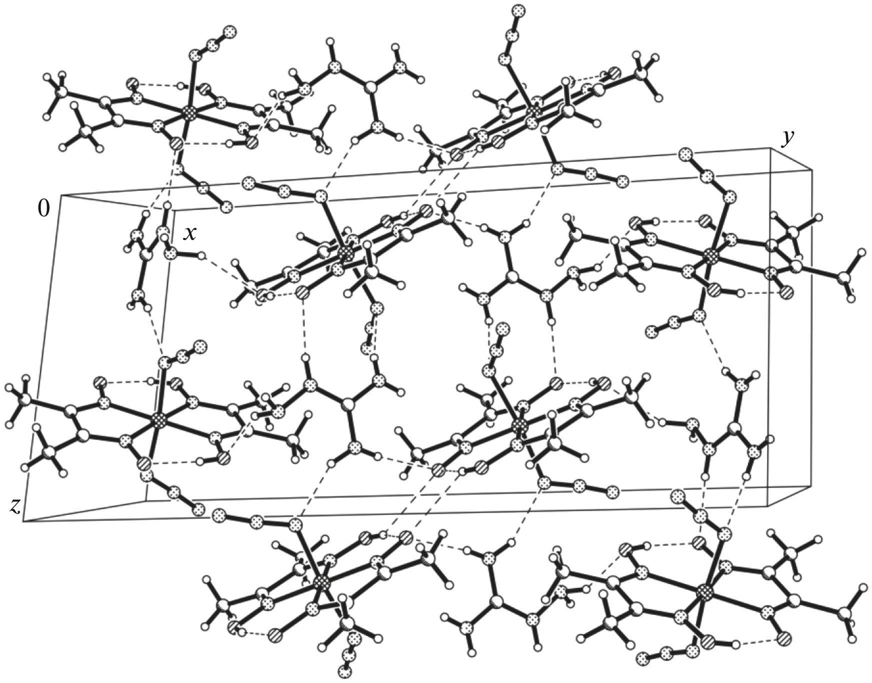

Fig. 5. Fragment of the crystal structure of **II**.

matic activity was 3.02–3.15 U/mL for **I** present in concentrations of 5–10 mg/L and 1.34 U/mL for **II** versus 1.26 U/mL in the control run; this is 239.7–250.0% relative to the maximum level of the control (5th day). Thus, the addition of complex **I** to the culture medium of the *Fusarium gibbosum* strain increases the activity of acid proteases by 140–150%. A common fact for both tested complexes is that the increase in the concentration to 15 mg/L leads to a considerable decrease in the acid protease activity.

For complex **I**, the rate of biosynthesis of neutral and alkaline proteases under the optimized conditions is similar to the enzyme formation rate in the control runs, reaching the maximum on the 5th day of culturing and being approximately at the level of the control. In the case of **II**, the maximum activity of neutral proteases falls on the 4th day of culturing and amounts to 2.85 U/mL (for 10 mg/L concentration), which is markedly (by 26.7%) lower than the maximum activity for the control, which is 3.61 U/mL on the 5th day. The maximum activity of alkaline proteases under the optimized conditions is observed on the 5th day of culturing and amounts to 2.94 U/mL (10 mg/L), which is also lower (by 11.6%) than the activity in the control run (3.28 U/mL). On the 6th day, the activity of neutral proteases with complex **I** drops to zero, while the activity of the control is substantially retained (1.47 U/mL); the activity of alkaline proteases varies from 2.18 to 0.5 U/mL in the presence of complexes

Table 4. Change in the proteolytic activity of the micromycete *Fusarium gibbosum* CNMN FD 12 strain under the action of complexes **I** and **II** during culturing (U/mL)

Compound	*c*, mg/L*	Acid (pH 3.6)			Neutral (pH 7.4)			Alkaline (pH 9.0)		
		4th day	5th day	6th day	4th day	5th day	6th day	4th day	5th day	6th day
I	5	0.50	0.84	3.02	2.10	3.36	0.00	1.68	3.44	2.18
	10	0.50	0.75	3.15	2.10	3.27	0.00	1.68	3.44	1.59
	15	0.25	0.25	1.43	1.90	2.35	0.04	1.43	2.43	0.59
II	5	0.38	0.55	1.34	2.52	0.34	0.00	1.26	1.43	0.00
	10	0.34	0.61	1.34	2.85	0.67	0.00	2.68	2.94	0.08
	15	0.42	0.52	1.26	2.18	0.84	0.00	2.26	0.92	0.00
Control		0.65	1.26	0.42	3.40	3.61	1.47	2.61	3.28	2.60

* *c* is concentration.

following the increase in the concentration from 5 to 15 mg/L; in the case of complex **II**, the activity disappears almost entirely, while that in the control is retained at 2.60 U/mL.

The assays have demonstrated that submerged culturing of the micromycete *Fusarium gibbosum* in the presence of complex **I** in the optimal concentration of 5–10 mg/L increases the activity of acid proteases by 140–150% and thus enables the manufacture of enzyme products of a specified composition.

