



Dihydrophenarsazine-based Arsenic-Thio Ethers – Preparation and Stabilization

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ABSTRACT

10-chloro-5,10-dihydrophenarsazine ('adamsite') was used as starting materials to prepare arsenic-thio ethers: 10-benzothiazolylsulphyde-5,10-dihydrophenarsazine and 10-phenylsulphyde-5,10-dihydrophenarsazine. The arsenic organic compounds were synthesized using potassium hydroxide and analyzed by various spectrometric instrumentations. The high toxic and high reactive 10-chloro-5,10-dihydrophenarsazine was converted into stable and low toxic compounds, which will be used as ligands for preparation of metal complexes and biological activity of new compounds will be studied.

INTRODUCTION

Despite the high toxicity of arsenic inorganic and organic compounds, arsenic has long history of medical applications for treating many diseases such as malignancies, leukemia's and other types of cancer [1,2]. Arsenic has high affinity toward sulfur and sulfur-containing compounds are used for binding to arsenic [3]. Arsenic organic compound p-glycineamidophenylarsonate Tryparsamide) was considered as a clinically effective for sleeping sickness [4], another compound – melarsoprol was used to treat trypanosomiasis [4,5]. On the other hand, Lewisite (β -chlorovinyl-dichloroarsine) and Adamsite (10-chloro-5, 10 dihydrophenarsazine) were used as chemical warfare agents. Adamsite is volatile, very reactive and high toxic compound. Therefore, its conversion into relatively non-

toxic substances have been subject of interest [6] and for applications as antimicrobial agents [7,8]. Our interest was concerned to the stabilization of reactive arsenic-chlorine center by arsenic- sulfur bond formation and attachment of phenyl and 2 mercaptobenzothiazole. The new compounds showed low toxicity, but as they contain many different atoms (arsenic, sulfur, nitrogen), would be showed antimicrobial activity and they serve as good complex-forming ligands for preparation of metal coordination compounds. The 10-chloro-5,10-dihydrophenarsazine thioethers were obtained in the two way: in neutral environment using BuLi, but because they are stable in the air and are not sensitive toward moisture, we prepared these compounds also with potassium hydroxide; the second way was easier and faster (Figure 1).

