



*J. Serb. Chem. Soc.* 77 (10) 1391–1399 (2012)  
JSCS–4360

## Cobalt(II) and cadmium(II) compounds with adamantane-1-sulfonic acid

MILENA ĐORĐEVIĆ<sup>1</sup>, DEJAN JEREMIĆ<sup>1#</sup>, KATARINA ANĐELKOVIĆ<sup>1\*\*</sup>,  
MAJA GRUDEN-PAVLOVIĆ<sup>1</sup>, VLADIMIR DIVJAKOVIĆ<sup>2</sup>,  
MAJA ŠUMAR RISTOVIĆ<sup>1#</sup> AND ILIJA BRČESKI<sup>1#</sup>

<sup>1</sup>Faculty of Chemistry, University of Belgrade, Studentski trg 12–16, 11000 Belgrade, Serbia  
and <sup>2</sup>Faculty of Sciences, University of Novi Sad, Trg D. Obradovića 4,  
21000 Novi Sad, Serbia

(Received 12 April, revised 11 May 2012)

**Abstract:** In this work, the syntheses and characterization of two novel compounds of adamantane-1-sulfonic acid (1-AdSO<sub>3</sub>H) with cobalt(II) and cadmium(II) are reported. The results of single crystal X-ray analysis of the compounds revealed that adamantane-1-sulfonate (1-AdSO<sub>3</sub><sup>−</sup>) in the monoanionic form plays different roles in the investigated compounds. Namely, while in compound [Co(H<sub>2</sub>O)<sub>6</sub>](1-AdSO<sub>3</sub>)<sub>2</sub>, six water molecules are coordinated to the cobalt(II) ion and 1-AdSO<sub>3</sub><sup>−</sup> serves as a counter ion, in compound [Cd(H<sub>2</sub>O)<sub>4</sub>(1-AdSO<sub>3</sub>)<sub>2</sub>], two molecules of 1-AdSO<sub>3</sub><sup>−</sup> are *trans*-coordinated to the cadmium(II) ion as a monodentate (O)-ligand and the other coordination sites are occupied by water molecules. The obtained compounds showed moderate activity against *Artemia salina*.

**Keywords:** X-ray structure determination; transition metal compounds; metal complexes; adamantane-1-sulfonate derivatives.

### INTRODUCTION

Selective and efficient activation of C–H bonds in aliphatic hydrocarbons is one of the major challenges in chemistry and is the subject of extensive research.<sup>1</sup> Nevertheless, sulfoxidation of saturated hydrocarbons, as well as their possible application, has seen much slower progress, although the resulting products are stable compounds, suitable to serve as ligands and to form a coordination bond *via* oxygen.

As a part of on-going efforts to investigate the coordination behavior of alkane sulfonates,<sup>2,3</sup> two novel compounds of 1-AdSO<sub>3</sub>H with cobalt(II) (**1**) and cadmium(II) (**2**) are presented in this work.

\* Corresponding author. E-mail: kka@chem.bg.ac.rs

# Serbian Chemical Society member.

doi: 10.2298/JSC120419051D

Adamantane and its derivatives have gained much attention in the recent years, due to their significant biological activity.<sup>4</sup> Coordination compounds of 1-adamantane derivatives are known only for the amino ( $-\text{NH}_2$ ),<sup>5,6</sup> and mercapto- ( $-\text{SH}$ ) derivatives.<sup>7,8</sup> It is noteworthy that information about compounds of 1- $\text{AdSO}_3\text{H}$  with metal ions, both salts and coordination compounds, are very sparse.<sup>9</sup> Therefore, to the best of our knowledge and according to the Cambridge Structural Database (CSD), herein the first crystal structures of any of the compounds of 1- $\text{AdSO}_3\text{H}$  are presented. Evaluation of the biological activity of the synthesized compounds also formed part of this study.

## EXPERIMENTAL

### *General procedures*

For the synthesis of 1- $\text{AdSO}_3\text{H}$ , the method of sulfoxidation of alkane using an  $\text{SO}_2/\text{O}_2$  mixture in the presence of a catalytic amount of vanadium(IV) species  $[\text{VO}(\text{acac})_2]$  was employed.<sup>10</sup> This method was modified. Hence, unlike the original procedure, the gas was continuously blown through the mixture. Yield: 64 %.

