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ANTONIO DE ULLOA, DISCOVERER OF PLATINUM

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ABSTRACT

Don Antonio de Ulloa, member of a distinguished Spanish family, was born in 1716 and died in 1795. He studied physics and mathematics and was a member of many scientific societies, including the Academy of Sciences of Paris and the Royal Society of London. He travelled widely in Europe and the Americas and occupied many important positions, including those of Frigate Captain, Commander of the Royal Squadron of the Spanish Armada, Governor of Huancavélica - Peru, Louisiana and Florida. In 1735, while member of a scientific expedition sent by the Spanish and French governments to South America to measure a degree of meridian in Quito, close to the equator, he discovered platinum in the mines of Lavadero or wash gold in the district of Chocó.

RESUMO

Don Antonio de Ulloa, membro de uma ilustre família espanhola, nasceu em 1716 e morreu em 1795. Ele estudou física e matemática e foi sócio de muitas entidades científicas, incluindo a Academia de Ciências de Paris e a Royal Society de Londres. Viajou extensivamente na Europa e nas Américas e ocupou muitos cargos importantes, entre eles, Capitão de Fragata, Comandante da Esquadra da Real Armada Espanhola, Governador de Huancavélica - Peru, da Louisiana e da Flórida. Em 1735, quando fazia parte de uma expedição científica enviada pelos governos da Espanha e da França à América do Sul para medir um arco de meridiano em Quito, perto do ecuador, descobriu a platina nas minas de Lavadero no Partido de Chocó.

KEYWORDS History of Chemistry, Platinum, Discovery of the Elements.

Contrarily to what is generally believed, many scientists that were born or lived in Latin America, made significant contributions to chemistry. Among them are Antonio de Ulloa (1716-1795), who was the first to take platinum to Europe and make this metal known in the Old World; Fausto and Juan José Delhuyar, discoverers of tungsten; Andrés Manuel Del Rio, discoverer of vanadium; José Luis Casaseca, founder of the Cuban Institute of Chemical Research; Alvaro Reynoso, father of modern sugar technology and Luis Frederico Leloir, Nobel laureate in chemistry. Notable contributions were also made by Horacio Damianovich in noble gas chemistry, Gustavo Fester and Xorge Alejandro Dominguez in natural products and Ernesto Giesbrecht in the chemistry of lanthanides.[1-10] More recently, in 1995, the Mexican chemist Mario Molina was awarded the Nobel Prize in Chemistry together with Paul Crutzen and F. Sherwood Rowland for their work dealing with the ozone layer.

Antonio De Ulloa, member of an illustrious Spanish family, was born in Seville in 1716 and died on the Island of León near Cadiz on July 5, 1795. He received a very good formal education and turned out a brilliant young physicist and mathematician. His first long travel was at the age of thirteen, when he participated in an expedition to Cartagena de Indias (Carthagena, Colombia). Upon his return to Cadiz in 1732, after passing successfully a series of examinations, he enlisted as a naval guard.

In 1735 the Academy of Sciences of Paris nominated two scientific commissions to perform measurements of degrees of meridians. The first one, that travelled to Lapland and was to make measurements near the North Pole was headed by Louis Moreau de Maupertuis (1698-1759) and the Swedish scientist Anders Celsius (1701-1744). The second one, formed by Charles Marie La Condamine (1701-1774), Louis Godin (1704-1760) and Pierre Bouguer (1698-1758) was sent to Peru and Ecuador to measure a degree of meridian near Quito, close to the equator.[11-17]

Louis XV solicited an authorization from Philip V, King of Spain, who not anly gave approval and support, but also appointed two young officers (Frigate Lieutenants) of the Spanish Armada to accompany the French Commission, assist with the observations and measurements and help obtain new scientific knowledge about the shape and the dimensions of earth.[14-17]

The two young naval officers were Jorge Juan Santacilia (1713-1773) and Juan Antonio De Ulloa. The two left Spain in May 1735 and arrived in Cartagena on July 1, where they met the French scientists. They travelled together to Portobelo, Guayaquil and Quito and collaborated doing various types of astronomical measurements and observations. Ulloa worked mainly with La Condamine and Bouguer. Soon afterwards, in May 1736, the two young Spanish officers received secret military assignments and classified scientific tasks from the Viceroy of Peru that they performed for about eight years, when they

returned to Quito and engaged in astronomical observations at the Pueblo Viejo de Mira Observatory. Part fo the discoveries and observations made during the nine years of exploration have been described in the monumental work published by the two of them in Madrid in 1748. This work also includes the first description of platinum given below.[14]

"En el Partido del Chocó, habiendo muchas minas de *Lavadero,* como las que se acaban de explicar, se encuentran también algunas, en donde por estar disfrazado, y envuelto el *Oro,* con otros cuerpos metálicos, Jugos y Piedras, necesita para su beneficio el auxilio del *Azogue;* y tal vez se hallan minerales, donde la *Platina* (Piedra de tanta resistencia, que no es fácil romperla, ni desmenuzarla con la fuerza del golpe sobre *Yunque de Acero*), es causa de que se abandonen; porque ni la calcinación la vence, ni hay arbitrio para extraer el *Metal* que encierra, sino a expensas de mucho trabajo y costo" **.

** ***Relación Histórica del Viaje a la América Meridional hecho de orden de S. Mag. para medir algunos grados del meridiano terrestre y venir por ellos en conocimiento de la verdadera figura y magnitud de la Tierra, con otras observaciones astronómicas y físicas:*** Por Don Jorge Juan, Comendador de Aliaga en el Orden de San Juan, socio correspondiente de la Real Academia de Ciencias de París y Don Juan Antonio de Ulloa, de la Real Sociedad de Londres: Ambos capitanes de Fragata de la Armada. Impresa de orden del Rey Nuestro Señor en Madrid por Antonio Marín. Año de MDCCXLVIII - Primera Parte Tomo II. p. 606.

ANTONIO DE ULLOA (1716-1796)

SPANISH PHYSICIST, MATHEMATICIAN, NAVAL COMMANDER, DISCOVERER OF PLATINUM, GOVERNOR OF LOUISIANA AND FLORIDA, EXPLORER OF THE AMERICAS.

Mary Elvira Weeks in her book "*Discovery of the Elements*"[18] states the following:

> In the preface to his "Astronomical and Physical Observations," Jorge Juan said that Ulloa regarded platinum as a peculiar metal and anticipated that there must be special mines of it just as there are of gold and silver."
>
> De Ulloa described it as follows: "In the district of Chocò are many mines of Lavadero, or wash gold . . . several of the mines have been abandoned on account of the platina; a substance of such resistance that, when struck on an anvil of steel, it is not easy to be separated; nor is it calcinable; so that the metal, inclosed within this obdurate body, could not be extracted without infinite labour and charge . . . "

Apparently, the discovery of platinum in the district of Chocō on the Pacific Coast of present day Colombia occurred in 1735, during the initial part of the expedition from Cartagena to Quito and both scientists were very much aware of its importance.[11]

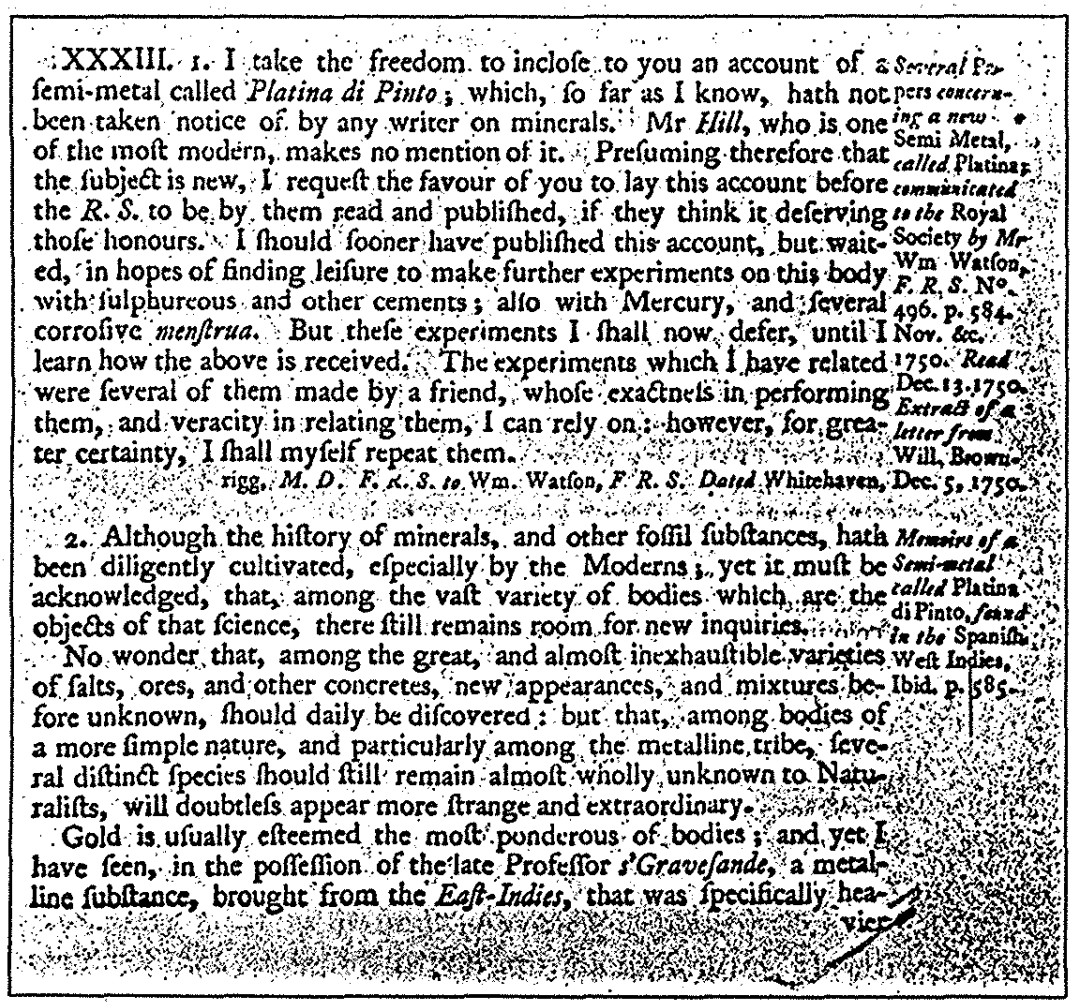
In May of 1745, after completing the military and scientific missions, the two officers made arrangements to return to Spain. In order to avoid the risk of loosing the results of the scientific work, they embarked separately and Jorge Juan arrived safely in Europe. On the other hand, Antonio De Ulloa travelled on the French frigate *Dēlivrance* that was captured by the British. Some of the more compromising documents in De Ulloa's possession were thrown in the sea; the rest were confiscated by the British and he was made prisoner. He only returned to Madrid on July 25, 1746. Apparently, he was treated well and was presented to Martin Folkes, president of the Royal Society. When he petitioned the Admiralty for the return of his papers, the Duke of Bedford affirmed that war between nations should not hinder the progress of science and he was allowed to travel to London and receive back his documents.[11,18]

After his return to Spain, De Ulloa did not devote much effort to platinum. The studies were continued by Fausto Delhuyar (1755-1833) and Pierre Francois Chabaneau (1754-1842) and gave Spain a practical monopoly of this metal for many years.[11-13]

Besides the British, many other scientists became interested in platinum. They included Scheffer, Bergman, Berzelius, Baumē, Buffon, Lavoisier, Macquer, Marggraf and others.

Antonio De Ulloa devoted his time to other activities. He travelled widely in Europe on scientific missions. For example, in 1755, he visited Sweden and was elected member of the Swedish Academy. He reorganized the teaching of medicine in Spain, established the textile industry, improved the arsenals and the mining of mercury. In 1758 he was named Governor of Huancavēlica, Peru and superintendent of the mercury mines. In 1765 he was named Governor of Louisiana, in 1766 Governor of Florida and in 1772 Commander of the Spanish Fleet.[19-21]

In 1750, Brownrigg sent a sample of a mineral containing *"Platina di Pinto"* to Sir William Watson of the Royal Society. Brownrigg had obtained the sample from the metallurgist[11,18] Charles Wood during a trip to Jamaica, West Indies. It was contraband from Carthagena, Colombia. Sir William Watson analyzed the sample and presented the results to the Royal Society on December 13, 1750. A copy of the page of the *Philosophical Transactions Abridgement* containing Watson's communication and Brownrigg's letter is given below.



XXXIII. 1. I take the freedom to incloſe to you an account of a ſemi-metal called *Platina di Pinto*; which, ſo far as I know, hath not been taken notice of by any writer on minerals. Mr *Hill*, who is one of the moſt modern, makes no mention of it. Preſuming therefore that the ſubject is new, I requeſt the favour of you to lay this account before the *R. S.* to be by them read and publiſhed, if they think it deſerving thoſe honours. I ſhould ſooner have publiſhed this account, but waited, in hopes of finding leiſure to make further experiments on this body with ſulphureous and other cements; alſo with Mercury, and ſeveral corroſive *menſtrua*. But theſe experiments I ſhall now defer, until I learn how the above is received. The experiments which I have related were ſeveral of them made by a friend, whoſe exactneſs in performing them, and veracity in relating them, I can rely on: however, for greater certainty, I ſhall myſelf repeat them.

Several Papers concerning a new Semi Metal, called Platina; communicated to the Royal Society by Mr Wm Watſon, F. R. S. N°. 496. p. 584. Nov. &c. 1750. Read Dec. 13. 1750. Extract of a letter from Will. Brownrigg, M. D. F. R. S. to Wm. Watſon, F. R. S. Dated Whitehaven, Dec. 5, 1750.

2. Although the hiſtory of minerals, and other foſſil ſubſtances, hath been diligently cultivated, eſpecially by the Moderns; yet it muſt be acknowledged, that, among the vaſt variety of bodies which are the objects of that ſcience, there ſtill remains room for new inquiries.

No wonder that, among the great, and almoſt inexhauſtible varieties of ſalts, ores, and other concretes, new appearances, and mixtures before unknown, ſhould daily be diſcovered: but that, among bodies of a more ſimple nature, and particularly among the metalline tribe, ſeveral diſtinct ſpecies ſhould ſtill remain almoſt wholly unknown to Naturaliſts, will doubtleſs appear more ſtrange and extraordinary.

Memoirs of a Semi-metal called Platina di Pinto, found in the Spaniſh Weſt Indies. Ibid. p. 585.

Gold is uſually eſteemed the moſt ponderous of bodies; and yet I have ſeen, in the poſſeſſion of the late Profeſſor *s'Graveſande*, a metalline ſubſtance, brought from the *Eaſt-Indies*, that was ſpecifically hea-

vier

In many chemistry books written in English, Sir William Watson is considered the sole and exclusive discoverer of platinum.

REFERENCES

1. M. Roche, *Science, 194,* 806 (1976).
2. G. Weinberg, *Interciencia, 3(2),* 72 (1978).
3. J. A. Schufle and L. G. Ionescu, *J. Chem. Educ., 53,* 174 (1976).
4. L. G. Ionescu and J. A. Schufle, *J. Chem. Educ.,55,*583 (1978).
5. L. G. Ionescu and J. A. Shufle, *N. Mex. J. Science, 21(1),* 41 (1978).
6. L. G. Ionescu, R. A. Yunes and J. A. Schufle, *J. Chem. Educ., 59,*304 (1982).
7. L. G. Ionescu, R. A. Yunes and J. A. Schufle, *N. Mex. Highlands Univ. J., 4(1),* 32 (1983).
8. L. G. Ionescu, *South. Braz. J. Chem., 2,* 1 (1994).
9. L. G. Ionescu and C. A. Perazzolo, *South Braz. J. Chem., 3,* 1 (1995).
10. L. G. Ionescu, *South. Braz. J. Chem.,4,* 1 (1996).
11. R. Osorio O., *"Historia de la Quimica en Colombia",* Publ. Geol. Esp., Ingeminas, Bogotã, Colombia, 1982.
12. M Bargallõ, *" La Amalgamación de los Minerales de Plata en Hispanoamérica Colonial",* Compañia Fundidora de Fierro y Acero de Monterrey, Mexico, D.F., 1969.
13. M. Bargallõ, *La Mineria y Metalurgia en la América Española durante la Epoca Colonial",* Fondo de Cultura Económica, Mexico, D.F., 1955.
14. J. Jorge and J. A. De Ulloa, *"Relación Histórica del Viaje a la América Meridional hecho de Orden de S. Mag. para Medir Algunos Grados del Meridiano Terrestre y Venir por Ellos en Conocimiento de la Verdadera Figura y Magnitud de la Tierra, con Otras Observaciones Astronómicas y Físicas",* Antonio Marin, Madrid, 1748.
15. J. Jorge and A. De Ulloa, *"A Voyage to South America",* Vols. 1,2, Lockyer Davis, London, 1772.
17. C. M. La Condamine, *"Relation abregée d'un voyage fait dans l'interieur de l'Amérique Meridionale",* Paris, 1745.
18. M. E. Weeks, *"Discovery of the Elements",* Published by Journal of Chemical Education, Easton, Pa., USA, 1945.
19. A. Phelps, *"Louisiana, a Record of Expansion",* Houghton, Mifflin and Company, Boston, 1903.
20. A. De Ulloa, *"Relacion circunstanciada del gobierno y superintendencia de la Real Mina de Azougues de la Vila de Guancavélica por el capitan de la Real Armada, desde el 4 de noviembre de 1758 hasta el 14 de mayo de 1762",* Guancavélica, 1762.
21. A. De Ulloa, *"Noticias americanas. Entretenimientos físico-históricos sobre América Meridional y Septentrional Oriental, climas y producciones en las tres especies vegetales, animales y minerales",* Madrid, 1772.

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ADSORPTION OF GASEOUS SUBSTANCES ON CHEMICAL AND ELECTROLYTIC MANGANESE DIOXIDE

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ABSTRACT *The adsorption of mercury , arsine, hydrocyanic acid and hydrogen sulfide on amorphous chemical manganese dioxide (CMD) and electrolytic manganese dioxide (EMD) has been investigated. Variables such as agitation time, pH, temperature, mass of adsorbent and concentration of adsorbate were studied. The adsorption process obeys a Freundlich type isotherm over the concentration range investigated. Wads of Luffa cylindrica Roem were used as substrate for CMD production. For gaseous substances this amorphous material showed better sorption capacity than EMD.*

KEY WORDS: manganese dioxide, pollutants, adsorption, isotherms

RESUMO *A adsorção de mercúrio, arsina e dos ácidos cianídrico e sulfídrico sobre o dióxido de manganês amorfo preparado químicamente (CMD) e o dióxido de manganês eletrolítico (EMD) foi estudado. As variáveis investigadas foram: tempo de agitação e de contato, pH, temperatura, massa do adsorvente e concentração do adsorvato. A reação obedece a isoterma de adsorção de Freundlich no intervalo de concentração estudado. Como substrato para a produção do dióxido de manganês utilizou-se aparas da bucha Luffa cylindrica Roem. Nos estudos com substâncias gasosas, este material amorfo mostrou capacidade de adsorção superior ao dióxido de manganês eletrolítico.*

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INTRODUCTION

There is a wide variety of manganese (IV) oxides whose structures have been extensively investigated. Among these oxides, most attention has been focused on electrolytic manganese dioxide for which the electrochemical and catalytic activity behaviour have been investigated[1].

X-ray studies showed that MnO_2 prepared by chemical reaction is amorphous with higher porosity than the electrolytic manganese dioxide[2]. Although progress has been made in the characterization of MnO_2 with respect to structure and electrochemical behavior, some aspects remain unexplained. The reason why certain forms of MnO_2, for instance, the γ modification, are highly reactive and may undergo electrochemical reduction at high rates, while other forms, for instance, the β modification, are relatively inactive, are still not fully understood[3].

One of the potential methods of removing pollutants from aqueous systems is the adsorption on iron, aluminum and manganese oxides.On the surface of manganese dioxide as much as 0.28 mole of lead ion can be adsorbed per mole of Mn(IV) at pH 6 as reported by Laitinen and Gadde[4]. The adsorption process of gaseous pollutants has different mechanisms from the aqueous phase, so that very little information is available for the mercury adsorption[5].

While there is no doubt that hydrous metal oxides are important sinks and modes of transport for heavy metals in the environment, the quantitative magnitude of this role is not known for a variety of natural waters[6].Hydrous oxides in aqueous solutions carry a surface charge which is very pH dependent. The pH of solution relative to the point of zero charge (PZC) affects the counter ion type adsorption of cations and anions. At pH values higher than PZC, cation adsorption is generally favored, whereas anion adsorption is favored by pH values less than PZC. (PZC of manganese dioxide is approximately 2,8)[7].

Manganese dioxide has been used as a sorbent for collection of radionuclides from water samples, collecting a known volume of water through identical MnO_2-impregnated cartridges connected in series[8]. Using this procedure the adsorption efficiency of an element and the activity were calculated. The redox mechanism was observed when two different oxidation states were investigated. After contact with MnO_2 plutonium(III) is oxidized to Pu(IV) and no higher oxidation states were observed[9]. The catalytic oxidation properties of manganese dioxide have also been investigated using organic (n-hexane or n-octane) compounds by gas chromatography.It was observed that doped EMD has a better catalytic activity[10].

The present research focuses upon the adsorption of toxic substances on manganese dioxide. The adsorption of mercury, mercuric ion, hydrogen sulfide, arsine, and hydrocyanic acid have been investigated.

EXPERIMENTAL

Chemicals

The reaction of 0.5 $mol.l^{-1}$ $KMnO_4$ (250 ml) with wads (3.5g) of dry **Luffa cylindrica Roem** , 10 ml of 50% (m/v) of sodium silicate, and 10 ml of 1.5 $mol.l^{-1}$ H_2SO_4 was employed for CMD production. The mixture was transferred to a 1000 ml flask with vigorous shaking and kept at room temperature. After 24 hours, 20 ml of 2 $mol.l^{-1}$ H_2SO_4 were added with strong agitation. The filtration of this black gel like solution was performed using a vaccum pump and washing several times with distilled water.The amorphous CMD produced was dried at 80°C , powdered to 100 mesh,and dried again at 80°C for 2 hours.

Brown granular EMD, sample n° 9, International Common Sample with surface area of 45m^2 BET was purchased from Trona Chemicals (USA). All solutions were prepared using doubly distilled deionized water. Analytical-reagent grade chemicals were used without further purification.

Procedure:

Figures 1 and 2 show the apparatus used for adsorption studies of hydrogen sulfide, arsine, hydrocyanic acid and mercury on manganese dioxide.

Hydrogen sulfide evolution and adsorption. The following chemicals were added to flask A, and to tubes B and C respectivelly:

A) 10 ml of 12 mol.l^{-1} HCl (Merck) and variable amounts of FeS (ferrous sulfide-technical grade-Aldrich).

B) 0.500 g of Manganese dioxide and pieces of glass wool.

C) 10,0 ml of As(III) solution (996 μg/ml), prepared from As_2O_3 (Aldrich-USA).

After 45 minutes of reaction at room temperature, tube B was disconnected from A, and the filtration of solution in tube C was performed using quantitative filter paper. The remained arsenic(III) in tube C was transferred to an erlenmeyer flask and determined by titration with standard iodine solution according to the procedure of Skoog et al[11] .

Hydrocyanic acid adsorption. The adsorption studies of hydrocyanic acid on MnO_2 was performed using the following chemicals:

A) 10 ml of 6 mol.l^{-1} HCl (Merck) + variable amounts of KCN (Merck).

B) glass wool + 0.500 g of MnO_2.

C) 10 ml of 0.25 mol.l^{-1} NaOH (Reagen).

After 75 minutes, tube B was disconnected from A and the HCN concentration in tube C was determined by UV-VIS spectrophotometry with the pyridine and barbituric acid method [12] .

Arsine generation and adsorption. The adsorption of AsH_3 , generated by reduction of standard As(III) solution with $SnCl_2$ and Zn (powder) in acidic medium, on CMD and EMD were studied with the following chemicals:

A) 5 ml of 12 mol.l^{-1} HCl + 5 ml of 0.01 mol.l^{-1} KIO_3 (Aldrich) + 0.2 ml of 0.001 mol.l^{-1} $SnCl_2$ (Merck). After the initial reduction of As(III), 1.5 g of Zn (powder-Merck) were added into the the flask to AsH_3 generation.

B) 0.500 g MnO_2 + glass wool wetted in 1 mol.l^{-1} lead acetate (Reagen).

C) 10 ml of 0.1 mol.l^{-1} TRIS (tris(hydroxymethyl)aminomethane-Sigma) + 0.5 ml of 0.002 mol.l^{-1} $AgNO_3$ (Aldrich). The arsine after reaction with Ag^+, was determined by differential pulse polarography using a solution of 0.1 mol.l^{-1} TRIS and HCl as supporting electrolyte[13].

To the polarographic cell containing 2 ml of pure mercury and 10.0 ml of supporting electrolyte, 1.0 ml of sample collected in flask C was added. Deaeration was performed with pure nitrogen for 15 minutes and the polarogram recorded from 0 to -1.6 volts with the following apparatus and conditions: Polarograph (Radelkis-Hungary-OH-107), a platinum wire as reference electrode, scan rate (2 mV.sec^{-1}), pulse amplitude (50 mV.sec^{-1}), and sensibility of 0.2 μA.

Mercury adsorption. The conventional mercury purification and distillation apparatus was modified for mercury adsorption on MnO_2. A 100 mm length and 10 mm of internal diameter PVC

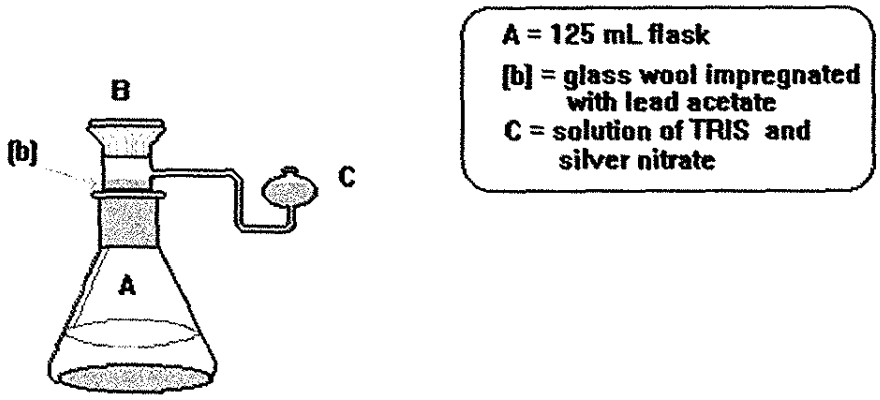


Figure 1. Apparatus used for arsine generation

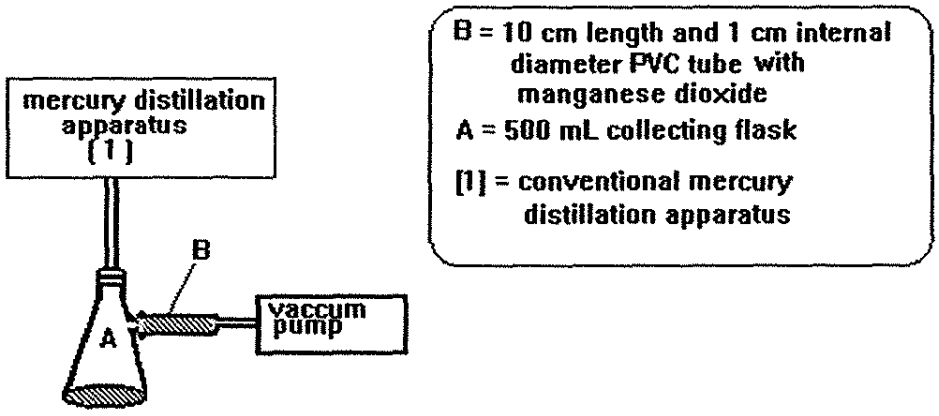


Figure 2. Apparatus for mercury adsorption

tube was connected between the collecting flask and the vaccum pump (Figure 2). Pieces of dry **Luffa cylindrica Roem** were used at the extremity and the CMD inside the tube was changed every 48 hours of continuous operation. The mercury concentration, after washing the CMD with nitric acid, was determined by cold vapor atomic absorption spectrometry (CVAAS) according to the procedure of Akif et al[14] , with the following conditions: Atomic absorption spectrometer (CG AA 7000 ABC) and a mercury hollow cathode lamp as source, λ = 253.7 nm. Carrier gas used was pure nitrogen (White Martins). $SnCl_2$ (Merck) was used as 10% (m/v) solution (12.0 g of $SnCl_2$. 2 H_2O was weighed into a 100 ml flask, dissolved by 18 ml of diluted HCl (1:1), and diluted to the mark with distilled water).

Mercuric ion adsorption. The adsorption of 7.4 $\mu g.ml^{-1}$ of Hg^{2+} solution, prepared from $Hg(NO_3)_2$-Aldrich, on MnO_2 was performed using a 500 ml flask with a thermometer. A mechanical mixer was used for agitation, and the system was immersed in a thermostatic bath.The mercuric ion solution was transferred to the flask, the pH adjusted to 4.5, and the experiment started when MnO_2 was added to the solution. In previous paper[10] it was observed that EMD particles were stronger than CMD in liquid solution. Due to these better physical characteristics the adsorption studies of Hg^{2+} were performed on EMD.