REFERENCES

1. Coropceanu, E.D., Rija, A., Lozan, V., et al., *Cryst. Growth Des.*, 2016, vol. 16, p. 814.
2. Coropceanu, E.D., Bologa, O.A., Arsene, I., et al., *Russ. J. Coord. Chem.*, 2016, vol. 42, no. 8, p. 516.
3. Allen, F.H., *Acta Crystallogr., Sect. B: Struct. Sci.*, 2002, vol. 58, p. 38.
4. Moggach, S.A., Galloway, K.W., Lennie, A.R., et al., *CrystEngComm*, 2009, vol. 11, p. 2601.
5. Xiang, J., Man, W.-L., Yiu, Sh.-M., et al., *Chem.-Eur. J.*, 2011, vol. 17, p. 13044.
6. Samus', I.D., Taran, G.G., Mazus, M.D., et al., *Koord. Khim.*, 1993, vol. 19, no. 2, p. 149.
7. Begley, M.J., Hubberstey, P., and Walton, P.H., *J. Chem. Soc., Dalton Trans.* (1972–1999), 1995, p. 957.
8. Begley, M.J., Eisenstein, O., Hubberstey, P., et al., *J. Chem. Soc., Dalton Trans.* (1972–1999), 1994, p. 1935.
9. Hubberstey, P. and Falshaw, C.P., *J. Chem. Res.*, 1982, vol. 176, p. 1809.
10. Ritche, L.K. and Harrison, W.T.A., *Acta Crystallogr., Sect. E: Struct. Rep. Online*, 2007, vol. 63, p. m617.
11. Pickardt, J. and Kuhn, B., *Z. Naturforsch., A: Phys. Sci.*, 1996, vol. 51, p. 1701.
12. Aitken, D.J., Albinati, A., Gautier, A., et al., *Eur. J. Inorg. Chem.*, 2007, p. 3327.
13. Polyakova, I.N., Malinina, E.A., Drozdova, V.V., and Kuznetsov, N.T., *Crystallogr. Rep.*, 2009, vol. 54, no. 5, p. 831.
14. Fischer, N., Joas, M., Klapotke, T.M., and Stierstorfer, J., *Inorg. Chem.*, 2013, vol. 52, p. 13791.
15. Zubkov, S.V., Seifulina, I.I., Starikova, Z.A. et al., *Koord. Khim.*, 1996, vol. 22, no. 6, p. 666.
16. Savel'eva, Z.A., Larionov, S.V., Romanenko, G.V., et al., *J. Struct. Chem.*, 1995, vol. 36, no. 5, p. 855.
17. Mitin, N.I., Lagutkin, N.A., and Chapurina, L.F., *Khim.-Farm. Zh.*, 1983, no. 5, p. 565.
18. Treshchalina, E.M., Konovalova, A.L., Pryanov, M.A., et al., *Dokl. Akad. Nauk SSSR*, 1979, vol. 248, no. 5, p. 1273.
19. *CrysAlis RED. Version 1.171.34.76*, Oxford Diffraction Ltd., 2003.
20. Sheldrick, G.M., *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 2008, vol. 64, no. 1, p. 112.
21. Ciloci, A., Tiurina, J., Lupascu, G., et al., *Brevet de invenţie MD*, 4186. 2012-11-30.
22. Gracheva, I.M., Grachev, Yu.P., Mosichev, M.S., et al., *Laboratornyi praktikum po tekhnologii fermentnykh preparatov* (Laboratory Works on Enzyme Product Technology), Moscow: Legk. pishch. prom., 1982, p. 36.
23. Liu, X., Zhang, B.F., Wang, X., et al., *Acta Crystallogr., Sect. E: Struct. Rep. Online*, 2004, vol. 60, p. m538.
24. Melnic, E., Bourosh, P., Rija, A., et al., *Russ. J. Coord. Chem.*, 2012, vol. 38, no. 9, p. 623.
25. Miminoshvili, E.B., Miminoshvili, K.E., Beridze, L.A., and Zazashvili, S.R., *J. Struct. Chem.*, 2006, vol. 47, no. 4, p. 782.
26. Savel'eva, Z.A., Romanenko, G.V., Podberezskaya, N.V., and Larionov, S.V., *Polyhedron*, 1996, vol. 15, p. 3581.
27. Li, F., Bi, Ya., Zhao, W., et al., *Inorg. Chem.*, 2015, vol. 54, p. 2050.
28. Varbanets, L.D., Rzaeva, O.N., Avdiyuk, E.V., et al., *Mikrobiol. Zh.*, 2007, vol. 69, no. 3, p. 11.
29. Bivol, Ch., Lazaresku, A., Turte, K., and Rudik, V., *Izv. Akad. Nauk Resp. Moldova. Nauki o Zhizni*, 2012, no. 2(317), p. 149.
30. Dulcevscaia, G., Kravtsov, V., Macaev, F., et al., *Polyhedron*, 2013, vol. 52, p. 106.
31. Desyatnik, A.A., Gerbeleu, N.V., Coropceany, E.B., et al., *Russ. J. Coord. Chem.*, 2002, vol. 28, no. 2, p. 135.
32. Ciloci, A., Bivol, C., Stratan, M., et al., *The Annals of Oradea University. Biology Fascicle*, 2012, vol. 19, no. 2, p. 128.
33. Bourosh, P., Coropceany, E.B., Ciloci, A., et al., *Russ. J. Coord. Chem.*, 2013, vol. 39, no. 11, p. 777.
34. Shubchins'ka, A.S., Varbanets, L.D., Seifullina, I.I., et al., *Mikrobiol. Zh.,* 2008, vol. 70, no. 4, p. 3.
35. Seifullina, I.I., Martsinko, E.E., Minacheva, L.Kh., et al., *Ukr. Khim. Zh.*, 2009, vol. 75, no. 1, p. 3.

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