1- $\text{AdSO}_3\text{H}\cdot\text{H}_2\text{O}$  (1.0 g, 4.2 mmol) was dissolved in methanol of technical purity. Into the clear solution of 1- $\text{AdSO}_3\text{H}$ , cobalt(II) acetylacetonate (0.64 g, 2.5 mmol) was added. The obtained suspension was digested for 10 min on an ultrasonic bath at 20 °C. The reaction mixture was filtered and the filtrate was left for 7 days to crystallize at room temperature. The obtained brick-red crystals of the cobalt(II) complex had grown to a size of 5 mm and were suitable for crystallographic analyses. Yield of complex **1**: 58 %.

The cadmium(II) complex was prepared by the same procedure except cadmium(II) acetylacetonate (**3**) (0.78 g, 2.5 mmol) was added into the clear solution of 1- $\text{AdSO}_3\text{H}$ . After 7 days of crystallization at room temperature, the obtained colorless crystals of the cadmium(II) complex had grown to a size of 1 mm and were suitable for crystallographic analyses. Yield of complex **2**: 57 %.

Elemental analyses (C and H) were performed by standard micro-methods using an ELEMENTARVario ELIII C.H.N.S O analyzer.

### *X-ray crystallography*

The selected single crystals of the title compounds **1** and **2** were glued onto glass threads. The diffraction data were collected on an Oxford Diffraction KM4 four-circle goniometer equipped with Sapphire CCD detector. The crystal to detector distance in both cases was 45.0 mm and graphite monochromated  $\text{MoK}\alpha$  ( $\lambda = 0.71073$  Å) X-radiation was employed in the measurements. A frame width of  $1^\circ$  in  $\omega$ , for 21.7 and 20.3 s, was used to acquire each frame for **1** and **2**, respectively. More than a hemisphere of three-dimensional data was collected in all measurements. The data were reduced using the Oxford Diffraction Program CrysAlisPro.<sup>11</sup> A semi-empirical absorption correction based upon the intensities of equivalent reflections was applied, and the data were corrected for Lorentz, polarization, and background effects. The scattering curves for neutral atoms, together with anomalous-dispersion corrections, were taken from International Tables for X-ray Crystallography.<sup>12</sup> The structures were solved by direct methods,<sup>13</sup> and the figures were drawn using Mercury.<sup>14</sup> The refinements were based on the  $F^2$  values and performed by full-matrix least-squares<sup>15</sup> with all non-H atoms anisotropic. The positions of all non H-atoms were located by direct methods. The positions of hydrogen

atoms were found from the inspection of the difference Fourier maps. The final refinement included atomic positional and displacement parameters for all non-H atoms.

The non-H atoms were refined anisotropically, while H sites of the water molecules were refined with isotropic displacement parameters. However, at the final stage of the refinement, H atoms belonging to the corresponding ligand were positioned geometrically (C–H, 0.97–0.98 Å) and refined using a riding model with fixed isotropic displacement parameters. The crystal data and refinement parameters are listed in Table I.

TABLE I. Crystal data and structure refinement for the obtained compounds

Compound	[Co(H <sub>2</sub> O) <sub>6</sub> ](1-AdSO <sub>3</sub> ) <sub>2</sub> ( <b>1</b> )	[Cd(H <sub>2</sub> O) <sub>4</sub> ](1-AdSO <sub>3</sub> ) <sub>2</sub> ( <b>2</b> )
Chemical formula	C <sub>20</sub> H <sub>42</sub> CoO <sub>12</sub> S <sub>2</sub>	C <sub>20</sub> H <sub>38</sub> CdO <sub>10</sub> S <sub>2</sub>
Formula weight	597.606	615.053
Wavelength, Å	0.71073	0.71073
Temperature, K	295(2)	295(2)
Crystal system	monoclinic	monoclinic
Space group	C2/m	C2/m
<i>a</i> / Å	11.058(5)	7.459(3)
<i>b</i> / Å	7.103(3)	10.488(4)
<i>c</i> / Å	18.099(8)	15.896(5)
$\beta$ / °	106.057(5)	91.662(4)
<i>V</i> / Å <sup>3</sup>	1366.13(11)	1243.0(8)
<i>Z</i>	2	2
<i>D</i> <sub>calc</sub> / g cm <sup>-3</sup>	1.453	1.643
$\mu$ / mm <sup>-1</sup>	0.84	1.10
<i>F</i> (000)	634	636
( $\theta_{\min}$ – $\theta_{\max}$ ) / °	3.5–25.0	3.4–25.0
Diffraction measured fraction, $\theta_{\max}$	0.998	0.998
Refined difference density, max/min	0.352/–0.220	0.64/–0.50
Reflection collected/unique/greater ( <i>R</i> <sub>int</sub> )	2350/1309/1147 (0.023)	2286/1167/1136 (0.022)
Data/restraints/parameters	1309/0/104	1167/0/94
Goodness-of-fit on <i>F</i> <sup>2</sup>	1.082	1.032
<i>R</i> indices (all data)	0.0442	0.0428
Final <i>R</i> indices [ <i>I</i> > 2 $\sigma$ ( <i>I</i> )]	0.0367	0.0414