RESULTS AND DISCUSSION

Table 1 shows the (%) adsorption of H_2S on CMD and EMD, based on the theoretical mass of H_2S generated. In this table, 100% adsorption means that no H_2S reacted with the standard solution of As^{3+}, keeping the original concentration of As^{3+} in flask C.The following reactions are related to the adsorption of H_2S indicated by $(H_2S)_{ads.}$

Flasks A). $FeS\,(s) + 2\,HCl \rightarrow H_2S\,(g) + Fe^{2+} + 2\,Cl^-$

B) $H_2S\,(g) + MnO_2\,(s) \rightarrow (H_2S)_{ads.}\,/\,MnO_2$

C) H_2S (excess) $+ As^{3+} \rightarrow As_2S_3\,(s)$

Due to the high concentration of As^{3+} used (996 $\mu g.ml^{-1}$), the remaining As^{3+} in flask C was accordingly titrated with iodine, and the H_2S sorbed on MnO_2 was calculated by the difference of (H_2S) in flasks A and C.

Table 2 shows the HCN adsorption on MnO_2 , with the following reactions in flasks A, B, and C respectivelly:

A) $KCN + HCl \rightarrow HCN\,(g) + KCl$

B) $HCN\,(g) + MnO_2\,(s) \rightarrow (HCN)_{(ads.)}\,/MnO_2$

C) $HCN\,(g)$ (excess) $+ NaOH \rightarrow NaCN + H_2O$

The spectrophotometric method of barbituric acid was employed for (CN^-) determination. The difference among the total cyanide concentration and the CN^- that remained in flask A plus the cyanide collected in flask C represents the $(HCN)_{(ads.)}$

Table 3 shows the adsorption of arsine on MnO_2 and the following reactions could be considered:

Table 1.Percentage (m/m) of hydrogen sulfide adsorption on MnO_2 (*)

sample number	mass of FeS (g) used	theoretical mass of H_2S generated (mg)	(%) adsorption on CMD	EMD
1	0.500	194	100	95
2	0.850	329	100	84
3	0.925	358	100	81
4	0.950	368	96	78
5	1.000	384	87	75

(*) % adsorption based on theoretical mass of H_2S generated. Average of three determinations with an estimated error of ± 6 % .

Table 2.Percentage (m/m) of HCN adsorption on MnO_2 (#)

sample number	theoretical mass of HCN generated (mg)	(%) adsorption on CMD	EMD
1	49	100	100
2	313	100	100
3	326	96	85

(#) % adsorption based on the theoretical mass of HCN generated. Average of three determinations with an estimated error of ± 6 % .

Table 3.Percentage (m/m) of AsH_3 adsorption on MnO_2 (*)

Sample number	theoretical mass of AsH_3 generated (mg)	% adsorption on CMD	EMD
1	26	100	100
2	63	100	100
3	158	98	90

(*) % adsorption based on theoretical mass of AsH_3 generated. Average of five determinations with an approximate error of ± 4 %.

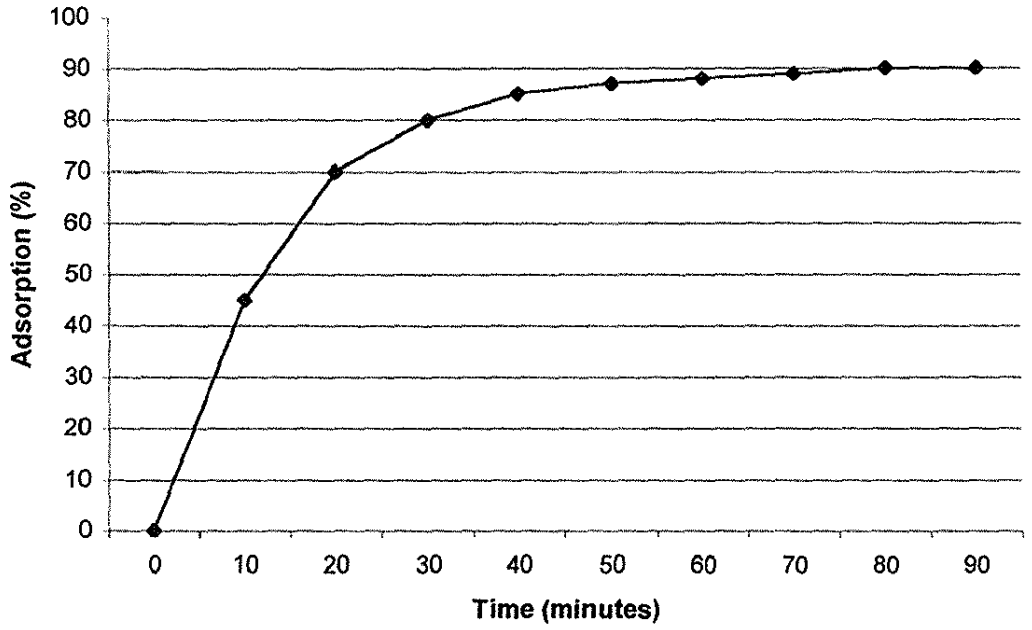
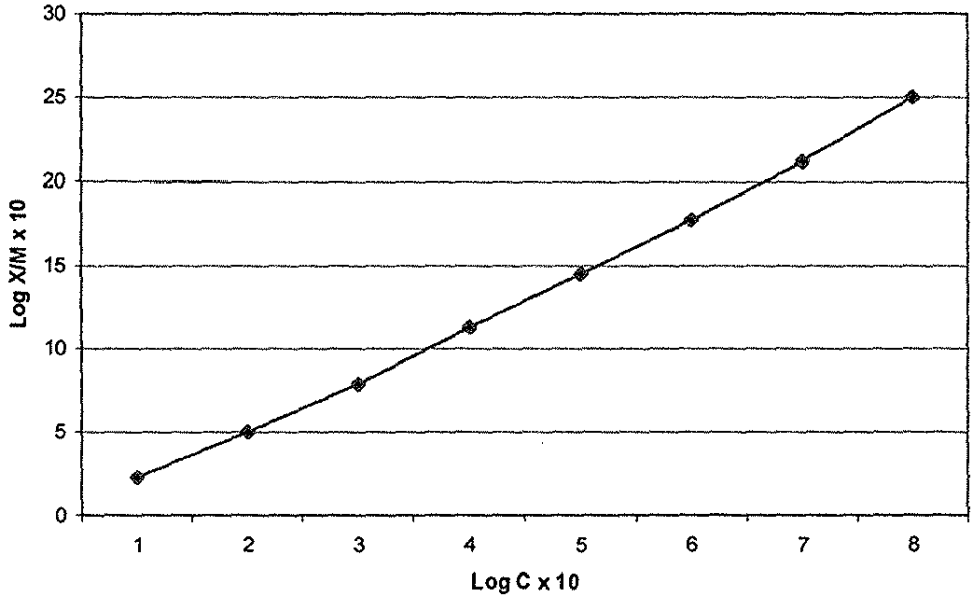


Figure 3. Dependence of contact and shaking time for Hg^{2+} adsorption on Electrolytic Manganese Dioxide (EMD)



X/M = concentration ratio of adsorbate (Hg^{2+}) and adsorbent (EMD). C = Hg^{2+} concentration in solution determined by cold vapor atomic absorption spectrometry using $SnCl_2$ as reducing reagent.

Figure 4. Freundlich adsorption isotherm of Hg^{2+} on Electrolytic Manganese Dioxide (EMD)

A). $As^{3+} + 3\ Zn(s) + 6\ HCl\ (aq.) \rightarrow AsH_3\ (g) + 3\ ZnCl_2 + 3\ H^+$

B). $AsH_3\ (g) + MnO_2\ (s) \rightarrow (AsH_3)_{(ads.)}/MnO_2$

$H_2S\ (g) + Pb^{2+} \rightarrow PbS\ (s) + 2\ H^+$

C). $6\ Ag^+ + AsH_3\ (g) \rightarrow As^{3+}\ (aq.) + 6\ Ag(s) + 3\ H^+$

$As^{3+} + 3\ e = As(s) \qquad E = -0.45$ volts (polarographic cell)

As^{3+}(aq.) is an electroactive substance and its concentration was determined by differential pulse polarography . The lead acetate used in (B) was to prevent MnO_2 from sulphide contamination[15]. For instance, this method was used in determination of arsenic in bituminous coal with high sulfur concentration.

The adsorption studies of elemental mercury were carried out using the classical mercury distillation apparatus, and the following reactions could be considered:

B) distilled mercury collecting flask: $Hg\ (l) \leftrightarrow Hg\ (g)$

A) $Hg(g) + MnO_2\ (s) \rightarrow (Hg)_{(ads.)}/MnO_2$

$(Hg)_{(ads.)}/MnO_2 +$ diluted $HNO_3 \rightarrow Hg(l) + H_3O^+ + NO_3^- + MnO_2\ (s)$

The concentration of Hg(l) was determined by CVAAS. The mercuric ion adsorption on MnO_2 represented by $(Hg^{2+})_{(ads.)}$ was performed with the following reactions:

Hg^{2+} (aq.) (pH = 4.5) $+ MnO_2\ (s) \rightarrow (Hg^{2+})_{(ads.)}/MnO_2$

$(Hg^{2+})_{(ads.)}/MnO_2 +$ diluted $HNO_3 \rightarrow Hg^{2+}(aq.) + H_3O^+ + NO_3^- + MnO_2\ (s)$

$Hg^{2+}\ (aq.) + SnCl_2 \rightarrow Hg(l) + Sn^{4+} + 2\ Cl^-$

The concentration of mercury was also determined by CVAAS. Figure 3 shows the dependence of shaking and contact time for Hg^{2+} adsorption on EMD. The adsorption efficiency increased at higher temperature (60°C) if compared with room temperature(25°C). At 60°C and pH 4.5 , that is slightly higher than the PZC of MnO_2, the adsorption process is very high from time zero until 30 minutes of reaction. It was also observed that in liquid media the adsorption efficiency of EMD was better than CMD. However, Freundlich isotherm were followed for both adsorption process (Figure 4).

The studies performed using manganese dioxide as adsorbent and gaseous substances as adsorbates showed some differences between CMD and EMD. Due to its porosity, the sorption efficiency of H_2S , HCN , AsH_3, and Hg were higher on CMD. On the other hand, EMD has better physical characteristics and efficiency for adsorption in liquid media. It was also observed that the adsorption of Hg^{2+} on MnO_2 changes the pH quickly. Starting at 4.5, the pH increases to 6.5 after 30 minutes of adsorption.

Acknowledgment

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REFERENCES

1. T. Ohzuku, M. Kitagawa and T. Hirai, **J. Electrochem.,Soc.,137,** 40 (1990).
2. S. Bach, J.P.P.Ramos, N. Baffier and R.Messina,.**Electrochim. Acta., 36 (10),** 1595-1603 (1991).
3. P. Ruetschi, **J. Electrochem. Soc.,Electrochemical Science and Technology**,December, 2737-2745, (1984).
4. R. R. Gadde and H.A.Laitinen, **Anal. Chem.,46,**2022-2026(1974).
5. Y. Otani, H. Emi, C. Kanaoka, I. Uchijima and H. Nishino, **Environ. Sci. Technol., 22 (6),** 708-711(1988).
6. J.J. Morgan and W. Stumm, **J. Colloid Sci. 19,** 347-359 (1964).
7. H. Tamura and M. Nagayama, **Progress in Batteries & Solar Cells, 5,** 143-147 (1984).
8.M.T.Crespo,J.L..Gascon and M.L.Acena,**The Science of the Total environment, 130/131,**383-391(1993).
9. M.T.Crespo, M.L. Acena and P.P.Galan,**J. Radioanal. Nucl. Chem.,Letters 166(4),**299-308(1992).
10. J. Nozaki and H. Zhou,**Química Nova, 20 (1),** 15-17 (1992).
11. D. Skoog, D.M. West and F.J. Holler, " **Analytical Chemistry. An Introduction".** Sixth Edition, Saunders College Publishing, New York, 1994.
12. J. Nozaki and J.C.R. Azevedo,**IchemE, The Second UK Congress of Biotechnology. Vol. 1 (1),** 76-78(1994).
13.J.Nozaki, E. Nogami and G.M.Oliveira,XI CIBAE-IX SIBEE-Congresso Iberoamericano de Eletroquímica.Simpósio Brasileiro de Eletroquímica e Eletroanalítica, Aguas de Lindoia-MG., vol. 1 (1), 480-482(1994).
14. M. Akif, S.A. Seckin and O.Y. Ataman, **Inter. J. Environ. Anal. Chem.,26,** 1-17 (1986).
15. M. Zygmunt, **"Spectrophotometric Determination of Elements",**.John Willey & Sons, New York,1976, p. 131-141.

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SOME COMPLEXES OF COPPER(II) WITH N,N'-DISUBSTITUTED DITHIOOXAMIDES DERIVED FROM α - AMINOACIDS AND α - AMINOACID ESTERS

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ABSTRACT

The binuclear copper(II) complexes $Cu_2(L-4H)(H_2O)_2$ (L = N,N'-bis (carboxymethyl) dithiooxamide - GlyDTO and N,N'-bis(1-carboxyethyl) dithiooxamide - AlaDTO) and $Cu_2(L'-2H)Cl_2$ (L' = methyl or ethyl ester of L) were synthesized. The structure of the complexes were studied employing IR, electronic and ESR spectroscopy and conductivity measurements. The IR data indicate that the ligands act as bistridentates, with N, S, O - coordination to the copper(II) ion.

RESUMO

Os complexos binucleares de cobre (II) $Cu_2(L-4H)(H_2O)_2$ (L= N,N'-bis(carboximetil) ditiooxamida -GlyDTO e N,N'-bis (l-carboxietil) ditiooxamida - AlaDTO e $Cu_2(L'-2H)Cl_2$ (L' = éster de metila ou etila de L) foram sintetizados. A estrutura dos complexos foi estudada usando técnicas de espectroscopia eletrônica, no infravermelho e de ressonância do spin do eletron. Os resultados obtidos no infravermelho indicam que os ligantes são bis-tridentados, com coordenação do N,S e O com o íon de Cu(II).

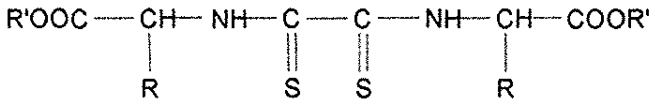
KEYWORDS: ethanedithioamides, copper(II) complexes, ESR spectroscopy, square planar complexes.

INTRODUCTION

In the last years, O. Kahn and coworkers have described several copper(II) binuclear complexes with N,N' - dithiooxamides derived from aminoacids, peptides and esters of aminoacids or peptides[1,2]. Recently, the synthesis, crystal structure and magnetic properties of binuclear copper(II) complexes bridged by dithiooxamidate group were reported[3-5]. The magnetic behaviour of these compounds revealed that the metal centers were strongly coupled in an antiferromagnetic way[2].

N,N' - disubstituted dithiooxamides have interesting properties as complexing agents, since it is possible to obtain ionic, neutral or polymeric metal complexes depending on the pH of the solution, solvent or metal salt[6,7]. Internal rotation around the C-C bond in the molecules of dithiooxamides allows the preparation of complexes of trans or cis configuration[8].

In this paper we describe the synthesis of the Cu(II) complexes with N,N'-disubstituted dithiooxamides:



R = R' = H, N,N' - bis (carboxymethyl)ethanedithioamide (L_1 - GlyDTO)
R = CH_3; R' = H, N,N' - bis (1-carboxyethyl)ethanedithioamide (L_2 - AlaDTO)
R = H; R' = CH_3, N,N' - bis (methoxycarbonylmethyl)ethanedithioamide (L_3 - GlyOMeDTO)
R = R' = CH_3, N,N' - bis (1-methoxycarbonylethyl)ethanedithioamide (L_4 - AlaOMeDTO)
R = H; R' = CH_2-CH_3, N,N' - bis (ethoxycarbonylmethyl)ethanedithioamide (L_5 - GlyOEtDTO)
R = CH_3; R' = CH_2-CH_3, N,N' - bis (1-ethoxycarbonylethyl)ethanedithioamide (L_6 - AlaOEtDTO).

The L_4 ligand has been structurally characterized. The results are indicative of a trans configuration of the molecule[9]. Upon loosing two protons, this molecule is expected to play the role of a novel bis(tridentate)bichelating ligand. The structure of the complexes were deduced from IR, electronic and ESR spectra and conductivity measurements.

EXPERIMENTAL PART

Materials. All solvents and chemicals were AR grade and used without further purification. The ligands L_1 - L_6 were prepared according to literature methods[2,10].

Preparation of the complexes. The complexes $Cu_2(L - 4H)(H_2O)_2$ type were prepared by adding 0,236 g (1 mmole) of L_1 (or 0.264 g, 1 mmole of L_2) to a solution of 0.5 g (2 mmole) of $CuSO_4 \cdot 5H_2O$ in 10 ml of water. The mixture was stirred during half an hour. The resulting solid was filtered after two days, washed with hot water and dried under vacuum. These complexes are insolubles in the usual solvents. The complexes $Cu_2(L' - 2H)Cl_2$ type were prepared by adding 0.264 g (1 mmole) of L_3 (or 0.292 g, 1 mmole of L_4 and L_5 or 0.320 g, 1mmole of L_6) to a solution of 0.270 g (2 mmoles) of

$CuCl_2$ in 10 ml ethanol. The mixture was stirred during 15 minutes. The resulting solid was filtered, washed with ethanol and dried under vacuum. The complexes are very soluble in DMF.

Physical measurements. Elementary analyses were been performed with a Carlo Erba L1108 automatic analyzer (C, H). Copper contents of the complexes were determined by a conventional method[11]. IR spectra were recorded on a FT-IR BIORAD FTS spectrophotometer in the 4000 - 500 cm^{-1} and on a SPECORD M80 Carl Zeiss Jena spectrophotometer in the 500 - 250 cm^{-1}, in KBr pellets. The electronic spectra of complexes with ligands L_1 and L_2 were obtained by the diffuse reflectance method, using MgO as a dilution matrix with SPECORD M40 Carl Zeiss Jena. The electronic spectra of complexes with ligands L_3 - L_6 were studied with a SHIMADZU UV 160A spectrophotometer, using DMF solutions. The ESR spectra of copper(II) complexes were recorded on polycrystalline powders at room temperature with a ART-5 spectrometer operating in the X-band at 100 kHz modulation. In order to determine the g values, we used Mn^{2+} ion in a CaO matrix as standard.. Conductivities were measured at room temperature in DMF with a HACH TDS - meter.

RESULTS AND DISCUSSION

The coordination behaviour of GlyDTO and AlaDTO was studied by isolating and characterizing the binuclear neutral cobalt(II) complexes[12]. The analytical results and conductivity values for the complexes are given in Table 1. The molar conductance of 10^{-3}M DMF solutions of the complexes were found to be in the range 5.8-10.8 $ohm^{-1}\cdot cm^2\cdot mol^{-1}$. The complexes may be regarded as essentially nonelectrolytes.

Selected IR spectral data are summarized in Table 2. Figures 1 and 2 shows the spectra of L_1 ligand and $Cu_2(L_1\text{-}4H)(H_2O)_2$ complex. Differences between the infrared spectra of the ligands and those of all their copper complexes are confined to regions of 3200, 1700, 1500 and 890 cm^{-1}. The loss of the two protons of the carboxy group of the GlyDTO and AlaDTO is confirmed by the disapearance of the $\nu_{CO}(CO_2)$ vibration[1], at 1712 cm^{-1} and 1715 cm^{-1} respectively, as can be seen in Figures 1 and 2. The frequency at ~3200 cm^{-1} assigned to ν(NH) vibration disappears in all spectra of the complexes. This shows that a deprotonation of the N-H group has occured upon coordination.

The ν(CN) vibration for ligands is assigned to the intense band at 1516, 1495, 1517, 1532, 1519 and 1526 cm^{-1} respectively. The same vibration is found in the spectra of all complexes at a higher frequency (1582, 1574, 1579, 1556, 1580 and 1553 cm^{-1} respectively). This increase in frequency can be explained as resulting from a greater double bond character of the carbon - nitrogen bond upon complex formation[13].

The band involved between 845 - 899 cm^{-1} for ligands, assigned to the ν(CS) vibration is shifted to 834 - 874 cm^{-1} for complexes. The frequency decrease can be explained by the lesser double bond character of carbon - sulphur bond upon complexation[14]. In the infrared spectra, below 500 cm^{-1}, almost all the bands of the ligands are observed in the spectra of the complexes and the few distinct new bands can be assigned to complex modes. The assignments of the new far infrared bands to ν(CuO) (340 - 352 cm^{-1}), ν(CuS) (325 - 335 cm^{-1}) and ν(CuN) (260 - 290 cm^{-1}) are in agreement with literature data[13,15,16].

Table 1. Elementary analysis and molar conductivities of the complexes.

Complex	Colour	%C		%H		%Cu		Λ_M
		exp.	calc.	exp.	calc.	exp.	calc.	($ohm^{-1}\cdot cm^2\cdot mol^{-1}$)
$Cu_2(L_1 - 4H)(H_2O)_2$	dark-green	17.89	18.18	2.40	2.02	31.98	32.32	*
$Cu_2(L_2 - 4H)(H_2O)_2$	dark-green	22.17	22.64	2.98	2.83	30.04	30.18	*
$Cu_2(L_3 - 2H)Cl_2$	brown	20.63	20.82	2.43	2.16	27.56	27.76	10.85
$Cu_2(L_4 - 2H)Cl_2$	brown	24.32	24.53	2.97	2.82	26.05	26.17	10.49
$Cu_2(L_5 - 2H)Cl_2$	brown	24.27	24.53	2.93	2.82	25.98	26.17	5.8
$Cu_2(L_6 - 2H)Cl_2$	brown	27.56	27.85	3.65	3.48	24.36	24.75	5.9

* These complexes are insolubles in DMF.

Table 2. Infrared bands (cm^{-1}) of ligands and complexes.

Compound	ν(NH) (CSNH)	ν(CO) (CO_2)	ν(CN) (CSN)	ν(CS)
L_1	3237	1712	1516	895
$Cu_2(L_1 - 4H)(H_2O)_2$	-	-	1582	869
L_2	3224	1715	1495	886
$Cu_2(L_2 - 4H)(H_2O)_2$	-	-	1574	834
L_3	3225	1734	1517	889
$Cu_2(L_3 - 2H)Cl_2$	-	1656	1579	864
L_4	3177	1737	1532	845
$Cu_2(L_4 - 2H)Cl_2$	-	1664	1556	836
L_5	3229	1731	1519	899
$Cu_2(L_5 - 2H)Cl_2$	-	1647	1580	874
L_6	3193	1735	1526	863
$Cu_2(L_6 - 2H)Cl_2$	-	1667	1553	859

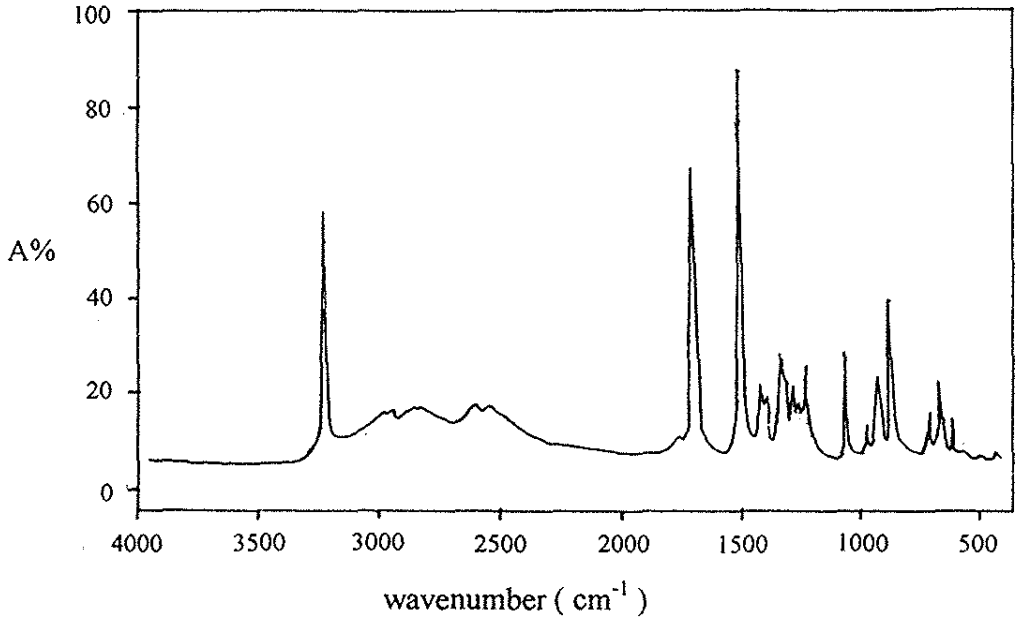


Fig. 1. IR spectrum of $C_2S_2(NHCH_2COOH)_2$ (L_1)

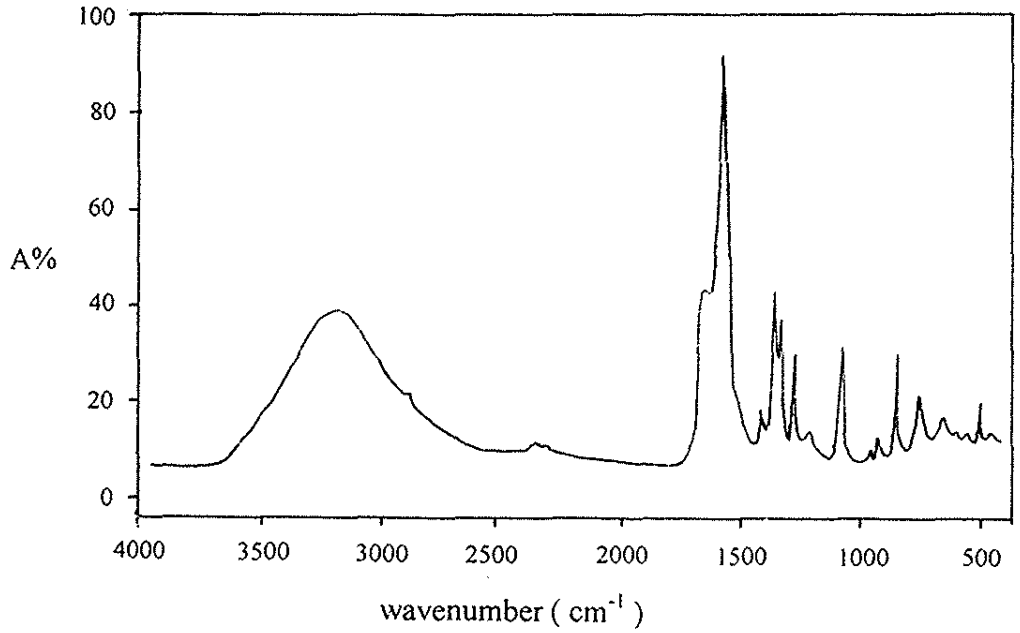


Fig. 2. IR spectrum of $Cu_2(L_1\text{-}4H)(H_2O)_2$ complex

Table 3. Electronic spectra of the complexes (λ_{max} in nm).

Complex	Assignments		
	$\pi \rightarrow \pi^*$	$\sigma(S) \rightarrow Cu(II)$ CT	d - d
$Cu_2(L_1 - 4H)(H_2O)_2$	333	440	606
$Cu_2(L_2 - 4H)(H_2O)_2$	327	468	634
$Cu_2(L_3 - 2H)Cl_2$	348	488	615
$Cu_2(L_4 - 2H)Cl_2$	320	485	630
$Cu_2(L_5 - 2H)Cl_2$	342	478	620
$Cu_2(L_6 - 2H)Cl_2$	332	472	638

Table 4. ESR data for the copper(II) complexes.

