N-Allyl-N-Benzoyl-Bisthiourea as N,O,S-Atom Containing Ligand for Determination of Bi(III)

Maksym Fizer[1*], Ruslan Mariychuk[2], Oksana Fizer[3], Mykhaylo Slivka[1], Vasyl Lendel[1]

[1]Department of Organic chemistry, Faculty of Chemistry, Uzhhorod National University, 88000, Uzhhorod, Nadordna sq. 3, Ukraine, E-mail: mmfizer@gmail.com Phone: +380994630446, [2]Department of Ecology, Faculty of Humanities and Natural Sciences, University of Prešov in Prešov, 08116, 17th November str. 1, Prešov, Slovakia, [3]Department of Analytical chemistry, Faculty of Chemistry, Uzhhorod National University, 88000, Uzhhorod, Nadordna sq. 3, Ukraine

Abstract: We developed a simple, accurate, sensitive and reliable method for the selective determination of Bi(III), which is based on spectrophotometric measurement of water soluble yellow bismuth-ligand complexes. The linear calibration ranges and limit of detection for the proposed method was $1.00 \cdot 10^{-6}$ - $1.00 \cdot 10^{-3}$ and $2.00 \cdot 10^{-8}$ mol/L, respectively. The complexes were prepared in mixing of sample with the organic-solvent solution of chelating agent. The influence of the organic solvent amount was studied. Chelating agent were firstly synthesized though the reaction of thiosemicarbazides with aroyl isothiocyanates. The mentioned ligands are bisthioureas with sulfur, nitrogen and oxygen donor atoms. The quantum-chemical calculations were carried out for detailed understanding of the complex formation reaction for received compounds.

Keywords: spectrophotometry; Bismuth; thiosemicarbazides; aroyl isothiocyanates

1   Introduction

Development of fast and reliable methods for determination of small quantities of Bismuth in natural samples is an important task. Bismuth is widely used in different parts of industry. Bismuth is a metal that is mostly consumed in the production of low-melting alloys and metallurgical additives [1], as a substitute for the toxic lead in ammunition [2].

Bismuth-containing pigment based on platelet-shaped crystals of bismuth oxide chloride (BiOCl) and greenish yellow pigment based on bismuth orthovanadate (BiVO$_4$) have been known for a long time [3].

Some bismuth-containing complex oxides could be activated by visible light and mineralize organic pollutants [4]. Furthermore, visible light-responsive photocatalysts like Bi_2WO_6, $BiVO_4$ and Bi_2MoO_6 were also described [5].

Human exposure mainly occurs during production and use of pharmaceuticals such as Pepto-Bismol (Bismuth Subsalicylate) and Bismuth Citrate, an over-the counter drug to treat minor upsets of the digestive system [6, 7].

Bismuth containing drugs is used for eradication of Helicobacter pylori in peptic ulcers [8, 9, 10], treatment of syphilis and tumours [11], reduction of the renal toxicity of cisplatin [12, 13].

In recent years, bismuth has been promoted as a "green element", however, the bio-availability and toxicity of bismuth is still not very well described. Bi-containing compounds are considered to be slightly adsorbed through both respiratory and gastrointestinal tracts but information on uptake and metabolism is still scarce [14].

In one investigation was shown that Bi^{3+} ions, at concentration of 60 μg/ml, may reduce normal sperm metabolism by inhibition of sperm creatine kinase, which probably is an important cause of infertility in men. [15].

There are some reports that the digestion of bismuth and its compounds may result in kidney damage, gingivitis, rheumatic pain, fever and problems in hepatic function [16, 17].

Unlike organic pollutants, metals cannot be degraded easily and accumulate throughout the food chain, producing potential human health risks and ecological disturbances [18]. That is why, the elaboration of bismuth-detection techniques is actual.