CCDC-844771 (**2**) and CCDC-844772 (**1**) 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](http://www.ccdc.cam.ac.uk/data_request/cif).

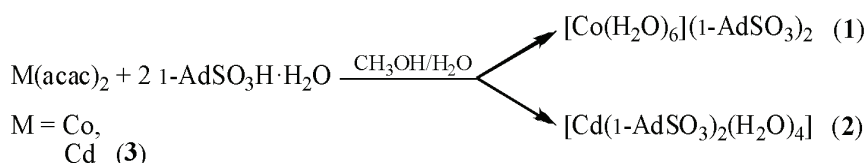
#### Biological activity evaluation – the brine shrimp test

A teaspoon of lyophilized eggs of the brine shrimp *Artemia salina* was added to 1 L of artificial sea water containing several drops of yeast suspension (3 mg of dry yeast in 5 mL distilled water), and air was passed through the suspension thermostated at 28 °C, under illumination for 24 h. Complex **2** and Cd(acac)<sub>2</sub> (**3**) were dissolved in DMSO. Since complex **1** is insoluble in DMSO and water, appropriate amounts of the compound dissolved in methanol were applied on paper disks (diameter 8 mm), and the solvent was evaporated. In a glass vial, 1–2 drops of yeast extract solution, 10–20 hatched nauplii in 5 mL of artificial seawater, and finally solutions of the tested compounds were added. For each concentration,

three determinations were performed. The vials were left at room temperature under illumination for 24 h, and afterwards the surviving nauplii were counted. The lethal concentration 50 ( $LC_{50}$ ) was defined as the concentration of a substance that causes the death of 50 % of the nauplii. DMSO was inactive under the applied conditions.

## RESULTS AND DISCUSSION

According to the procedure described in experimental section, 1-AdSO<sub>3</sub>H as well as its derivatives with cobalt(II) **1** and cadmium(II) **2** were synthesized (Scheme 1) and characterized.



Scheme 1. Reaction of 1-AdSO<sub>3</sub>H with the starting Co(II) and Cd(II) compounds.

*1-AdSO<sub>3</sub>H*. Anal. Calcd. for C<sub>10</sub>H<sub>16</sub>O<sub>3</sub>S: C, 55.56; H, 7.41 %. Found: C, 56.58; H, 7.39 %.

*Cobalt complex 1*. Anal. Calcd. for C<sub>20</sub>H<sub>42</sub>CoO<sub>12</sub>S<sub>2</sub>: C, 40.20; H, 7.04 %. Found: C, 40.24; H, 7.01 %.

*Cadmium complex 2*. Anal. Calcd. for C<sub>20</sub>H<sub>38</sub>CdO<sub>10</sub>S<sub>2</sub>: C, 39.06; H, 6.18 %. Found: C, 39.10; H, 6.12 %.

