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Crystal structures and spectral properties of new Cd(II) and Hg(II) complexes of monensic acid with different coordination modes of the ligand

Research Article

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Abstract: The single crystal X-ray structures and the spectroscopic properties of complexes of monensic acid ($C_{36}H_{62}O_{11}\cdot H_2O$) with toxic metal ions of Cd(II) and Hg(II) are discussed. The cadmium(II) complex (**1**) is of composition $[Cd(C_{36}H_{61}O_{11})_2(H_2O)_2]$ and crystallizes in the monoclinic system (space group *P*2(1), Z = 2) with a = 12.4090(8), b = 24.7688(16), c = 14.4358(11) Å, β = 91.979(7)°. Two ligand monoanions are bound in a bidentate coordination mode to Cd(II) via the carboxylate and the primary hydroxyl oxygens occupying the equatorial plane of the complex. The axial positions of the inner coordination sphere of Cd(II) are filled by two water molecules additionally engaged in intramolecular hydrogen bonds. The Hg(II) complex (**2**), $[Hg(C_{36}H_{60}O_{11})(H_2O)]$, crystallizes in the orthorhombic system (space group *P*2(1)2(1)2(1), Z = 4) with a = 12.7316(2), b = 16.4379(3), c = 18.7184(4) Å. The monensic acid reacts with Hg(II) in a tetradentate coordination manner via both oxygen atoms of the carboxylate function and oxygens of two hydroxyl groups. The twofold negative charge of the ligand is achieved by deprotonation of carboxylic and secondary hydroxyl groups located at the opposite ends of the molecule. Hg(II) is surrounded by five oxygen atoms in a distorted square pyramidal molecular geometry.

Keywords: *Monovalent polyether ionophore • Heavy metal complexes*

1. Introduction

Monensic acid ($C_{36}H_{62}O_{11}$, Scheme 1) is among the polyether ionophorous antibiotics widely used in veterinary medicine as coccidiostats [1-3]. The pharmacological activity of this compound is due to its high affinity to complex with sodium ions and to transport them through cellular membranes via an electroneutral mechanism [4,5]. The disturbance of the osmotic balance of the cells initiates biochemical processes eventually leading to cell death. The selectivity of monensic acid towards alkali metal ions is well studied and decreases in the order $Na^+ > K^+ > Rb^+ > Li^+ > Cs^+$ [6-19]. The monensic acid binds monovalent alkali ions in a hydrophilic cavity where the metal ion is either six- or seven-fold coordinated. The formation of overall neutral complexes is secured by deprotonation of the carboxylic group as both oxygen atoms are engaged in "head-to-tail" type intramolecular hydrogen bonds with the hydroxyl groups located at the opposite site of the ligand anion.

At the present we have reported that monensins (monensic acid or sodium monensin ($C_{36}H_{61}O_{11}Na$)) form complexes of different stoichiometry with divalent ions of some biometals [20-25]. The mononuclear

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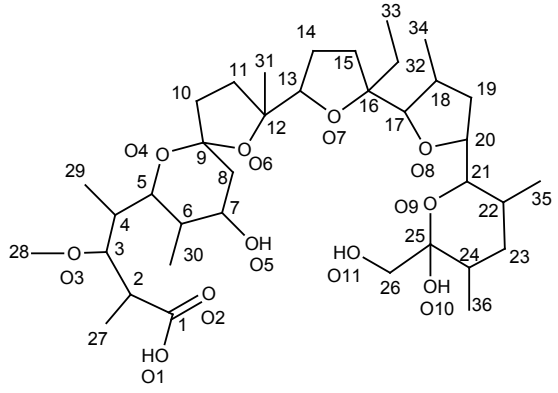
metal(II) complexes of the monoanion of monensic acid showed enhanced bactericidal activity towards *Bacillus subtilis* and *Bacillus mycoides* compared to the non-coordinated antibiotic, although the nature of the metal(II) ion should be considered when discussing the antimicrobial properties of these new compounds [25].

On the other hand, it has been demonstrated that monensin is effective for the treatment of lead(II) intoxication reducing significantly Pb(II) concentration in rats, treated with $PbCl_2$ [26]. The same authors earlier suggested the formation of various monensin complex species containing Pb(II) [27], although to the best of our knowledge there is still no data regarding the solid state structures of these compounds. To access the potential application of monensin as an antidote for treatment of intoxications with other heavy metals like cadmium or mercury, detailed investigations on its complexation ability towards divalent metal ions are required. Herein, we report the synthesis, single crystal X-ray structures and spectroscopic properties of the complexes of anions of monensic acid A with the toxic metal ions of Cd(II) and Hg(II).

2. Experimental Procedure

2.1. Physical measurements

For the performance of IR spectral analysis (in a nujol mull) a Specord 75-IR (Carl-Zeiss, Germany) was used. FAB-mass analysis was performed on Fisons VG Autospec (Micromass Instruments, UK). ^{1}H (600.13 MHz) and ^{13}C (150.92 MHz) spectra were acquired on an AVANCE AV600 II+ NMR spectrometer (Bruker, Germany). All spectra were recorded in $CDCl_3$ at room temperature. TMS was used as an internal standard for the ^{1}H and ^{13}C spectra. Unambiguous assignment of the signals was made on the basis of the gradient enhanced versions of COSY, TOCSY, HSQC, HMBC and ROESY experiments (Bruker pulse library programs: cosygpmfqf, dipsi2etgpsi, hsqcedetgpsisp2.2, hmbcgplpndqf, roesyph.2, 2007). The chemical shift values of the individual protons in the complexes have been determined from the HSQC spectra. Elemental analysis data (C, H, O) were obtained with VarioEL V5.18.0 Elemental Analyzer (Elementar Analysensysteme GmbH, Hanau, Germany). The metal content was determined by AAS on a Perkin Elmer 1100 B (Waltham, USA) apparatus using stock standard solution (1000 mg mL^{-1}, Merck). Working reference solutions were prepared after suitable dilution.