There are many techniques for the determination of Bismuth in various types of samples – such as flame atomic absorption spectrometry (FAAS) [19, 20], inductively coupled plasma mass spectrometry (ICP-MS) [21], atomic fluorescence spectrometry [22], potentiometric analysis [23] and spectrophotometry [24; 25]. Some of these techniques such as ICP-MS usually have enough sensitivity for the determination of Bi at trace level, but suffer from matrix interferences and is not available in many laboratories due to its high cost. FAAS is simple, low cost, highly selective, but due to the relatively poor sensitivity, direct determination of trace amounts of bismuth is problematic.

The sensitivity and detection limit for the analyte determination can be significantly improved by the combination of a separation/pre-concentration with the instrumental technique of analysis. 2-Mercaptobenzothiazole (MBT), with sulfur and nitrogen donor atoms, as a chelating agent has been used for the separation and pre-concentration of bismuth [26]. The objective of our studies is improving of photometric determination of Bi(III) by complexation with variation of ligands nature.

2   Experimental

2.1   Computational Investigation

All calculations were performed with MOPAC2012 program [27, 28, 29, and 30]. Graphical results were presented with Jmol program [31] and Gabedit [32].

2.2   Chemical Synthesis

Synthesis of Compounds L[1,2]. (General Method). NH_4SCN (13 mmol) was dissolved in acetonitrile (100 ml) at 60-70°C. The solution was cooled to 35-40°C and aroyl chloride (10 mmol) was added with stirring. The suspension obtained was stirred for 15-20 min and then a solution of corresponding thiosemicarbazide (10 mmol) in acetonitrile (50 ml) was added. Stirring was continued for 30 min at 45-50°C. Solvent was removed under reduce pressure. The residue was mixed with cold water. The precipitate of product L[1,2] was filtered off, washed with water, and dried in the air. The precipitate was recrystallized from suitable solvent and dried in the air.

N-{[2-(methylcarbamothioyl)hydrazino]carbonothioyl}benzamide   (L[1]) obtained in 71% yield; m.p. 190-192 °C. IR (cm^{-1}): 3250 (N-H); 1700 (C=O); 1480-1600 (C=S, C-N); 1200-1300 (N-N, Ph, C-N). 1H NMR (DMSO-d6): δ = 3.06 (d, 3H, CH3N), 6.45-13.10 (NH, Ph, NH, NH, NH). Anal. Calcd for $C_{10}H_{12}N_4OS_2$, %: C, 44.76; H, 4.51; N, 20.88; O, 0.96; S, 23.90. Found, %: C 44.39; H 4.20; N 19.71; S 22.94.

N-{[2-(prop-2-en-1-ylcarbamothioyl)hydrazino]carbonothioyl}benzamide (L[2]) obtained in 57% yield. m.p. 144-146 °C. IR (cm^{-1}): 3250 (N-H); 1700 (C=O); 1480-1600 (C=S, C-N); 1200-1300 (N-N, Ph, C-N). 1H NMR (DMSO-d6): δ = 4.17 (m, 2H, CH2N), 5.25-5.38 (dd, 2H, CH2=), 5.88 (m, 1H, =CH-), 6.41-13.03 (NH, Ph, NH, NH, NH). Anal. Calcd for $C_{12}H_{14}N_4OS_2$, %: C, 48.96; H, 4.79; N, 19.03; S, 21.78. Found, %: C 47.84; H, 4.87; N, 18.40; S, 21.19.

2.3   Analytical Procedure

For the investigation we used two different samples: $TlBiSe_2$ − semiconductor, and a tablet of "Vicairum" - combined drug for treating stomach.

$TlBiSe_2$. A sample was dissolved in 5 ml of concentrated HNO_3. Mixture was evaporated with boiling, 5 ml of H_2SO_4 solution (1:1) was added and evaporated again. Obtained residue was diluted with bi-distilled water (about 30 ml) and filtered. Water was added to this solution till average 50.0 ml. An aliquot of 5ml of this solution was dissolved in 95 ml of water to get 100 ml of sample solution.

Vicairum. A pill of "Vicairum" was dissolved in 5 ml of concentrated HNO_3. Mixture was diluted with bi-distilled water (about 30 ml) and filtered. Water was

added to this solution till average 100.0 ml. An aliquot of 2 ml of this solution was dissolved in 98 ml of water to get 100 ml of sample solution.