### X-ray analysis

The results of the single crystal X-ray analysis revealed that the structural units of **1** are [Co(H<sub>2</sub>O)<sub>6</sub>]<sup>2+</sup> and 1-AdSO<sub>3</sub><sup>-</sup> additionally connected by strong hydrogen bonds, while the structural units of **2** are neutral [Cd(H<sub>2</sub>O)<sub>4</sub>(1-AdSO<sub>3</sub>)<sub>2</sub>] complex molecules mutually well separated, in which two 1-AdSO<sub>3</sub><sup>-</sup> coordinate as monodentate (O)-ligands in the *trans* position. The structural units in **1** and **2** are involved in the formation of 2D networks of hydrogen bonds. In both compounds, the central ions are in a slightly distorted octahedral environment, consisting of six O-atoms of water molecules in **1**, or four O-atoms of water molecules and two O-atoms of sulfonate fragments in **2**. Structural units in both compounds exhibit a high degree of internal symmetry, as the majority of atoms that build up the 1-AdSO<sub>3</sub><sup>-</sup> in **1** and **2** occupy a special position  $4i$  (*m*), while the central ions are placed in positions  $2b$  and  $2d$  ( $2/m$ ) of the  $C2/m$  space group, respectively (Figs. 1 and 2). Pertinent crystallographic data for the two structures are given in Table I, the labeling schemes and corresponding symmetry elements are given in Figs. 1 and 2. Selected bond lengths and angles are listed in Table II. Both structures appear similar at the supramolecular level, caused by the relatively small number of hydrogen bonds (Table III). Hydrogen atoms from water molecules are involved in strong hydrogen bonding with free oxygen atoms of

the sulfonate fragment, building a 2D network of hydrogen bonds both along the *a* and *b* axes. As a result, along the *c* axis, “sandwiches” of thickness less than the size of axis *c* can be distinguished (Figs. 3 and 4). These “sandwiches” are on both outer sides covered with Ad-fragments, on which proper SO<sub>3</sub> groups are attached and oriented towards the core of the “sandwich”. The core consists of metal ions that are in **1** coordinated with six H<sub>2</sub>O molecules, whereas in **2** the metal ions are coordinated with two O atoms from monodentate AdSO<sub>3</sub> ligands in the apical positions and four H<sub>2</sub>O molecules in the equatorial plane. The distances between the “sandwiches” correspond to the C–C van der Waals contacts between the opposing Ad-fragments.

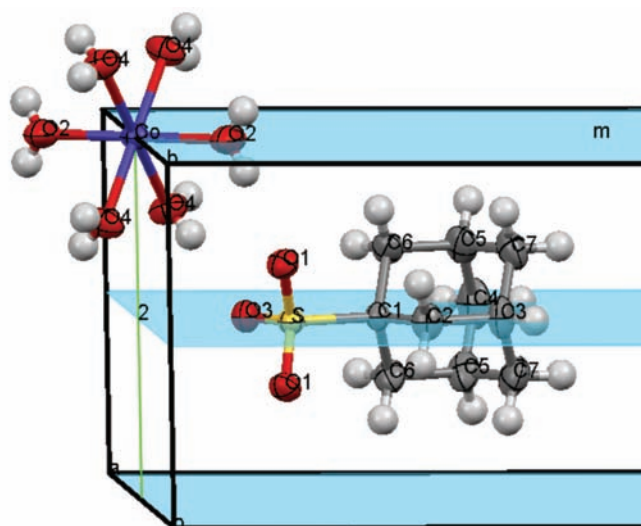


Fig. 1. Hexaaquacobalt(II)adamantane-1-sulfonate (**1**).

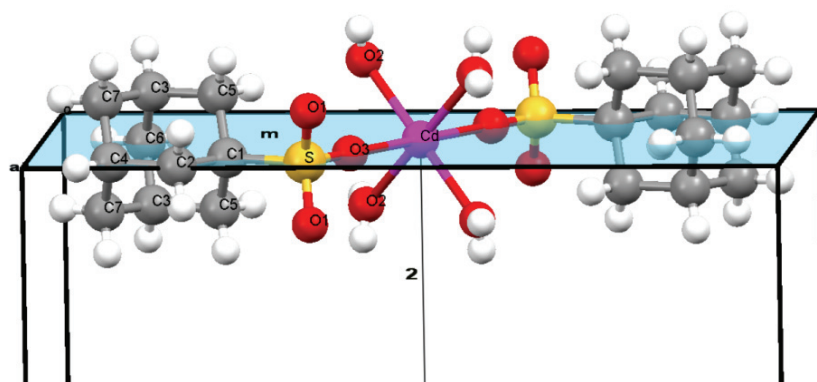


Fig. 2. Tetraaquabis(adamantane-1-sulfonato)cadmium(II) (**2**).