Scheme 1. Structure and numbering sequence of monensic acid A

2.2. Materials

All chemicals used were of reagent grade. Sodium monensin A was supplied from BIOVET Ltd. (Sofia, Bulgaria). $Cd(CH_3COO)_2 \cdot 2H_2O$, $Hg(NO_3)_2 \cdot H_2O$ and Et_4NOH were purchased from Fluka (Buchs, Switzerland). Acetonitrile (MeCN), MeOH and HCl were received from Merck (Darmstadt, Germany).

2.3. Synthesis of monensic acid monohydrate ($C_{36}H_{62}O_{11} \cdot H_2O$)

The monensic acid A monohydrate was prepared from sodium monensin (711 mg, 1 mmol) as previously reported [28]. Yield 589 mg, 85%. Anal. Calcd. for $C_{36}H_{64}O_{12}$ (%): H, 9.36; C. 62.77; O, 27.87. Found: H, 8.97; C, 62.95; O, 27.60. ^{1}H-NMR (600 MHz, δ (multiplicity, intensity, *J-coupling(s)*, assignment), $CDCl_3$): 6.25 (br, 1-OH, 10-OH (sharp), 11-OH, H_2O), 4.50 (br d, 1H, *7.9*, 5-OH), 4.33 (ddd, 1H, *10.8*, *5.9*, *2.9*, 20CH), 4.07 (dd, 1H, *11.6*, *2.1*, 5CH), 4.03 (d, 1H, *4.0*, 17CH), 3.94 (dd, 1H, *10.5*, *2.7*, 21CH), 3.86 (br s, 1H, 7CH), 3.69 (d, 1H, *11.2*, $26CH_2$'), 3.50 (d, 1H, *11.2*, $26CH_2$"), 3.44 (dd, 1H, *10.7*, *4.6*, 13CH), 3.37 (s, 3H, $28OCH_3$), 3.22 (dd, 1H, *10.2*, *2.1*, 3CH), 2.62 (dq, 1H, *10.2*, *6.7*, 2CH), 2.25-2.13 (4H, 18CH, $15CH_2$', 4CH, $19CH_2$'), 2.10 (m, 1H, 6CH), 1.98 (dd, 1H, *14.2*, *3.5*, $8CH_2$'), 1.97 (dd, 1H, *12.3*, *8.4*, $10CH_2$'), 1.89 (dt, 1H, *11.9*, *8.7*, $11CH_2$'), 1.74-1.52 (m, 5H, $8CH_2$", $11CH_2$", $10CH_2$", $14CH_2$), 1.55 (m, 2H, $32CH_2$), 1.52-1.33 (m, 5H, $23CH_2$', 24CH, $15CH_2$", $19CH_2$", $23CH_2$"), 1.48 (s, 3H, $31CH_3$), 1.35 (m, 1H, 22CH), 1.27 (d, 3H, *6.7*, $27CH_3$), 1.10 (d, 3H, *6.9*, $29CH_3$), 0.95 (t, 3H, *7.4*, $33CH_3$), 0.92 (d, 3H, *6.9*, $34CH_3$), 0.88 (d, 3H, *7.1*, $30CH_3$), 0.87 (d, 3H, *6.4*, $36CH_3$), 0.85 (d, 3H, *6.5*, $35CH_3$).

2.4. Synthesis of $[Cd(C_{36}H_{61}O_{11})_2(H_2O)_2]$ (1)

To a solution of $C_{36}H_{62}O_{11} \cdot H_2O$ (172 mg, 0.25 mmol in 2 mL H_2O and 20 mL MeCN), Et_4NOH (90 μL, 0.25 mmol, 40% in H_2O) was added. The mixture was

stirred to full dissolution of the ligand. The already dissolved $Cd(CH_3COO)_2 \cdot 2H_2O$ (133 mg, 0.5 mmol in 2 mL H_2O) was slowly added to the solution of monensic acid. The reaction mixture was stirred for 15 min to give white precipitates of composition $[Cd(C_{36}H_{61}O_{11})_2(H_2O)_2]$ (**1**). The solid phase was filtered off, washed with MeCN to remove unreacted reagents and dried at r.t. Yield 242 mg, 65%. Anal. Calcd. for $C_{72}H_{126}O_{24}Cd$ (%): H, 8.53; C, 58.11; Cd, 7.55. Found: H, 8.37; C, 57.59; Cd, 7.46. The slow concentration of diluted reaction mixture (within 24 h) leads to the formation of colourless crystals of **1** as $[Cd(C_{36}H_{61}O_{11})_2(H_2O)_2] \cdot 5MeCN$. The complex is soluble in MeOH, EtOH, $CHCl_3$ and possesses a limited solubility in MeCN. ^{1}H-NMR (600 MHz, δ (assignment), $CDCl_3$) 8.97 (OH), 6.69 (OH), 5.09 (OH-5), 4.90 (H_2O), 4.30 (20CH), 4.13 (17CH), 3.99 (21CH), 3.97 (5CH), 3.75 (7CH, 26CH_2'), 3.62 (26CH_2"), 3.46 (13CH), 3.33 (28OCH_3), 3.19 (3CH), 2.54 (2CH), 2.23 (6CH, 18CH, 19CH_2), 2.14 (15CH_2'), 2.08 (4CH), 1.94 (8CH_2', 10CH_2'), 1.89 (11CH_2), 1.66 (8CH_2"), 1.62 (14CH_2), 1.56 (10CH_2"), 1.51 (32CH_2, 23CH_2'), 1.45 (31CH_3), 1.42 (15CH_2"), 1.39 (24CH), 1.32 (23CH_2"), 1.26 (22CH), 1.18 (27CH_3), 1.09 (29CH_3), 0.91 (33CH_3), 0.90 (34CH_3), 0.85 (30CH_3), 0.82 (35CH_3, 36CH_3).