Complex	g_1	$g_\parallel$	g_2	$g_\perp$	g_3	g_{iso}
$Cu_2(L_1 - 4H)(H_2O)_2$						2.18
$Cu_2(L_2 - 4H)(H_2O)_2$						2.18
$Cu_2(L_3 - 2H)Cl_2$		2.27		2.14		
$Cu_2(L_4 - 2H)Cl_2$						2.16
$Cu_2(L_5 - 2H)Cl_2$						2.11
$Cu_2(L_6 - 2H)Cl_2$	2.40		2.15		1.87	

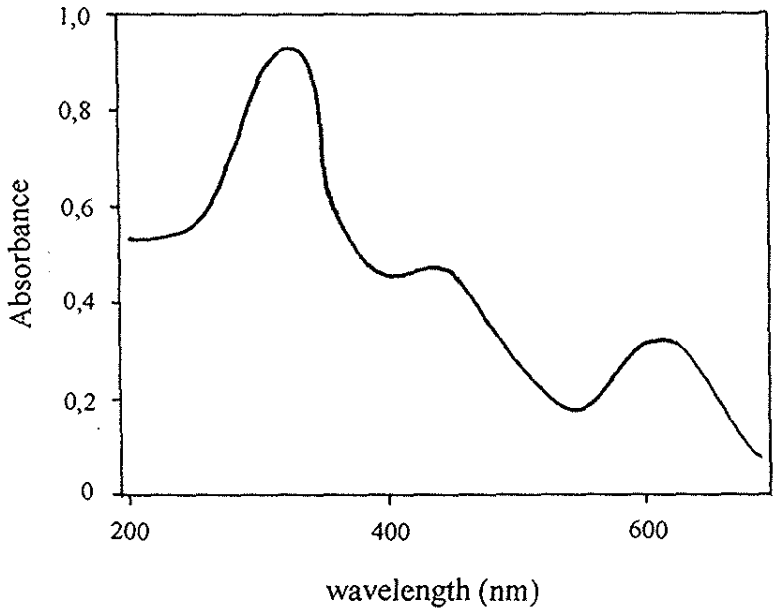


Fig. 3. UV-VIS spectrum of $Cu_2(L_1\text{-}4H)(H_2O)_2$ complex

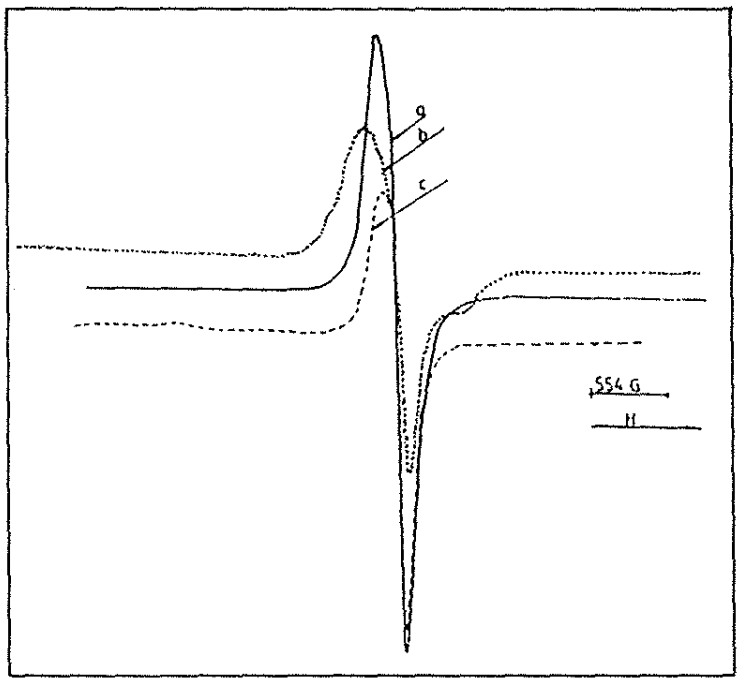


Fig. 4. ESR spectra of $Cu_2(L_1\text{-}4H)(H_2O)_2$ (a), $Cu_2(L_6\text{-}2H)Cl_2$ (b) and $Cu_2(L_3\text{-}2H)Cl_2$ (c) complexes

The assignments of the absorption bands from the electronic spectra of the complexes are reported in Table 3. The UV - VIS spectrum of the $Cu_2(L_1\text{-}4H)(H_2O)_2$ complex in the solid state is given in Figure 3. The spectra of the complexes exhibit a very strong and very broad band at about 440 - 488 nm. This band involves the $\sigma(S) \rightarrow d_{x2-y2}$ (Cu(II)) ligand $\rightarrow$ metal charge transfer transition[2,17]. This S (thioamide) $\rightarrow$ copper(II) transition appears at lower energy when the ligand field is weak (halogen donor atom) as compared to the case when the ligand field is strong (oxygen donor atom)[2]. The band at 606 - 638 nm is due to a d - d transition.. For $Cu_2(L\text{-}4H)(H_2O)_2$ complexes the wavelength of the d- d bands are fairly typical of square - planar stereochemistry with the $CuSNO_2$ cromophore[2]. The d - d bands observed in the spectra of $Cu_2(L'\text{-}2H)Cl_2$ complexes seem to indicate a square - planar symmetry around the Cu(II) ion[17].

ESR spectra of some of the complexes are shown in Figure 4. The g values for all complexes are given in Table 4. The powder ESR spectra of $Cu_2(L\text{-}4H)(H_2O)_2$ complexes exhibit an almost symmetrical signal. The g values are in agreement with literature data for similar complexes[1]. The g values of $Cu_2(L'\text{-}2H)Cl_2$ complexes are similar with literature data for other N,N' - disubstituted dithiooxamide complexes[18]. No $\Delta M_S = 2$ signal is detected, probably because of the very weak magnitude of the zero field splitting[1]. Considering the g values, a predominant d_{x2-y2} ground state is indicated[18]. As the covalency increases, the energies of the excited states rise, so that the orbital contribution to g become less effective and g becomes closer to the free electron value[19].

REFERENCES

1. J. J. Girerd, O. Kahn, *Angew. Chem. Int., Ed. Engl. Supl., 94(5)*, 953, (1982).
2. R. Veit, J. J. Girerd, O. Kahn, F. Robert, Y. Jeannin, Nabil El Murr, *Inorg. Chem., 23(26)*, 4448, (1984).
3. H. Okawa, N. Matsumoto, M. Koikawa, K. Takedo, S. Kida, *J. Chem. Soc. Dalton Trans, 10*, 1383, (1990).
4. N. Xing, B. Jianchun, S. Yueming, J. Tongshun, *Hecheng Huaxue, 4(3)*, 267, (1996), (C. A. 126: 180336s).
5. N. Xing, B. Jianchun, S. Yueming, C. Chenxin, *Wuji Huaxue Xuebao, 12(2)*, 218, (1996), (C. A.125: 211038f).
6. Q. Y. Ye, Y. Nakano, G. R. Frauenhoff, D. R. Whitcomb, F. Takusagawa, D. H. Busch, *Inorg. Chem., 30(7)*, 1503, (1991).
7. R. Baggio, M. T. Garland, M. Perec, *J. Chem. Soc. Dalton Trans., 6*, 987, (1995).
8. R. E. Carter, J. Sanström, *J. Phys. Chem., 76(5)*, 642, (1972).
9. L. Stoicescu, I. Strenger, unpublished results.
10. R. N. Hurd, G. De La Mater, G. C. Mc Elheny, R. J. Turner, V. H. Wallingford, *J. Org. Chem., 26*, 3980, (1961).
11. A. I. Vogel, *"A Text Book of Quantitative Inorganic Analysis"*, Longmans London, 3rd ed., p. 358, 1961.

12. A. Castineiras, M. C. F. Vidal, R. Carballo, *Trans. Met. Chem. (London), 20(5)*, 477, (1995).
13. B. Slootmaekers, S. P. Perlepes, H. O. Desseyn, *Spectrochim. Acta, 45A(12)*, 1211, (1989).
14. H. O. Desseyn, W. A. Jacob, M. A. Herman, *Spectrochim. Acta, 25A*, 1685, (1969).
15. A. W. Herlinger, S. L. Wenhold, T. V. Long, *J. Am. Chem. Soc., 92(22)*, 6474, (1970).
16. G. Peyronel, G. C. Pellacani, A. Pignedoli, G. Benetti, *Inorg. Chim. Acta, 5(2)*, 263, (1971).
17. B. Slootmaekers, S. P. Perlepes, H. O. Desseyn, *Spectroscopy: An International Journal, 4*, 265, (1985).
18. L. Antolini, A. C. Fabretti, G. Franchini, L. Menabue, G. C. Pellacani, H. O. Desseyn, R. Dommise, H. C. Hofmans, *J. Chem. Soc. Dalton Trans., 8*, 1921, (1987).
19. R. V. Parish, *"NMR, NQR, EPR and Mössbauer Spectroscopy in Inorganic Chemistry"*, Ellis Horwood Ltd., New York, p.189, 1990.

SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY
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DIFFERENTIAL PULSE POLAROGRAPHIC DETERMINATION OF ARSENIC IN BITUMINOUS COAL

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ABSTRACT. *Differential pulse polarography was employed for the determination of arsenic in bituminous coal from Figueiras, Parana, Brazil. The dried coal sample was crushed to ~ 100 mesh, ashed and treated with reducing reagents in acidic media. The arsine generated was collected and selectively oxidized to As^{3+} using an absorbing solution of 0.1 mol.L^{-1} [tris(hydroximethyl) aminomethane] (TRIS) and 0.002 mol.L^{-1} silver nitrate. A solution of TRIS and hydrochloric acid, pH ~ 1, was used as supporting electrolyte for differential pulse polarographic determination of As^{3+} in the concentration range 0.05 - 0.60 μg/mL. The average arsenic concentration found was 69.0 ± 2.6 mg.kg^{-1} and was in agreement with the spectrophotometric method using silver-diethyldithiocarbamate-pyridine.*

RESUMO. *O teor de arsênio em carvão betuminoso de Figueiras, Estado do Paraná, Brasil, foi determinado por polarografia de pulso diferencial. Após a secagem o carvão foi triturado a ~ 100 mesh, calcinado e, a seguir, tratado com agentes redutores em meio ácido. A arsina foi coletada e seletivamente oxidada a As^{3+} utilizando como solução absorvedora o TRIS [tris(hidroximetil)aminometano] 0,1 mol.L^{-1} e nitrato de prata 0,002 mol.L^{-1} .Uma solução de TRIS e ácido clorídrico, pH ~1, foi utilizada como eletrólito suporte na determinação de As^{3+} por polarografia de pulso diferencial, no intervalo de concentrações de 0,05 a 0,60 μg.mL^{-1}. A concentração média do arsênio encontrado foi de 69,0 ± 2,6 mg.kg^{-1} concordando com o método clássico espectrofotométrico de dietilditiocarbamato de prata e piridina.*

Key words: arsenic, bituminous coal, differential pulse polarography, spectrophotometry.

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INTRODUCTION

Arsenic is a constituent of numerous minerals and is found most frequently in association with sulfur, especially as arsenopyrite, palladium as arsenopalladinite, gold, uranium, etc [1]. Soils associated with gold deposits contain between 300 and 5000 p.p.m. of arsenic compounds. This association of arsenic with valuable elements has led to suggestion of its use as a geological prospecting marker. The arsenic content of plants could be used as a biogeochemical indicator, in particular, as a pathfinder element for gold [2].

Arsenic is also present in coal, shale oil, and petroleum. The redistribution of arsenic by fossil combustion has important environmental consequences. Natural phenomena such as wheathering, antropogenic imputs, biological and volcanic activity are responsible for the emission of arsenic into the atmosphere [3,4].

Coal produces up to 30 % of its weight as fly ash after combustion, and increased coal usage presents problems regarding the disposal of this material[5]. Arsenic concentrations in groundwater are usually below 5 $\mu g.L^{-1}$, but geochemical mobilization, contaminated soils in industrial regions and the use of arsenic pesticides lead locally to enhanced concentrations [6,7,8]. In natural waters the speciation and distribution of dissolved arsenic are influenced by the differential scavenging of As(III) and As(V) by iron and manganese oxides[9,10]. Generally, adsorption of arsenite is relatively lower as compared to arsenate ions[7].This paper presents a novel procedure for arsine generation and determination of As(III) in bituminous coal by means of differential pulse polarography(DPP).

EXPERIMENTAL

Apparatus

A polarograph (Radelkis-Hungary-OH-107), with a platinum wire in contact with mercury pool as reference electrode, scan rate (2 $mV.sec^{-1}$) , pulse amplitude (50 $mV.sec^{-1}$), sensitivity of 0.2 μA, and mercury dropping time of 2 sec were employed. Spectrophotometric determination of As:DDTC: pyridinium complex[11] was performed with UV-VIS spectrophotometer Beckman DU-70 and 1 cm quartz cubets.

Reagents

Nitric acid (d = 1.40, Merck); hydrochloric acid, 37%, Merck; tris(hydroxymethyl)aminomethane, 99 % - TRIS, Sigma, and standard reference of bituminous coal (3.72 $mg.kg^{-1}$), National Institute of Standards and Technology-USA were used. The following chemicals (Aldrich-USA) were also employed:Thallium(III) nitrate trihydrate,98 %; tellurium(IV) chloride, 99 %; germanium tetrachloride; selenium(I) chloride; antimony(III) oxide, 99%; tin(II) chloride, 98%; Arsenic free granulated zinc ,100 mesh; silver nitrate, 99%; potassium iodide, 99%; arsenic(III) oxide, 99%; diethyldithiocarbamic acid, silver salt, 99%; AgDDTC; pyridine, 99%.

Arsine generation

Coals samples were obtained from the **CNEN** (National Commission of Nuclear Energy - Brazil) site located 3 miles northwest of Figueiras, Paraná, Brazil. Figueiras has one of the most important deposits of bituminous coal in Paraná State, mainly because of its

uranium content (see Table 1).Dried coal samples were ground to ~ 100 mesh and 3.00 g were transferred to a porcelain crucible and ignited at 450°C for 3 hours. After cooling, the sample was transferred to a flask A as shown in Figure 1. Five mL of concentrated HCl , 5.0 mL (0.1 mol.L^{-1}) KI , 0.50 mL (1.0 mol.L^{-1}) $SnCl_2$, and 1.50 g of granulated Zn were also added to the same flask[11] . After conecting the flasks A and B, the arsine generated in flask A was absorbed in flask C with a solution of 0.020 M $AgNO_3$ and 0.10 M TRIS , at pH 6.2 . The absorbed arsine was then selectively oxidized to As^{3+} in this medium. The glass wool and lead acetate in flask B were used for sulfide hydrogen absorption.

Differential pulse polarographic determination of As^{3+}

An acidic solution , pH ~ 1 , of 0.10 mol/L TRIS-HCl was employed as supporting electrolyte for DPP measurements at the dropping mercury electrode. An aliquot of 1.00 mL of standard solution of As^{3+} prepared from As_2O_3 was added to the polarographic cell containing 2 mL of pure mercury, and 10.0 mL of supporting electrolyte. Deaeration was performed with pure nitrogen for 15 minutes and the polarograms recorded from 0 to - 1.6 volts. The optimum concentration range observed in the polarographic cell was 0.05 - 0.60 μg(As).mL^{-1} as measured from standard curves.

Two different methods of standard addition were used for arsenic determination in bituminous coal. 1) Addition of known concentration of As^{3+} to the flask used for arsine generation, recording the polarogram after addition of the sample (1.00 mL) to the polarographic cell with a known concentration of As^{3+} . This polarogram was compared with the polarogram of the sample added to the polarographic cell, without addition of standard solution of As^{3+} for arsine generation . 2) A polarogram with a known concentration of As^{3+} was recorded . A new polarogram was recorded again after addition of the sample (1.00 mL) to the polarographic cell. Standard reference of bituminous coal (3.72 mg (As).kg^{-1}) was used to compare the efficiency of the proposed method.

The classical spectrophotometric method of Gutzeit measuring the color formed by the reaction of arsine and a solution of silver diethyldithiocarbamate (AgDDTC)-pyridine was also used for comparative purposes[11]. Interference studies of substances that also form volatile hydrides were performed after addition of 10μg.ml^{-1} of each solution to flask (A) before arsine generation.

RESULTS AND DISCUSSION

As^{3+} recorded from acidic media undergoes three distinct reduction steps(Figure 2). The only important peak for quantitative purposes is E_p = -0.45 volts where the reaction is diffusion-controlled and proportional to the As^{3+} concentration in the polarographic cell.

The following reactions probably occur in flasks A (arsine generation[11]), B(selective oxidation to As^{3+}) , and the polarographic cell respectively:

$$As_2O_5\,(s) + 10\,H^+ + 4\,e \Rightarrow 2\,As^{3+} + 5\,H_2O$$

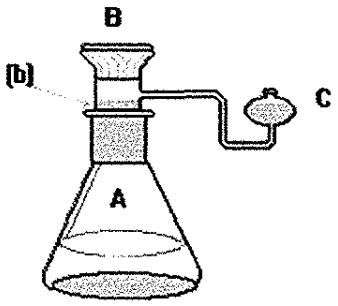
$$As^{3+} + 3\,Zn(s) + 6\,HCl\,(aq.) \Rightarrow AsH_3\,(g) + 3\,ZnCl_2 + 3\,H^+ \qquad (A)$$

$$6\,Ag^+ + AsH_3(g) \Rightarrow As^{3+}(aq.) + 6\,Ag(s) + 3\,H^+ \qquad (B)$$

$$As^{3+}(aq.) + 3\,e = As(s) \qquad E_p = -0.45 \text{ volts} \qquad (\text{polarographic cell})$$

Table 1. Coal Reserves in Parana State[12]

District	coal (tonne - in situ)	% of total
Ortigueira	2,227,000	2.9
Figueiras	31,200,000	40.4
Telemaco Borba	1,800,000	2.3
Sapopema	42,000,000	54.4
Total	77,277,000	100



A = 125 mL flask
[b] = glass wool impregnated with lead acetate
C = solution of TRIS and silver nitrate

Figure 1. Apparatus used for arsine generation

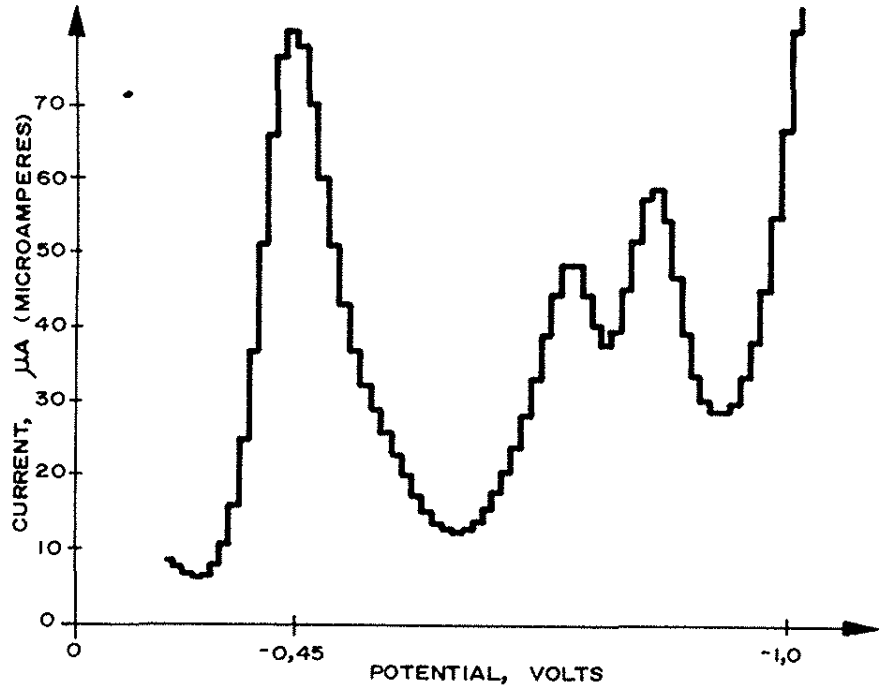


Figure 2. Differential pulse polarography (DPP) of As^{3+} in TRIS-HCL as supporting electrolyte.

Table 2. Arsenic Found in Bituminous Coal from Figueiras, PR., Brazil.

Samples	spectrophotometry ($mg.kg^{-1}$)	DPP ($mg.kg^{-1}$)*
1	68.77	67.26
2	64.78	66.89
3	69.49	73.00
4	65.03	67.81
5	71.04	72.77
6	64.54	69.14
7	69.18	70.16
8	72.24	72.64
Average	68.06 ± 2.99	69.96 ± 2.57

Spectrophotometric conditions: $\lambda = 540$ nm; range of As^{3+} concentration 0.5 - 3.0 μg/mL

(*) Average of 5 determinations.

DPP = Differential Pulse Polarography.

The I_p observed at - 0.45 volts was proportional to As^{3+} concentration. No interferences were observed with tellurium (IV) , thallium (III), germanium(IV), antimony (III) , and selenium(I). Table 1 summarizes some important coal deposits in Parana State, Brazil. Figueiras is the most important reserve because of its uranium content[12] . Table 2 shows the arsenic content found in bituminous coal from Figueiras by DPP (differential pulse polarography) and spectrophotometric methods.

The proposed method of arsenic determination by differential pulse polarography is very simple and useful for a complex samples like bituminous coal. Using the standard addition method for arsine generation, the recovery of As(III) was almost complete and no systematic error was observed. The results were in agreement with the spectrophotometric method using silver diethyldithiocarbamate-pyridine solution.

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REFERENCES

1. A. Kabata and H. Pendias, **"Trace Elements in Soils and Plants"**,.CRC Press, 2nd edition, New York, 1992.
2. W.R. Cullen and J.K. Reimer, **Chem. Rev., 89** , 713-764 (1989).
3. A. Chaterjee, D. Das, B.K. Mondal, T.R. Chawdhury, G. Samanta and D. Chakraborti, **Analyst, 120,** 643-650 (1995).
4. S. Caroli, **Element Speciation in Bioinorganic Chemistry**. Chapter 13. Arsenic Speciation and Health Aspects, vol. 135, John Wiley & Sons, Inc., 1996, p. 445-463.
5. H. H. Schobert," **Coal, the Energy Source of the Past and Future**", American Chemical Society, Washington,DC , 1987, 298 pp.
6. R. B. Smart, and H. Li, **Analytica Chimica Acta 325,** 25-32 (1996).
7. S.A. Wasay, M.J. Haron, A. Uchiumi and S. Tokunaga,. **Water Res., 30, (5),** 1143-1148 (1996).
8. W. Drichaus, R. Seith and M. Jekel, **Water Res., 29 (1),** 297-305 (1995).
9. E.I. Ochiai, **J. Chem. Education, 72, (6),** 479-484 (1995).
10. H.M. Spliethoff, R.P. Mason and H.F.Hemond, **Environ. Sci. Technol., 29, (8),** 2157-2161(1996).
11. Z. Marczenko, **"Spectrophotometric Determination of Elements"**,. John Willey & Sons, New York , 1976, p. 131-141.
12. MINEROPAR - Minerais do Paraná. Potenciais e perspectivas para o carvão mineral do Estado do Paraná. Curitiba, Governo do Estado do Paraná, Brasil, 1985, 126 p.

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PHENOXATHIIN CHEMISTRY. SYNTHESIS BASED ON 2-ω-BROMOACETYLPHENOXATHIIN

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ABSTRACT

Starting from 2-ω-bromoacetylphenoxathiin and using the Kornblum reaction the corresponding glyoxal **2** was synthesized. This was used for the syntheses of the monoxime **3**, dioxime **4** and quinoxalinyl **5** derivatives. By treatment with thiourea 4-(2-phenoxathiinyl)-2-aminothiazole hydrobromide 7 was obtained. Some new ammonium and phosphonium salts was also prepared.Chemical and spectral data supporting the structure of the newly synthesized compounds are also presented.

RESUMO

Começando com 2-ω-bromoacetilfenoxatiina e usando a reação de Kornblum, o glioxal correspondente 2 foi sintetizado. Este foi usado para a síntese dos derivados da nomoxima 3, dioxima 4 e do quinoxalinil 5. O hidrobrometo de 4-(2-fenoxatiinil)-2-aminotiazol 7 foi obtido através de tratamento com uréia. Alguns sais novos de amônio e fosfônio também foram preparados. Dados espectrais e químicos que comprovam a estrutura dos compostos novos sintetizados são apresentados.

KEYWORD: Phenoxathiin, ammonium salts, thiazole, glyoxime.

INTRODUCTION

Phenacyl-, heteracylhalide respectively are important reagents for organic synthesis which allow access to sulfonium, ammonium, phosphonium or selenonium salts. Starting from these substances, through the respective ylides, various heterocyclic compounds can be obtained [1-9].

The present paper describes the synthesis of some new products based on 2-ω-bromoacetylphenoxathiin according with the scheme 1 and 2 and is part of a systematic research connected with structure-biological activity of compounds of the phenoxathiin class.

EXPERIMENTAL

Melting points were determined in an open capillary and are uncorrected. IR spectra were recorded in KBr pellet with an UR-20 apparatus.

^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Gemini 300 spectrometer using $CDCl_3$, DMSO-d_6 as solvent and TMS as internal standard. MS spectra were performed on JEOL GC mate spectrometer.

Thin layer chromatography (TLC) was performed on plates of silica gel 60-254 (Merck), unidimensional technique. Detection of compounds was done by UV light (λ=254 nm), iodine and sulfuric acid spray.

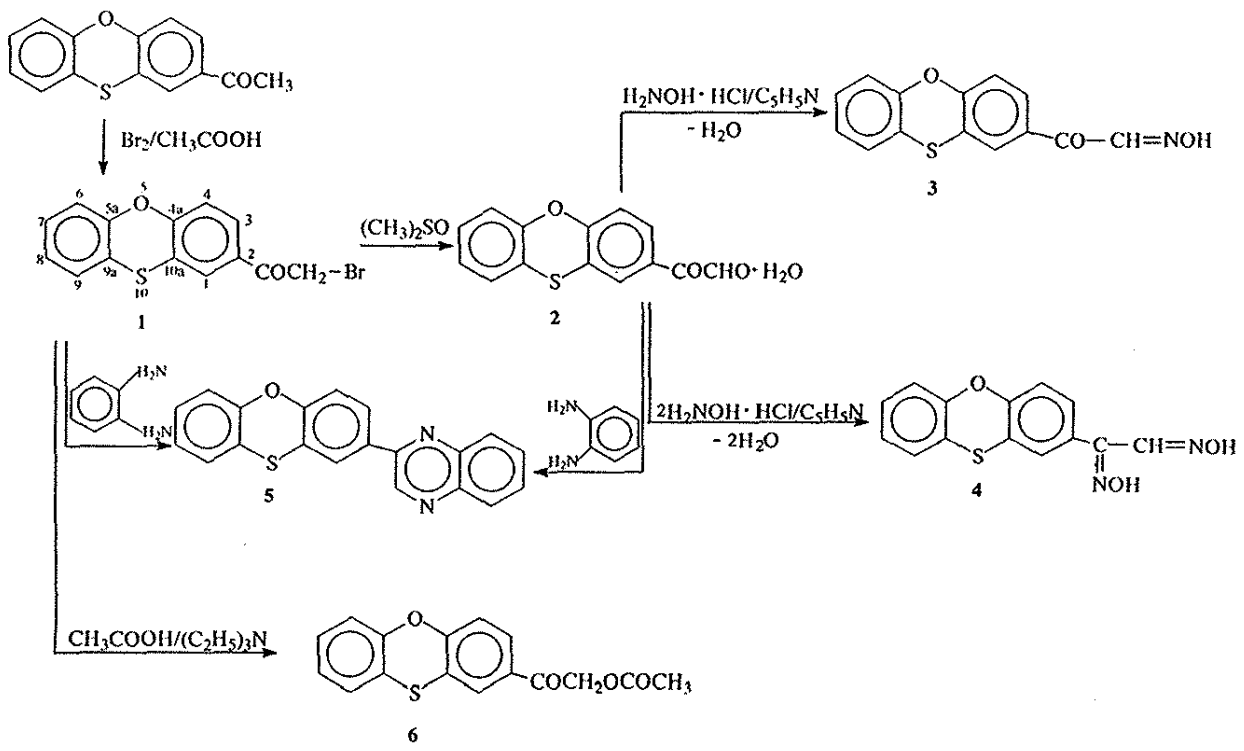
2-ω–Bromoacetylphenoxathiin (**1**):

To a solution of 15 g (0.0062 mole) of 2-acetylphenoxathiin (m.p.=118-119°) in 70 mL glacial acetic acid, 3.2 mL (9.92g; 0.062 mole) of bromine in 30 mL glacial acetic acid were added, under heating at 50-60° and stirring. After cooling , the precipitate was filtered off, washed with water, affording 17.2 g of the compound **1** (86.5%).m.p.=146-147°.

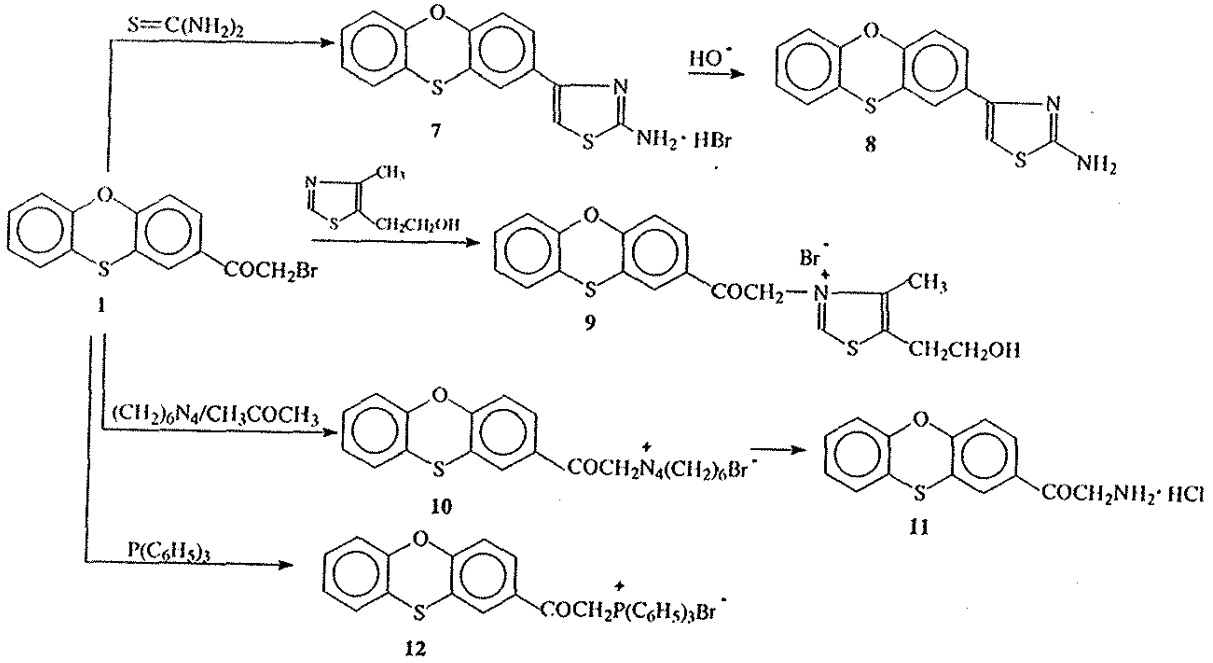
After recrystallisation from glacial acetic acid, yellow crystals with m.p.=147-149° were obtained. For the purified 2-ω-bromoacetylphenoxathiin, the literature indicates the following melting points: 134[10], 128-131[12], 144-145[11].