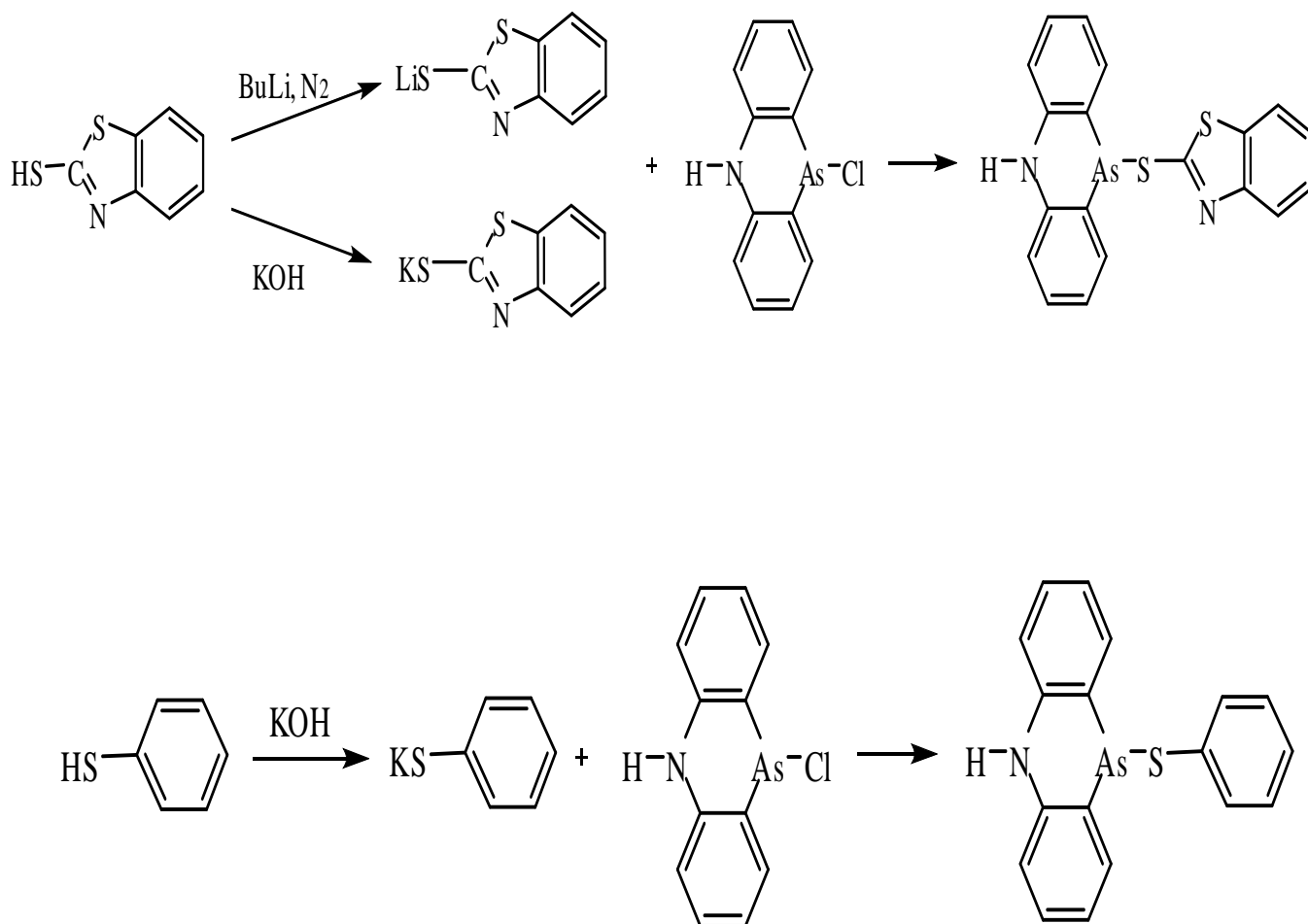


Figure 1: Preparation of 5-Chloro-5,10- Dihydrophenarsazine thio-ethers.

*10-benzothiazolylsulphyde-5,10 dihydrophenarsazine
(compound 1)*

2.0 g of 2-mercaptobenzothiazole in 16 mL of THF was placed in 3-neck flask and 8.3 mL of BuLi (1.6 M in hexane) was added by dropwise under N₂. The reaction was carried out at 0°C. After adding of BuLi, the reaction mixture was stirred for 2 hours at room temperature. The orange precipitate was formed during lithiation of 2-mercaptobenzothiazole. 3.3 g of 5-Chloro-5,10-

Dihydrophenarsazine dissolved in 20 mL of THF was then added dropwise under ice. The color the reaction mixture was changed from orange to dark red and white precipitate was formed. The mixture was kept at room temperature overnight under stirring and was filtrated under nitrogen. The white solid was removed by filtration and solvents were evaporated from filtrate. The product several times was recrystallized in acetone and/or acetonitrile to give yellow crystals. Yield: 69.3%, MS SEI m/z 408 (M⁺) (Figure 2); FT-IR, cm⁻¹: 3340-3400 (νHN), 470 (νAs-C_{ar}), 635 (νAs-C_{alk}); UV-vis, nm: 323 (Figure 3).