2.5. Synthesis of $[Hg(C_{36}H_{60}O_{11})(H_2O)]$ (2)

$Hg(NO_3)_2 \cdot H_2O$ (171 mg, 0.5 mmol) was dissolved in 5 mL H_2O and was mixed with a solution of monensic acid (172 mg, 0.25 mmol in 10 mL mixed solvent (H_2O : MeCN = 1 : 10)) containing Et_4NOH (90 μL, 0.25 mmol, 40% in H_2O). The reaction mixture was stirred for 15 min at room temperature. The solvent was slowly evaporated to give the complex $[Hg(C_{36}H_{60}O_{11})(H_2O)]$ (**2**) as yellowish precipitates in 24 hours. The compound was purified by washing with MeCN/H_2O and dried at room temperature. Yield 166 mg, 75%. Anal. Calcd. for $C_{36}H_{62}O_{12}Hg$ (%): H, 7.04; C, 48.72; Hg 22,60. Found: H, 6,76; C, 47.82; Hg, 22.00. The slow concentration of diluted reaction mixture within 48 h leads to the formation of colourless crystals of **2** as $[Hg(C_{36}H_{60}O_{11})(H_2O)] \cdot 2H_2O$. The complex is soluble in MeOH, EtOH, $CHCl_3$ and is not soluble in MeCN. ^{1}H-NMR (600 MHz, δ (assignment), $CDCl_3$) 4.40 (OH-5, H_2O), 4.31 (20CH), 4.05 (17CH), 4.04 (5CH), 3.90 (21CH), 3.80 (7CH), 3.50 (26CH_2), 3.45 (13CH), 3.34 (28OCH_3), 3.22 (3CH), 2.68 (2CH), 2.23 (18CH), 2.18 (19CH_2), 2.11 (4CH), 2.06 (6CH), 1.97 (8CH_2'), 1.95 (10CH_2'), 1.88 (11CH_2), 1.69 (8CH_2"), 1.64 (10CH_2", 14CH_2'), 1.55 (14CH_2", 32CH_2'), 1.49 (23CH_2', 32CH_2", 24CH), 1.46 (31CH_3), 1.38 (15CH_2), 1.33 (23CH_2"), 1.26 (22CH), 1.22 (27CH_3), 1.05 (29CH_3), 0.91 (33CH_3), 0.90 (34CH_3), 0.85 (36CH_3), 0.84 (30CH_3), 0.83 (35CH_3).

2.6. Structure analysis and refinement

Data collection, structure solution and refinement of complexes **1** and **2** are given in Table 1. Data sets were collected at 115(2) K (**1**) and at 112(2) K (**2**) on an Oxford Diffraction Sapphire2-CCD diffractometer operating with Mo-Kα radiation (λ = 0.71073 Å) and equipped with a graphite monochromator. The structures were solved using direct methods [29]. The coordinates of non-hydrogen atoms were refined by full matrix least squares with anisotropic thermal parameters [30]. Hydrogen atoms were isotropically refined with a riding model. CCDC 754039 (**1**) and 754040 (**2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

3. Results and Discussion

3.1. Single crystal X-ray structures of complexes 1 and 2

The monensic acid reacts with some divalent metal ions in the presence of an organic base to form mononuclear complexes of composition $[M(C_{36}H_{61}O_{11})_2(H_2O)_2]$ (M = Mn, Ca, Zn, *etc.*) [22-25]. The Cd(II) derivative of the monoanion of monensic acid (**1**) reported now is isostructural with the compounds reported previously [22-25], while Hg(II) reacts with the dianion of monensic acid to form a unique complex of composition $[Hg(C_{36}H_{60}O_{11})(H_2O)]$ (**2**).

The ORTEP diagram of Cd(II) dimonensinate $[Cd(C_{36}H_{61}O_{11})_2(H_2O)_2]$, **1**, and its crystal packing are depicted in Figs. 1a and 1b, respectively. Selected bond length distances and angles are presented in Table 2. As can be seen, two monoanions of monensic acid coordinate to Cd(II) via the oxygens of carboxylate function (O(1)) and primary hydroxyl group (O(11)), situated at the opposite ends of the ligand molecule. Therefore, the resulting bonds Cd-OOC and Cd-OH formed are referred to as being of the "head-to-tail" type. The bidentate coordination mode of both ligands to Cd(II) causes formation of two 22-membered pseudo cycles in the macromolecule of the complex. Each of these cycles is further stabilizing by water molecules bound to monensin anions via intramolecular hydrogen bonds (Fig. 1c, Table 3). The H-bonds – O(2)-O(11), O(5)-O(6) and O(5)-O(10) – additionally support the cyclization of the ligand. No intermolecular bonds were observed in the crystal packing of **1** (Fig. 1b).