2-Phenoxathiinylglyoxal hydrate (**2**):

SCHEME 1



SCHEME 2



A mixture of 3 g (0.009 mole) 2-ω-bromoacetylphenoxathiin and 17.5mL dimethyl sulfoxide was heated at 40° up to dissolving . The solution was maintained 72 hours at room temperature and then poured into 100 mL water. The precipitate was filtered off and washed with water. The yield of **2** was about 2.54 g (99.2%) m.p.=117-125°. After recrystallisation from 90% acetic acid m.p.=132-134°.[lit[12] m.p.=130-132°]. TLC: Rf=0.77 (chloroform-methanol 4.5 : 0.5 v/v; detection: sulfuric acid spray - spot violet-red). IR(cm^{-1}): 3400(large bands characteristic to aldehyde hydrate), 1690 (CO), 830(γ_{2CH}), 742(γ_{4CH}); ^{1}H-NMR(DMSO-d_6, δppm): 7.92(d,1H,H-1), 7.91(dd,1H,H-3), 7.26(m,1H,H-9), 7.24(m,1H,H-7), 7.20(d,1H,H-4), 7.12(td,1H,H-8), 7.10(dd,1H,H-6), 6.83(d,2H,OH), 5.61(t,1H,$CH(OH)_2$); ^{13}C-NMR (DMSO-d_6, δppm): 194.22(CO), 154.59(C-4a), 150.36(C-5a), 130.42(C-2), 130.11(C-1), 128.53 (C-7), 128.39(C-3), 127.04(C-9), 125.59(C-8), 119.12 (C-10a), 118.12 (C-9a), 117.82(C-6), 117.63(C-4), 89.57($CH(OH)_2$).

2-Phenoxathiinylglyoxal monoxime (**3**):

To 2 g (0.0073 mole) of 2-phenoxathiinylglyoxal hydrate, 10 mL pyridine and 10 mL methanol, 0.5 g (0,0072 mole) of hydroxylamine hydrochloride were added. The mixture was kept at room temperature for 6 hours, then was poured into ice-water. The precipitate was filtered and 1.42g (71.7%) crystals with m.p.=181-183°, were obtained. After recrystallisation from ethanol m.p.=182.5-186°.TLC: Rf=0.70 (chloroform : methanol 4.5 : 0.5 v/v; detection sulfuric acid spray - violet spot); ^{1}H-NMR(DMSO-d_6,δppm): 12.73(s, 1H, NOH), 8.01(s, 1H, CH), 7.87(d, 1H, H-1), 7.84(dd, 1H, H-3), 7.27(m, 1H, H-9), 7.25(m, 1H, H-7), 7.20(d, 1H, H-4), 7.13(td, 1H, H-8), 7.11(dd, 1H, H-6); ^{13}C-NMR(DMSO-d_6, δppm): 186.56(CO), 154.62(C-4a), 150.28(C-6a), 147.61(CH=NOH), 132.74(C-2), 130.31(C-1), 128.61(C-3), 128.56(C-9), 127.05(C-7), 125.62(C-8), 119.22(C-10a), 117.99(C-9a), 117.83(C-6), 117.58(C-4).

Anal. calcd. for $C_{14}H_9NO_3S$: S, 12.46 , Found: S, 12.13.

2-Phenoxathiinylglyoxal dioxime (**4**):

To a mixture of 1 g (0.0036 mole) of 2-phenoxathiinylglyoxal, 0.7 g (0.01 mole) of hydroxylamine hydrochloride, 14 mL pyridine and 14 mL methanol were added. The reaction mixture was refluxed one hour, then was

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concentrated under low pressure and the obtained residue was poured in water to give 1.03g (99%) of **4**. The dioxime recrystallised from methanol leads to crystals with m.p.=212.5-213.5°. TLC: Rf=0.63 (chloroform-methanol 4.5:0.5 v/v; detection sulfuric acid spray-spot violet bleu); IR(cm^{-1}): 3200-3300, 1450 (OH), 1615 and 950 (C=NOH), 830(γ_{2CH}), 742 (γ_{4CH}); ^{1}H-NMR (DMSO-d_6, δppm): 11.99 and 11.98 (s, 2H, NOH), 7.85 and 8.44(s,1H,-CH=N-), 7.43(d,1H,H-1), 7.41(dd,1H,H-3), 7.26(m,1H,H-9), 7.23(m,1H,H-7), 7.12(m,1H,H-8), 7.11(d,1H,H-4), 7.10(m,1H,H-6); ^{13}C-NMR(DMSO-d_6, δppm): 140.39 and 147.44(-CH=N-), 151.54(C-4a), 150.99(C-5a), 149.44(>C=NOH), 130.81(C-2), 128.44(C-1), 128.38(C-7), 127(C-9), 126.81(C-3), 125.22(C-8), 118.64(C-10a), 118.64(C-9a), 117.73(C-4), 117.20(C-6). MS: 286(M^+).

Anal. calcd. for $C_{14}H_{10}N_2O_3S$: S,11.20; Found S, 10.92.

2-(2'-Quinoxalinyl)phenoxathiin (**5**):

A: According to the literature indications[10], from 0.85g (0.026 mole) of 2-ω-bromoacetylphenoxathiin, 0.866g (99.7%) crystals with m.p.=173-175°, were obtained.

B: o-Phenylendiamine (0.21g, 0.0018 mole) was added to a solution of 2-phenoxathiinylglyoxal(0.51g, 0.0018 mole) in 20 mL ethanol, under heating until a solution was obtained. The mixture was refluxed one hour, maintained at room temperature 24 hours, then filtered off and 0.46g (75.4%) crystal were obtained. m.p.=194-196° [lit[10] m.p.=174°]. Compound was recrystallised from methyl ethyl cetone, m.p.=199-200°. TLC: Rf=0.41 (benzene : ethyl acetate 4.5 : 0.5 v/v ;detection-sulfuric acid spray-spot violet) ; IR(cm^{-1}): 1610(C=N); 1245(C-O-C); 825(γ_{2CH}); 750(γ_{4CH}).

Anal. calcd. for $C_{20}H_{12}N_2OS$: S, 9.76 ; Found S, 9.49.

2-Phenoxatiinylcarbonylmethyl acetate (**6**):

To a mixture of 0.46 mL (0.48g, 0.008 mole,d=1.049) acetic acid, 10 mL dimethylformamide and 1mL (0.73 g.0.007 mole, d=0.726) triethylamine, 1.6 g (0.005 mole) of 2-ω-bromoacetylphenoxathiin were added. The reaction mixture was lightly warm for 5 minutes, and maintained at room temperature for 24 hours. The solid product was filtered off, and water was added to filtrate.

The new precipitate, which was formed, was filtered, washed with water and air-dried to provide **6** (1.29g, 86.6%). This was recrystallised from ethanol to yield a solid, m.p.=132.5-133.5. TLC: Rf=0.68 (chloroform : ethanol 9.5:0.5 - v/v ; detection: sulfuric acid spray- spot dark-red); IR(cm^{-1}): 1750(CO); 1690(CO); 1220(C-O-C); 825(γ_{2CH}); 765(γ_{4CH}); ^{1}H-NMR($CDCl_3$, δppm): 7.63(s, 1H, H-1), 7.61(d, 1H, H-3), 6.94-7.13(m, 5H, H-4 -H-8), 5.23(s, 2H, CH_2), 2.21(s, 3H, CH_3); ^{13}C-NMR($CDCl_3$, δppm): 190.03(CO), 170.23($COOCH_3$), 155.84(C-4a), 150.63(C-5a), 130.56(C-2), 127.94(C-1), 127.68(C-3), 126.62(C-9), 126.48(C-7), 125.11(C-8), 120.81(C-10a), 118.32(C-9a), 117.72(C-6), 117.72(C-4), 65.58(CH_2), 20.43(CH_3);

Anal. calcd. for $C_{16}H_{12}O_4S$; S,10.67; Found S, 10.45.

4-(2-Phenoxathiinyl)-2-aminothiazole hydrobromide (7):

To 0.5 g (0.0015 mole) of 2-ω-bromoacetylphenoxathiin in 20 mL isopropanol, 0.25 g (0.0032 mole) of thioyrea was added and was refluxed for one hour. The precipitate formed on cooling, was filtered off and washed with isopropanol to yield 0.5 g (84.7%) of compound 7. m.p.=273-275°. TLC: Rf=0.12 (petroleum ether : ethyl ether : dichloromethane : ethyl acetate -7.5 : 1 : 2 : 1 -v/v/v/v; detection sulfuric acid spray- spot bleu).

4-(2-Phenoxathiinyl)-2-aminothiazole (**8**):

To 0.25 g (0.00065 mole) of 7 in 3 mL water, 1.2 mL of sodium hydroxide were added until pH=9-10. The obtained precipitate was filtered off and air-dried to give 0.18 g (91.8%) of compound **8** with m.p.=176-177°. TLC: Rf=0.14 (petroleum ether : ethyl ether : methylene chloride ; ethyl acetate 7.5 : 1: 2 : 1 v/v/v/v, detection : sulfuric acid spray- spot light violet); IR(cm^{-1}):3425, 3365, 3275, 1620 (NH_2), 1435,1465 (thiazole nucleus), 830(γ_{2CH}), 745(γ_{4CH}); ^{1}H-NMR(DMSO-d_6, δppm); 7.63(d,1H,H-1), 7.60(dd, 1H,H-3), 7.19-7.25(m,2H,H-7;H-9), 7.07-7.10(m,3H,H-4;H-6;H-8), 7.05(s, 1H,thiazoleH-5), 7.00(s,2H,NH_2); ^{13}C-NMR (DMSO-d_6, δppm):168.25(thiazole C-2), 151.13(C-5a), 150.14(C-4a), 148.17(thiazoleC-4), 132.02(C-2), 128.29(C-9), 127.00(C-1), 125.33(C-7), 125.06(C-3), 123.69(C-8), 119.09(C-10a), 118.81(C-9a), 117.71(C-6), 117.71(C-4), 101.55(thiazoleC-5); MS: 298(M^+);

Anal. calcd. for $C_{15}H_{10}N_2OS_2$: S,21.49; Found S, 21.73.

3-(2-Phenoxathiinylcarbonylmethyl)-5-(2-hydroxyethyl)-4-methylthiazolium bromide (**9**):

To a solution of 0.5 g (0.0015 mole) of 2-ω-bromoacetylphenoxathiin in 10 mL anhydrous toluene , 0.2 mL (0.0017 mole) of 5-(2-hydroxyethyl)-4-methylthiazole were added. The reaction mixture was refluxed 30 minutes. The precipitate formed, on cooling, was filtered off to give the crude compound **9** (0.5g, 70.4%). After recrystallisation from ethanol and trituration with a mixture of dichloromethane - toluene (1:1-v/v), white crystals with m.p.=228-229° were obtained. TLC: Rf=0.33 (butanol : acetic acid : water -4 : 1 :1 v/v/v); detection sulfuric acid spray - spot light violet. IR(cm^{-1}): 3465, 3310 (NH_2), 1472, 1440(thiazole nucleus), 840(γ_{2CH}), 760(γ_{4CH}); ^{1}H-NMR(DMSO-d_6, δppm): 10.15(s, 1H, thiazole H-2); 7.83(m, 2H, H-1;H-3), 7.06(m, 5H, H4;H-6 - H-9), 6.33(s, 2H, $COCH_2$), 3-3.6(m, 4H, CH_2CH_2), 2.25(s, 3H, CH_3);

Anal. calcd. for $C_{20}H_{18}BrNO_3S_2$: S, 13.8; Found S, 14.02.

1-(2-Phenoxathiinylcarbonylmethyl)hexamethylentetraminiu bromide (**10**):

The quaternisation reaction was done by the method used for the synthesis of triethylammonium salt [24], but using anhydrous acetone as a solvent. Yellow crystals with m.p.=187-189° (96.7%) were obtained. TLC: Rf=0.67 (butanol : acetic acid : water; detection: sulfuric acid spray - spot light violet); IR(cm^{-1}): 1685(CO); 1400(CH_2-N<); 1235(C-O-C); 832(γ_{2CH}); 765(γ_{4CH}).

Anal. calcd. for $C_{20}H_{21}BrN_4O_2S$: S, 6.94; Found S, 7.25.

1-(2-Phenoxathiinylcarbonylmethyl)amine hydrochloride (**11**):

A mixture of 3 g (0.0065 mole) of **10**, 5 mL conc. hydrochloric acid and 15 mL ethanol, was stirred at room temperature for 5 hours. After 48 hours, the solvent was removed and the precipitate was filtered off and dried to afford 1.5 g (78.5%) of the compound **11**. m.p.=275-278°(charing). TLC: Rf=0.56 (butanol : acetic acid : water 4:1:1 v/v/v; detection sulfuric acid spray-spot violet); IR(cm^{-1}): 1400(CH_2-N<), 1250(C-O-C), 818(γ_{2CH});

770(γ_{4CH}); ^{1}H-NMR(DMSO-d_6, δppm): 7.90(d, 1H, H-1), 7.85(dd, 1H, H-3), 7.24-7.29(m, 3H, H-4;H-7;H-9), 7.12-7.17(m, 2H, H-6;H-8), 4.55(s, 2H, CH_2), 4.01(s, 3H, $^+NH_3$); ^{13}C-NMR(DMSO-d_6, δ ppm): 182.73(CO), 147.5(C-4a), 142.18(C-5a), 122.51(C-2), 120.79(C-1), 120.58(C-3), 119.32(C-9), 118.9(C-7), 117.7(C-8), 112.4(C-10a), 109.9(C-9a), 109.8(C-6), 109.8(C-4), 38.86(CH_2).

Anal. calcd. for $C_{14}H_{12}ClNO_2S$: S, 10.91; Found : S, 11.17.

1-(2-Phenoxathiinylcarbonylmethyl)triphenylphosphonium bromide **(12)**:

To a solution of 0.25 g (0.0007 mole) of 2-ω-bromoacetylphenoxathiin in 10 mL anhydrous toluene, 0.2 g (0.00076 mole) of triphenylphosphine were added. The reaction mixture was refluxed for 30 minutes and the precipitate formed was filtered off. After drying 0.35 g (79.5%) of the compound **13**, were obtained. m.p.=279-281°-TLC: Rf=0.67 (butanol-acetic acid: water 4:1:1-v/v/v; detection sulfuric acid spray - spot violet intense); IR(cm^{-1}): 3010-3050 (phenyl), 2853, 2910(CH_2), 1660(CO), 1240(C-O-C), 822(γ_{2CH}), 750(γ_{4CH}); ^{1}H-NMR(DMSO-d_6, δ ppm): 7.8-7.9 (m,2H,H-1;H-3), 7.43-7.7(m, 8H, H-4;H-7;H-9 and phenyl), 6.94-7.05(m, 2H, H-6;H-8), 5.73 and 6.11(s, 2H, CH_2).

Anal. calcd. for $C_{32}H_{24}BrPO_2S$: S, 5.49; Found : S, 5.82.

RESULTS AND DISCUSSION

Through bromination in acid medium, 2-acetylphenoxathiin forms the corresponding brominated derivative **1**[10-12]. This compound, subject to the Kornblum oxidation reaction in the presence of dimethyl sulfoxide turns into a glyoxilic derivative **2** with a 99% yield. The literature[13] describes the synthesis of product **2** only through the oxidation of 2-acetylphenoxathiin with selenium dioxide, in the presence of dioxane.

The phenoxathiinylglyoxal **2** was characterized through the monoxime **3** and the corresponding dioxime **4** (scheme 1).

By using the reaction with o-phenylendiamine, product **2** leads to the 2-(2-quinoxalinyl)phenoxathiin **5** with 75.4% yield. The same product was

also obtained from 2-ω-bromoacetylphenoxathiin with o-phenylendiamine with 69.8% yield. These two methods lead to compounds **5** with the same m.p.=199-200°.

The reaction between 2-ω-bromoacetylphenoxathiin with o-phenylendiamine is also described in the literature [10], but the melting points of the product is indicated at 174°. This temperature difference might be explained through the fact that the starting substance used by the authors of the paper[10] , contained traces of 3-acetylphenoxathiin. The presence of this isomer in the 2-acetylphenoxathiin synthesis was recently confirmed[14].

In this synthesis a brominated derivative with m.p.=148-149° obtained from 2-acetylphenoxathiin, having a m.p.=118-119° was used.

The article[10] indicates a m.p.=113° of the brominated derivative (of course contaminated with the isomer from position 3)

Considering the fact that the phenacyl esters are used in the organic synthesis as protective groups of carbonyl, hydroxyl and phenol functions[15-18], the obtaining of such a compound was followed also in the case of 2-ω-bromoacetylphenoxathiin.

Thus by treatment of the brominated derivative **1** with acetic acid in the presence of triethylamine the compound **6** is obtained (scheme 1).

The literature mentioned the antimicrobial activity of certain quaternary ammonium salts based on 2-methyl-3-chloromethylphenoxathiin, towards Gram-positive and Gram-negative germs[19]. Taking into consideration all these factors, these researches was extensioned for the compounds obtained through the quaternisation reaction of 2-ω-bromoacetylphenoxathiin.

The products which were synthesized are indicated in scheme 2. The reaction between 2-ω-bromoacetylphenoxathiin and thiourea leads to compound **7**. Treated with sodium hydroxide solution it turns into 4-(2-phenoxathiinyl)-2-aminothiazole **8.**

A thiazolic derivative **9** is also obtained through the reaction between brominated derivative **1** with 5-(2-hydroxyethyl)-4-methylthiazole.

A quaternary ammonium salt was also synthesized through the reaction between 2-ω-bromoacetylphenoxathiin and hexamethylenetetramine, compound **10** beeing thus synthesized. Reaction of triphenylphosphine with 2-ω-bromoacetylphenoxathiin gives compund **12**.

The synthesized products were characterized by spectral methods (IR, NMR, MS) and their purity was confirmed by thin layer chromatography (TLC).

In the IR spectra of the compounds **1-12**, a series of bands is remarked, characteristic for both the phenoxathiin nucleus and the substituent grafted on the aromatic ring.

For the phenoxathiin nucleus the vibrations at 750-760 cm^{-1} (γ_{4CH}), 810-815 cm^{-1} (γ_{2CH}), 1070-1090 cm^{-1} (ν_{C-S}) and 1210-1240 cm^{-1} (ν_{C-O-C}) are characterized. All these values are according to the literature data [20-23]. In the 1405-1580 cm^{-1} range five bands appear also characteristic for the phenoxathiinic nucleus. Absorption bands of the substituents grafted in the position 2 of the phenoxathiin nucleus were also identified. Thus characteristic for compound **2** is the absorption at 1690 cm^{-1}, assigned to the valence vibrations of the carbonyl group. The lack of this band in the structure of compounds **3** and **4** and the appearance of a band at 1610-1620 cm^{-1}, which characterized the $\nu_{C=N}$ vibration, confirms the oxime structure.

For compound **6**, the ν_{CO} at 1740 cm^{-1} vibration, assigned to the acetoxy group is characteristic.

For compounds **7-9** characteristic bands of the thiazole nucleus (1435-1465 cm^{-1}) and ν_{NH} 3275, 3425 cm^{-1} appear; for the ammonium salts **10-11** the absorption appear at 1400 cm^{-1}.

The main absorption bands which are characteristic of the substances **1-12**, are presented in the experimental part of this paper.

The ^{1}H- and ^{13}C-NMR spectra for the synthesized compounds were also recorded and interpreted, the respective chemical shifts being presented within the experimental part.

The signal assignments were made by comparison to the literature data regarding derivatives series of the 2-substituted phenoxathiin [14].

Analyzing the ^{1}H-NMR spectra for the substances which were synthesized, we found out that the chemical shifts of H_1 and H_3 protons are influenced by the electron-withdrawing effect of the substituents from position 2. In this way a deshielding takes place with the same signals to those for phenoxathiin.

The influences of the substituent in position 2 are much less evident on the H_4 as well as for the protons from the unsubstituted benzene ring. For the methylene group in position 2 in compounds **1**, **6**, **9-12** the resonance signals appears as a singlet in the range δ=4.86-6.33 ppm. For compound **12**, because of the three big volumes of the phenyl groups the both

methylenic protons are no longer equivalent giving signals as singlet at δ=5.73 and 6.11 ppm, while the molecule adopts a rigid conformation.

In the ^{1}H-NMR spectrum of the compound **8** the signal at δ=7.00 ppm is assigned to the two protons from the amino group. This signal disappears when the spectrum is recorded in the presence of D_2O.

For compound **3** the deshielding produced by the functional groups (CO or C=NOH) makes the protons H-1 to appear at lower field at 7.8-7.9 ppm compared to the compound **4** were a normal shielding takes place at approximately Δδ=0.5 ppm.

The multiplicity of the signals shows a *cis*-coupling J_{34}=8.0-9.1 Hz as well as a *meta*-coupling J_{13}=2.0-2.2 Hz, which makes the proton to appear as doublet with the small coupling constant and the H_3 as a doublet of doublets in which the couplings with H-4 and H-1 are found again. The H-4 proton appears at δ=7.1-7.2 ppm as a doublet with J_{43}=8.0-9.1 Hz. When the ketone **3** turns into oxime **4**, the value of this coupling decrease approximately 1Hz.

The protons H-6 - H-9 from the unsubstituted ring appear in the δ=7.1-7.26 ppm range, the most shielding proton being H-6 and the most deshielding being H-9. To assign the proton resonances of these compounds two dimensional experiments (2D), COSY H-H; COSY H-C were made[25].

The proton of the aldehyde group from the glyoxal hydrate **2** appears as a triplet at δ=5.61 ppm with a 7.0 Hz coupling with hydroxyl groups (evinced through the deuteration).

The ^{1}H- and ^{13}C-NMR spectra for the dioxime **4** indicates the presence of the *sin* and *anti* isomers for the oxyminic groups. The following pairs of chemical shifts (δ ppm) appear: 11.87 , 11.56 (NOH); 7.85 (CH=N) and 12.00 , 11.99 (NOH) ; 8.44 (CH=N).

The ^{13}C-NMR spectra confirm the asymetric substitution of the phenoxathiin ring. Generally speaking, the assigments for the unsubstituted ring were revealed by spectra comparison with the derivatives of this class which were previously described[14, 26], as well as through heteronuclear corelation experiments (COSY H-C).

Regarding the antimicrobial activity of the synthesized derivatives, compound **9** is specially remarkable against Gram-positive bacteria.

CONCLUSIONS

Eight new products based on 2-ω-bromoacetylphenoxathiin were synthesised and characterised through mass, IR, NMR (^{1}H- and ^{13}C- at 300 and 100 Mhz) spectra. The purity of the products was confirmed by means of TLC.

Upon the antimicrobial screening an activity of compound **9** against various Gram-positive strains was observed.

REFERENCES

1.N.N.Suronov, Jn.J.Smuschevici, N.N.Marianovskaia and A.V.Sulima, *Khim. Farm. Zh.*, **2**, 10-14 (1970)

2.A.N.Grinev,*Khim.Farm.Zh.*, **5**, 6 (1970)

3.W.W.Lotz and J.Gosselck, *Tetrahedron*, **29**, 917 (1973)

4.D.Gavriliu, S.Stoia and O.Maior, *Rev.Chim.(Buc.)*, **47**, 326-331 (1996)

5.A.V.Samet, A.M.Sestopalov and V.V.Semenov, *Khim.Ghet.Soed.*, **8**, 1136-1139 (1996)

6.L.Jukic, U.Bratusek, M.Skof, J.Svete and B.Stanovnik,*Khim. Ghet.Soed.*, **11/12**, 1510-1514 (1996)

7.R.A.Kuroianov, A.N.Markosian, S.A.Vartanian and D.Z.Partev, *Arm.Khim.J.*, **34**, 603 (1983)

8.J.W.Lown and J.P.Maser,*Chem.Communications*, 247 (1970)

9.I.K.Moiseev, M.N.Zemotova and N.V.Macarova, *Khim.Ghet.Soed.*, **7**, 247 (1994)

10.E.Lescot, N.Ph.Buu-Hoi and N.D.Xuong, *J.Chem.Soc.*, 2408-2411 (1956)

11.G.Vasiliu and O.Maior,*Anal.Univ.Bucharest*, **XIII(1)**, 103-111 (1964)

12.H.Dehne and V. Mass, *Ztf. Chem.*, **28**, 296-298 (1988)

13.E.L.Anderson,*U.S. 3,117,121 / 7 Ian. 1964*, C.A. 1964, **61**, 666 (1964)

14.S.Florea, H.O.Kalinovski, O.Maior and D.Gavriliu,*Polish J. Chem.*, **70**, 36-40 (1996)

15.J.C.Sheehan and K.Umezewa, *J.Org.Chem.*, **38**, 3771-3773 (1973)

16.H.D.Durst, *Tetrahedron Letters*, **28**, 2421-2424 (1974)

17.M.Bodanszky and J.Martinez, *J.Org.Chem.*, **43**, 3071-3073 (1978)

18.C.C.Yang and R.B.Merrifield, *J.Org.Chem.*, **41**,1032-1040 (1976)

19.O.Maior,*Rev.Chim.(Buc.)*, **20**(12), 593-595 (1969)

20.H.Mantsch and O.Maior, *Rev.Roum.Chimie* , **10**(11), 1245-1253 (1965)

21.N.Marziano, G.Montaudo and R.Passerini, *Ann.Chim.(Ital.),* **52,** 121-125 (1962)

22.A.R.Katrizki and A.P.Ambler, *Physical Methods in Heterocyclic Chemistry-Infrared Spectra*, 2nd edition Academic Press, New York, N.Y., USA 1963, pp. 161

23.K.J. Sacs, W.S.Saari, C.L.Mohoney and I.M.Gordan, *J.Org.Chem,* **25**, 1590-1592 (1960)

24.D.Gavriliu, S.Stoia, S.Florea and O.Maior, *Anal. Univ. Bucharest*, **VI** pp. 105-112 (1997)

25.R.R.Ernst, G. Bodenhausen and A.Wokoum, *Principles of Nuclear Magnetic Resonance One and Two Dimensions,* Oxfords University Press, Oxford, England, 1990

26.R.R.Klein,P.D.N.Svoronos and C.F.Hammer, *J.Chem.Educ.,* **66**, 870-872 (1989)

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PHENOXATHIIN CHEMISTRY. NEW CARBONYL COMPOUNDS AND DERIVATIVES

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ABSTRACT

Starting with 2-acetylphenoxathiin , 2-ω-bromoacetylphenoxathiinyl-10,10-dioxide **2** was obtained. By means of the Kornblum reaction the corresponding glyoxal **4** was synthesized. From compound **2**, the aminothiazole **3** and the 1,4-diketone **7** were also obtained. By the reaction of 2-ω-bromoacetylphenoxathiin **8** and sodium acetylacetonate "one pot" synthesis of 1,4-diketone **9** was performed. Compound **9** was converted to pyrrolophenoxathiin **11** and 1,4-diketone **7**. Starting with the brominated derivative **8** the aminoketones **12** and **13** were obtained. The new compounds were caracterised by spectral methods (^{1}H- and ^{13}C-NMR, IR, MS).

RESUMO

O composto 2-ω-bromoacetilfenoxatiinil-10,10-dioóxido 2 foi obtido a partir de 2-acetilfenoxatiina. Usando a reação de Kornblum, o glioxal correspondente 4 foi sintetizado. A partir do composto 2 foram obtidos o aminotiazol 3 e a dicetona 7. A síntese da dicetona 9 foi obtida reagindo 2-ω-bromoacetilfenoxatiina 8 com acetilacetonato de sódio. O composto 9 foi convertido para a pirolofenoxatiina 11 e a 1,4-dicetona 7. As aminocetonas 12 e 13 foram obtidas a partir do derivado bromado 8. Os novos compostos foram caracterizados usando métodos espectroscópicos (ressonância magnética nuclear de ^{1}H e ^{13}C, infravermelho e espectrometria de massa).

KEYWORD: Phenoxathiin, 1,4-Diketones, Oximes, α-Bromoketones

INTRODUCTION

Phenoxathiin and its derivatives have been the subject of continnous research because of their multiple uses and because of multiple theoretical problems related to the reactivity of this class of heterocyclic compounds [1-8].

This paper describes the synthesis of carbonyl derivatives based on 2-acetylphenoxathiin as shown in Schemes 1 and 2. Through the action of oxidizing agents (hydrogen peroxide in acetic acid [9], chromic acid [10,11], potassium permanganate[12] or peracetic acid [12]) on the phenoxathiin nucleus the corresponding 10-oxide or 10,10-dioxide are formed.

EXPERIMENTAL PART

Melting points were determined in an open capillary and are uncorrected . IR spectra were recorded in KBr pellet with an UV-20 apparatus. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Gemini 300 spectrometer using $CDCl_3$, DMSO-d_6 as solvent and TMS as internal standard. MS spectra were performed on JEOL GCmate spectrometer.

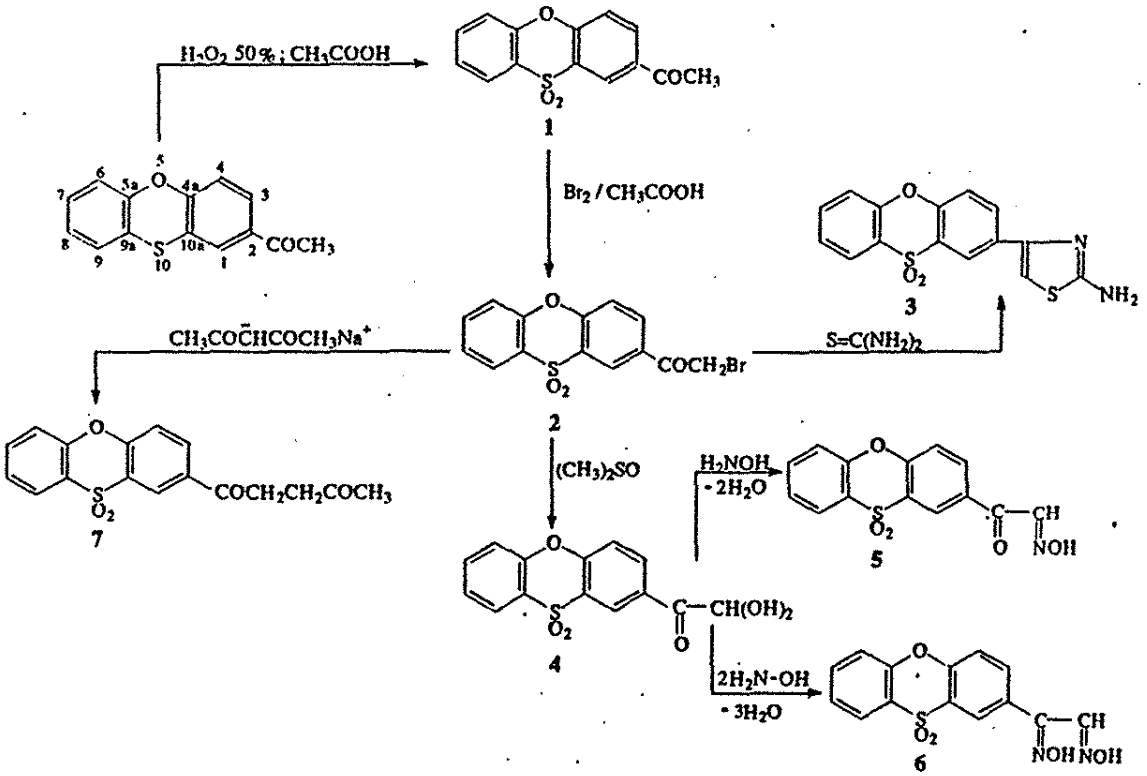
Thin layer chromatography (TLC) was performed on plates of silica gel 60-254 (Merck), unidimenssional technique. Detection of compounds was done by UV light (λ 254 nm), iodine and sulfuric acid spray.