The measurement of analytical signal was carried out in the mentioned manner. Results are presented in the Table.1.

Table.1.

Determination of Bi (III) (n =3, tα =4,30, α = 0,95).

| Sample	m of sample, g	m Bi in sample, g	Calculated, μg/ml	Observed, μg/ml	$\bar{X}$	S_r	$\bar{X}\pm\Delta X$
TlBiSe$_2$	0.10260	0.03753	37.53	36.9 36.7 35.7	36.43	0.018	36.43±2.76
"Vicairum"	1.05620	0.15079	30.16	28.7 30.1 27.9	28.9	0.039	28.90±4.79

A spectrophotometer Shimadzu UV-2600 was used spectroscopic measurements. Measurement of the absorbency of the solution was made at 440 nm.

3   Results and Discussion

In our work we decided to combine few donor groups for receiving the new ligand with synergistic effect of atoms. For this purposes we synthesized substituted N,N'-bisthioureas which contain mercapto group for the formation of strong Sulphur-Metal covalent bond, carbonyl and amino group for the additional coordinate bonds and formation of stable complexes.

The starting ligands N-{[2-(R-carbamothioyl)hydrazino]carbonothioyl}benzamide **L**[1,2] (Scheme 1) was obtained from N-R-thiosemicarbazide and benzoyl isothiocyanate. We determined physical and chemical characteristics of synthesized organic ligands (stability, solubility, IR spectroscopy spectra, UV spectroscopy spectra, NMR spectra, etc.). It was noted that obtained bisthioureas **L**[1,2] are not stable upon heating – the reaction of hydrogen sulphide elimination was occurred with formation of corresponding triazoles **T**[1,2] which are not an object of this study.

Scheme 1.

R = CH$_3$ (**L^1**), CH$_2$=CHCH$_2$ (**L^2**)   **L^{1,2}**   undesirable **T^{1,2}**
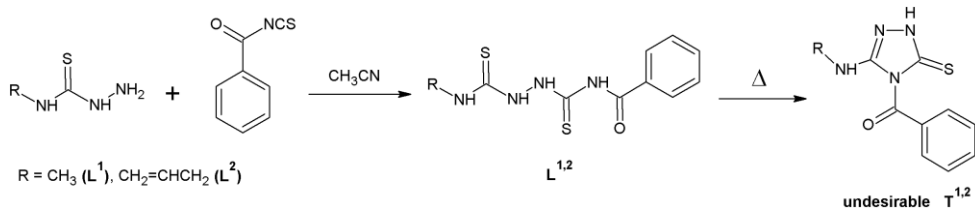
We investigated the reaction conditions of Bi^{3+} ions with N-({2-[(R-amino)carbonothioyl]hydrazino} carbonothioyl) benzamides **L^{1,2}** in water solution (Scheme 2). It must be noted that yellow complex is formed in this reaction, but we were unable to separate this complex in necessary minimal quantity for identification. In the case of using highly concentrated solutions black Bismuth Sulphide was precipitated and Bi-**L^{1,2}** formation was not observed.

Therefore, for detailed understanding of the complex formation reaction for **L^{1,2}** compounds was carried out quantum-chemical calculations. The semi-empirical PM6 method was chosen as a method of calculation, because it was developed for a wide range of compounds and atoms, including transition and heavy metals [27]. The calculations were carried out using MOPAC2012 [28, 29]. The Fig. 1 presents hypothetical structure for **Bi-L^1** complex. Selected PM6 semi-empirical method gives satisfactory settlement for bond lengths of Bi-X (where X = N, O, S) [30]. HOMO orbital were calculated to find the reaction centre of ligands molecules: As can be seen form the picture 2 HOMO orbital which is response for the reaction with cations located on the Sulphur atom, so at first Bi-S bond will be formed with the next formation of Bi-N and Bi-O coordination bonds.

Scheme 2.