The molecular geometry of the complex can be

Table 1. Crystal data and structure refinement for compounds **1** and **2**.

Compound	Complex 1	Complex 2
Formula	$C_{82}H_{141}N_5O_{24}Cd$	$C_{36}H_{66}O_{14}Hg$
Formula weight	1693.4	923.5
Crystal system	Monoclinic	Orthorhombic
Space group	P2(1)	P2(1)2(1)2(1)
Z	2	4
Cell constants (Å, °)		
a	12.4090(8)	12.7316(2)
b	24.7688(16)	16.4379(3)
c	14.4358(11)	18.7184(4)
β	91.979(7)	90.00
V [A^3]	4434.3(5)	3917.40(13)
Absorption coeffcient [mm^{-1}]	0.320	3.993
Crystal size [mm^3]	0.18×0.07×0.03	0.12×0.05×0.05
D_{Calcd} [g cm^{-3}]	1.268	1.566
F(000)	1816	1896
2θ range [°]	2.94 - 25.08	3.14 - 27.57
No. reflections measured	17994	51023
No. unique reflections	13816 (Rint = 0.0855)	8970 (Rint = 0.0691)
No. observed reflections	4629 (I > 2σ(I))	6827 (I > 2σ(I))
No. parameters	1017	469
R indices (I > 2σ(I))	R1 = 0.0517	R1 = 0.0282
	wR2 = 0.0623	wR2 = 0.0428
R indices (all data)	R1 = 0.1670	R1 = 0.0452
	wR2 = 0.0782	wR2 = 0.0442
GOF	0.564	0.783
Final difference peaks (eÅ^{-3})	+0.389, –0.408	+1.085, –0.709

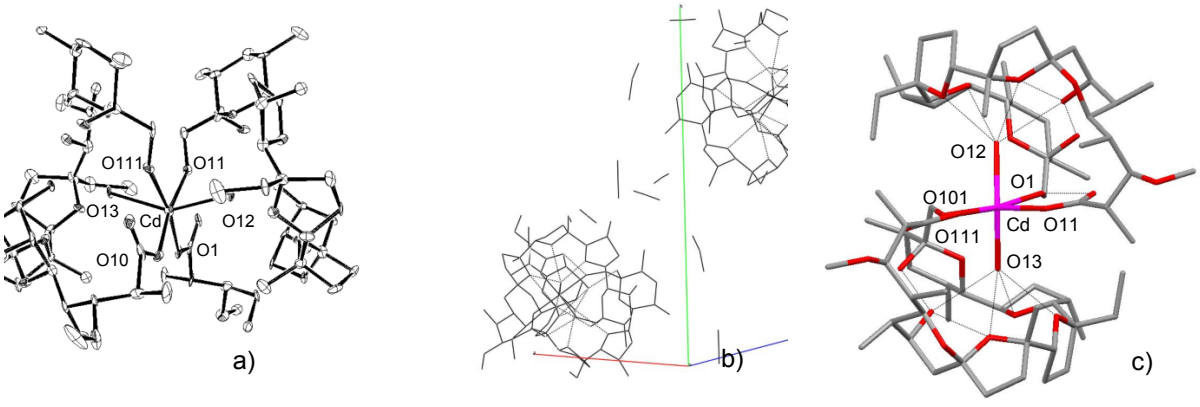


Figure 1. (a) ORTEP drawing of complex **1** at the 30% probability level (Protons and solvent molecules are omitted for clarity); (b) Crystal packing of **1**; c) Intramolecular hydrogen bonding (dotted lines) observed in **1**.

described as a distorted octahedron. The equatorial plane of **1** consists of four oxygen atoms (O(1), O(11), O(101), O(111)), originating from both monensinate anions. Two water molecules (O(12), O(13)) occupy axial sites in the inner coordination sphere of the metal ion. The octahedron is significantly distorted as the value of the H_2O-Cd-H_2O (O(12)-Cd(1)-O(13)) angle deviates significantly (*ca.* 30°) from the ideal one (180°). The data presented in Table 2 are in a good agreement with an observation reported previously that the divalent metal ion affects the H_2O-M-OH_2 angle and that it decreases with increasing ionic radii of the metal ion but does not significantly reflect on the value of other O-M-O angles [25]. The M-O coordination bond distances depend on the size of the metal ion radii also and increase with increasing ion radii.

The molecular formula of (**1**) $[Cd(C_{36}H_{61}O_{11})_2(H_2O)_2]$ was assigned and was confirmed by elemental analysis of the bulk phase. The crystals of the complex were grown by slow evaporation of MeCN/H_2O solution and contain additionally five molecules of MeCN that do not affect the main coordination sites of the ligand and do not participate in additional intra- and intermolecular bonding with the complex unit.

In contrast to all known divalent metal complexes of monensic acid, mercury(II) reacts with the ligand

Table 2. Selected bond lengths (Å) and angles (°) for complex **1**.

Cd(1)-O(1)	2.216(6)	O(1)-Cd(1)-O(101)	89.1(2)
Cd(1)-O(101)	2.233(6)	O(101)-Cd(1)-O(111)	86.3(2)
Cd(1)-O(11)	2.370(5)	O(111)-Cd(1)-O(11)	99.02(19)
Cd(1)-O(111)	2.340(6)	O(11)-Cd(1)-O(1)	86.4(2)
Cd(1)-O(12)	2.324(5)	O(1)-Cd(1)-O(111)	171.36(19)
Cd(1)-O(13)	2.337(5)	O(101)-Cd(1)-O(11)	171.8(2)
		O(12)-Cd(1)-O(13)	149.55(18)

Symmetry operation: x, y, z

Table 3. Intramolecular H-bonds (Å) observed in the structure of complex **1**.