2-Acetylphenoxathiin-10,10-dioxide **1** and 2-ω-bromoacetylphenoxathiin **8** were obtained according to references [18] and [19] respectively.

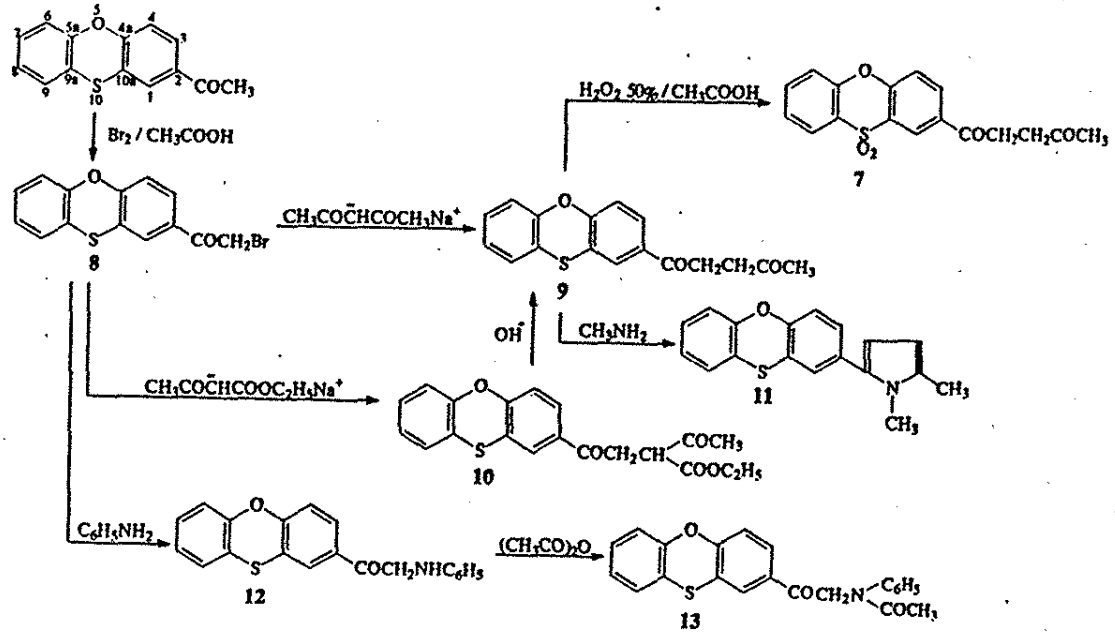
2-ω-Bromoacetylphenoxathiinyl -10,10-dioxide (**2**):

To a heated solution (40-50°) of 10 g (0.036 mole) 2-acetylphenoxathiin-10,10-dioxide in 160 mL glacial acetic acid, 1.9 mL(5.89g; 0.037 mole) bromine in 50 mL glacial acetic acid was added. The solid was filtered after 24 hours, washed with water and dried to give the compound **2** (10.3 g, 79.9%) with m.p. 198-199°. TLC: Rf 0.72 (chloroform : methanol-

SCHEME 1



SCHEME 2



4.5 : 0.5- v/v ; Detection iodine vapors); IR(cm^{-1}): 1700(νCO); 1285, 1140, 560(SO_2); 1210(νC-O-C); 860(γ2CH); 755(γ4CH) (phenoxathiin nucleus). ^{1}H-NMR(DMSO-d_6, δppm): 8.61(s, 1H, H-1); 8.35(d, 1H, H-3); 8.11(d,1H, H-9) ; 7.85(t, 1H, H-7); 7.74(d, 1H, H-4); 7.63(d, 1H, H-6); 7.58(t, 1H, H-8) 5.05(s, 2H, CH_2); ^{13}C-NMR(DMSO-$_6$; δppm): 189.58(CO); 154.02(C-4a); 150.50(C-5a); 135.45(C-3); 134.80(C-7); 130.96(C-2); 126.25(C-1); 124.72(C-8); 124.72(C-10a); 124.34(C-9a); 123.14(C-9); 120.16(C-4); 119.35(C-6); 33.9(CH_2).

Anal. Calcd. for $C_{14}H_9BrO_4S$: S, 9.12; Found: S, 9.26.

4-(2-Phenoxathiinyl-10,10-dioxide)-2-aminothiazole (**3**):

A mixture of 0.5 g (0.0014 mole) 2-ω- bromoacetylphenoxathiin-10,10-dioxide, 0.15 g (0.0019 mole) thiourea and 30 mL anhydrous isopropanol was refluxed on a water bath during an hour. The resulting precipitate was filtered and suspended in 8 mL of water. A solution of 8% sodium hydroxide was added up to pH 9-10. The solid was filtered off and dried giving 0.35 g (76%) of **3** with m.p. 294-296°. TLC: Rf 0.09 (petroleum ether : ethyl ether : dichloromethane : ethyl acetate - 7.5 : 1 : 2 : 1 - v/v/v/v. Detection: iodine vapors). IR (cm^{-1}): 3425, 3375, 3280 (νNH$_2$); 1623, 1470, 1430 (thiazole nucleus); 1280, 1150, 560(SO_2); 1230(νC-O-C); 832(γ2CH); 748(γ4CH) (phenoxathiin nucleus); ^{1}H-NMR(DMSO-d_6; δppm):8.41(d, 1H, H-1); 8.20(dd, 1H, H-3); 8.08(d, 1H, H-9); 7.82(t, 1H, H-7); 7.60(d, 1H, H-4); 7.59(d, 1H, H-6); 7.54(t, 1H, H-8); 7.28(s, 1H, CH-thiazole); 7.20(s, 2H, NH_2); ^{13}C-NMR(DMSO-d_6; δppm): 168.61(thiazole C-2); 150.81(C-5a); 149.57(C-4a); 147.00(thiazole C-4); 135.06(C-2); 132.18(C-7); 131.50(C-3); 125.58(C-8); 124.43(C-1); 124.19(C-10a); 123.04(C-9a); 119.47(C-9); 119.13(C-6); 119.13(C-4); 103.28(thiazole C-5); MS: m/z 330 (M^+, 100%).

Anal. Calcd. for $C_{15}H_{10}N_2S_2O_3$: S, 19.41; Found: S,19.75.

2-(2-Phenoxathiinyl-10,10-dioxide)-glyoxal hydrate (**4**):

A solution of 5 g (0.014 mole) 2-ω- bromoacetylphenoxathiin-10,10-dioxide in 30 mL dimethyl sulfoxide was obtained by heating to 50°. The mixture was maintained for 48 hours at room temperature, then was poured in water. The resulting solid was filtered. The yield was 4.3 g (99.9%) of compound **4**.

Crystals with m.p. 128.5-129.5° were formed by recrystallization from an ethanol-water mixture (1:3 -v/v). TLC: Rf 0.74 (chloroform : methanol-4.5 : 0.5 - v/v; Detection: iodine vapors). IR(cm^{-1}): 3400(νOH); 1700(νCO); 1300, 1160, 555(SO_2); 1275(νC-O-C); 815(γ2CH); 755(γ4CH) (phenoxathiin nucleus)). ^{1}H-NMR(DMSO-d_6, δppm): 8.72(s, 1H, H-1); 8.38(d, 1H, H-3); 8.09(d, 1H, H-9); 7.83(t, 1H, H-7); 7.71(d, 1H, H-4); 7.63(d, 1H, H-6); 7.57(t, 1H, H-8); 7.40 (d, 2H, OH); 5.48 (t, 1H, CH); ^{13}C-NMR (DMSO-d_6, δppm): 192.15(CO); 154.00(C-4a); 150.76(C-5a); 135.51(C-7); 135.51(C-3); 130.30(C-2); 126.30(C-8); 125.51(C-1); 124.56(C-10a); 124.52(C-9a); 123.24(C-9); 119.91(C-4); 119.46(C-6); 96.15 ($CH(OH)_2$).

Anal. Calcd. for $C_{14}H_{10}O_6S$: S, 10.46; Found: S, 10.58

2-(2-Phenoxathiinyl-10,10-dioxide)glyoxal monoxime (**5**):

To 1.1 g (0.0036 mole) of 2-(2-phenoxathiinyl-10,10-dioxide)glyoxal hydrate, 0.25 g (0.0036 mole) hydroxylamine hydrochloride, 6 mL pyridine and 6 mL methanol were added. The mixture was maintained at room temperature for 24 hours and then was poured in ice-water. The precipitate was removed by filtration, washed by water and dried. The yield of product **5** was 0.9 g (82.6 %) with m.p. 165-166°. After four recrystallization from ethanol m.p.186-187° (des.). TLC: Rf 0.69 (chloroform : methanol - 4.5 : 0.5 - v/v; Detection: iodine vapors); IR(cm^{-1}): 1640(νCO); 1230(νC-O-C); 1290, 1155, 515(SO_2); 860(γ2CH); 755(γ4CH) (phenoxathiin nucleus). ^{1}H-NMR(DMSO-d_6; δppm): 8.70(d, 1H, H-1); 8.32(dd, 1H, H-3); 8.09(dd, 1H, H-9); 8.00(s, 1H, CH); 7.85(m, 1H, H-7); 7.71(d, 1H, H-4); 7.62(dd, 1H, H-6); 7.60(m, 1H, H-8); ^{13}C-NMR(DMSO-d_6; δppm): 186.10(CO); 153.53(C-4a); 150.45(C-5a); 148.19(CH=NOH); 135.50(C-3); 135.33(C-7); 132.50(C-2); 126.11(C-8); 125.61(C-1); 124.20(C-10a); 124.06(C-9a); 123.05(C-9); 119.64(C-4); 119.28(C-6).

Anal. Calcd. for $C_{14}H_9O_5NS$: S, 10.57 ; Found: S, 10.61

2-(2-Phenoxathiinyl-10,10-dioxide)glyoxal dioxime (**6**):

To 1.1 g (0.0036 mole) of 2-(2-phenoxathiinyl-10,10-dioxide)glyoxal hydrate were added 0.7 g (0.01 mole) hydroxylamine hydrochloride, 14 mL pyridine and 14 mL methanol. The mixture was refluxed for 2 hours, then cooled off and poured in water. The resulting solid was filtered after 24

hours. After drying 0.91g (79.6%) of compound **5** was obtained, m.p. 204-205°.

Recrystallization from a mixture of ethanol and water (1 : 3 - v/v) gave the compound **6**. m.p. 209-210°. TLC: Rf 0.54 (chloroform : methanol - 4.5 : 0.5 - v/v; Detection: iodine vapors); IR(cm^{-1}): 1590(νC=NOH); 1225(νC-O-C); 1280,1155,520(SO_2); 870(γ2CH); 720(γ4CH) (phenoxathiin nucleus); ^{1}H-NMR(DMSO-d_6; δppm): 11.99 and 11.98 (s, 2H, NOH); 8.25(d, 1H, H-1); 8.09(dd, 1H, H-9); 8.04(dd, 1H, H-3); 7.94(s, 1H, CH); 7.86(m, 1H, H-7); 7.66(d, 1H, H-4); 7.64 (dd, 1H, H-6); 7.56(m, 1H, H-8); ^{13}C-NMR (DMSO-d_6; δppm): 150.77(C-4a); 150.65(C-5a); 148.60 (C=NOH); 147.42 (CH=NOH); 135.21(C-7); 136.00(C-3); 131.10(C-2); 125.79(C-8); 124.36(C-9a); 123.99(C-10a); 123.60(C-1); 123.04(C-9); 119.20(C-6); 118.64(C-4). MS: m/z 318(M^+, 25%).

Anal. Calcd. for $C_{14}H_{10}N_2O_5S$: S, 10.07 ; Found: S, 10.12.

2-[2-(Phenoxathiinyl-10,10-dioxide)carbonyl]ethyl methyl ketone (7):

A. A mixture of 0.97g (0.0027 mole) 2-ω-bromoacetylphenoxathiin-10,10-dioxide, 0.86g (0.007 mole) sodium acetylacetonate and 10 mL anhydrous ethanol was lightly heated during 15 minutes, then poured in water(Note 1). The precipitate was filtered and 0.6 g (66.7%) of compound **7** were obtained. m.p. 145-146°.

Note 1: Any increased of reaction time and strong heating may result in a decrease of the reaction yield.

B. To 0.6 g (0.002 mole) of compound **9** dissolved in 5 mL glacial acetic acid, 1 mL of 50% hydrogen peroxide were added, upon heating, then after 30 minutes another 1 mL 50% hydrogen peroxide was added. The mixture was refluxed for 90 minutes, then was cooled and the precipitate was filtered off. The yield of compound **7** was 0.45 g (68.2%) with m.p. 144-146° (Note 1).

Note 1: If water was added to the filtrate 0.1 g further product was obtained.

2-[2'-(Phenoxathiinyl-10,10-dioxide)carbonyl]ethyl methyl ketone recrystallized from methanol lead to crystals with m.p. 146-147°.TLC: Rf 0.17 (benzene : ethylacetate - 9 : 1 - v/v); IR(cm^{-1}): 1715(νCOCH$_3$); 1685(νCO); 1300, 1150, 565(SO_2); 1275(νC-O-C); 840(γ2CH); 765(γ4CH) (phenoxathiin nucleus).

Anal. Calcd. for $C_{17}H_{14}O_5S$: S, 9.70; Found: S, 9.48.

2-(2-Phenoxathiinylcarbonyl)ethyl methyl ketone (**9**):

A. A mixture of 3.49 g (0.011 mole) 2-ω- bromoacetylphenoxathiin, 3.46 g (0.028 mole) sodium acetylacetonate (Note 1) and 20 mL anhydrous ethanol were refluxed for 30 minutes, then cooled off. The solid was filtered and 3.18 g (98.15%) of product **9** with m.p. 121-122° were obtained.

Note 1: Sodium acetylacetonate was obtained according to reference [16].

B. To 0.55 g (0.0015 mole) of product **10,** 2.5 mL 4% sodium hydroxide was added. The mixture was boiled for 50 minutes. After cooling for 30 minutes at room temperature the solid was filtered and washed with 0.5 mL 12N sulfuric acid. The yield of diketone **9** was 0.14 g (31.8%).

2-(2-Phenoxathiinylcarbonyl)ethyl methyl ketone recrystallized from acetone had the m.p. 126-127°. TLC: Rf 0.33 (Benzene : ethyl acetate - 9:1 - v/v; Detection:sulfuric acid spray - red-violet spot); IR(cm^{-1}):1701(νCOCH$_3$); 1680(νCO); 1270(νC-O-C); 820(γ2CH); 750(γ4CH) (phenoxathiin nucleus); ^{1}H-NMR(DMSO-d_6; δppm): 7.81(d, 1H, H-1); 7.78(dd, 1H, H-3); 7.20-7.26(m, 2H, H-7 and H-9); 7.15(d, 1H, H-4); 7.08-7.13(m, 2H, H-6 and H-8); 3.14 and 2.76(-CH_2-); 2.13(CH_3); ^{13}C-NMR(DMSO-d_6, δppm): 207.02($COCH_3$); 196.65(CO); 154.49(C-4a); 150.32(C-5a); 133.34(C-2); 128.48(C-1); 128.41(C-3); 127.01(C-9); 126.90(C-7); 125.53(C-8); 119.49(C-10a); 118.12(C-9a): 117.77(C-4); 117.70(C-6); 36.6 and 32.01(-CH_2-); 29.65(CH_3); MS: m/z 298 (M^+, 60%).

Anal. Calcd. for $C_{17}H_{14}O_3S$: S, 10.74; Found: S,10.51.

2-(2-Phenoxathiinylcarbonyl)-1-(ethoxycarbonyl)ethyl methyl ketone (**10**):

A mixture consisting of 1.16 g (0.0036 mole) 2-ω- bromoacetyl-phenoxathiin, 1.44 g sodium ethylacetoacetate (Note 1) was lightly heated up to dissolving and further heated for another 5 minutes. A white precipitate was formed which was filtered and the solution was thoroughly cooled. The resulting precipitate was filtered and 0.87 g (65.1%) of compound **9** were obtained with m.p. 88-93° (Note 1).

Note 1 : The sodium ethylacetoacetate was obtained according to reference [20].

Compound **10** recrystallized from anhydrous ethanol has the m.p. 93-94°. TLC: Rf 0.15 (benzene : ethyl acetate - 9 : 1 - v/v; Detection: sulfuric acid spray - blue spot); IR(cm^{-1}): 1735($\nu COOC_2H_5$); 1710($\nu COCH_3$); 1670(νCO); 1275($\nu C\text{-}O\text{-}C$); 815($\gamma 2CH$); 752($\gamma 4CH$) (phenoxathiin nucleus); ^{1}H-NMR (DMSO-d_6; δppm): 7.9(s, 1H, H-1); 7.73(d, 1H, H-3); 7.1-6.96(m, 5H, H-4 - H-9); 4.23(q, 2H, CH_2); 4.11(t, 1H, CH); 3.43(d, 2H, CH_2); 2.36(s, 3H, CH_3); 1.3(t, 3H, CH_3);

Anal. Calcd. for $C_{20}H_{18}O_5S$: S,8.65; Found: S, 8.82.

1,5-Dimethyl-2-(2-phenoxathiinyl)-pyrrole (**11**):

A mixture consisting of 0.75 g (0.0025 mole) diketone **9** and 4 mL ethanol was lightly heated until clearing of the solution after which 4 mL of 30% methylamine and 4 mL ethanol were added. The mixture was heated during 30 minutes at 75-80°, then kept at room temperature for 12 hours. The resulting solid was filtered and 0.72 g (97.3%) of compound **11** with m.p. 113-114° was obtained. The product recrystallized from ethanol has a m.p. 116-117°. TLC: Rf 0.70 (benzene : ethylacetate -9 : 1 -v/v); IR(cm^{-1}): 3450 (νNH_2); 1220($\nu C\text{-}O\text{-}C$); 830($\gamma 2CH$); 755($\gamma 4CH$) (phenoxathiin nucleus); MS: m/z 293(M^+, 100%).

Anal. Calcd. for $C_{18}H_{15}NOS$: S, 10.92; Found: S, 10.76.

2-ω- Anilinoacetylphenoxathiin (**12**):

To 1.62 g (0.005 mole) of 2-ω-bromoacetylphenoxathiin and 10 mL anhydrous ethanol, 1mL (1.07 g; 0.01 mole) of aniline was added. The mixture was stirred at room temperature for 24 hours, then refluxed for 15 minutes. After cooling the mixture was poured in water. The solid was filtered and 1.6 g (95.24%) of compound **12** with m.p. 165-170° was obtained.

The product recrystallised from ethanol led to crystals with m.p. 174-175°. TLC: Rf 0.60(benzene : ethyl acetate - 9 : 1 - v/v; Detection: sulfuric acid spray - violet spot); IR(cm^{-1}): 3380(νNH_2); 1680(νCO); 1270($\nu C\text{-}O\text{-}C$); 820($\gamma 2CH$); 749($\gamma 4CH$) (phenoxathiin nucleus). ^{1}H-NMR(DMSO-d_6; δppm): 7.95(s, 1H, H-1); 7.88(d, 1H, H-3); 7.27-7.18(m, 3H, H-4, H-7 and

H-9); 7.13-7.06(m, 2H, H-6 and H-8); 7.04(t, 2H, H^{metha}-aniline); 6.66(d, 2H, H^{ortho}-aniline); 6.54(t, 1H, H^{para}-aniline); 4.60 (d, 2H, CH_2); 4.35(s, 1H, NH); ^{13}C-NMR(DMSO-d_6; δppm): 194.89(CO); 154.73(C-4a); 150.31(C-5a); 148.01 (C^1-aniline); 131.98(C-2); 128.77(C^{metha}-aniline); 128.53(C-1); 128.44(C-3); 127.05(C-9); 127.02(C-7); 125.59(C-8); 119.60(C-10a); 118.08(C-9a); 117.81(C-6); 117.81(C-4); 116.16(C^{para}-aniline); 112.47(C^{ortho}-aniline); 49.76(CH_2); MS: m/z 333(M^+, 40%).

Anal. Calcd. for $C_{20}H_{15}O_2SN$: S, 9.61; Found: S, 9.40.

2-(ω-N-Acetylanilino)acetylphenoxathiin (**13**):

A mixture of 0.7 g (0.002 mole) of compound **12** and 10 mL acetic anhydride was heated for 4 hours, then maintained at room temperature for 24 hours. The reaction mixture was poured in water and the solid was filtered off and washed with water. The yield was 0.65 g (82.5%) of compound **13**. After recrystallization from acetic acid crystals with m.p. 182-183° were obtained. TLC: Rf 0.15 (benzene : ethyl acetate - 9:1 - v/v ; Detection: sulfuric acid spray - green spot) IR(cm^{-1}): 1690(νCOCH$_3$); 1650(νCO); 1270(νC-O-C); 830(γ2CH); 760(γ4CH) (phenoxathiin nucleus). ^{1}H-NMR(DMSO-d_6; δppm): 7.9(s, 1H, H-1); 7.76(d, 1H, H-3); 7.1-6.96(m, 5H, H-4 - H-9); 7.20-7.00(m, 5H, aniline); 5.08(s, 2H, CH_2); 2.00(s, 1H, CH_3).

Anal. Calcd. for $C_{22}H_{17}NO_2S$: S, 8.91; Found: S, 8.72.

RESULTS AND DISCUSSION

By oxidizing reaction with hydrogen peroxide in acetic acid on 2-acetylphenoxathiin, the corresponding 10,10-dioxide product **1** is obtained (see Scheme 1).

By bromination of compound **1** in acetic acid, 2-ω-bromoacetylphenoxathiin-10,10-dioxide, **2,** is formed.

The brominated derivative is the starting material in the synthesis of compound **3** (through its reaction with thiourea) and upon the Kornblum oxidizing reaction with dimethyl sulfoxide to dicarbonylic compound **4** is obtained which has been characterized by oximes **5** and **6**.

2-ω-Bromoacetylphenoxathiin-10,10-dioxide has been used for the synthesis of a substituted 1,4-diketone **7** (Scheme 1).

The same compound has been also obtained from 2-ω-bromoacetylphenoxathiin **8** (Scheme 2).

The reaction occurs in two steps. The diketone **9** is initially obtained which, oxidized with 50% hydrogen peroxide, turns into compound **7** . The literature described the use of acetylacetone in a two steps synthesis of the $R\text{-}CH_2CH_2COCH_3$ type ketone through an alkylation - splitting method [14,15]. Product **9** has been directly synthesized with sodium acetylacetonate in ethanol medium according to reference [16] applied to phenetyl ketones. This derivative oxidized with hydrogen peroxide turns into compound **7**. Another way for obtaining compound **9** is the reaction between 2-ω-bromoacetylphenoxathiin with sodium ethylacetoacetate when compound **10** is formed . The latter in an alkaline medium turns in substituted 1,4 diketone **9**. The synthesis of derivative **9** has been performe because of the well-known importance of 1,4-diketones which are often used as intermediates for the preparation of heterocycles. Thus, the synthesis of a derivative with a pyrrolic nucleus was performed by the action of methylamine on 1,4-diketonic compound **9** according to the Paal-Knorr reaction [17] resulting in substance **11**.

Substance **12** was obtained from 2-ω-bromoacetylphenoxathiin with aniline in alcohol medium. This compound by treating with acetic anhydride turns into the corresponding acetyl derivative **13**.

The synthesized products were characterized by mass spectrometry, IR and NMR spectra, while purity was confirmed by TLC. The main absorption bands and chemical shifts for the synthesized compounds, as well as the Rf values are presented in the experimental section of the paper.

CONCLUSIONS

Ten new compounds of the phenoxathiin class were synthesized and characterised by chemical and physico-chemical methods.

The "one pot" synthesis of the 1,4-diketones **7** and **9** from the corresponding ω-bromoketones and sodium acetoacetonate was described.

By the Kornblum reaction the glyoxal **4** was synthesized and from this compound the mono- and dioximes **5** and **6** were obtained.

Using methylamine, compound **9** and the Paal-Knorr reaction, the pyrrolophenoxathiin **11** was synthesized.

REFERENCES

1. J.P.Linduske and F.A.Morton, *J.Econ.Entomol.*, **41**, 43 (1948); Chem. Abstr. **42**, 6048 (1948).
2. W. Reifshneider, *U.S.A. 3.299.098* (1967); Chem. Abstr. **66**, 95056 (1967).
3. L.R.Rudnich, N.C.Rowe, D.A. Law and G.A.Naghipur, *U.S.A. 5.286.396* (1994); Chem. Abstr. **120,** 303137 (1994).
4. V.Antony, *Eur. Pat. Appl.EP. 270252* (1988); Chem. Abstr. **110**, 39009 (1989).
5. F.A.Lehmann, *Germ. Pat. 1.078.839* (1960); Chem. Abstr. **55**, 16232 (1961).
6. D.Gavriliu and O.Maior, *Anal. Univ.Craiova*, **1**, 103-109 (1995).
7. R.M.Norton, H.L.White and B.R.Cooper, *Drug Dev.. Res.*, **25(3)**, 229 (1992); Chem. Abstr. **116**, 247858 (1992).
8. E.D.Savin, V.I. Nedelkin, D.V.Zverev, *Khim. Ghet. Soed.*, **3,** 392-296,(1997).
9. H. Gilman and D.L.Esmay, *J.Amer.Chem.Soc.*,**74,** 2021-2024 (1952).
10. F. Mauthner, *Chem. Ber.*, **39**, 1340-1347 (1906).
11. M.Tomita and T.Ikeda, *J.Pharm.Soc.Japan,* **58**, 780 (1938).
12. H.K. Drew, *J.Chem.Soc.*, 511-524 (1928).
13. O.Maior and E.Cohn, *Rev. Chim. (Bucharest)*, **15**, 358-359 (1964).
14. S.Boatman, T.M.Harris and C.R.Hauser, *J.Org.Chem.*, **30,** 3321-3324 (1965).
15. A.W.Johnson, E.Markham and R.Price, *Org. Synth.*, **42**, 75-76 (1962).
16. A.Nicolae, O.Maior and A.Paun, *Rev. Chim. (Bucharest)*, **45**, 361-367 (1994).
17. O.Maior, A.Nicolae, S.Florea, *Reactii nominalizate in chimia organica*, Ed. Briliant-Bucuresti, Romania. 1996, pp 231.
18. O.Maior, *Anal. Univ. Buc.*, **XIV(2),** 105-111 (1965).
19. A.Nicolae, D.Gavriliu, O.Maior and C.Draghici, *South. Braz. J. Chem.* in press.
20. E.Jung. and J.Schindewahn, *Germ. Pat.* 2.336.394 (1974).

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THE PREPARATION AND SOME REACTION OF 2,2-DIPHENYL-1-(3,6-DINITRO-4-COUMARINYL) HYDRAZYL FREE RADICAL.

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ABSTRACT

The new persistent 2,2-diphenyl-1-(3,6-dinitro-4-coumarinyl)hydrazyl free radical **4** was obtained by potassium permanganate or lead dioxide oxidation of the corresponding 2,2-diphenyl-1-(3,6-dinitro-4-coumarinyl)hydrazine **3**; hydrazine **3** reacts with nitrous acid to give successively the 2-(p-nitrophenyl)-2-phenyl-1-(3,6-dinitro-4-coumarinyl) hydrazine **6** and 2,2-(p-nitrophenyl)-1-(3,6-dinitro-4-coumarinyl) hydrazine 7. Compound **6** rezults also from free radical **4** and sodium nitrite in the presence of 15-C-5 crown ether. The structure of new compounds was confirmed by means of TLC,UV-Vis,^{1}H-NMR, IR and for the free radicals by the EPR spectra.

RESUMO

O novo radical livre estável 2,2-difenil-1-(3,6-dinitro-4-cumarinil)hidrazila 4 foi obtido pela oxidação da 2,2-difenil-1-(3,6-dinitro-4-cumarinil) hidrazina correspondente 3 com permanganato de potássio ou dióxido de chumbo. A hidrazina 3 reage sucessivamente com ácido nitroso para formar a 2-(p-nitrofenil)-2-fenil-1-(3,6-dinitro-4-cumarinil) hidrazina 6 e a 2,2-(p-nitrofenil)-1-(3,6-dinitro-4-cumarinil) hidrazina 7. O composto 6 também é formado pelo radical livre 4 e nitrito de sódio na presença do éter de coroa 15-C-5. A estrutura dos novos compostos foi confirmada por meio de cromatografia em camada delgada, ultravioleta, infravermelho, RMN de ^{1}H e de espectra de ressonância paramagnética de elétrons.