L^{1,2}   **Bi-L^{1,2}**   **T^{1,2}**
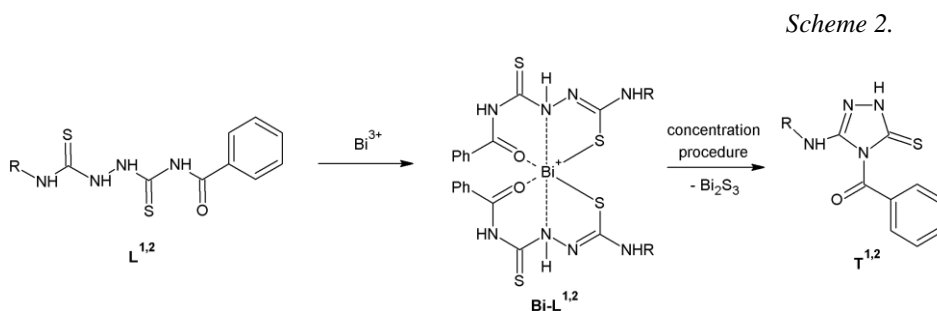
Starting 10^{-3} M solution of Bismuth was prepared with dissolving of precise sample analytical purity metallic Bismuth in nitric acid. Working standard solutions were prepared by double-distilled water dilution. The solutions of ligands were prepared by dissolving of precise sample of bisthiourea (1mmol) in 100ml of solvent (methanol, dioxane, dimethylformamide – DMF), C = 10^{-2} mol/L. For controlling pH we used 1 M buffer solutions – ammonia buffer (NH$_4$OH+NH$_4$Cl) and acetic buffer solution (CH$_3$COONa+CH$_3$COOH).
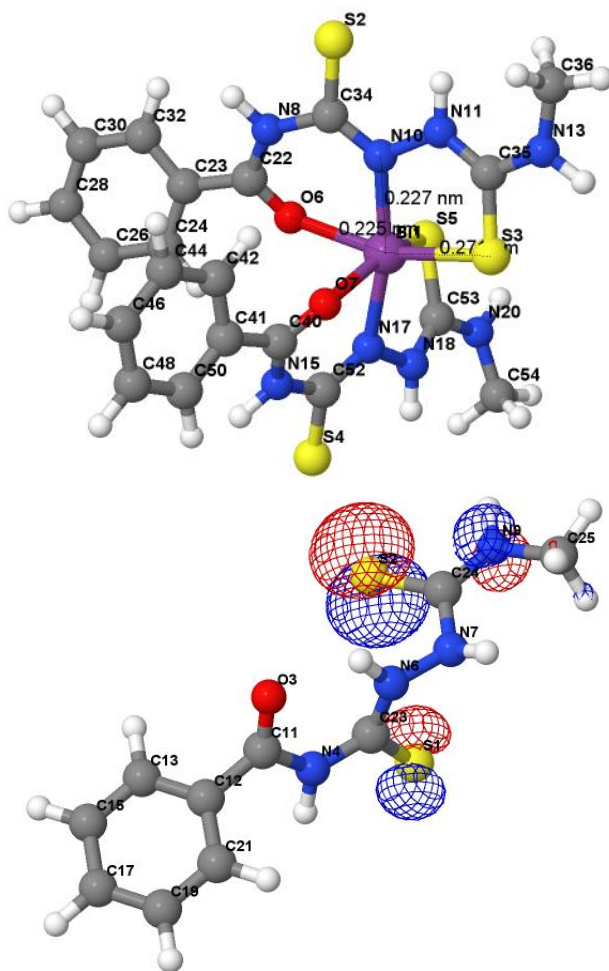
Figure 1

Hypothetical structure for Bi-L^1 complex

pH is an important factor that influence on the formation of complex. So we investigated the conditions with the formation of maximum amount of complex and maximum optical density. It was established that coloured complexes are not produced in acidic conditions with pH<3. In the region of pH=4-8 the clear yellow colour was observed, which can be controlled by spectrophotometer, but with further increasing of pH it was still increasing of optical density but this effect was due to formation of opalescence. In the case of **L^1** - opalescence was observed beginning from pH = 9.5 and higher, but for **L^2** this line was even smaller - precipitation begins from pH = 8.5 (Fig. 2). According to this we used **L^1** in our standard technique of Bi(III) determination.