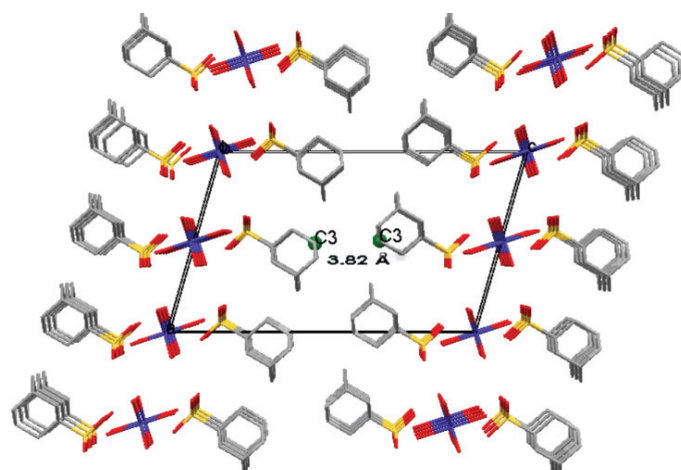
TABLE II. Selected bond lengths, Å, and angles, °, for complexes **1** and **2**

[Co(H <sub>2</sub> O) <sub>6</sub> ](1-AdSO <sub>3</sub> ) <sub>2</sub> ( <b>1</b> )		[Cd(1-AdSO <sub>3</sub> ) <sub>2</sub> (H <sub>2</sub> O) <sub>4</sub> ] ( <b>2</b> )	
Co–O2	2.043(3)	Cd–O2	2.233(4)
Co–O4	2.088(2)	Cd–O2 <sup>a</sup>	2.233(4)
O2–Co–O2 <sup>b</sup>	180.00	Cd–O3	2.250(5)
O4–Co–O4 <sup>c</sup>	180.00	S–O1	1.449(3)
O2–Co–O4	89.13(10)	S–O1 <sup>d</sup>	1.449(3)
O2–Co–O4 <sup>b</sup>	90.87(10)	S–O3	1.429(5)
O4–Co–O4 <sup>b</sup>	84.45(14)	S–C1	1.798(6)
O4–Co–O4 <sup>e</sup>	95.55(14)	O2–Cd–O3	92.4(2)
S–O3	1.457(2)	O2–Cd–O2 <sup>f</sup>	93.3(3)
S–O1	1.457(2)	O3–S–O1	112.1(2)
S–O1 <sup>g</sup>	1.457(2)	O3–S–O1 <sup>d</sup>	112.1(2)
S–C1	1.797(3)	O1–S–O1 <sup>d</sup>	112.1(3)
O3–S–O1	112.46(8)	O1–S–C1	107.0(2)
O1–S–O1 <sup>g</sup>	111.59(14)	O1 <sup>d</sup> –S–C1	107.0(2)
O3–S–C1	106.51(14)	O3–S–C1	106.2(3)
O1–S–C1	106.68(9)	Cd–O3–S	179.6(4)

<sup>a</sup>  $-x+1, y, -z+1$ ; <sup>b</sup>  $-x+1, y, -z$ ; <sup>c</sup>  $-x+1, -y+2, -z$ ; <sup>d</sup>  $x, -y, z$ ; <sup>e</sup>  $x, -y+2, z$ ; <sup>f</sup>  $-x+1, y, -z+1$ ; <sup>g</sup>  $x, -y+1, z$

TABLE III. Hydrogen bonding in complexes **1** and **2**

Bond	D–H, Å	H···A, Å	D···A, Å	D–H–A, °	Symmetry operation
<b>1</b>					
O4–H <sub>A</sub> ···O3	0.74(3)	2.04(3)	2.770(3)	171(3)	$(-x+1, -y+1, -z)$
O4–H <sub>B</sub> ···O1	0.78(3)	2.05(3)	2.815(3)	170(3)	$(-x+1/2, y+1/2, -z)$
O2–H <sub>C</sub> ···O1	0.76(3)	1.99(3)	2.742(3)	167(3)	$(x, y+1, z)$
<b>2</b>					
O2–H1···O1	0.73(6)	2.08(6)	2.802(6)	167(6)	$(x-1/2, y-1/2, z)$
O2–H2···O1	0.82(6)	1.92(6)	2.739(6)	176(6)	$(x-1, -y, z)$

Fig. 3. Packing of the structural units in **1** with a view along the axis *b*.