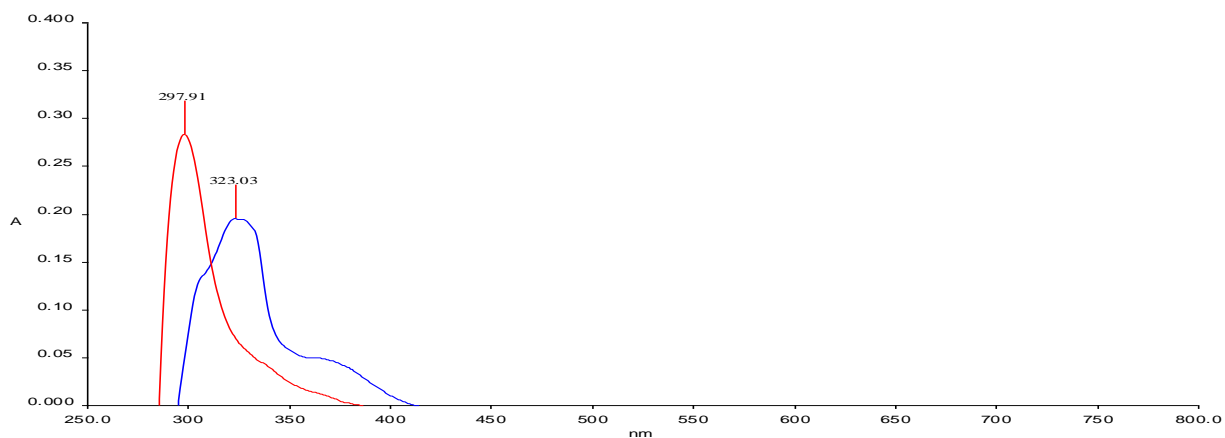


Figure 2: UV-vis spectra of compound 1 (blue) and compound 2 (red).

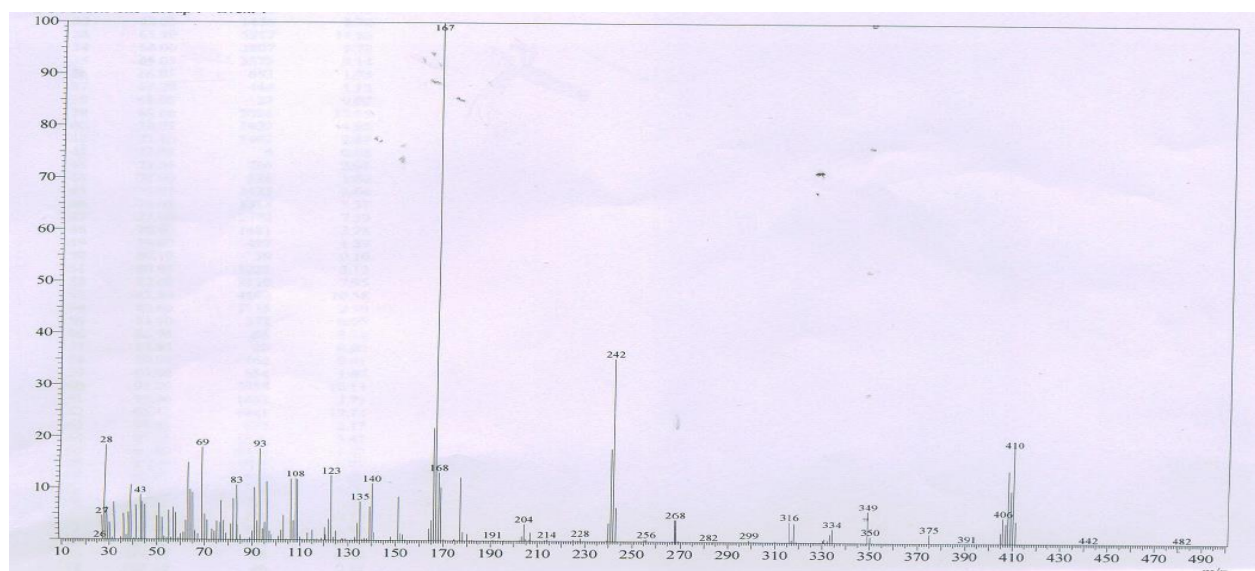
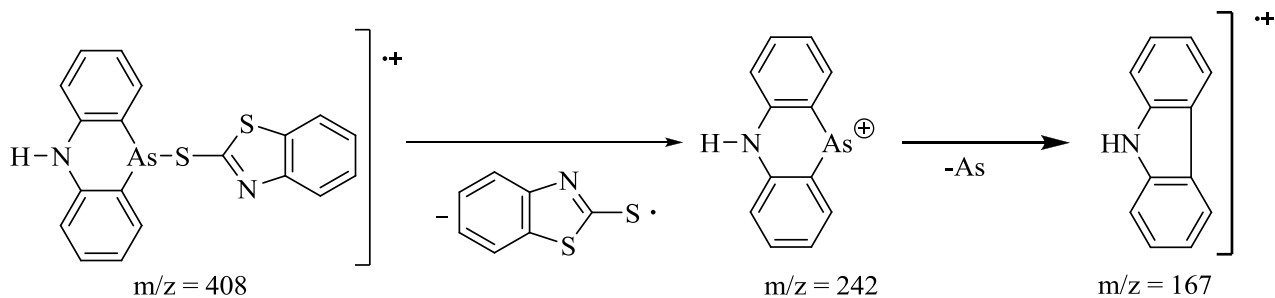