O(2)-O(11)	2.522	O(102)-O(111)	2.527
O(5)-O(6)	2.810	O(105)-O(106)	2.801
O(5)-O(10)	2.734	O(105)-O(110)	2.699
O(5)-O(12)	2.876	O(105)-O(13)	2.842
O(6)-O(12)	2.945	O(106)-O(13)	2.937
O(7)-O(12)	2.716	O(107)-O(13)	2.705
O(8)-O(12)	2.897	O(108)-O(13)	2.873

Symmetry operation: x, y, z

Table 4. Selected bond lengths (Å) and angles (°) for complex **2**.

Hg(1)-O(1)	2.050(3)	O(1)-Hg(1)-O(2)	49.30(1)
Hg(1)-O(2)	2.921(3)	O(2)-Hg(1)-O(11)	79.07(9)
Hg(1)-O(10)	2.057(3)	O(11)-Hg(1)-O(10)	76.09(10)
Hg(1)-O(11)	2.524(2)	O(10)-Hg(1)-O(1)	153.76(10)
Hg(1)-O(12)	2.580(3)	O(1)-Hg(1)-O(11)	125.39(11)
		O(2)-Hg(1)-O(10)	155.14(9)

Symmetry operation: x, y, z

in the presence of base to form a unique complex of composition $[Hg(C_{36}H_{60}O_{11})(H_2O)]$ confirmed by elemental analysis of the bulk phase. Complex **2** crystallizes as $[Hg(C_{36}H_{60}O_{11})(H_2O)]\cdot 2H_2O$ due to the additional inclusion of water molecules in the crystals grown from MeCN/H_2O solution.

Complex **2** consists of a dianion of monensic acid bound in a tetradentate coordination manner to Hg(II) ion via the carboxylate (O(1)), carboylate (O(2)), secondary hydroxylate (O(10)) and primary hydroxyl (O(11)) oxygens (Fig. 2a). Selected bond lengths and angles are presented in Table 4. In the structure of **2**, the carboxylate / carboylate and hydroxyl / hydroxylate oxygens of monensic acid dianion, respectively, are placed at the opposite sites of the ligand molecule thus their coordination to Hg(II) affording the antibiotic cyclization. At all, the mercury(II) ion is surrounded by five oxygen atoms in a distorted square pyramidal environment. The four oxygen atoms O(1), O(2), O(10), O(11), originating from the ligand, occupy the basal plane in the inner coordination sphere of the metal ion. Placed at the axial position is a water molecule (O(12)), that participates additionally in a number of hydrogen bonds with the monensic acid dianion (Fig. 2b, Table 5).

The Hg-O bond length distances vary in a wide range from 2.050 Å (Hg(1)-O(1)) to 2.921 Å (Hg(1)-O(2)) indicating strong interaction of the metal ion with carboxylate (O(1)) and secondary hydroxylate (O(10)) oxygens accompanied by weaker bonding with carboylate (O(2)), primary hydroxyl (O(11)) and water (O(12)) oxygens, respectively. In contrast to the divalent metal complexes of monensic acid monoanion reported previously, Hg(II) coordinates preferentially to the secondary hydroxylate oxygen atom rather than to the primary hydroxyl one, as well as a bidentate coordination mode of carboxylate group is observed for the first time in divalent metal complexes of monensic acid anion. Four complex units complete the crystal packing of **2** attached by interacting with one other by intra- and intermolecular H-bonds of various origins due to the inclusion of water molecules (Fig. 2c, Table 5).

The crystallographic studies showed that Cd(II) and Hg(II) react with the anions of monensic acid to form two different type of complexes. While compound **1** exhibits a structure already found for some divalent metal complexes of monensic acid monoanion [22-25], the complex **2** represents the first example where an unusual tetradentate coordination mode of a dianion of the polyether ionophore monensic acid to the metal(II) ion is observed. It should be mentioned that the ion of Hg(II) does not “enter” the cavity of the ligand to form a shell-like complex as was observed for sodium monensinate. The Hg(II) structure reported is unique and confirms the ability of the ligand to form complexes with divalent toxic metal ions.

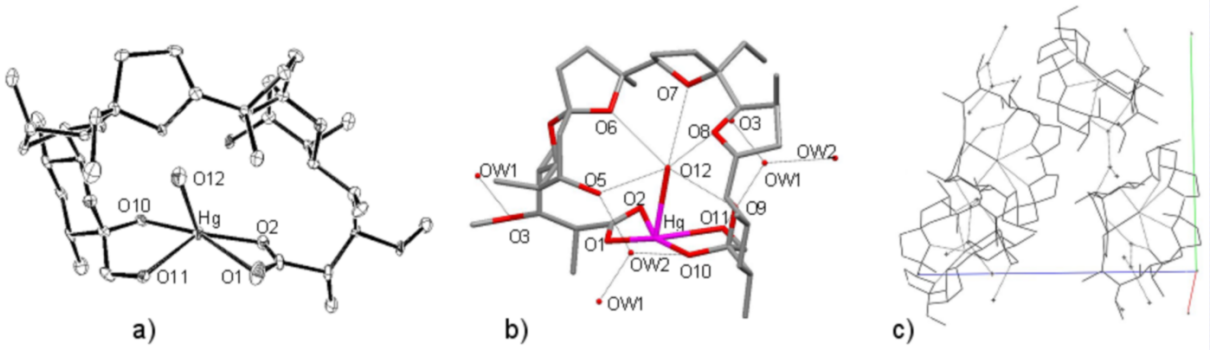


Figure 2. (a) ORTEP drawing of complex **2** at the 50% probability level (Protons and solvent molecules are omitted for clarity); (b) Intramolecular H-bonds (dotted lines) observed in **2**; (c) Crystal packing of **2**.

