

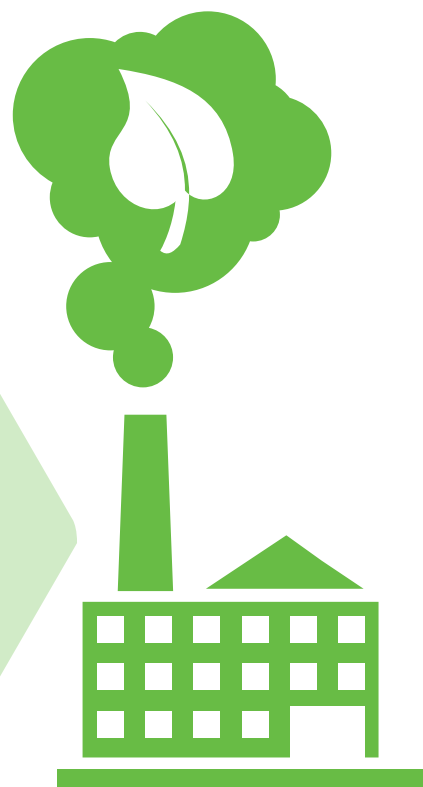
PROCEEDINGS OF

**THE INTERNATIONAL SYMPOSIUM
ON ANALYTICAL AND ENVIRONMENTAL
PROBLEMS, WITH SPECIAL EMPHASIS
ON HEAVY METAL IONS AS CONTAMINANTS**

24 September 2012

Edited by
Zoltán Galbács

18.



**SZAB
SZEDED, HUNGARY**



Hungary-Romania
Cross-Border Co-operation
Programme 2007-2013

European Union
European Regional Development Fund



Two countries, one goal, joint success!

INTERACTION OF As(III) WITH THIOLATE-CONTAINING MOLECULES

Béla Gyurcsik, Attila Jancsó, Levente Szekeres

University of Szeged, Department of Inorganic and Analytical Chemistry, H-6720 Szeged,
Dóm tér 7, Hungary;
e-mail: GYURCSIK@CHEM.U-SZEGED.HU

ABSTRACT

The aqueous solutions of arsenous acid with thiolate containing organic ligands such as the meso and racemic forms of 1,4-dithiol-butane-2,3-diol, (dithioerythritol – dte and dithiothreitol - dtt) as well as 2,3-dimercaptopropanol (called also British anti-Lewisite (BAL) or Dimercaprol) were investigated. pH-mertric titrations were performed in solutions with different molar ratios of As(III) and the ligands. The pK_a values for $As(OH)_3$, and the ligands determined from these data were in good agreement with the literature data. In all investigated systems containing both $As(OH)_3$ and one of the ligands, the deprotonation steps appeared at a higher pH in the titration curves, than in those of the individual components. This unusual observation was explained by the condensation reactions between the reagents taking place in the $pH < 8$ range. In some of these systems the pH-metry was combined with NMR and UV spectroscopic measurements. We observed the complexes with 1:1 As(III):ligand composition as being the major species in aqueous solutions. In the case of As(III)-dte system we could crystallize the complex of 1:1 composition from ethanolic solution.

INTRODUCTION

Study of the chemistry of arsenic is important because of its well-known toxic effect. The limit of the arsenic concentration in drinking water is 10 $\mu\text{g/L}$ according to the EU-regulations. Still more than 1.5 million people in Hungary (>50 millions world-wide) have to drink water containing arsenic in concentrations above this limit. [1–3] As(III) is 25–60 times more toxic than As(V) [4], but the removal of arsenic from drinking water is possible only for As(V) by ion-exchange or precipitation methods in form of $AlAsO_4$ or $FeAsO_4$. Although new sophisticated methods are being developed, so far there is no efficient, selective, and economic way to eliminate As(III) from drinking water. Since in neutral aqueous solution As(III) is present as $As(OH)_3$, we tried to find ligands that form stable complexes with this form. Recent investigations showed that As(III) has high affinity towards thiolate-containing molecules. Among the sulfur-containing molecules interacting with As(III), glutathione, as one of the most important examples in the living cell, has been studied. Scott et al. isolated the tris(glutathionate)-As(III) complex and characterized it by mass spectrometry. [5] The recent equilibrium study of the complex formation of As(III) with cysteine (H_2cys) and glutathione [6] showed the formation of $[As(Hcys)_3]$ and $[As(Hgs)_3]^{3-}$ complexes. The ligands bound As(III) via their sulfur atoms forming thioester bonds.

Thus, the biological effect of arsenic may be assigned to its binding potential to the thiolate-containing functional groups of biomolecules. The better knowledge of these interactions may lead us to understanding the biological effects and new therapies based on arsenic chelation. Dithiothreitol (dtt) has been shown in biological experiments to enhance arsenic trioxide-induced apoptosis in several different leukemia cell lines, a promise of an effective drug for

leukemia. [7] At the same time BAL was recommended for treatment of arsenic, gold, mercury, and lead poisoning. [8]

There are no systematic data on the solution chemistry of arsenic(III) with thiolate-containing ligands in the literature. In this work we compared the interactions between arsenous acid and the meso and racemic forms of 1,4-dithiol-butane-2,3-diol, (dithioerythritol – dte and dithiothreitol – dtt, respectively) as well as 2,3-dimercaptopropanol (BAL) in aqueous solutions studied by pH-metric, UV, NMR spectroscopic and X-ray crystallographic methods.