Figure 3: MS-spectrum of compound 1.

10-phenylsulphyde5,10-dihydrophenarsazine (compound 2) was synthesized in the same way. The product several times was recrystallized in acetone and/or acetonitrile to give yellowish-green crystals. Yield: 61.4%, MS SEI m/z

351 (M^+); FT-IR, cm^{-1} : 3340-3400 (ν_{HN}), 478 (ν_{As-Car}), 630 ($\nu_{As-Calk}$); UV-vis, nm : 298. NMR spectra are given in Figures 4-6.



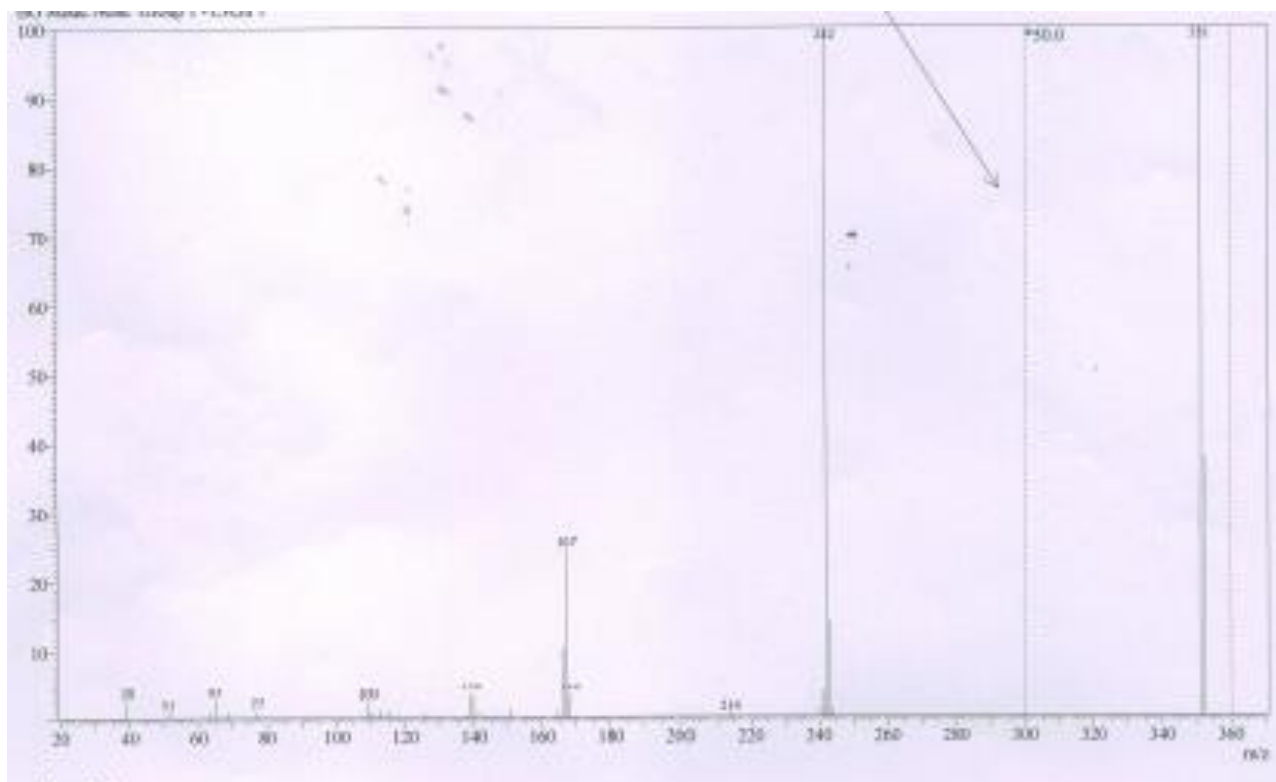
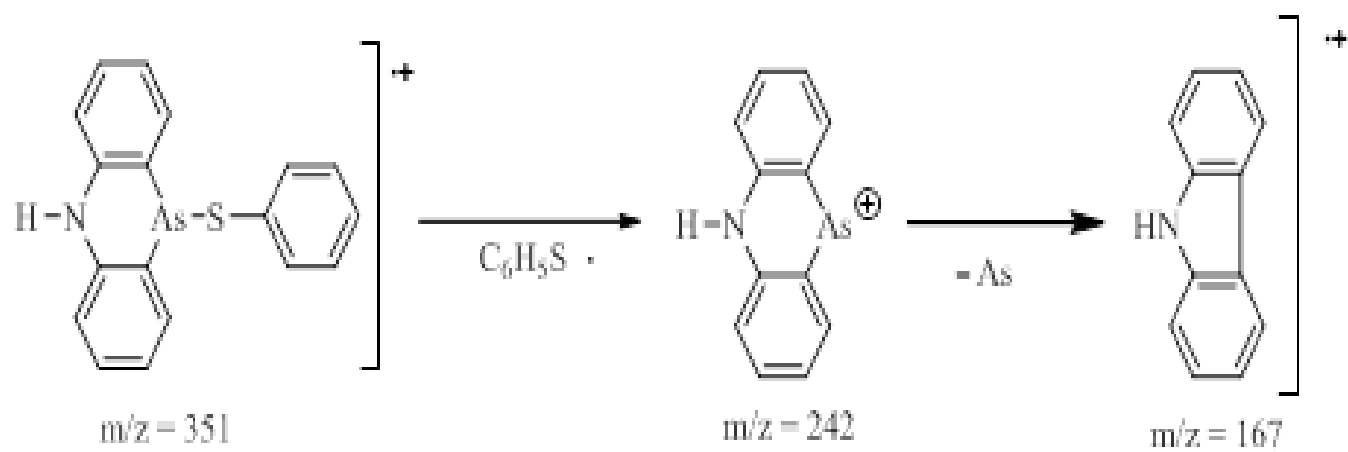