Table 5. Hydrogen bonds (Å) observed in the structure of complex **2**.

O(5)-O(12)	2.791	O(11)-OW(1)	2.712
O(6)-O(12)	2.829	O(10)-OW(2)	2.723
O(7)-O(12)	2.979	O(5)-OW(2)	2.897
O(8)-O(12)	2.837	O(3)-OW(1)[a]	2.903
O(9)-O(12)	3.031	OW(1)-OW(2) [b]	2.764

Symmetry operation: x, y, z; [a] 1-x,0.5+y,1.5-z; [b] 2-x, 0.5+y, 1.5-z

3.2. Spectroscopic study of complexes 1 and 2

The spectroscopic properties of new complexes were studied to obtain additional information, which is important when no single crystals of monensin complexes can be prepared.

Infrared spectra of monensic acid and new metal(II) complexes were recorded in a nujol mull and were related to the blank spectrum. The band at 1700 cm^{-1} in the IR spectrum of monensic acid monohydrate is attributed to the stretching vibration of the carboxylic function while the presence of water molecule and hydroxyl groups in the molecule resulted in the appearance of two bands at 3520 cm^{-1} and 3320 cm^{-1}, respectively [21].

The bands observed at 1550 cm^{-1} and 1400 cm^{-1} in the IR spectrum of Cd(II) complex **1**, are assigned to asymmetric and symmetric stretching vibrations of the carboxylate anion, respectively [22-25]. The band at 3480 cm^{-1} is attributed to the stretching vibration of the hydroxyl group from water molecules both coordinated to Cd(II) and engaged in hydrogen bonds. The participation of ligand hydroxyl groups in coordination and hydrogen bonds broadens the peak observed at 3320 cm^{-1}. The IR data obtained for **1** are consistent with the refined crystal structure.

The IR spectrum of Hg(II) complex, **2**, possesses bands at 1650 cm^{-1} ($\nu_a(COO^-)$) and 1410 cm^{-1} ($\nu_s(COO^-)$), respectively, assigned to the stretching vibrations of the carboxylate anion. The value of $\Delta = 240\ cm^{-1}$ ($\Delta = \nu_a(COO^-) - \nu_s(COO^-)$) is in agreement with the crystallographic data proving the bidentate coordination mode of carboxylate function [31]. The broad bands observed at 3500 cm^{-1} and in the range from 3400 to 3200 cm^{-1} confirm the presence of water molecules and monensin hydroxyl groups participating in coordination and hydrogen bonds.

The major ions observed in the FAB-MS spectrum of **1** are shown in Scheme 2. The presence of peaks assigned to **1a-1d** confirms the coordination of monensic acid to Cd(II). In the FAB-MS spectrum of complex **2** the major peaks are assigned to $[Hg(C_{36}H_{61}O_{11})]^+$ (m/z 871.4; 93%) and $[Hg(C_{36}H_{60}O_{11})]Na]^+$ (m/z 893.4; 63%). The presence of $[(C_{36}H_{62}O_{11})Na]^+$ (m/z 693.4; 10% (**1**), 25% (**2**)) is in accordance with the affinity of monensic acid to bind sodium ions originating from the glass and/or matrix used (3-nitrobenzylalcohol) and are in agreement with the data previously reported [32-38].

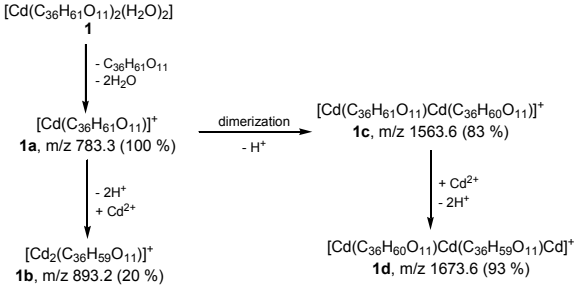
^{1}H-NMR data of complexes **1** and **2** (600 MHz, $CDCl_3$) are presented in the Experimental Procedure. ^{13}C {^{1}H}-NMR data are listed in Table 6. Original NMR spectra of **1** and **2** (^{1}H, ^{13}C{^{1}H} and HSQC) are presented as Supplementary data and can be viewed on the web.

The ^{13}C-NMR chemical shifts of Cd(II) dimonensinate, **1**, are almost in agreement with the data of mononuclear divalent monensin complexes already reported [23,25]. The significant downfield shift of δ, observed for C(1), C(2), C(25), C(27) (Table 6), confirm that these carbon atoms are in close proximity to the Cd(II) ion. Coordination of the hydroxyl groups and water molecules in **1** participating additionally in various hydrogen bonds is reflected in the ^{1}H-NMR spectrum of the complex. The signals at 5.09 ppm and 4.64 ppm are assigned to OH(5) and H_2O, respectively. The signals at 8.97 ppm and 6.69 ppm, belonging to the hydroxyl groups OH(10) and OH(11), could not be assigned, despite their clear

Table 6. $^{13}C\{^1H\}$ NMR chemical shifts (150 MHz, $CDCl_3$/TMS) of monensic acid and complexes **1**-**2**.