It was noted that probes with different solutions of ligands have different optical density. In the case of dioxane, and especially DMF the optical density was much lower. Indeed, when we add pure solvent like dixane or DMF instead of water during the preparation of probe there were no any colour formation. Obviously that these solvents act as destructors of complex. In other investigations we used only methanol solution.
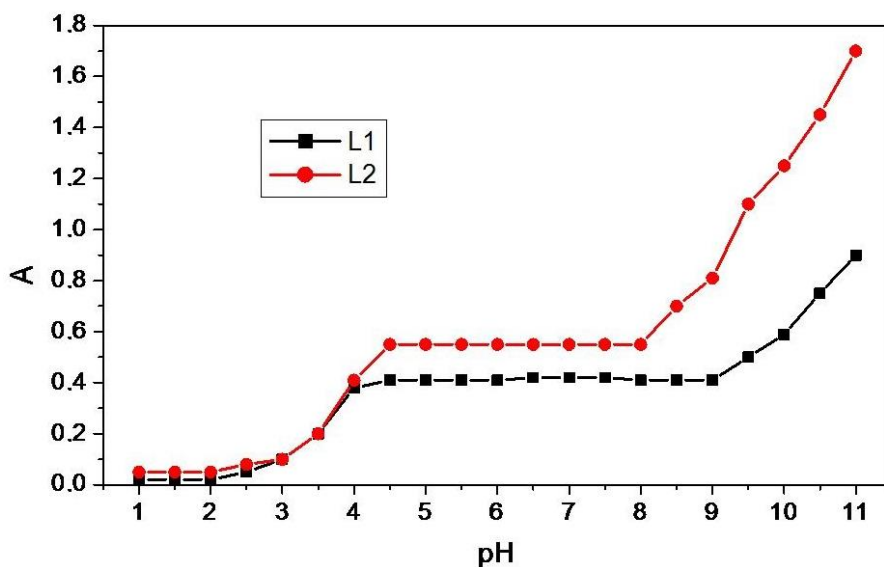

Figure 2

Optimal pH region is 4-8.

Beer–Lambert–Bouguer law is correct in the range of $1.00 \cdot 10^{-6}$-$2.00 \cdot 10^{-3}$ and limit of detection for the proposed method is $2.00 \cdot 10^{-8}$ mol/L (Fig. 3).
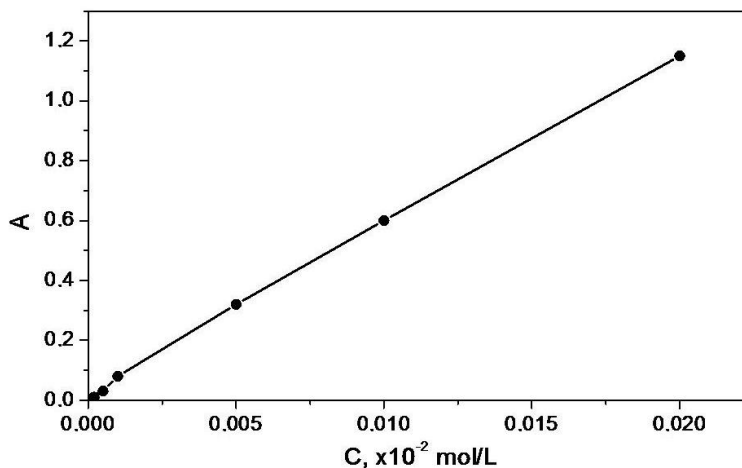
Figure 3

Dependence of optical density with concentration of Bi(III).