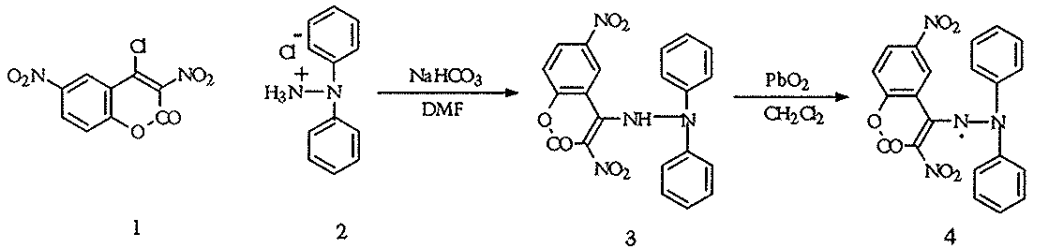
KEYWORDS : Free Radicals, Nitro-Coumarins, Diphenylhydrazines, Crown ethers.

INTRODUCTION

The first persistent free radical of hydrazyl type 2,2-diphenyl-1-picrylhydrazyl (DPPH·) was synthesized by Goldschmidt and Renn [1] in 1922.

The interest of scientists for this substance and its analogues continues to recive attention due to their implications in diverse acid-base or redox proceses (the generation or scavenger the short life radical species), aplications in analytical chemistry,etc.[2-8]

In this paper we report the synthesis of an new hydrazyl-type free radical where the picryl moiety from DPPH· was substituted with a heterocyclic ring, the 3,6-dinitrocoumarinyl respectively in order to investigate its chemical reactivity. It involves the reaction of 3,6-dinitro-4-chloro-2H-1-benzopyran-2-one[9] **1** with 1,1-diphenyl-hydrazin hydrochloride[10] **2** in the presence of an excess of $NaHCO_3$, in DMF or ethanol,, to give 2,2-diphenyl-1-(3,6-dinitro-4-coumarinyl)hydrazin **3** (DPCH). This compound in the presence of PbO_2 or $KMnO_4$ suspended in dichloromethane or anhydrous acetone respectively, is transformed in 2,2-diphenyl-1-(3,6-dinitro-4-coumarinyl)hydrazyl 4 free radical (DPCH·).



1 2 3 4

EXPERIMENTAL

Melting points (uncorrected) were determined in open capillary. IR spectra were recorded in KBr pellet with an UR-20 apparatus. Thin-layer chromatography (TLC) was realized on silica gel Merck plates. Unidimensional technique and visualisation was done with iodine.The EPR spectra were recorded at room temperature on a JES-3B(JEOL) spectrometer with 100 kHz field modulation using the X-band frequency.The parameter of the EPR spectra were measured and compared with those of Fremy's salt (a_N= 13.0 G).UV-Vis spectral determination were performed with a Specord UV-Vis spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian Gemini-300 MHz instrument in DMSO-d_6

2,2-Diphenyl-1-(3,6-dinitro-4-coumarinyl) hidrazine **3**

To 0.81 g (3 mmol) 3,6-dinitro-4-chloro-2H-1-benzopyran-2-one **1** in 8 mL DMF, 0.78 g (3.5 mmol) 1,1-diphenylhydrazine hydrochloride **2** and 0.63 g (7 mmol) $NaHCO_3$ were added and the reaction mixture was stirred at room temperature for two hours.The mixture was poured into 150 mL water.The precipitate was filtered off, washed with water and dried.The crude product (1.03 g 82.4 %) was recrystallized from ethanol or methanol to give yellow crystals with m.p. 170-171°. TLC R_f 0.63 (toluene-ethyl acetate 7:3 v/v). The substitution in this reaction, the DMF with ethanol or isopropanol, lowered yield and a more impure product was obtained. UV-Vis.(CH_2Cl_2) λ_{max} 344 nm (log ε = 3.94) ; in basic medium (treatment of CH_2Cl_2 solution with 0.01 M NaOH in methanol) the corresponding salt **5** has λ_{max} 444 nm (log ε = 4.00) . IR (KBr cm^{-1}) 3255 (NH) 1730,1690 (CO) 1610 (C=C) 1545,1350 (NO_2); ^{1}H-NMR (δ ppm): 11.56(s,1H,N-H); 9.48(d,1H;5;J_{57}=2.39)8.56(dd,1H;H-7;J_{75}=2.33);7.71(d,1H;H-8;J_{87}=9.21);7.38(t,4H;H-11,H-13,H-17,H-19);7.17(m,6H;H-10,H-12,H-14,H-16,H-18,H-20). ^{13}C-NMR(DMSO, δ ppm): 155.27(C=O); 112.86(C-3); 143.92(C-4); 116.60(C-4a); 121.04(C-5); 144.04 (C-6); 128.33(C-7); 119.10(C-8); 154.85(C-8a); 145.52(2C,C-9,C-15); 119.99(4C, C-10,C-14,C-16,C-20); 129.01(4C,C-11,C-13,C-17,C-19); 124.51(2C,C-12,C-8). Anal.Calcd.for $C_{21}H_{14}O_6N_4$(418.37)found:N,13.2(calcd.N,13.38)

2,2-Diphenyl-1-(3,6-dinitro-4-coumarinyl)hydrazyl free radical **4**

Ten milligrams (0.024 mmol) of compound **3** were oxidized by stirring in 20 mL anhydrous dichloromethane or anhydrous acetone solution with an excess of $KMnO_4$ (0.1 g 0.63 mmol) or PbO_2. The color of the reaction mixture changed from yellow to violet. Inorganic compounds were then filtered off.The filtrate is adequately stable for physical measurements or some chemical reactions. EPR spectra (Fig.1) UV-Vis (CH_2Cl_2) λ_{max} 515 nm.The violet solution of free radical **4** passes easily to hydrazine **3** (evinced by TLC) by stirring it for five minutes with 5 % aqueous ascorbic acid.

2-(p-Nitrophenyl)-2-phenyl -1-(3,6-dinitro-4-coumarinyl) hydrazyne **6**

Method A. To 0.2 g (0.48 mmol) **3** in 75 mL dichloromethane were added 1 g (14.5 mmol) of sodium nitrite.Then were added with stirring durring five minutes at room temperature 75 mL HCl 1 M . The organic layer was washed with water and dried over anhydrous sodium sulphate.The solvent was removed and 0.16 g (72.7 %) **6** crude product results. After preparative TLC or recrystallization from 7:3 toluene / ethyl acetate the yelow-brown product has m.p. 165-166°. TLC R_f 0.18 (CH_2Cl_2 - ethanol 9.5 : 0.5). UV-Vis (CH_2Cl_2) λ_{max} 308 nm (log ε = 4.03). In basic medium the corresponding salt, λ_{max} 435 nm (log ε = 4.20). IR (KBr cm^{-1}) : 3240 (NH) 1710 (CO) 1615 (C=C) 1540, 1350 (NO_2). ^{1}H-NMR (δ ppm) 11.42(s,1H,N-H);7.75-9.52(m,3H,H-5,H-7,H-8); 7.2-7.56(m,9H,H-10,H-11,H-13,H-14,H-16,H-17,H-18,H-19,H-20).
Anal.Calcd.for $C_{21}H_{13}O_8N_5$(463.37) found:N,14.9(calcd.N,15.10)

Method B. To a solution of **4** free radical in dichloromethane, obtained from 20 mg (0.048 mmol) compound **3**, 100 mg (0.45 mmol) 15-C-5 crown ether and 80 mg (1.16 mmol) sodium nitrite were added. After two hours of stirring at room temperature (the colour changed to redish-brown) the reaction mixture was filtered. The filtrate was washed with water and with HCl 1 M and then dried over anhydrous sodium sulphate. The TLC and UV-Vis analysis proved the presence of compound **6**.

2,2- (p-Nitrophenyl)- 1 - (3,6-dinitro-4-coumarinyl) hydrazine **7**

To 0.2 g (0.48 mmol) compound **3** in 75 mL dichloromethane were added 75 mL HCl 1 M. Then were added in portions, with stirring, during a period of two hours 1.5 g (21.74 mmol) of sodium nitrite. The stirring was continued at room temperature for 24 hours.The dichloromethane layer was separated, washed with water and dried over anhydrous sodium sulphate. The solvent was removed and 0.2 g (83.3 %) **7** were obtained. After crystallization from ethanol, the yellow product had m.p. 204-205°. TLC R_f 0.09 (CH_2Cl_2 - ethanol 9.5 : 0.5).
UV-Vis (CH_2Cl_2) λ_{max}356 nm (log ε = 3.57). In basic medium the corresponding salt, λ_{max} 459 nm (log ε = 3.70). IR (KBr cm^{-1}) : 3260 (NH) 1695 (CO) 1620 (C=C) 1530, 1345 (NO_2). ^{1}H-NMR(δ ppm):11.39(s,1H;N-H);9.29(d,1H;H-5;J_{57}=1.8);8.54(dd,1H;H-7;J_{78}=9;J_{75}=1.9);7.84(d,1H;H-8;J_{87}=8.90);7.18(d,4H,H-10,H-14,H-16,H-20;J=7.92); 8.5(d,4H,H-11,H-13,H-17,H-19;J=7.92).
Anal.Calcd.for $C_{21}H_{12}O_{10}N_6$(508.37) found:N,16.21 (calcd.N,16.52).

Oxidation of compounds **6** *and* **7** *to the corresponding free radicals* **8** *and* **9**.

The 2- (p-nitrophenyl) - 2 - phenyl -1 - (3,6 -dinitro -4 -coumarinyl) hydrazyl free radical **8** and 2,2 - (p - nitrophenyl) - 1 - (3,6 - dinitrocoumarinyl) hydrazyl free radical **9**, was synthesised from corresponding hydrazines **6** and **7** with $KMnO_4$ or PbO_2 as described for the preparation of free radical **4**. EPR spectra (Fig.1) UV-Vis (CH_2Cl_2) λ_{max} 507 nm for **8** and λ_{max} 502 for the free radical **9** .

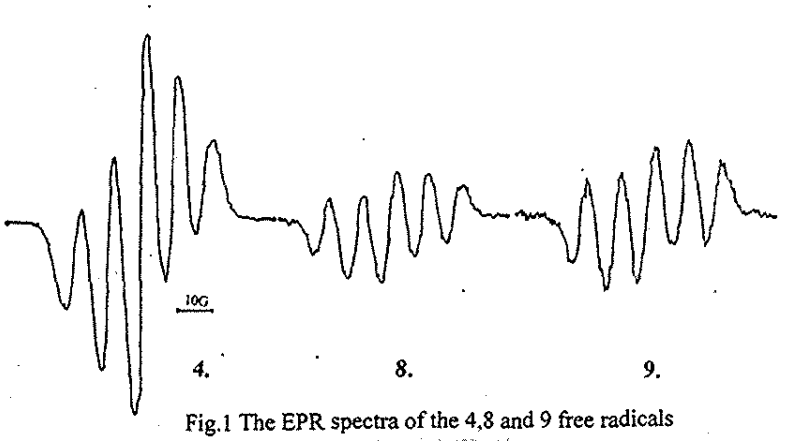
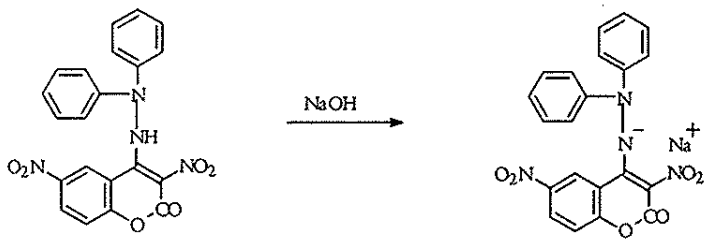


Fig.1 The EPR spectra of the 4,8 and 9 free radicals

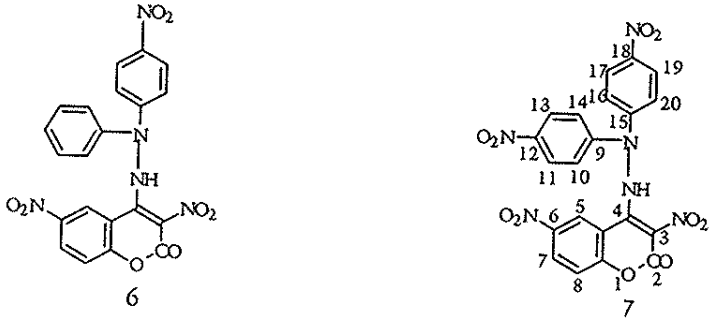
RESULTS AND DISCUSSION

2,2-Diphenyl-1-(3,6-dinitro-4-coumarinyl)hydrazyl free radical is stable in solution for 24 hours ; it was not obtained in solid state and the characteristic violet colour for the radical solution in dichloromethane (λ_{max} 515 nm) slowly became yelow-brown, losing its EPR signal. The EPR spectrum is similar with DPPH· (5 lines $a_{N(2)}$ = 9.0 G). DPCH· passes easily to hydrazine **3** (λ_{max}. 344 nm) by stirring it with an aqueous ascorbic acid solution. The hydrazinic hydrogen in **3** shows an acid character (especialy influenced by -NO_2 group from position 3 in the coumarinic ring) confirmed by reaction with alkaline hydroxide in ethanol (the same behaviour like DPPH)[11,12]



3 5

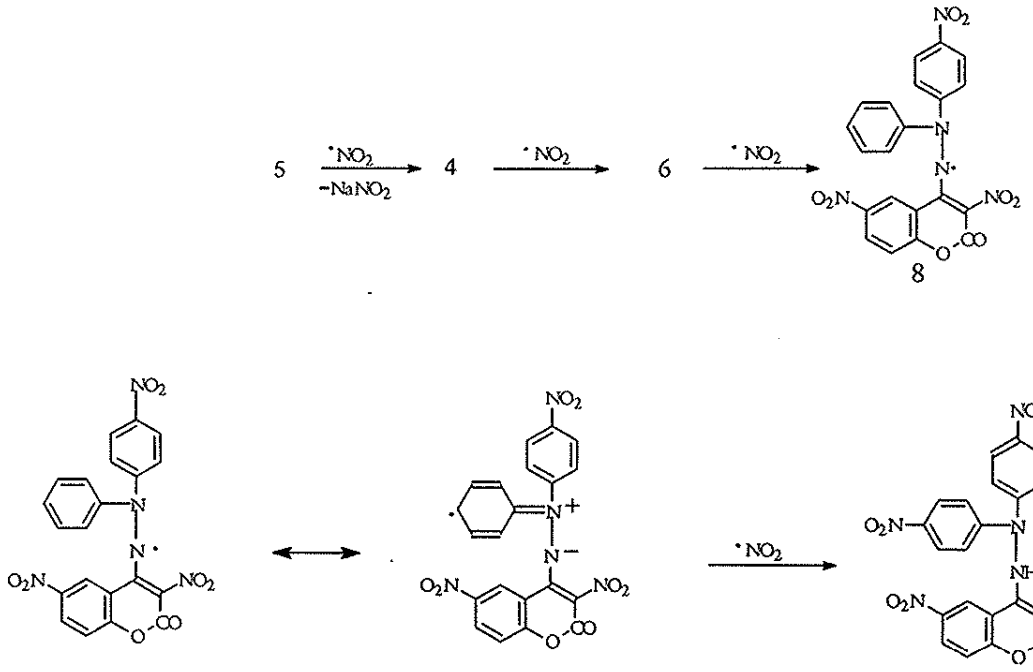
The reaction is accompanied by the colour change of the reaction mixture from yellow (λ_{max}.in dichloromethane, 344 nm) to red (λ_{max} 444 nm), corresponding to salt **5**. Similarly to DPPH [8,13], the ·NO_2 radical reacts with **3** or **4** to give a tri and tetranitro hydrazines mixture **6** and **7**, which were separated by TLC and identified :



6 7

Their oxidation with PbO_2 or $KMnO_4$ leads to the corresponding free radicals confirmed "in situ" by EPR.(Fig.1)

The substances **6** and **7** were also obtained from dichloromethane solution of salt **5**, by NO_2 bubbling that leads first to compound **4**, which traps NO_2 in excess giving the corresponding substituted nitrohydrazines :



DPCH· is a good radical scavenger.The reaction of DPCH· or the corresponding hydrazine DPCH with sodium nitrite in the presence of 15-C-5 crown ether affords the selective formation of 2-phenyl-2-(p-nitrophenyl)-1-(3,6-dinitro-4-coumarinyl) hydrazine **6**.The mecanism may by represented as follows :

i) The electron transfer reaction :

$$DPCH^{\cdot} + NO_2^- \rightarrow DPCH^- + {}^{\cdot}NO_2$$

Due to DPCH· **4** high hydrophobicity, it is necessary to transport the nitrite anion from the solid phase to organic phase (CH_2Cl_2) as a supramolecular complex $(15\text{-C-5...Na})^+NO_2^-$ consequently :

$$NaNO_2 + 15\text{-C-5} \rightarrow (15\text{-C-5...Na})^+ NO_2^-$$

ii) The persistent free radical **4** reacts with the supramolecular complex yielding the nitro free radical ·NO_2 :

$$\mathbf{4} + (15\text{-C-5...Na})^+ NO_2^- \rightarrow (15\text{-C-5...Na})^+DPCH^- + {}^{\cdot}NO_2$$

iii) The nitro free radical generated in this way, is trapped by the excess of radical **4** forming compound **6** :

$$\mathbf{4} + {}^{\cdot}NO_2 \rightarrow \mathbf{6}$$

2-(p-Nitrophenyl)-2-phenyl-1-(3,6-dinitrocoumarinyl)hydrazine **6** was confirmed by TLC, and after the separation and oxidation,the presence of the corresponding free

radical **8** was proved by EPR " in situ". A similar behaviour was also observed for DPPH[14].

The compounds **6** and **7** can be prepared also from **3** with nitrous acid at the room temperature. The reaction proceeds if sodium nitrite is added to the biphasic system containing **3** dissolved in dichloromethane and dilute hydrochloric acid (aqueous phase). After shaking well for 5 min. compound **6** is formed (yield 70 %).A larger contact time (24 h stirring) yields substance **7** (yield about 70 %). This method is simple and efficient for the selective synthesis of the compounds **6** and **7** respectively. Nitrous acid generated in this reaction probably cames form nitrogen oxides. Nitrogen dioxide will be generated *via* oxidation the hydrazyl radicals which finally will go to compounds **6** and **7** respectively. In conclusion, DPCH can participate both in proton and electron transfer reactions depending of the reaction partners. Compounds **3, 6** and **7** have acid character and show different distributions in the biphasic system water - organic solvent, depending on aqueous state pH. The extraction yields of compounds **3, 6** and **7** in buffered aqueous solution / dichloromethane 1:1 (v/v)- obtained in the dichloromethane phase are given as massic percent :

Compounds	pH 7	pH 9	pH 11 (Titrisol Merck)
3	0	8	44
6	0	53	81
7	63	87	95

It can be observed that the extractions are more efficient at high pH and the yields increase with increasing acidity of the hydrazine derivative, (due to additional nitro groups) the order being **3** < **6** < **7**

CONCLUSIONS

The hydrazines **3, 6** and **7** were synthesised and characterised by TLC, UV-Vis, IR, ^{1}H-NMR and EPR (after oxidation to the corresponding hydrazyl-free radicals).

The substitution of the picryl-moiety by 3,6-dinitrocoumarinyl one affords hydrazines with same chemical behaviour but the corresponding free radicals are less stable, having shorter life-times comparing to DPPH$^{\cdot}$

Of the set of hydrazyl free radicals described here, the unsubstituted one DPCH$^{\cdot}$, appears to be the most stable.

The syntheses of mono and dinitro derivatives of DPCH involved interphase processes with NO_2 as homolytical reagent.

REFERENCES

1. S.Goldschmidt and K.Ren, *Ber.*, **55**, 628 (1922)
2. A.R. Forrester, S.M. Hay and R.H. Thomsar "Organic Chemistry of Stable Free Radical", Academic Press, New York, N.Y., USA, 1968
3. M.M.Chen, A.F.D'adamo and R.I.Walter, *J.Org.Chem.*,**26**,2721 (1961)
4. W.W.Parish, P.Statt and M.Mc.Constand, *J.Org.Chem.*,**43**,4577 (1978)
5. P.F.Currie, J.W.Quail, A.C.Rusk and J.A.Weil, *Can.J.Chem.*,**61**,1760 (1983)
6. K.C.Brown and J.A.Weil, *Can.J.Chem.*,**64**, 1836 (1986)
7. P.Ionita, T.Constantinescu, N.Caldararu, C.Luca,M.T.Caproiu and A.T.Balaban *New.J.Chem.*, **21**,511 (1977)
8. L.Gille, U.Prosch and R.Stroesser, *Radiat.Phys.Chem.*,**40**, 461 (1992)
9. M.Kules, M.Trkovnik and A.Juric, *Acta Pharm.Jugosl.*,**34**, 81 (1984)
10. R.H.Poirier, E.J.Kahler and F.Benington, *J.Org.Chem.*,**17**, 1437 (1952)
11. C.Luca, P.Ionita and T.Constantinescu, *Rev.Roum.Chim.*,**39**, 1141 (1994)
12. J.A.Weil and G.A.Jansonis, *J.Org.Chem..*,**27**, 1248 (1962)
13. J.A.Weil, K.V.Sane and J.M.Kinkadl, *J.Phys.Chem.*,**65**, 710 (1961)
14. C.Luca, P.Ionita, T.Constantinescu and M.T.Caproiu.,*Rev.Roum.Chim.*-in press.

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FORMATION OF MICELLES OF CETYLTRIMETHYLAMMONIUM BROMIDE IN WATER-GLYCEROL SOLUTIONS

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ABSTRACT

The micellization of cetyltrimethylammonium bromide (CTAB), in glycerol and aqueous solutions of glycerol was studied by means of surface tensiometry. The critical micellar concentration (CMC) was determined at 25 °C and 40 °C and thermodynamic parameters such as the free energy of micellization (ΔG^{o}_{mic}), enthalpy (ΔH^{o}_{mic}) and entropy (ΔS^{o}_{mic}) of micellization were also measured. At 40 °C, CTAB forms micelles in pure glycerol and in the entire range of water-glycerol solutions. For 25 °C, the CMC ranged from 9.2 x 10^{-4} M in pure water to 8.5 x 10^{-3} M for solutions containing 90% glycerol by volume. The corresponding values obtained for ΔG^{o}_{mic} were -4.14 and -2.82 kcal/mole; for ΔH^{o}_{mic} were -1.03 kcal/mole and -3.73 kcal/mole and for ΔS^{o}_{mic} were +10.43 and -3.10 e.u. Addition of glycerol decreases the spontaneity of micelles formation of CTAB in water.

RESUMO:

O processo de micelização do brometo de cetiltrimetilamônio (CTAB) em glicerol e soluções aquosas de glicerol foi estudado por métodos de tensiometria superficial. A concentração micelar crítica (CMC) foi determinada a 25 °C e 40 °C e parâmetros termodinâmicos tais como a energia livre (ΔG^{o}_{mic}) de micelização, entalpia (ΔH^{o}_{mic}) e entropia (ΔS^{o}_{mic}) de micelização também foram medidos. A uma temperatura de 40 °C, CTAB forma micelas em glicerol puro e na faixa inteira de soluções aquosas de glicerol. Para 25 °C, a CMC variou de 9,2 x 10^{-4} M em água pura até 8,50 x 10^{-3} M para soluções aquosas contendo 90% de glicerol por volume. Os valores correspondentes obtidos para ΔG^{o}_{mic} foram -4,14 kcal/mole e -2,82 kcal/mole; com ΔH^{o}_{mic} = -1,03 kcal/mole e -3,73 kcal/mole e com ΔS^{o}_{mic} = +10,43 e -3,10 e.u., respectivamente. A adição de glicerol diminuiu a espontaneidade do processo de micelização de CTAB em água.

KEYWORDS: Micellization, Cetyltrimethylammonium Bromide (CTAB), Critical Micellar Concentration, Glycerol, Water-Glycerol Solutions.

INTRODUCTION

As a part of our systematic study of the process of micellization in non-aqueous solvents and water solutions containing various cosolvent or additives[1-16], we have also investigated the formation of micelles of the surfactant cetyltrimethylammonium bromide (CTAB) in pure glycerol and water solutions containing glycerol.

The subject of the effect of cosolvents on micelle formation has been originally treated by Ray and Nemethy[17-19] and has been reviewed in the literature[11,20];

Glycerol and ethylene glycol form intra- and intermolecular hydrogen bonds. Experimental studies involving various techniques, including NMR, for aqueous solutions of glycerol and ethylene glycol have shown the existence of intra- and intermolecular hydrogen bonding and have indicated that the hydrogen bonds between either one of the two and water are stronger than those among themselves[21-23].

Both have been employed in protein conformation studies and as simple membrane simulators. Being dense liquids, they approximate portion of membranes in terms of their anhydrous environment. Glycerol has been used as a viscous agent in the construction of media close to the intracellular environment during the investigation of the allosteric enzyme glycogen phospharylase b[24]. Reactivation effects by glycerol and ethylene glycol of inactivated δ-aminolevulinic acid synthetase were reported. It was indicated that the protein conformation around the pyridoxal 5'-phosphate binding site of synthetase was stabilized by the two polyprotic alcohols[25].

EXPERIMENTAL PROCEDURE

The glycerol used was analytical reagent grade supplied by Merck do Brasil S.A., Rio de Janeiro. It was employed without any additional treatment or purification. Cetyltrimethylammonium bromide, $CH_3(CH_2)_{15}N^+(CH_3)_3\ Br^-$ (CTAB), was purchased from Aldrich Chemical Company, Milwaukee, Wisconsin, USA. It was recrystallized twice from ethyl alcohol and dried under vacuum for two days. Deionized distilled water was used for the preparation of all the solutions.

All solutions were prepared volumetrically at the following percentages by volume of glycerol: 0.00; 10.0; 20.0; 30.0; 40.0; 50.0; 60.0; 70.0; 80.0; 90.0 and 100%. All of them containing at least fifteen different concentrations of CTAB. The surface tension of the water-CTAB-glycerol solutions was measured at 25 °C, 40 °C and sometimes 32 °C by means of a Fisher Model 21, Semi-Automatic Tensiometer. Ten milliliters aliquots of the solutions were placed in a Petri dish with a diameter of 6 cm. The temperature of the solutions was brought to the chosen temperature using a water bath and the Petri dish was kept at the desired temperature by placing it in a container through which water was circulated from the constant temperature bath. The tensiometer was set a constant height. The final surface tension of any solution was the average of at least three independent measurements.

The critical micellar concentrations (CMC's) were determined from plots of the concentration of the surface tension of the solutions versus the concentration or the logarithm of the concentration of CTAB. The marked change in the plots was taken as an indication of micelle formation and the inflection point was considered to correspond to the CMC.

The thermodynamic parameters ΔG°_{mic}, ΔH°_{mic} and ΔS°_{mic} were determined using standard equations[26,27] derived on the basis of the assumption that the process of micellization involves the

formation of a distinct micellar phase at the CMC and that the concentration of monomers in solution is constant, once micelles are formed. The experimental accuracy in the values determined for ΔG°_{mic} is about ± 100 cal/mole. On the other hand, ΔH°_{mic} and ΔS°_{mic} are more approximate since they were calculated on the basis of measurements at two or three temperatures only.

RESULTS AND DISCUSSION

Some typical experimental results obtained for the surface tension of CTAB in water-glycerol solutions at 25 °C are illustrated in Figure 1.

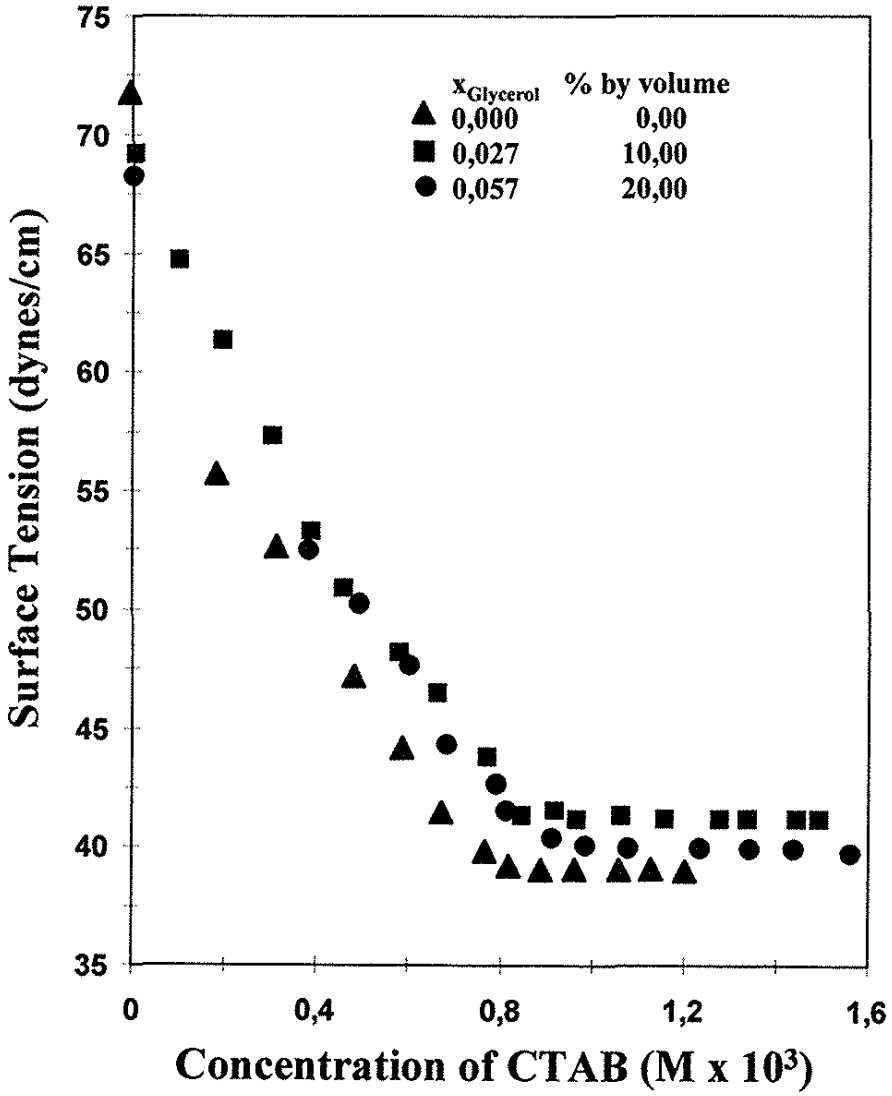

Figure 1. Plot of Surface Tension versus Concentration of Cetyltrymethylammonium Bromide (CTAB) for the Water-CTAB-Glycerol System at 25 °C.