MATERIALS AND METHODS

Measurements were performed using dithioerythritol (dte) from Fluka and dithiothreitol (dtt) and 2,3-dimercaptopropanol (BAL) from Sigma-Aldrich. Two kinds of As(III) solution were used: anhydrous As_2O_3 (Merck) was dissolved in 0.1 M sodium hydroxide solution (Sigma-Aldrich) and a commercial sodium arsenite solution (Sigma-Aldrich). NaOH stock solution (Sigma-Aldrich) was standardized against potassium hydrogen phthalate. The concentration of the As(III) solution was determined pH-metrically by simultaneous refinement of the pK_a and the concentration of the arsenous acid from at least three parallel titrations. The detailed description of the crystallization of the As(III) $\text{H}_3\text{dte}^{3-}$ coordination compound, and the conditions of the spectroscopic measurements were described elsewhere. [9]

RESULTS

pH-metric titrations were performed in the aqueous solutions of both the binary systems for determining the pK_a values of the individual components and the ternary systems to follow the eventual reaction occurring between them. All calculated pK_a values were in good agreement with the previously published ones in the literature. The titrations of the ternary systems were conducted in the systems with various As(III):Lig molar ratios. A characteristic example of As(III):BAL = 1:1 system is shown on Figure 1. In all cases the simulated curve for a reaction mixture without any reaction assumed displayed lower pH than the experimental curve, suggesting that instead of the consumption of OH^- -ions, rather the liberation of these ions was observed.

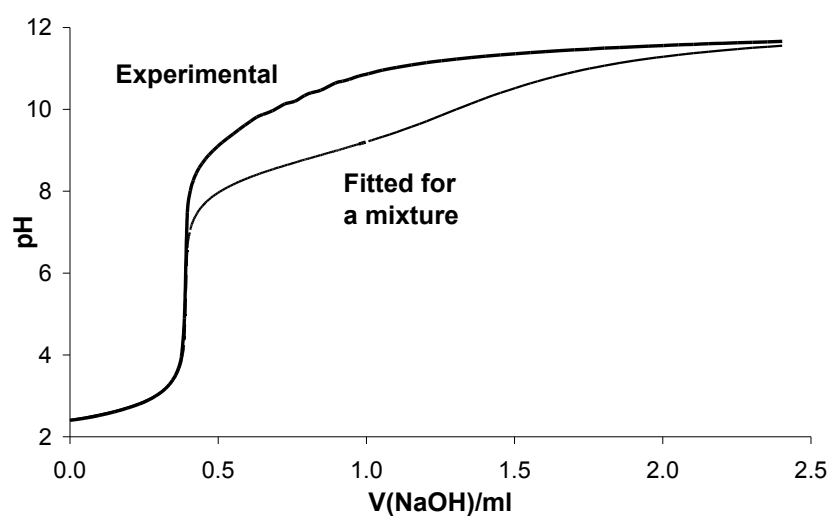


Figure 1. The comparison of the experimental pH-metric titration curve of the As(III):BAL = 1:1 system with that simulated for the same system assuming that no reaction takes place in the mixture.

This phenomenon is unusual in the systems where the competition between protons and metal ions may occur. Therefore, we proposed that condensation reactions occur between the thiol groups of the organic ligands and the hydroxyl groups of the arsenous acid. This reaction should take place at lower pH than the pK_a of the organic ligand, and it is not directly detectable by pH-metry. As a consequence of such a reaction the deprotonation of the thiol groups can not be observed on the titration curve.

To prove that the condensation reaction takes place 1H NMR measurement were performed in the systems. Figure 2. shows the recorded spectra at pH = 6.0 for the dte and As(III):dte 1:2 system.