Figure 4: MS-spectrum of compound 2.



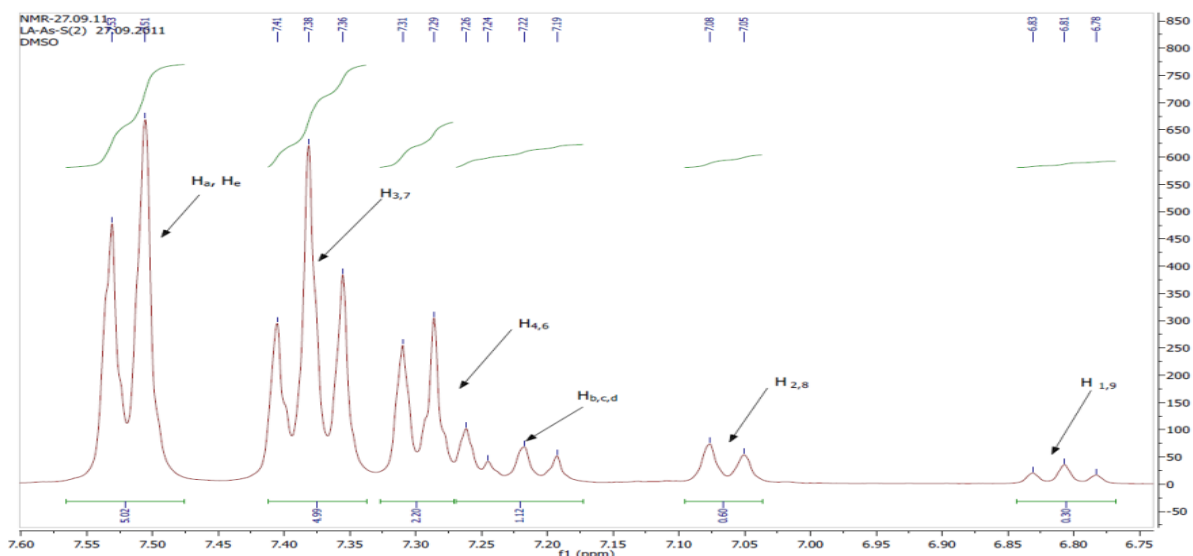


Figure 5: $^1\text{H-NMR}$ of $\text{HN}(\text{C}_6\text{H}_4)_2\text{AsS}(\text{C}_6\text{H}_5)$ in DMSO-d_6 .

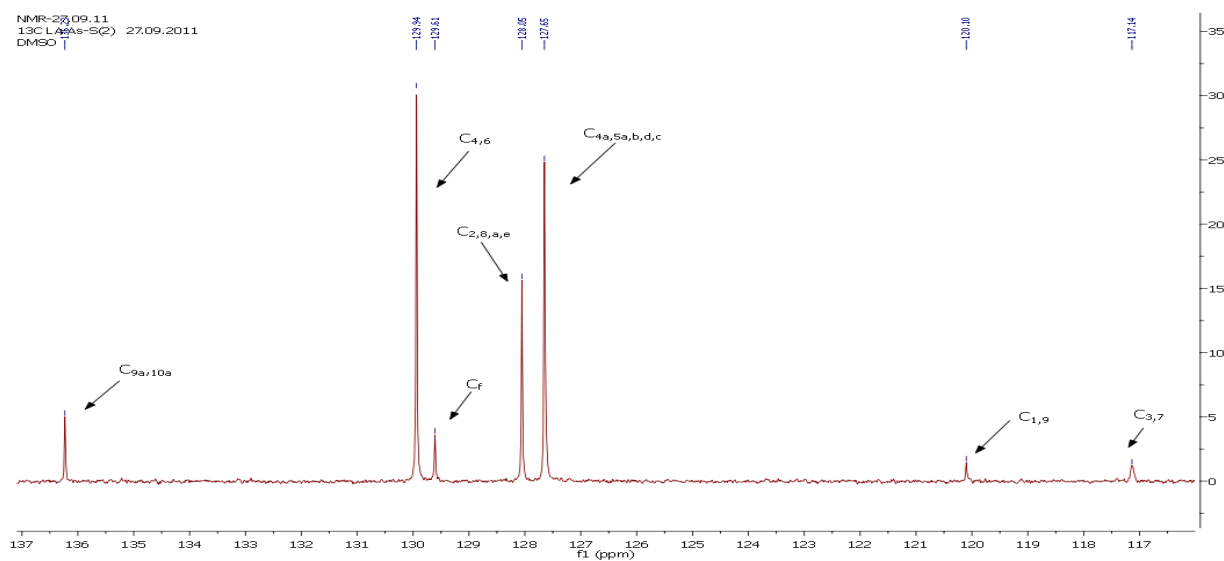


Figure 6: $^{13}\text{C-NMR}$ of $\text{HN}(\text{C}_6\text{H}_4)_2\text{AsS}(\text{C}_6\text{H}_5)$ in DMSO-d_6 .

CONCLUSION

10-chloro-5,10-dihydrophenarsazine ('adamsite') was used as starting materials to prepare arsenic-thio ethers: 10-benzothiazolylsulphyde-5,10 dihydrophenarsazine and 10-phenylsul-phide-5,10-dihydrophenarsazine.

The arsenic organic compounds were synthesized using potassium hydroxide and analyzed by various spectrometric

instrumentations. The high toxic and high reactive 10-chloro-5,10-dihydrophenarsazine was converted into stable and low toxic compounds, which will be used as ligands for preparation of metal complexes and biological activity of new compounds will be studied.

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