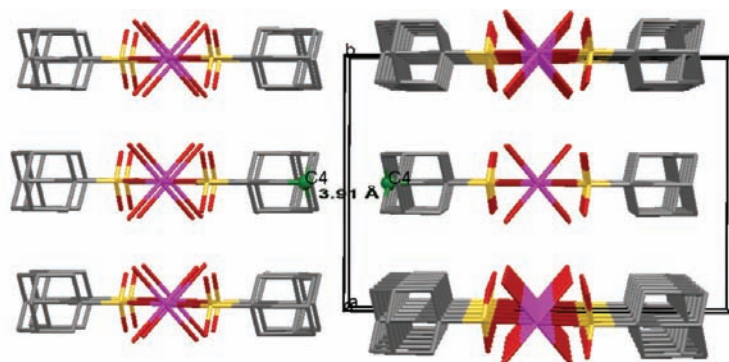


Fig. 4. Packing of the coordination units in **2** along the axis *a*.

#### Biological activity

In the *A. salina* test, which shows a good correlation with cytotoxic activity,<sup>16</sup> all the substances had  $LC_{50}$  values in either the millimolar range or high micromolar range (Table IV). The tetraaquabis(adamantane-1-sulfonato)cadmium(II) complex (**2**) was more active than the starting Cd(II) compound **3**, probably due to its higher lipophilicity.

TABLE IV. Toxic effect (expressed as  $LC_{50}$  values) of the investigated compounds against *A. salina*

Compound	$LC_{50}$ / mM
$[\text{Co}(\text{H}_2\text{O})_6](1\text{-AdSO}_3)_2$ ( <b>1</b> )	3.05
$[\text{Cd}(\text{H}_2\text{O})_4(1\text{-AdSO}_3)_2]$ ( <b>2</b> )	0.74
$\text{Cd}(\text{acac})_2$ ( <b>3</b> )	3.03

#### CONCLUSIONS

In this work, the first crystal structures of inorganic compounds of 1-AdSO<sub>3</sub>H were reported. While in compound  $[\text{Co}(\text{H}_2\text{O})_6](1\text{-AdSO}_3)_2$ , six water molecules are coordinated to the cobalt(II) ion and 1-AdSO<sub>3</sub><sup>-</sup> serves as a counter ion, in the  $[\text{Cd}(\text{H}_2\text{O})_4(1\text{-AdSO}_3)_2]$  compound, 1-AdSO<sub>3</sub><sup>-</sup> acts as monodentate ligand and coordinates to the cadmium(II) ion through the oxygen atom in a monoanionic form. The phenomenon that 1-AdSO<sub>3</sub><sup>-</sup> accomplished coordination with the Cd(II) ion but not with Co(II) can perhaps be explained by hard-soft-acid-base principle.<sup>17-19</sup> In fact, it is more likely that the soft cadmium can make a coordination bond with a relatively soft alkane sulfonate group (much softer than the sulfate group), as opposed to the harder cobalt. Rigidity and hydrophobicity of the adamantane residue proved to be a difficulty in further attempts to synthesize adamantane-1-sulfonate compounds. The obtained compounds were tested against *A. salina* and showed moderate activity. Due to higher lipophilicity of compound **2**, it was more active than the starting Cd(II) compound **3**.

*Acknowledgement.* The authors are grateful to the Ministry of Education, Science and Technological Development of the Republic of Serbia for financial support (Project No. 172017).

## ИЗВОД

НОВА ЈЕДИЊЕЊА КОБАЛТА(II) И КАДМИЈУМА(II) СА  
АДАМАНТАН-1-СУЛФОНСКОМ КИСЕЛИНОМ

МИЛЕНА ЂОРЂЕВИЋ<sup>1</sup>, ДЕЈАН ЈЕРЕМИЋ<sup>1</sup>, КАТАРИНА АНЂЕЛКОВИЋ<sup>1</sup>, МАЈА ГРУДЕН-ПАВЛОВИЋ<sup>1</sup>,  
ВЛАДИМИР ДИВЈАКОВИЋ<sup>2</sup>, МАЈА ШУМАР РИСТОВИЋ<sup>1</sup> и ИЛИЈА БРЧЕСКИ<sup>1</sup>

<sup>1</sup>Хемијски факултет, Универзитет у Београду, Студентски шир 12–16, 11000 Београд и <sup>2</sup>Природно-математички факултет, Универзитет у Новом Саду, Трт Д. Обрадовића 4, 21000 Нови Сад