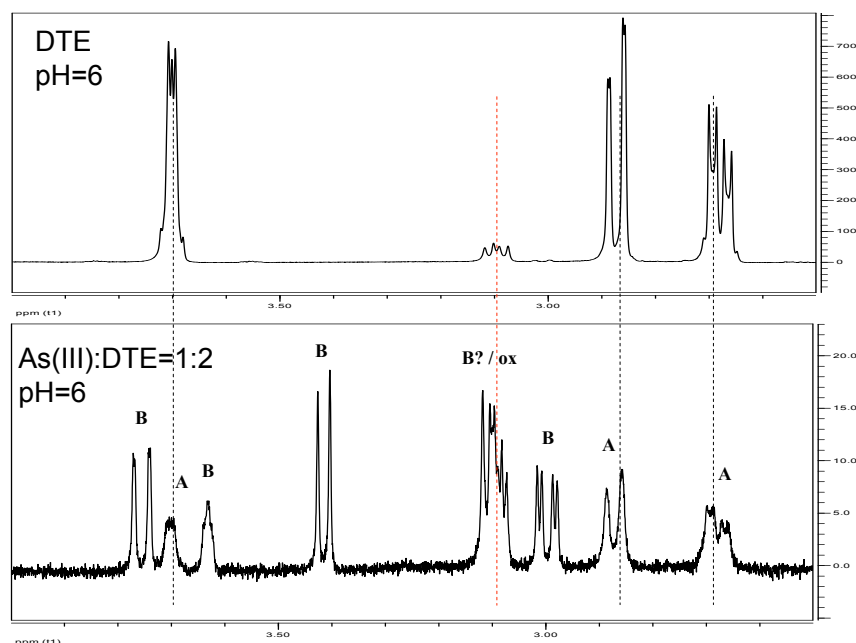
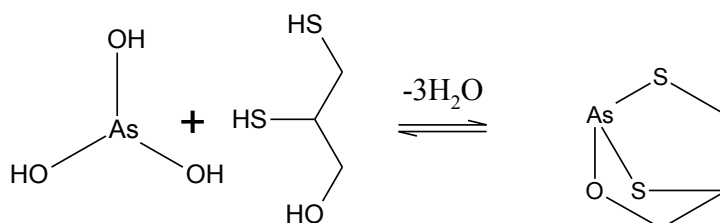


Figure 2. 1H NMR spectra of the dte solutions at pH value of 6.0, and that of the As(III):dte 1:2 system at pH 6.0. [9]

It can be observed, that the signals were multiplied in the presence of As(III). This suggests that there is a slow exchange between the free and bound dte, and also that the symmetry of the free ligand is broken by the adduct formation. This means that not only the thiol, but one of the ligand hydroxy groups also participates in the condensation, reacting with the third hydroxyl group of the $As(OH)_3$. Similar reaction was observed with BAL, as well, at low pH (Scheme 1.)



Scheme 1. The schematic representation of the condensation reaction between $As(OH)_3$ and BAL.

The product of the condensation reaction was crystallized from ethanolic solution in case of dte, and the structure has been proved by X-ray crystallography.

CONCLUSIONS

Our studies proved that $\text{As}(\text{OH})_3$ forms stable adducts with thiol and hydroxy groups of organic ligands possessing both types of functional groups. This reaction can be considered as to be quantitative in aqueous solutions at $\text{pH} \sim 7.0$. Thus it could be applied for the capture of As(III) from drinking water. Although thiolates are easily oxidized or bound strongly to heavy metal ions, their use in biotechnological water purification could be a promising perspective.

LIST OF REFERENCES

- [1] Smith, A. H., Lopipero, P. A., Bates, M. N. and Steinmaus, C. M. (2002) Public health. Arsenic epidemiology and drinking water standards, *Science* 296, 2145-2146.
- [2] Hungarian regulation of the quality of the drinking water - 201/2001. (X. 25.) Korm. Rendelet az ivóvíz minőségi követelményeiről és az ellenőrzés rendjéről
- [3] Lubin, J. H., Beane Freeman, L. E. and Cantor, K. P. (2007) Inorganic arsenic in drinking water: an evolving public health concern, *J. Natl. Cancer Inst.* 99, 906-907.
- [4] Fazal, M. A., Kawachi, T. and Ichion, E. (2001) Extent and Severity of Groundwater Arsenic Contamination in Bangladesh, *Water Int.* 26, 370-379.
- [5] Scott, N., Hatlelid, K. M., MacKenzie, N. E. and Carter, D. E. (1993) Reactions of arsenic(III) and arsenic(V) species with glutathione, *Chem. Res. Toxicol.* 6, 102-106.
- [6] Rey, N. A., Howarth, O. W. and Pereira-Maia, E. C. (2004) Equilibrium characterization of the As(III)-cysteine and the As(III)-glutathione systems in aqueous solution, *J. Inorg. Biochem.* 98, 1151-1159.
- [7] Gurr, J-R., Bau, D-T., Liu, F., Lynn, Sh. and Jan, K.-Y. (1999) Dithiothreitol enhances arsenic trioxide-induced apoptosis in NB4 cells, *Mol. Pharm.* 56, 102-109.
- [8] Klassen C.D. (2002) Heavy metals and heavy metal antagonists. In: Hardman J, Limbird LE, eds. Goodman and Gilman's The Pharmacological Basis of Therapeutics. New York, NY: McGraw-Hill, 851-1875.
- [9] Kolozsi A., Lakatos A., Galbács G., Madsen A.Ø., Larsen E. and Gyurcsik B. (2008) A pH-metric, UV, NMR, and X-ray crystallographic study on arsenous acid reacting with dithioerythritol, *Inorg. Chem.* 47, 3832-3840.

ACKNOWLEDGMENTS

HURO/1001/232/2.2.2 – METCAP, TÁMOP-4.2.1./B-09/1, TÁMOP-4.2.2/B-10/1-2010-0012, János Bolyai Research Grant from the Hungarian Academy of Sciences.