C-atom	δ_{ligand}, ppm	δ_1, ppm	Δ_1 [a]	δ_2, ppm	Δ_2 [b]
1	177.09	181.46	4.37	178.15	1.06
9	107.79	107.48	−0.31	107.62	−0.17
25	96.99	98.68	1.69	97.91	0.92
16	86.18	87.17	0.99	86.34	0.16
12	85.14	84.97	−0.17	85.30	0.16
17	85.11	84.66	−0.45	84.26	−0.85
13	83.42	84.33	0.91	82.93	−0.49
3	81.56	82.05	0.49	81.53	−0.03
20	77.01	77.31	0.30	77.34	0.33
21	73.83	73.32	−0.51	73.60	−0.23
7	70.74	70.51	−0.23	70.74	0.00
26	67.98	66.80	−1.18	67.64	−0.34
5	67.01	67.78	0.77	67.20	0.19
28	58.03	57.86	−0.17	57.91	−0.12
2	41.94	43.97	2.03	41.56	−0.38
10	38.36	38.50	0.14	38.53	0.17
4	36.70	37.20	0.50	36.74	0.04
23	36.59	36.57	−0.02	36.54	−0.05
24	35.68	35.74	0.06	32.83	−2.85
18	34.45	34.37	−0.08	34.41	−0.04
6	34.54	34.24	−0.30	34.40	−0.24
8	34.03	34.20	0.17	34.04	0.01
11	33.73	33.84	0.11	33.67	−0.06
22	32.80	33.18	0.38	32.83	0.03
19	32.58	32.62	0.04	32.46	−0.12
15	31.49	32.62	1.13	31.34	−0.15
32	31.19	30.79	−0.40	30.37	−0.82
14	27.88	27.66	−0.22	27.32	−0.56
31	27.69	27.44	−0.25	27.52	−0.17
35	17.54	17.49	−0.05	17.52	−0.02
36	16.32	16.80	0.48	16.61	0.29
27	15.66	16.80	1.14	15.76	0.10
34	15.75	15.60	−0.15	15.84	0.09
29	10.37	11.10	0.73	10.91	0.54
30	10.75	10.66	−0.09	10.35	−0.40
33	8.61	8.70	0.09	8.36	−0.25

[a] $\Delta_1 = \delta_1 - \delta_{ligand}$, *[b]* $\Delta_2 = \delta_2 - \delta_{ligand}$.



Scheme 2. Major products observed in the FAB-MS spectrum of **1**.

separation with some broadening due to exchange with the water molecules.

The carbon atoms in close proximity to the Hg(II) center in the ^{13}C-NMR spectrum of **2** are less up- or downfield shifted than the corresponding atoms in **1** and monensic acid. The observed Δ_2-values ($\Delta_2 = \delta_2 - \delta_{MonH}$) of these atoms (C(1), C(2), C(25), C(27)) are smaller most probably due to the tetradentate coordination of the ligand to the Hg(II) ion. The smaller down- and upperfield shifts, detected for the other carbon atoms in the spectra of **2**, indicate that additional conformational changes take place in the structure of the complex in solution. It should be noted that a high upfield shift (–2.85 ppm) was detected for C(24) that could not be easily explained.

4. Conclusions

Cadmium(II) complex of monensic acid $[Cd(C_{36}H_{61}O_{11})_2(H_2O)_2]$, **1**, was isolated and its structure solved by single crystal X-ray diffraction. The complex consists of Cd(II) ions placed in a distorted octahedral environment determined by two ligand monoanions acting in a bidentate coordination mode and two water molecules. Monensic acid reacts with Hg(II) to form a unique complex of composition $[Hg(C_{36}H_{60}O_{11})(H_2O)]$, **2**, in which the ligand is bound in a tetradentate coordination manner to Hg(II) to determine the basal plane of the compound. The Hg(II) ion possesses distorted square pyramidal geometry completed by coordination with a water molecule. Compound **2** crystallizes as $[Hg(C_{36}H_{60}O_{11})(H_2O)]\cdot 2H_2O$ and four complex units are attached to each other by various intermolecular H-bonds. The electroneutral Cd(II) and Hg(II)

compounds can be discussed as possible biological species formed due to the coordination of monensic acid in the case of intoxication with heavy metals in stock farming. To establish the possible application of the polyether ionophore monensic acid as an antidote a detailed *in vivo* investigation on experimental animals will be required.

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The supporting information contains ^{1}H, $^{13}C\{^{1}H\}$ and HSQC NMR spectra (in $CDCl_3$) of complexes $[Cd(C_{36}H_{61}O_{11})_2(H_2O)_2]$ (**1**) and $[Hg(C_{36}H_{60}O_{11})(H_2O)]$ (**2**).