All plots of surface tension versus the concentration of CTAB exhibited initial marked drops and subsequent leveled off. The inflection point in the given curve was taken as the CMC. At times, plots of surface tension versus the logarithm of the concentration of surfactant gave a better determination for the CMC. Results similar to those of Figure 1 were obtained for the entire range of water-glycerol solutions at 25 °C, 32 °C and 40 °C. A summary of the CMC's determined is given in Table I.

Table I. Critical Micellar Concentration (CMC) of Cetyltrimethylammonium Bromide (CTAB) in Aqueous Solutions of Glycerol

Percent of Glycerol by Volume (% vol.)	Mole Fraction of Glycerol (x_G)	CMC at 25 °C ($M \times 10^3$)	CMC at 40 °C ($M \times 10^3$)
0.00	0.000	0,92	1.00
10.0	0.027	0,98	1.15
20.0	0.057	1.10	1.25
30.0	0.095	1.23	1.45
40.0	0.142	1.50	1.90
50.0	0.197	1.90	2.50
60.0	0.270	2.50	3.70
70.0	0.366	3.50	5.20
80.0	0.498	6.00	8.50
90.0	0.687	8.50	11.50
100.0	1.000	*	18.00

* Surfactant precipitates.

The dependence of the critical micellar concentration of CTAB on the percent by volume and the mole fraction of glycerol at two temperatures is given in Figures 2 and 3, respectively.

The experimental values obtained for the thermodynamic functions, i.e., the standard free energy of micellization, ΔG°_{mic}, the enthalpy, ΔH°_{mic} and the standard entropy of micellization, ΔS°_{mic}, at 25 °C and 40 °C are given in Tables II and III. The results obtained at 25 °C are also illustrated in Figure 4.

The experimental results shown in Table I and Figure 2 indicate that the critical micellar concentration (CMC) increases with the rise in temperature. However, a strict thermodynamic analysis (Tables II and III) shows that the free energy of micellization is more negative at 40 °C, indicating that micelle formation is somewhat more favored by the slight increase in temperature. The critical micellar concentration is known to frequently depend on temperature, but in many cases the dependence is highly irregular. The nature of this effect is hard to predict because it depends on a series of factors related to the restructuring of water and the interactions between water and the surfactant. For example, in the case of N-alkylbetaines in water (C_{10} and C_{11}) the CMC decreases, reaches a minimum and then increases as a function of temperatures and for N-alkylbetaines (C_{12}) the CMC increases as a function of temperature[28,29]. For the case

Water-CTAB-Glycerol system interactions between water and glycerol and the surfactant must also be taken in consideration.

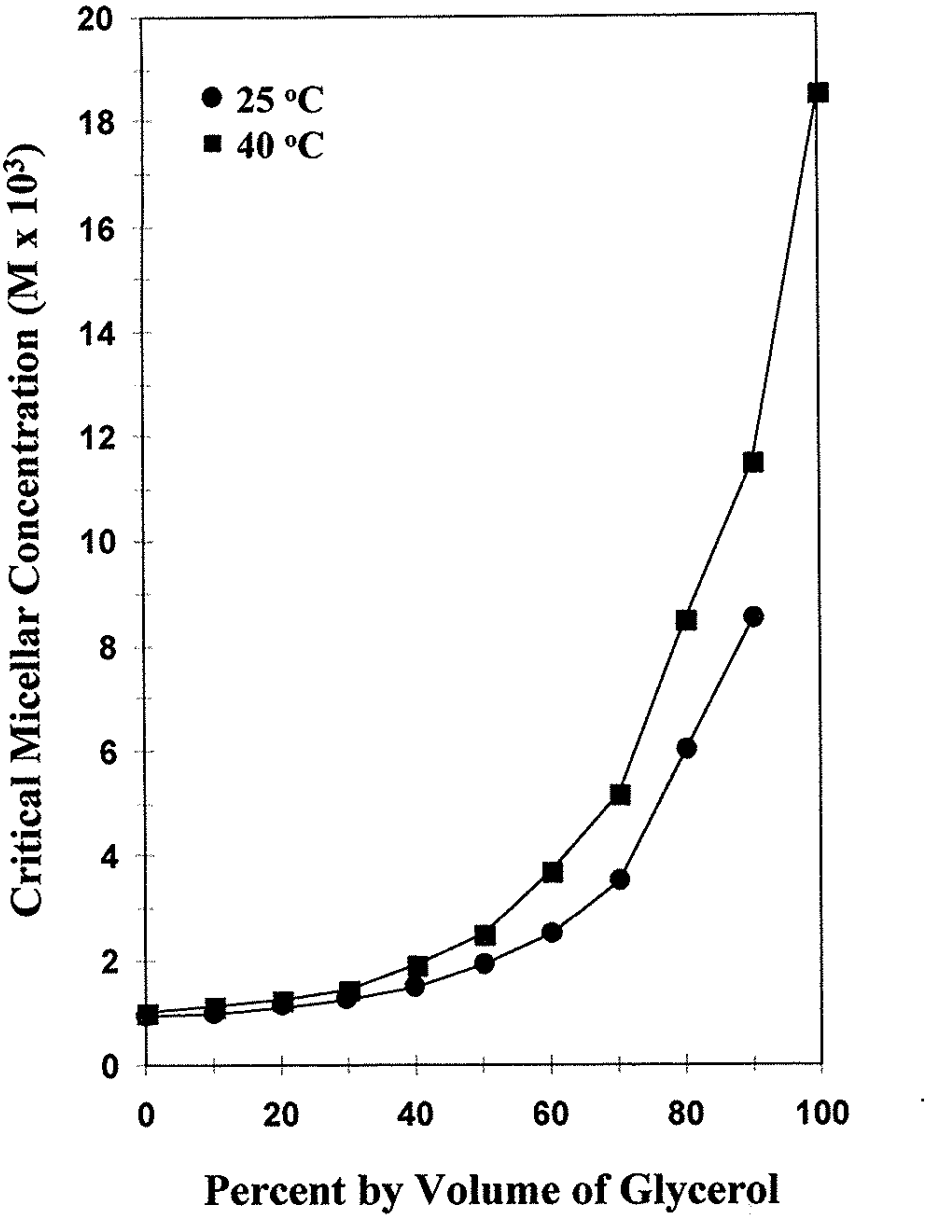

Figure 2. Dependence of the Critical Micellar Concentration of Cetyltrymethylammonium Bromide (CTAB) on the Percent by Volume of Glycerol for the Water-CTAB-Glycerol System.

The thermodynamic parameters shown in Tables II and III do not sort out the different types of interactions (water-surfactant, water-glycerol and glycerol-surfactant) as they were determined using equations derived for the micellization process in water[11]. In a wider sense, without starting

out water-cosolvent and surfactant-cosolvent interactions, the micellization process can be explained in terms of hydrophobic interactions and the break up of the water structure. Higher temperatures, on one hand, help disrupt the water structure, and on the other hand diminish hydrophobic interactions. At lower temperatures the effect is exactly the contrary. The net result is the balancing of two effects in the temperature range used.

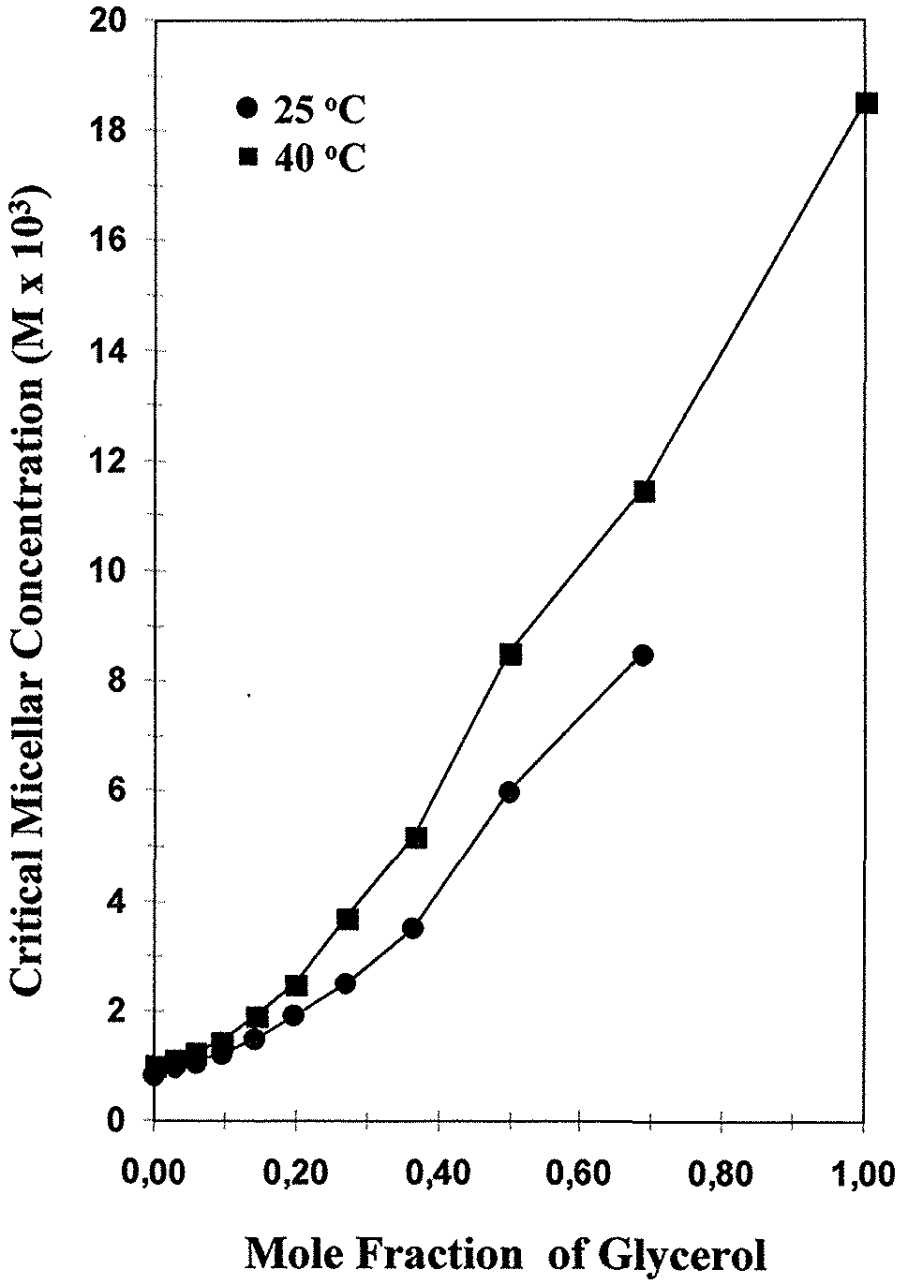

Figure 3. Dependence of the Critical Micellar Concentration of Cetyltrymethylammonium Bromide (CTAB) on the Mole Fraction of Glycerol for the Water-CTAB-Glycerol System.

Table II. Some Thermodynamic Properties for the Formation of Micelles of Cetyltrimethylammonium Bromide in Water-Glycerol Solutions at 25 °C.

Mole Fraction of Glycerol (x_G)	Free Energy of Micellization at 25 °C ΔG°_{mic} (kcal/mole)	Enthalpy of Micellization ΔH°_{mic} (kcal/mole)	Entropy of Micellization at 25 °C ΔS°_{mic} (e.u.)
0.000	-4.14	-1.03	+10.43
0.027	-4.10	-1.97	+ 7.14
0.057	-4.04	-1.58	+ 8.25
0.095	-3.97	-2.03	+ 6.51
0.142	-3.85	-2.92	+ 3.12
0.197	-3.71	-3.39	+ 1.07
0.270	-3.55	-4.84	- 4.33
0.366	-3.35	-4.89	- 5.17
0.498	-3.03	-4.30	- 4.26
0.687	-2.82	-3.73	- 3.10
1.000	*	*	*

* Surfactant precipitates.

Table III. Some Thermodynamic Properties for the Formation of Micelles of Cetyltrimethylammonium Bromide in Water-Glycerol Solutions at 40 °C.

Mole Fraction of Glycerol (x_G)	Free Energy of Micellization at 40 °C ΔG°_{mic} (kcal/mole)	Enthalpy of Micellization ΔH°_{mic} (kcal/mole)	Entropy of Micellization at 40 °C ΔS°_{mic} (e.u.)
0.000	-4.30	-1.03	+10.40
0.027	-4.21	-1.97	+ 7.15
0.057	-4.16	-1.58	+ 8.24
0.095	-4.07	-2.03	+ 6.51
0.142	-3.90	-2.92	+ 3.13
0.197	-3.73	-3.39	+ 1.09
0.270	-3.48	-4.84	- 4.34
0.366	-3.27	-4.89	- 5.17
0.498	-2.97	-4.30	- 4.25
0.687	-2.78	-3.73	- 3.03
1.000	-2.50	-	-

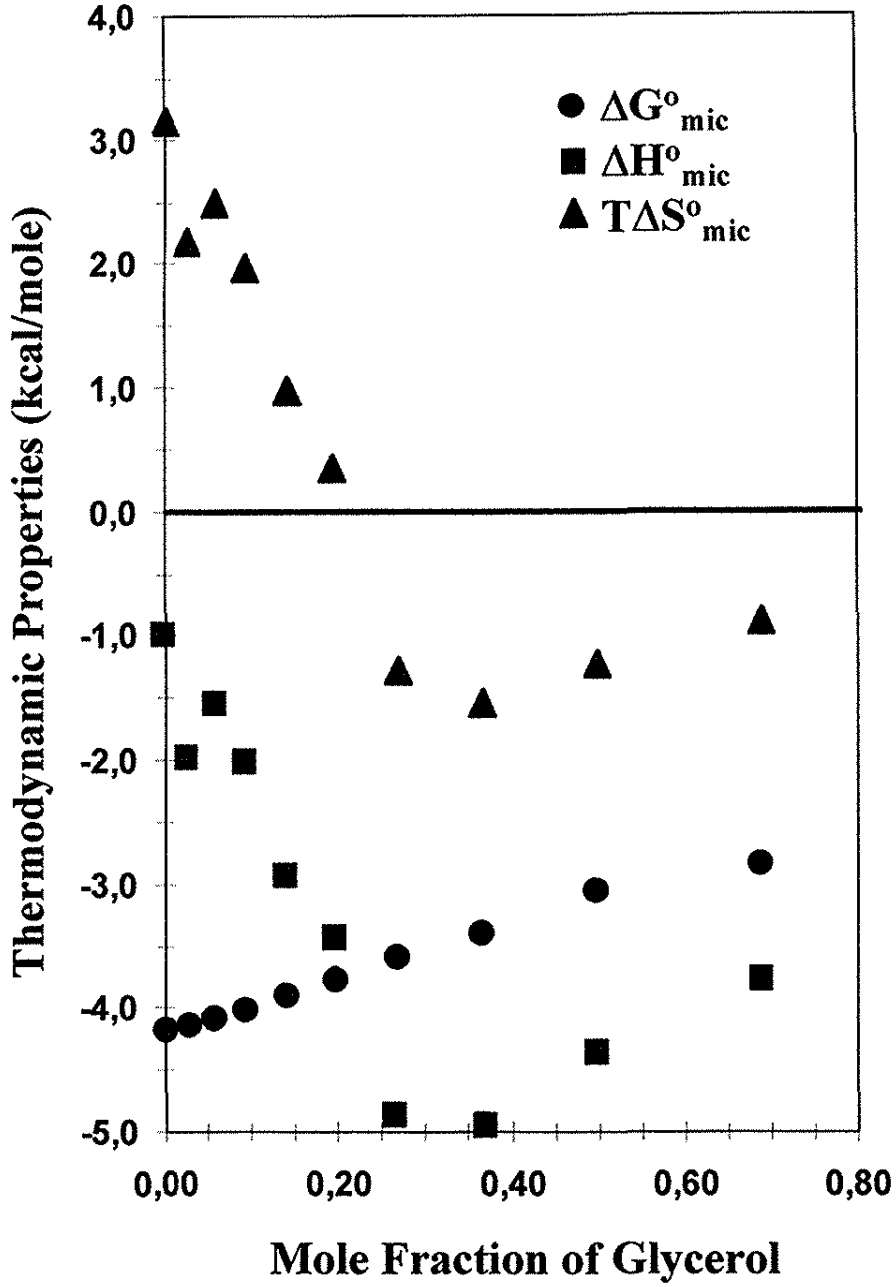

Figure 4. Plot of the Thermodynamic Properties as a Function of the Mole Fraction of Glycerol for the Water-CTAB-Glycerol Ternary System at 25 °C.

A careful analysis of the experimental results shows that at 40 °C the surfactant cetyltrimethylammonium bromide forms micelles in pure water, pure glycerol and the entire range of water-glycerol solutions. The free energy of micellization increases linearly from -4.30 kcal/mole (pure water) to -2.50 kcal/mole (pure glycerol), as can be seen in Table III. Attempts to determine CMC for CTAB in pure glycerol at 25 °C were not successful as the surfactant precipitates at a concentration higher than 14 x 10^{-3} M at this temperature. However, CTAB

forms micelles in water-glycerol solutions at this temperature up to the case of solutions containing 90% by volume of glycerol.

As can be clearly noted in Figure 4 and in Tables II and III, the addition of glycerol to water solutions containing CTAB has an inhibitory effect on micelle formation. This inhibitory effect can be explained by interactions between water and glycerol due to hydrogen bonding that eventually decrease the "hydrophobic" or "solvophobic" forces of the medium. As previously mentioned, it is well known that both glycerol and ethylene glycol form hydrogen bonds with water and disrupt the water structure[21-23].

Study of glycerol-water solutions by surface tensiometric measurements also showed the presence of interactions between the two solvents. This interaction reaches a maximum at mole fraction of glycerol of 0.18 and results in an excess surface free energy of 7dynes/cm somewhat higher than the values measured for ethylene glycol and formamide, that are similar polar solvents[30-31].

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REFERENCES

1. L. G. Ionescu and J. K. Tsang, *Rev. Roum. Biochim., 15*, 211 (1978).

2. L. G. Ionescu, T. Tokuhiro, B. J. Czerniawski and E. S. Smith, in "*Solution Chemistry of Surfactants*", K. L. Mittal, Ed., Plenum Press, New York, Vol. 1, p. 487 (1979).

3. T. Tokuhiro and L. G. Ionescu in "*Solution Chemistry of Surfactants*", K. L. Mittal, Ed., Plenum Press, New York, Vol. 1, p. 507 (1979).

4. L. G. Ionescu, T. Tokuhiro and B. J. Czerniawski , *Bull. Chem. Soc. Jpn., 52*, 922 (1979).

5. T. Tokuhiro, D. S. Fung and L. G. Ionescu,. *J. Chem. Soc. Faraday Trans. II, 75*, 975 (1979).

6. L. G. Ionescu and B. J. Czerniawski, *Rev. Roum. Biochim., 18*, 103 (1981).

7. L. G. Ionescu, and V. T. De Fávere in "*Solution Behavior of Surfactants: Theoretical and Applied Aspects*", K. L. Mittal and E. J. Fendler, Eds., Plenum Press, New York, Vol. 1, p. 407, 1982.

8. L. G. Ionescu, *Arch. Biol. Med. Exp., 12(2)*, 272 (1979).

9. L. G. Ionescu and D. S. Fung, *Bull. Chem. Soc. Jpn., 54*, 2503 (1981).

10. L. G. Ionescu, and D. S. Fung, *J. Chem. Soc. Faraday Trans. I, 77*, 2907 (1981).

11. L. G. Ionescu, L. S. Romanesco and F. Nome in "*Surfactants in Solution*", K. L. Mittal and B. Lindman, Eds., Plenum Press, New York, Vol. 2, p. 789, 1984.

12. L. G. Ionescu and P. E. De Brito Moreira, *Atual. Fís. Quim. Org., 2*, 79 (1984).

13. L. G. Ionescu, *Química Nova, 8(3)*, 191, (1985).

14. L. G. Ionescu and L. S. Romanesco, *Atual. Fís. Quim. Org., 3*, 109 (1985).

15. L. G. Ionescu, *Contrib. Cient. Tecnol. Santiago* (Chile), *NS*, 35 (1985).

16. L. G. Ionescu, T. H. M. do Aido and B. J. Kid, *Bol. Soc. Chil. Quim.*, *35*, 105 (1990).

17. A. Ray, *Nature*, *231*, 313 (1971).

18. A. Ray and G. Nemethy, *J. Phys. Chem.*, *75*, 809 (1971).

19. G. Nemethy and A. Ray, *J. Phys. Chem.*, *77*, 64 (1973).

20. L. Magid in "*Solution Chemistry of Surfactants*", K. L. Mittal, Ed., Plenum Press, New York, Vol. 1, p. 427, 1979.

21. M. Ueda, T. Urahata, A. Katyam and N. Kuroki, *Seni Gakkaishi*, *32*, T301 (1977).

22. V. D. Zinchenko, V. V. Mank and V. A. Mosiev, *Ukr. Khim. Zh.*, *41*, 371 (1977).

23. J. L. Beaudoin, *J. Chim. Phys.*, *74*, 268 (1977).

24. S. Damjanovich, B. Somogyi and J. Bot, *Stud. Biophys.*, *59*, 229 (1976).

25. T. Yubisui, M. Takeshita and Y. Yoneyama, *Experientia*, *32*, 3989 (1976).

26. N. Muller in "*Reaction Kinetics in Micelles*", E. H. Cordes, Ed., Plenum Press, New York, p. 1-23, 1973.

27. D. G. Hall, *Trans. Faraday Soc.*, *66*, 1351, 1359 (1970).

28. J. H. Fendler and E. J. Fendler, "*Catalysis in Micellar and Macromolecular Systems*", Academic Press: New York, 1975.

29. J. Swarbrick and J. Daruwala, *J. Phys. Chem.*, *73*, 2627 (1969).

30. S. M. H. Probst, MSc. Thesis, Universidade Federal de Santa Catarina, Florianópolis, S.C., Brazil, 1982, 135 pp.

31. L. G. Ionescu and L. S. Romanesco, *Atual. Fis. Quim. Org.*, *3*, 109 (1985).

SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY
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STUDY OF RENAL SORBITOLDEHYDROGENASE IN EXPERIMENTAL DIABETIC NEPHROPATHY

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ABSTRACT

The link between the polyol pathway and the occular complications of diabetes mellitus is explained by the excessive storage of sorbitol and the release of osmotic stress. The renal complications could also be explained by the osmotic hypothesis, but the polyol pathway activity is reduced in this case. The study of sorbitoldehydrogenase (SDH) activity, one of the enzymes involved in the catabolism of glucose by this pathway in renal and hepatic homogenates from diabetic animals shows a constant increase of the hepatic enzyme activity compared to that at the renal level. The different variation of the renal SDH activity can be explained by the effect of hyperglycemia on the active form of the enzyme and its inactivation by nonenzymatic glycosylation.

KEYWORDS: alloxan, polyol pathway, sorbitoldehydrogenase, aldose reductase, nonenzymatic glycosylation.

RESUMO

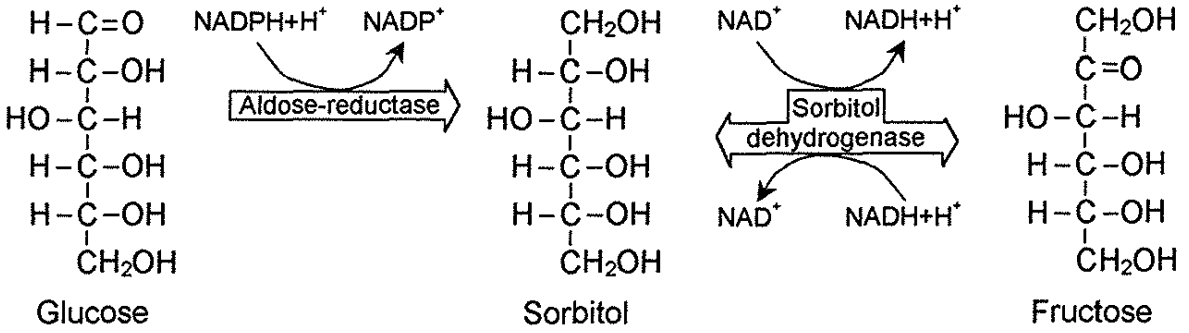
A relação entre o caminho metabólico do poliol e complicações oculares de diabetes mellitus é explicado através da armazenagem excessiva de sorbitol e da liberação da tensão osmótica. As complicações renais também poderiam ser explicadas através da hipótese osmótica, porém a atividade do caminho do poliol está reduzida neste caso. O estudo da atividade da sorbitoldehidrogenase (SDH), uma das enzimas envolvida no catabolismo da glicose através deste caminho, em homogenatos renais e hepáticos, provenientes de animais diabéticos, mostra um aumento contínuo da atividade da enzima hepática comparada à aquela a nível renal. O comportamento diferente da SDH renal pode ser explicado através do efeito da hiperglicemia sobre a forma ativa da enzima e a sua inativação por glicosilação nonenzimática.

INTRODUCTION

Only a small percent of total glucose (aprox. 5%) is transformed by the polyol pathway under normal conditions providing the sorbitol needed to maintain the hydroosmotic balance[1,2]. The polyol pathway is represented by two enzymes with different distribution:

- Aldosereductase (E.C.1.1.1.21), a $NADP^+$ dependent enzyme which acts in the medullary cells cytoplasm;
- Sorbitoldehydrogenase (E.C.1.1.1.14), a NAD^+ dependent enzyme from interstitial cells.

The two enzymes catalyse the transformation of glucose, first into sorbitol then to fructose (fig.1).



Aldosereductase has a low affinity (high K_m) for glucose and, thus, at the normal concentrations found in non-diabetic conditions, the metabolism of glucose by this pathway constitutes a very small percent. During hyperglycemia the intracellular level of glucose is eleveted and the transformation by the polyol pathway is intensified because of the insulin deficiency (between 11-30% depending on the organ involved)[3,4,5].

The storage of sorbitol and fructose in cells releases the osmotic stress[6].

The polyol pathway has different activity in lens, liver, kidney, retina, large and thin vessels and peripheral nerves[7].

The paper presents some of the results that we have obtained for renal and hepatic sorbitoldehydrogenase activity. They serve as an index for the polyol pathway in experimental diabetic nephropathy. The renal SDH activity depends on renal region, many data pointing out an increased activity in interstitial medullary cells[8].

MATERIAL AND METHODS

The experiment was performed on 32 male Wistar rats, weighing 230-280 g, kept under standardised feeding and bioclimatic conditions. To induce the experimental diabetes 24 of them were injected with a subcutaneous dose of 100 mg

alloxan/kg b.w. The animals were divided into three groups and sacrified at different periods after the onset of diabetic state:

- Group I, after 4 weeks;
- Group II, after 6 weeks;
- Group III, after 8 weeks.

The other 8 rats were part of the control group (c).

We used blood, liver and kidney samples to test the activity of sorbitoldehydrogenase.

Tissue homogenates were obtained in Tris-HCl buffer pH = 7,5 with an extraction ratio tissue/buffer = 1/10

We tested the sorbitoldehydrogenase activity with the Richterich's colorimetric method[9].

The total amount of tissue proteins was measured by the Lowry's method[9].

Serum glucose was measured by means of the o-toluidine colorimetric method.

RESULTS AND DISCUSSIONS

The experimental results, statistically processed, are illustrated in Table 1.

Soon after the alloxan administration we determined a triphasic variation of glucose values before the permanent hyperglycemia.

Figures 2 and 3 present the variation of hepatic and renal SDH activity for the three groups of treated animals compared to the control group.

Data from Figure 2 and Table 1 show a significant increase of hepatic SDH activity for the treated animals compared to the control group. The sorbitol pathway is a metabolic alternative for glucose in hyperglycemic conditions which follow the insulin deficiency in experimental diabetes.

This variation explains the hepatic origin of this enzyme.

At the same time, the alloxan "agression" also exacerbates the polyol pathway and the synthesis of the enzymes involved in this pathway increases in liver cells.

The high amount of sorbitoldehydrogenase in the liver was also confirmed by the increased concentration of SDH m-RNA[10].

The renal sorbitoldehydrogenase shows a different variation when compared to the hepatic enzyme (Table 1 and Figure 3).

Renal SDH activity increased for groups I and II compared to the control group, but the group III presented reduced activity.

Renal SDH activity increase is less significant as compared to the hepatic enzyme. Also, its variation doesn't correlate with serum glucose level.

The increased value of renal SDH activity is explained by the intensification of the polyol pathway and its decrease is caused by an intense glycation process.

Hyperglycemia enhances the nonenzymatic glycation of intracellular constituents and the active form of renal sorbitoldehydrogenase is transformed into an inactive one.