У овом раду приказана је синтеза и карактеризација два нова једињења адамантан-1-сулфонске киселине (1-AdSO<sub>3</sub>H) са кобалтом(II) и кадмијумом(II). Резултати рендгенске структурне анализе датих једињења указују да моноанјон адамантан-1-сулфоната (1-AdSO<sub>3</sub> показује различит афинитет према Co(II) и Cd(II) јонима). У комплексу [Co(H<sub>2</sub>O)<sub>6</sub>](1-AdSO<sub>3</sub>)<sub>2</sub>, шест молекула воде се координује за Co(II) јон, док 1-AdSO<sub>3</sub> има улогу контрајона. У комплексу [Cd(H<sub>2</sub>O)<sub>4</sub>](1-AdSO<sub>3</sub>)<sub>2</sub> два јона 1-AdSO<sub>3</sub> су координована за Cd(II) јон као монодентати у *trans* положају преко кисеоникових атома, док су остала координациона места заузета молекулима воде. Добијена једињења су показала умерену активност на *Artemia salina*.

(Примљено 12. априла, ревидирано 11. маја 2012)

## REFERENCES

1. F. Parrino, A. Ramakrishnan, H. Kisch, *Angew. Chem. Int. Ed.* **47** (2008) 7107
2. D. A. Jeremić, G. N. Kaluderović, S. Gómez-Ruiz, I. D. Brčeski, B. Kasalica, V. M. Leovac, *Cryst. Growth Des.* **10** (2010) 559
3. D. A. Jeremić, G. N. Kaluderović, S. Gómez-Ruiz, I. D. Brčeski, K. Anđelković, *Acta Crystallogr. C* **65** (2009) m143
4. A. Kozubík, A. Vaculová, K. Souček, J. Vondráček, J. Turánek, J. Hofmanová, *Met.-Based Drugs* **2008** (2008) 417897
5. F. D. Rochon, M. Doyon, I. S. Butler, *Inorg. Chem.* **32** (1993) 2717
6. M. Westerhausen, T. Bollwein, A. Pfitzner, T. Nilges, H. J. Deiseroth, *Inorg. Chim. Acta* **312** (2001) 239
7. A. P. Purdy, A. D. Berry, C. F. George, *Inorg. Chem.* **36** (1997) 3370
8. Y. Matsunaga, K. Fujisawa, N. Ibi, M. Fujita, T. Ohashi, N. Amir, Y. Miyashita, K. Aika, Y. Izumi, K. Okamoto, *J. Inorg. Biochem.* **100** (2006) 239
9. I. Hitoshi, Y. Hiroshi, E. Hiroyuki, S. Masaharu, A. Kimisuke, (Nippon Electric Co, Jpn. Kokai Tokyo Koho), JKXXAF JP 07070312 A 19950314 (1995)
10. Y. Ishii, K. Matsunaka, S. Sakaguchi, *J. Am. Chem. Soc.* **122** (2000) 7390
11. CrysAlis CCD and CrysAlis RED software (Version 1.171), Oxford Diffraction, Yarnton, Oxfordshire, UK, 2000
12. J. A. Ibers, W. C. Hamilton, Eds., *International tables for X-ray crystallography*, vol. 4, Kynoch, Birmingham, UK, 1974
13. A. Altomare, M. C. Burla, M. Cavalli, G. Cascarano, C. Giacovazzo, A. Gagliardi, A. G. Moliterni, G. Polidori, R. Spagna, *Sir97: A New Program For Solving and Refining Cryst*



*tal Structures*, Istituto di Ricerca per lo Sviluppo di Metodologie Cristallografiche CNR, Bari, 1997

14. I. J. Bruno, J. C. Cole, P. R. Edgington, M. K. Kessler, C. F. Macrae, P. McCabe, J. Pearson, R. Taylor, *Acta Crystallogr., Sect. B* **58** (2002) 389
15. G. M. Sheldrick, *Acta Crystallogr., Sect. A* **64** (2008) 112
16. B.N. Meyer, N.R. Ferrigni, J.E. Putnam, L.B. Jacobsen, D.E. Nichols, J.L. McLaughlin, *Planta Med.* **45** (1982) 31
17. R. G. Pearson, *J. Am. Chem. Soc.* **85** (1963) 3533
18. R. G. Pearson, *J. Chem. Educ.* **45** (1968) 581
19. R. G. Pearson, *J. Chem. Educ.* **45** (1968) 643.