The weight of sample taken for analysis should be such that the bismuth content is approximately 1 to 10 mg or if this is a solution with concentration diapason $1.00 \cdot 10^{-6}$-$2.00 \cdot 10^{-3}$ – take 1.00 ml of investigated solution. If the sample is solid or highly concentrated, the procedure [24] need to be applied. A sample of 1 ml is mixed with 1 ml of methanol solution of ligand $\mathbf{L^1}$, 1 ml of buffer solution and 2 ml of bi-distilled water. This mixture was let to stand for 10 min and optical density was measured using as a standard the same mixture except that instead of probe we add 1 ml of water.

4   Conclusion

The formation of the complex compounds of Bi(III) with N-{[2-(R-carbamothioyl) hydrazino] carbonothioyl} benzamide have been analysed by quantum-chemical calculations. The simple, accurate, sensitive and reliable method for the selective determination of Bi(III), which is based on spectrophotometric measurement of water soluble yellow bismuth-ligand complexes have been developed. The linear calibration ranges and limit of detection for the proposed method was $1.00 \cdot 10^{-6}$ - $1.00 \cdot 10^{-3}$ and $2.00 \cdot 10^{-8}$ mol/L, respectively.

6   Acknowledgments

7   References

[1]   Carlin, J.F. Bismuth. In: *U.S. Geological Survey Minerals Yearbook*, US Govement Printing Office, Washington. 2008. pp. 12.1-12.5.
ISBN 978-1-4113-3015-3

[2]   Pamamphlett, R. et al. Tissue uptake of bismuth from shotgun pellets, *Environ Res.*, 2000, **82**: pp. 258-262.

[3]   Völz, H. G. et al. Pigments, Inorganic. IN *Ullmann's Encyclopedia of Industrial Chemistry*. Wiley-VCH Verlag GmbH & Co. KgaA. Weinheim, Germany. 2006.   ISBN: 9783527306732

[4]   Liu, Y. et al. Enhanced photocatalytic degradation of organic pollutants over basic bismuth (III) nitrate/$BiVO_4$ composite. *Journal of Colloid and Interface Science*, 2010, **348**: pp. 211–215.

[5]   Zhang, L., Zhu, Y. A review of controllable synthesis and enhancement of performances of bismuth tungstate visible-light-driven photocatalysts. *Catal. Sci. Technol.*, 2012, **2**: pp. 694-706.

[6]   Larsen, A. et al. Gastrointestinal and systemic uptake of bismuth in mice after oral exposure. *Pharmacol Toxicol*, 2013, **93**: pp. 82-90.

[7]   Mahony, D. et al. Interaction of bismuth subsalicylate with fruit juices, ascorbic acid, and thiolcontaining substrates to produce soluble bismuth products active against Clostridium difficile. *Antimicrob Agents Chemother,* 2005, **49**: 1, pp. 431-433.

[8]   Malfertheiner, P. et al. Helicobacter pylori eradication with a capsule containing bismuth subcitrate potassium, metronidazole, and tetracycline given with omeprazole versus clarithromycin-based triple therapy: a randomised, open-label, non-inferiority, phase 3 trial. *Lancet.*, 2011, **377**: 9769, pp. 905-913.

[9]   Andrews, P.C. et al. Bismuth(III) saccharinate and thiosaccharinate complexes and the effect of ligand substitution on their activity against Helicobacter pylori. *Organometallics*, 2011, **30**: pp. 6283-6291.

[10]   Gisbert, J.P. Helicobacter pylori eradication: a new, single-capsule bismuth-containing quadruple therapy. *Nat Rev Gastroenterol Hepatol*. 2011, **8**: pp. 307-309.

[11]   Rosenblat, T.L. et al. Sequential cytarabine and alphaparticle immunotherapy with bismuth-213-lintuzumab (HuM195) for acute myeloid leukemia. *Clin Cancer Res.* 2010, **16**: pp. 5303-5311.

[12]   Leussink, B.T. et al.Renal epithelial gene expression profile and bismuth-induced resistance against cisplatin nephrotoxicity. *Hum. Exp. Toxicol.* 2003, **22**: pp. 535-540.

[13] Luo, Y. et al. In vitro cytotoxicity of surface modified bismuth nanoparticles. *J. Mater. Sci.: Mater. Med.* 2013, **23**: pp. 2563-2573.