References

[1] R.W. Taylor, R.F. Kauffman, D.R. Pfeiffer, In: J.W. Westley (Ed.) Polyether antibitocis: naturally occuring acid ionophores (Marcel Dekker, New York, 1982)
[2] R.F. Shumard, M.F. Callender, Antimicrob. Agents Chemother. 7, 369 (1967)
[3] J. Henri, C. Burel, P. Sanders, P.M. Laurentie, J. Vet. Pharmacol. Ther. 32, 451 (2009)
[4] B.C. Pressman, M. Fahim, Annu. Rev. Pharmacol. Toxicol. 22, 465 (1982)
[5] M.D. Ruff, In: J.W. Westley (Ed.) Polyether antibiotics: naturally occuring acid ionophores (Marcel Dekker, New York, 1982)
[6] M. Pinkerton, L.K. Steinrauf, J. Mol. Biol. 49, 533 (1970)
[7] W.K. Lutz, F.K. Winkler, J.D. Dunitz, Helv. Chim. Acta 54, 1103 (1971)
[8] L.K. Steinrauf, E.W. Czerwinski, M. Pinkerton, Biochem. Biophys. Res. Commun. 45, 1279 (1971)
[9] D.L. Ward, K.T. Wei, J.G. Hoogerheide, A.I. Popov, Acta Cryst, B34, 110 (1978)
[10] J.G. Hoogerheide, A.I. Popov, J. Solution Chem. 8, 83 (1979)
[11] W.L. Duax, G.D. Smith, P.D. Strong, J. Am. Chem. Soc. 102, 6725 (1980)
[12] P.Y. Barrans, M. Alleaume, G. Jeminet, Acta Cryst. B38, 1144 (1982)
[13] J. Garcla-Rosas, H. Schneider, B.G. Cox, J. Phys. Chem. 87, 5467 (1983)
[14] W. Pangborn, W.L. Duax, D. Langs, J. Am. Chem. Soc. 109, 2163 (1987)
[15] J. Rzeszotarska, E. Wagner-Czauderna, M.K. Kalinowski, J. Chem. Res. S 400 (1994)
[16] M. Mimouni, M. Hebrant, G. Dauphin, J. Juillard, J. Chem. Res. S 278 (1996)
[17] A. Huczyński, M. Ratajczak-Sitarz, A. Katrusiak, B. Brzezinski, J. Mol. Struct. 871, 92 (2007)
[18] S.O. Yildirim, V. McKee, F.Z. Khardli, M. Mimouni, T.B. Hadda, Acta Cryst. E64, m154 (2007)
[19] A. Huczynski, M. Ratajczak-Sitarz, A. Katrusiak, B. Brzezinski, J. Mol. Struct. 888, 224 (2008)
[20] P. Dorkov, I.N. Pantcheva, W.S. Sheldrick, H. Mayer-Figge, R. Petrova, M. Mitewa, J. Inorg. Biochem. 102, 26 (2008)
[21] I.N. Pantcheva, P. Dorkov, V. Atanasov, M. Mitewa, B.L. Shivachev, R.P. Nikolova, H. Mayer-Figge, W.S. Sheldrick, J. Inorg. Biochem. 103, 1419 (2009)
[22] I.N. Pantcheva, M. Mitewa, W.S. Sheldrick, I.M. Oppel, R. Zhorova, P. Dorkov, Curr. Drug Disc. Techn. 5, 154 (2008)
[23] I.N. Pantcheva, R. Zhorova, M. Mitewa, S. Simova, H. Mayer-Figge, W.S. Sheldrick, Biometals 23, 59 (2009)
[24] I.N. Pantcheva, R. Zhorova, M.I. Mitewa, W.S. Sheldick, In: M. Melnik, P. Segla, M. Tatarko (Eds.), Insights into coordination, bioinorganic and applied inorganic chemistry (Press of Slovak University of Technology, Bratislava, 2009) 257
[25] I.N. Pantcheva, J. Ivanova, R. Zhorova, M. Mitewa, S. Simova, H. Mayer-Figge, W.S. Sheldrick, Inorg. Chim. Acta 363, 1879 (2010)
[26] S.A. Hamidinia, W.L. Erdahl, C.J. Chapman, G.E. Steinbaugh, R.W. Taylor, D.R. Pfeiffer, Environm. Health Persp. 114, 484 (2006)
[27] S.A. Hamidinia, O.I. Shimelis, B. Tan, W.L. Erdahl, C.J. Chapman, G.D. Renkes, R.W. Taylor, D.R. Pfeiffer, J. Biol. Chem. 277, 38111 (2002)
[28] P.G. Gertenbach, A.I. Popov. J. Am. Chem. Soc. 97, 4738 (1975)
[29] G.M. Sheldrick, SHELXS-97, Program for Crystal Structure Solution (University of Göttingen, Germany, 1997)

[30] G.M. Sheldrick, SHELXL-97, Program for Crystal Structure Refinement (University of Göttingen, Germany, 1997)
[31] K. Nakamoto, Infrared and raman spectroscopy of inorganic and coordination compounds, 5th edition (Wiley, Toronto, 1997)
[32] J.W. Chamberlin, A. Agtarap, Org. Mass Spectrom. 3, 271 (1970)
[33] M.M. Siegel, W.J. McGahren, K.B. Tomer, T.T. Chang, Biomed. Environm. Mass Spectrom. 14, 29 (1987)
[34] D.E. Kiehl, R.K. Julian, A.S. Kennington, Rapid Comm. Mass Spectrom. 12, 903 (1988)
[35] V.M. Havlicek, M. Ryska, S. Pospisil, J. Mass Spectrom. 30, 1089 (1995)
[36] D.A. Volmer, C.M. Lock, Rapid Comm. Mass Spectrom. 12, 157 (1998)
[37] N.P. Lopes, C.B.W. Stark, H. Hong, P.J. Gates, J.Z. Staunton, Rapid Comm. Mass Spectrom. 16, 414 (2002)
[38] X.S. Miao, R.E. March, C.D. Metcalfe, Rapid Comm. Mass Spectrom. 17, 149 (2004)