[14] Urgast, D.S. et al. Multi-elemental bio-imaging of rat tissue from a study investigating the bioavailability of bismuth from shotgun pellets. *Anal. Bioanal. Chem.*, 2012, **404**: pp. 89-99.

[15] Ghaffari, M.A., Motlagh, B. In vitro effect of lead, silver, tin, mercury, indium and bismuth on human sperm creatine kinase activity: a presumable mechanism for men infertility. *Iranian Biomedical Journal,* 2011, **15**: pp. 38-43.

[16] Itoh, S.I. et al. Determination of bismuth in environmental samples with Mg-W cell – electrothermal atomic absorption spectrometry. *Anal. Chim. Acta*, 1999, **379**: pp. 169-173.

[17] Agrawal, K. et al. Flow-injection analysis spectrophotometric determination of bismuth in environmental and pharmaceutical samples. *Anal. Lett.* 2004, **37**: pp. 2163-2174.

[18] Nordberg, G.F. et al. Biomarkers of cadmium and arsenic interactions. *Toxicol. Appl. Pharmacol*. 2005, **206**: pp. 191-197.

[19] Chattopadhyay, P.; Nathan, S. Determination of bismuth in geological materials by flame atomic absorption spectrometry using a selective extraction technique. *Analyst*, 1991, **116**: 11, pp. 1145-1147.

[20] Şahan, S. et al. An on-line preconcentration/separation system for the determination of bismuth in environmental samples by FAAS. *Talanta*, 2010, **80**: pp. 2127-2131.

[21] Rahman, L. et al. Determination of mercury, selenium, bismuth, arsenic and antimony in human hair by microwave digestion atomic fluorescence spectrometry. *Talanta*, 2000, **52**: pp. 833-843.

[22] Pavlíčková, J. et al. Comparison of aqua regia and HNO_3-H_2O_2 procedures for extraction of Tl and some other elements from soils. *Anal. Bioanal. Chem.*, 2003, **376**: pp. 118-125.

[23] Ostapczuk, P. Present potentials and limitations in the determination of trace elements by potentiometric stripping analysis. *Anal. Chim. Acta*, 1993, **273**: pp. 35-40.

[24] Bendigo, B. B. et al. Spectrophotometric determination of bismuth in lead-base and tin-base alloys. *Journal of Research of the National Bureau of Standards*, 1951, **47**: 4, pp. 252-255.

[25] Satake, M.; Yamauchi, T. Solid-Liquid Separation after Liquid-Liquid Extraction. Spectrophotometric determination of bismuth after extraction of its 2-mercaptobenzothiazole complex with molten naphthalene. *Departmental Bulletin Paper, University of Fukui Repository*, 1977, **25:** 2, pp. 107-112. http://hdl.handle.net/10098/4496

[26] Shakerian, F. et al. Hydride generation atomic absorption spectrometric determination of bismuth after separation and preconcentration with modified alumina. *Journal of Separation Science*, 2014, **38**: pp. 677-682.

[27] Stewart, J.J.P. Optimization of parameters for semiempirical methods V: Modification of NDDO approximations and application to 70 elements. *J Mol Model.*, 2007, **13**: 12, pp. 1173-1213.

[28] Stewart, J.J.P. MOPAC2012. *Stewart Computational Chemistry*, http://openmopac.net

[29] Maia, J.D.C. GPU linear algebra libraries and GPGPU programming for accelerating MOPAC semiempirical quantum chemistry calculations. *Journal of Chemical Theory and Computation*. 2012, **8**: 9, pp. 3072-3081.

[30] Suzuki, H.; Matano, Y. *Organobismuth Chemistry,* Elsevier, ISBN 0-444-20528-4, Amsterdam, The Netherlands. 2001, 636 pp.

[31] Jmol: an open-source Java viewer for chemical structures in 3D. http://www.jmol.org/

[32] Allouche, A.R. Gabedit - A graphical user interface for computational chemistry softwares. *Journal of Computational Chemistry*, 2011, **32**: pp. 174-182.