Table 1

LEVELS OF SOME PARAMETERS IN EXPERIMENTAL DIABETIC NEPHROPATHY

Parameter	Control group ($\bar{x}$ ± SD)	Group I ($\bar{x}$ ± SD)	Group II ($\bar{x}$ ± SD)	Group III ($\bar{x}$ ± SD)
Serum glucose (mg/dl)	79.34±1.64	300.4±6.3	260.3±4.2	374.2±0.65
Hepatic SDH*	6.8±1.3	9.2±2.4	13.4±0.6	16.5±1.7
Hepatic SDH variation compared to the normal group	-	135%	195%	240%
Renal SDH*	0.78±0.12	0.81±0.92	0.98±0.24	0.80±0.42
Renal SDH variation compared to the normal group	-	105%	120%	102%

* SDH activity is measured in μmoles fructose/min/g of protein

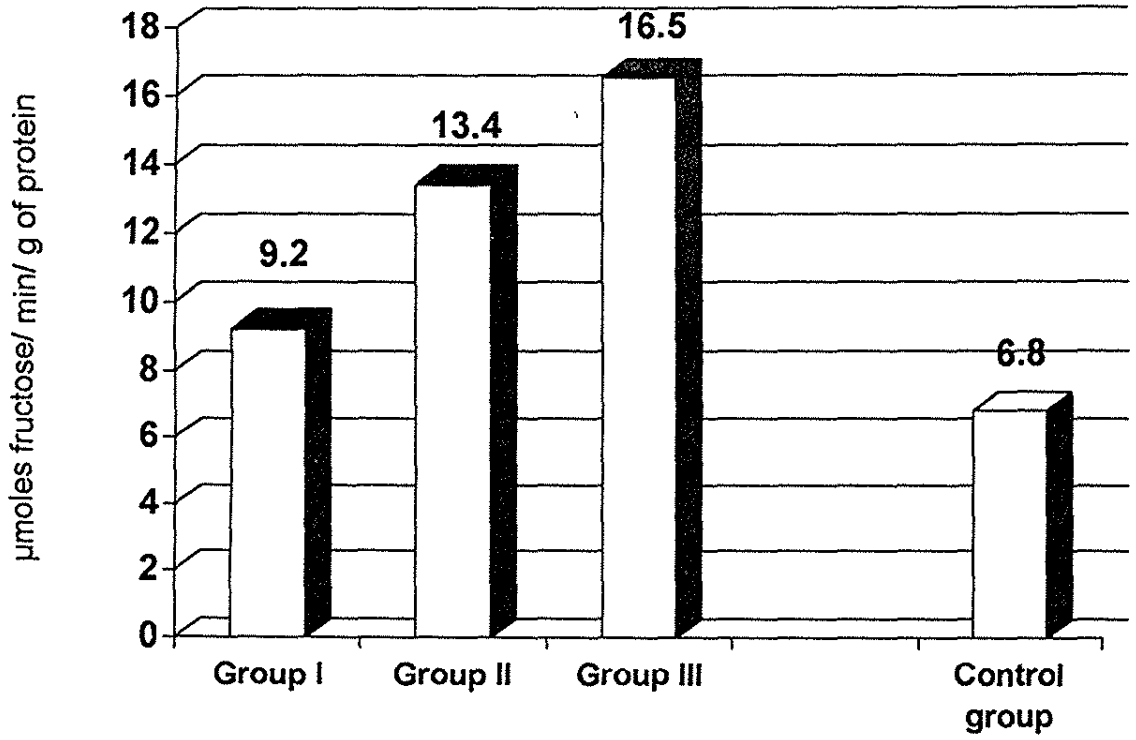


Fig.2. **Variation of hepatic SDH activity**

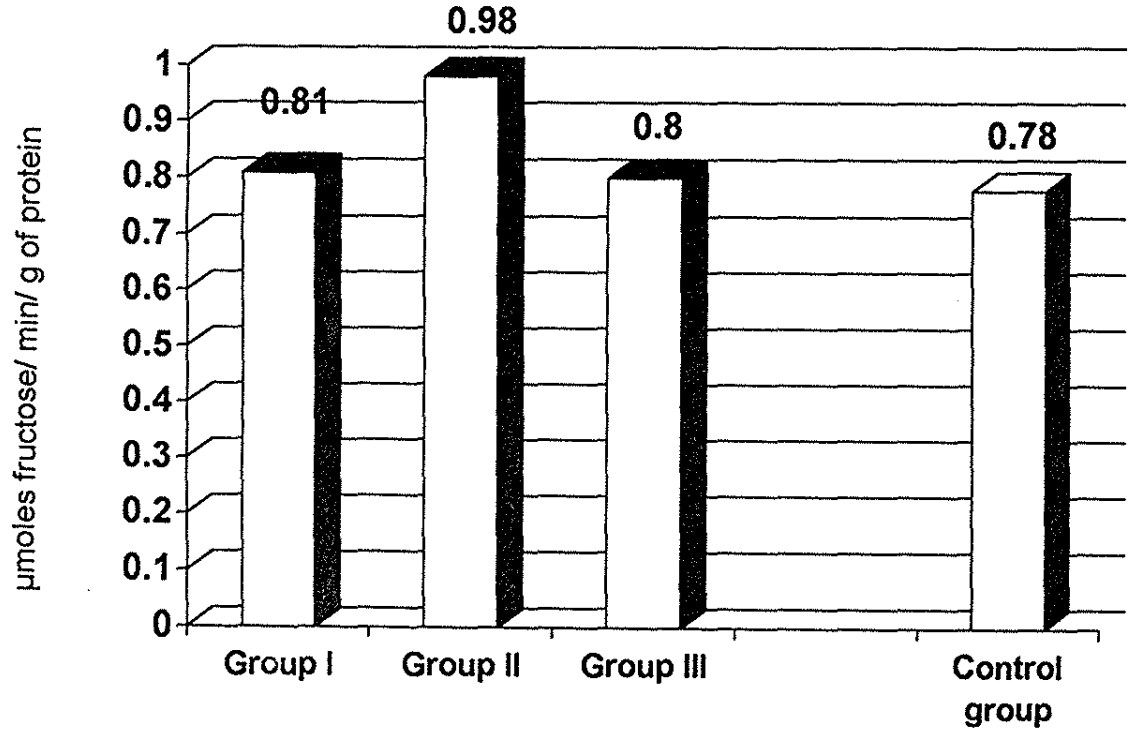


Fig.3. **Variation of renal SDH activity**

CONCLUSIONS

- The study of the polyol pathway intermediates and enzymes from the renal tuft is very important to explain the mesangial alterations associated with the renal complications of diabetes mellitus.
- The experimental model of diabetic nephropathy presents some similar conditions with diabetes mellitus caused by insulin deficiency.
- Both the activity of the enzymes involved and the relative preponderance of the polyol pathway intermediates showed changes.
- Although the SDH activity is modified, its variation does not correlate with hyperglycemia.

REFERENCES

1. I. Teodorescu-Exarcu, Patologie biochimica. Editura Medicala, Bucuresti, Romania, 1974.

2. C. Ionescu-Tirgoviste, Diabetologie moderna. Editura Tehnica, Bucuresti, Romania, 1997.

3. R. G. Gonzales, R. Barnett, J. Agnuyo, H. M. Cheng, L. T. Chylack, *Diabetes*, *33*, 196-199 (1984).

4. J. H. Kinoshita and C. Nishimura, *Diabetes Metabolism Rev.*, *4*, 323-337 (1988).

5. N. B. Ruderman, J. R. Williamson and M. Brownlee, *FASEB J.*, *6*, 2905-2914 (1992).

6. D. A. Greene, S. A. Latimer and A. F. Sima, *New Eng. J. Med.*, *316*, 77, 599-606 (1987).

7. V. Darie and M. Serban, *St. Cerc Biochim.*, *24*, 157-160 (1981).

8. R. W. Grunewald, J. J. Weber and R. K. Kinne, *Am. J. Physiol.*, 269, 696-701 (1995).

9. R. Richterich. Clinical Chemistry. Theory and Practice. Academic Press New York, London, 1969.

10. A. Hoshi, M. Takahashi, J. Fuji, T. Myint, H. Kaneto, K. Suzuki, J. Jamasaki, T. Kamada, N. Taniguchi, *Biochem. J.*, *318*, 119-123 (1996).

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SYNTHESIS STUDY OF NEW 2- SUBSTITUTED IMIDAZOLINES WITH POTENTIAL HYPOTENSIVE ACTIVITY

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ABSTRACT: *A theoretical study based on molecular mechanics and semi-empirical calculations of the condensation mechanism of methyl p-amidosulphonyl phenoxyacetate with ethylene diamine is reported. Synthesis of 17 new imidazolines derived from sulphonamidated phenoxyacetic acids is also described.*

RESUMO *Este trabalho relata os resultados de um estudo teórico baseado em mecânica molecular e cálculos semiempíricos para o mecanismo de condensação do metil-p-amidosulfonil fenoxiacetato com etileno diamina. A síntese de 17 novas imidazolinas derivadas de ácidos fenoxiacéticos sulfonamidados é também descrita.*

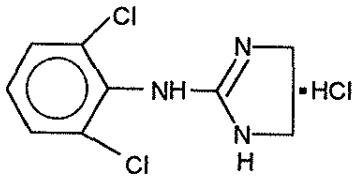
KEYWORDS: 2-substituted imidazoline, sulphonamidated phenoxyacetic acid derivatives, hypotensive imidazolines

INTRODUCTION

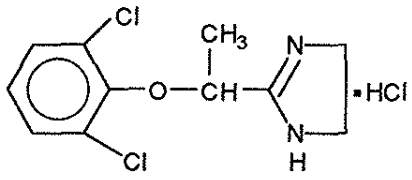
The systematic syntheses and pharmacological studies of numerous imidazolines substituted in the 2-position resulted in compounds with various biological activities (e.g. analgesic, antidepressant, antihelmintic, antihypertensive, vasopressor, hypotensive) [1].

Referring to the imidazolines acting on the high blood pressure only, these could be divided in two classes [1-3]. The first class consists in 2-substituted imidazolines with specific cardiovascular actions (e.g. Clonidine® and Lofexidine®). They have central antihypertensive properties being useful in treating the essential high blood pressure.

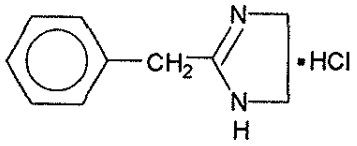
The imidazolines substituted in the 2- position which act on the vegetative nervous system are included in the second class. These ones (e.g. Periphen®) induce hypotensive responses being used for the periferic vasoconstricting disturbances.



Clonidine



Lofexidine



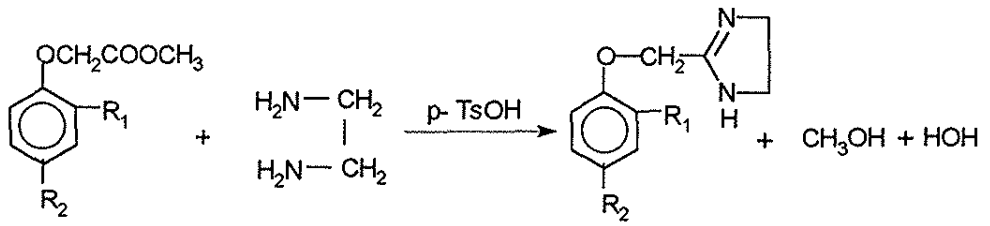
Periphen

In the present paper a study on the obtaining of some imidazolines derived from sulphonamidates phenoxyacetic acids with a possible hypotensive action (i.e. of second class type), is reported.

Some pharmacodynamical studies on such products [e.g. 2-(4-amidosulphonyl-phenoxymethylene)- imidazoline and 2-(4-amidosulphonyl-2-methyl-phenoxymethylene)-imidazoline] showed significant changes in arterial blood pressure when having been administred to dogs. In

addition, the sulphonamidated aryloxymethylene group exhibited an extremely low toxicity, even in high doses [4].

2- Substituted imidazolines have been synthesized by the condensation of ethylene diamine (EDA) with methyl esters of sulphonamidated phenoxiacetic acids in the presence of a condensing agent (p-toluenesulphonic acid, p-TsOH) and anhydrous methyl alcohol as solvent, following the scheme described below [4,5].



where: R_1= *Cl, CH*$_3$; R_2= SO_2NH_2, $SO_2NHC_2H_5$, $SO_2N(C_2H_5)_2$, $SO_2N(C_3H_7)_2$, $SO_2N(C_4H_9)_2$, *SO*$_2$*NH-i Pr, SO*$_2$*NH-t Bu, pyrrolydinosulphonyl, piperazinosulphonyl*

In order to obtain some theoretical informations on the condensation mechanism between esters and EDA in acid catalysis, a modelling study based on molecular mechanics and semi-empirical calculations has been performed.

EXPERIMENTAL AND METHODS

Computational Details

The modelling of the condensation process was done with the aid of the HyperChem 4.5 software.

All calculations have been performed after geometry optimization of the molecular systems. Both system optimization and semi- empirical calculations were carried out using the AM1 method [6].

Chemistry

Melting points were determined on a Boetzius micromelting point apparatus and were uncorrected. Infrared (IR) spectra were recorded on a UNICAM SP-100 apparatus using KBr pellets. Nuclear Magnetic Resonance

(^{1}H-NMR) spectra were recorded at 300.1 MHz in deuterated dimethylsulphoxide (DMSO-d_6) as solvent, at ambient temperature. Chemical shifts were referred to hexamethyldisiloxane (HMDS) used as an internal reference. Ultraviolet (UV) spectra were recorded on a UV-Visible Spectrophotometer as diluted methanol solutions. The nitrogen content of the compounds was determined by the Dumas method. All evaporations were performed under vacuum.

General Procedure

All the compounds were synthesized starting with 0.01 mole of methyl ester of the corresponding sulphonamidated phenoxyacetic acid and 0.015 mole EDA using *p*-TsOH and traces of sulfur as catalysts and anhydrous methanol (10 ml) as solvent. The reaction mixture was refluxed for 3-4 hours and the residue remaining after methanol removal by vacuum was treated with 25 ml water and allowed to stay till crystallization. The products obtained were purified from the appropriate solvent depending on their solubility.

RESULTS AND DISCUSSION

Our approach in clarifying the condensation reaction mechanism was based on two criteria: heats of formation, (ΔH_f), analyzed comparatively for three pairs of presumably formed species (denoted by A- H in the Figure 1) and bond lengths (δ) for the intermediates from which small molecules have to be eliminated.

Thus, according to the assumed mechanism the protonation, under the catalyst influence, of the methyl ester of *p*-amidosulphonyl-phenoxyacetic acid, taken as an example, can occur on either the ether oxygen or the carbonyl one giving the isomers denoted by A and B, respectively. Due to the great difference between the two values of ΔH_f corresponding to the A and B compounds, we supposed that only the formation of intermediate B is possible. That is why, only the attack of EDA on compound E is further considered.

For the binding of EDA at the carbon atom of the ester group, three intermediates are proposed as the structures C, D and E are depicting. Analyzing the ΔH_f values for the three compounds it can be observed that for

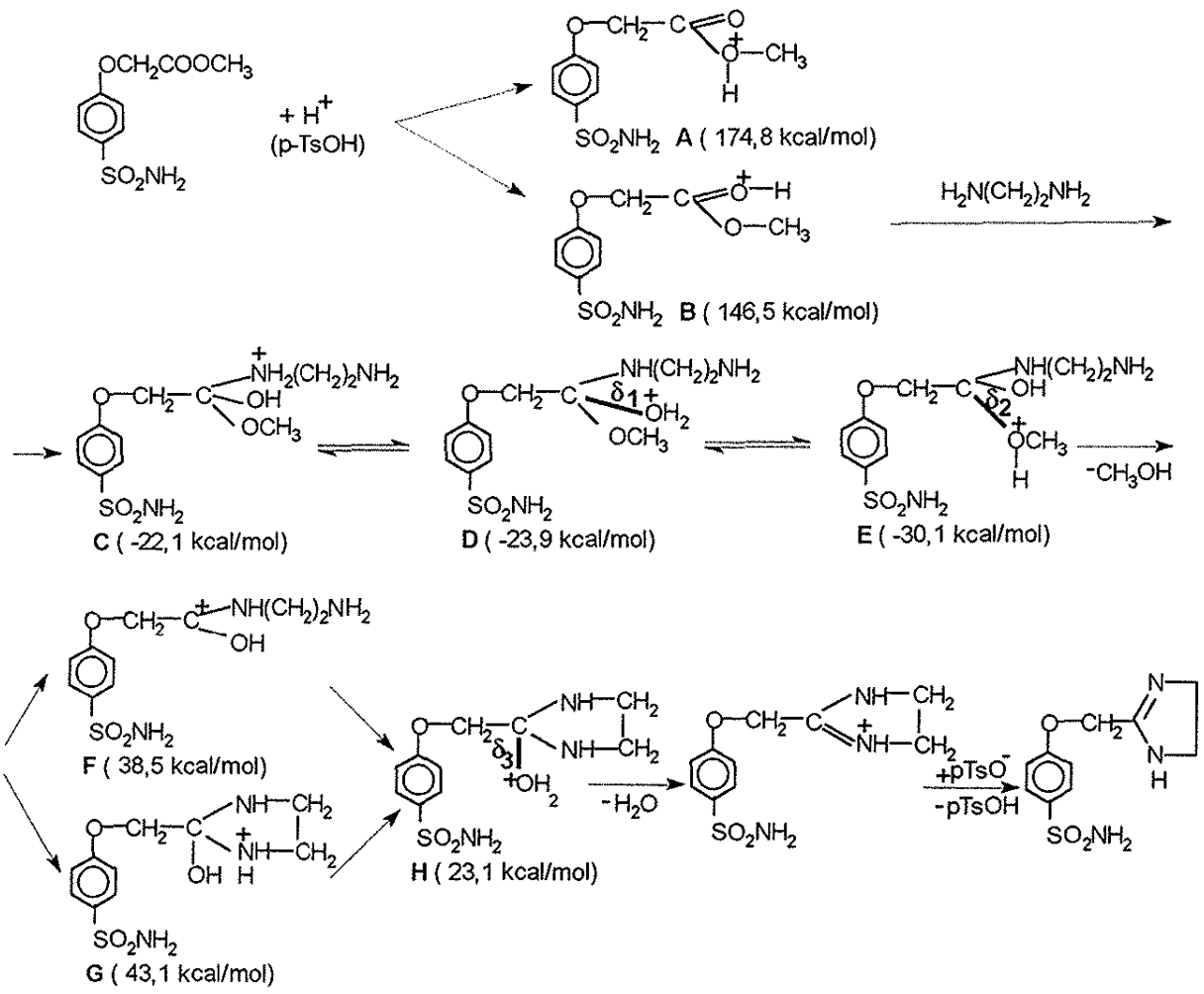


Figure 1. Acid catalyzed condensation of methyl p-amidosulphonyl phenoxyacetate with ethylene diamine.

the E intermediate the probability of formation is greatest. Consequently, we choose the E compound for the further transformation, by the elimination of one molecule of methanol. An additional argument for this choice consists in the difference between the length of the bonds δ_1 of 2,95 Å and δ_2 of 3,28Å which is indicative for the methanol molecule and not for the wateras leaving group.

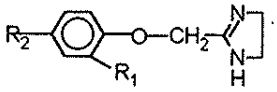
After methanol elimination from E two likely structures, denoted by F and G, respectively can be assumed. Since the difference in ΔH_f values of the two compounds is rather small (of 4.6 kcal/ mol) the conclusion that can be drawn is that both structures can be regarded as possible intermediates [7]. Thus, either carbocation F or intermediate G , obtained by a direct rearrangement of compound E , could virtually pass into the intermediate H , of lower ΔH_f value.

From the isomer H one water molecule is easily expelled, in agreement with the the abnormally great δ_3 length bond value, of 3.38 Å, giving thus the protonated 2-(4-amidosulphonyl-phenoxymethylene)-imidazoline.The expected product is obtained by exchanging proton with the conjugated base of catalyst (p-TsO^-).

In conclusion, according to the proposed mechanism, the condensation reaction of the methyl p-amidosulphonylphenoxyacetate with EDA, in acid catalysis, occurs in two main stages. The first step that involves the elimination of one molecule of methanol due to the attack of EDA on the ester and the second step, consists of cyclization and water elimination, the final product resulting by proton exchange with the catalyst.

Practically, seventeen imidazolines (Table 1) derived from sulphonamidated fenoxyacetic acids were obtained.

Table 1. Some properties of the imidazolines synthesized.



No.	R_1	R_2	Empirical Formula	M (g/mol)	M.p. (°C)	%N calc.	%N found	Recr. Solv.
1.	Cl	SO_2NH_2	$C_{10}H_{12}ClN_3O_3S$	289.5	230-231	14,5	14.25; 14.39	H_2O
2.	Cl	$SO_2NHC_2H_5$	$C_{12}H_{16}ClN_3O_3S$	317.5	172	13.22	13.05; 13.54	i-PrOH-HOH
3.	Cl	$SO_2N(C_2H_5)_2$	$C_{14}H_{20}ClN_3O_3S$	345,5	184	12,15	11,98; 12,01	i-PrOH-HOH
4.	Cl	$SO_2N(C_3H_7)_2$	$C_{16}H_{24}ClN_3O_3S$	373.5	115	11.24	11.34; 11.40	i-PrOH-H_2O
5.	Cl	$SO_2N(C_4H_9)_2$	$C_{18}H_{28}ClN_3O_3S$ HCl	438	129-130	9.59	9.47; 9.55	CH_3OH
6.	Cl	$SO_2NHCH(CH_3)_2$	$C_{13}H_{18}ClN_3O_3S$ HCl	368	183-185	11.41	11.09; 11.38	CH_3OH
7.	Cl	$SO_2NHC(CH_3)_3$	$C_{14}H_{20}ClN_3O_3S$ HCl	382	163-165	10.99	10.87; 11.03	CH_3OH
8.	Cl	pyrrolidinosulphonyl	$C_{14}H_{18}ClN_3O_3S$	333.5	167	12.59	12.25; 12.39	CH_3OH
9.	Cl	piperazinosulphonyl	$C_{14}H_{19}ClN_4O_3S$	358.5	258-260	15.62	15.49; 15.54	DMSO
10.	CH_3	$SO_2NHC_2H_5$	$C_{13}H_{19}N_3O_3S$	297	140	14.14	13.98; 14.02	C_2H_5OH-H_2O
11.	CH_3	$SO_2N(C_2H_5)_2$	$C_{15}H_{23}N_3O_3S$	325	189 - 190	12.92	12.55; 12.78	C_2H_5OH
12.	CH_3	$SO_2N(C_3H_7)_2$	$C_{17}H_{27}N_3O_3S$ HCl	389.5	175	10.78	10.69; 10.71	CH_3OH
13.	CH_3	$SO_2N(C_4H_9)_2$	$C_{19}H_{31}N_3O_3S$ HCl	417.5	171	10.059	9.98; 10.01	CH_3OH
14.	CH_3	$SO_2NHCH(CH_3)_2$	$C_{14}H_{21}N_3O_3S$ HCl	347.5	217	12.086	11.98; 12.05	CH_3OH
15.	CH_3	$SO_2NHC(CH_3)_3$	$C_{15}H_{24}N_3O_3S$ HCl	362.5	210	11.58	11.62; 11.52	CH_3OH
16.	CH_3	pyrrolidinosulphonyl	$C_{15}H_{21}N_3O_3S$	323	183-184	13.00	13.12; 13.08	CH_3OH- H_2O
17.	CH_3	piperazinosulphonyl	$C_{15}H_{22}N_4O_3S$	337	232	16.61	16.54; 16.59	DMF- H_2O

The imidazolines obtained are solid, amorphous substances with characteristic melting points. As free bases they are soluble in ethyl and methyl alcohol, acetone, dimethylsulfoxide, dimethylformamide, tetrahydrofuran and hot water.

The IR spectra, show characteristic bands as follows: 3050-3100, 2930-2950, 1600-1610, 1450-1490 cm^{-1} (imidazoline), 1080-1100 cm^{-1} (C⋯S); 1020- 1040 cm^{-1} (S⋯O); 1040- 1080 cm^{-1} (S⋯N); 1160-1180, 1300-1360 cm^{-1} (SO_2); 1200-1260 cm^{-1} (C⋯O) and 805-825, 870-885 cm^{-1} (1,2,4- substituted aromatic ring) [8-10].

The UV spectra show broad bands at approximately 220 nm.

The structures of 2-substituted imidazolines were finally confirmed by ^{1}H- NMR spectra. The chemical shifts assignments supported the expected structures being in close agreement with the Lofexidine® spectrum, taken as reference for the imidazoline ring [1].

CONCLUSIONS

The studies on the aryloxyalkylcarboxylic acids derivatives were continued by the synthesis of new compounds with potential hypotensive actions.

Seventheen new imidazolines have been prepared by the reaction of some methylic esters of sulphonamidated aryloxyalkylcarboxilic acids with ethylene diamine using acid catalysis.

A theoretically study based on molecular mechanics and semi-empirical calculations of the condensation mechanism of methyl p-amidosulphonyl phenoxyacetate with ethylene diamine is reported.

The structure of the compounds obtained have been elucidated by means of elementary analysis data and IR, UV and ^{1}H- NMR measurements.

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REFERENCES

1. H.Betzing, J. Biederman, *Arzneim.- Forsch./ Drug Res., 32(II), 8a,* 916 (1982).
2. C. Oniscu, *"Chimia si Tehnologia Medicamentelor"*, Ed. Tehnica, Bucuresti, 1988.
3. M. Rapin, *"Les 200 Médicaments Essentiels"*, Ed. Flammarion, Paris, 1983.
4. Gh. Botez, L. Enescu, *Bull. Inst. Polit. Iasi, VIIII(XII), (1-2),* 153 (1962).
5. C. Soldea, C. Oniscu, *Bull. Inst. Polit. Iasi, XXXVIII(XLII), (1-4),* 51 (1992).
6. M.J.S. Dewar, E.G. Zoehisch, E.F. Heally, J.J.P. Stewart, *J. Am. Chem. Soc., 107,* 3902(1985).
7. G.H. Loew, H.O. Villar, C. Cometta, J.J. Perez, *Int. J. Quantum Chem., 18,* 165(1991).
8. M. Avram , Gh. D. Mateescu, *"Spectroscopia in infrarosu. Aplicatii in chimia organica"*, Ed. Tehnica, Bucuresti, 1966.
9. A. T. Balaban, M. Banciu, I. Pogany, *"Aplicatii ale metodelor fizice in chimia organica"*, Ed. St. si Encicl., Bucuresti (1983).
10. E. Pretsch, Th. Clerc, J. Seibl, W. Simon, *Tables of Spectral Data for Stuctur. Determination of Orani. Compounds*, Springer Verlag, Berlin Heilderberg, New York, London, Paris, Tokio, Hong Hong, 1989.

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Synthesis and Characterization of New Oxovanadium(IV) Coordination Compounds with Pyrazol-5-one Azo Derivatives

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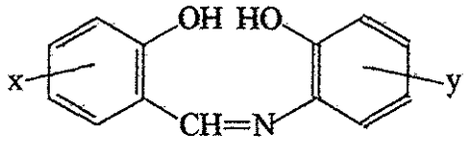
ABSTRACT

A new series of oxovanadium(IV) chelates containing bi-and tridentate pyrazol-5-one azo derivatives ligands of the type (1) $[VO(L)_2]$ and (2) $[VO(L)(H_2O)]$ have been prepared and characterized by elementary analysis, IR, electronic spectra, conductance measurements and molecular weights. The ligands coordinate through (O-N) donor system as monobasic and bidentate (HL) for the first type and through (O-N-O) donor system as dibasic and tridentate (H_2L) for the second type of complexes. The molecular weghts, the presence of the (V=O) stretching band around 950 cm^{-1} and the visible spectra suggest a monomeric penta-coordinated structure for these complexes.

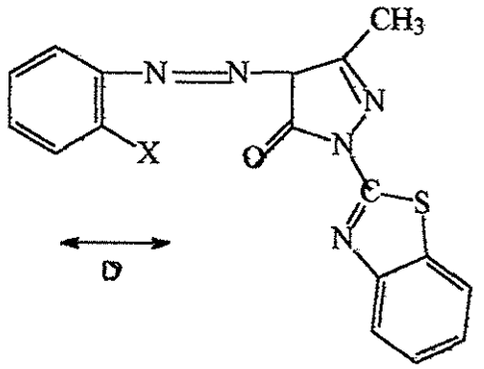
Keywords: oxovanadium(IV) coordination compounds, pyrazol-5-one, azo dye, UV, IR spectroscopie

INTRODUCTION

In recent years there has been considerable interest in the synthesis, magnetic and structural properties of oxovanadium(IV) complexes of bi- and tridentate Schiff bases[1,2,3]. Zelenstov[4] and Ginsberg[5] have suggested a dimeric structure for the complexes of oxovanadium(IV) with Schiff bases of the general formula:

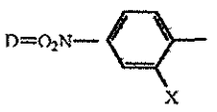


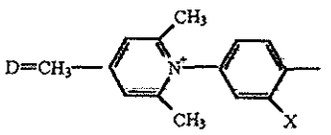
These results have suggested an investigation of the posibility of obtaining dimeric compounds of oxovanadium(IV) with bi- and tridentate 1-(2'-benzthyazolyl)-3-methyl-4-substituted-pyrazol-5-one azo derivatives of general formula:



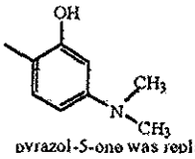
X = OH, COOH, H.
D = diazo component

The pyrazol-5-ore azo derivatives are very important pigments[6]. In the present paper we report the results of the study of the behavior of these new ligands with the vanadyl(IV) ion. It has been found that according to the nature of the substituents D and X two different types of complexes are obtained.
(*i*) complexes with the general formula $[VO(L)_2]$, in which the vanadium is linched to two azo derivatives obtained as the anionic part L of the following HL ligands.

HL1  X = H

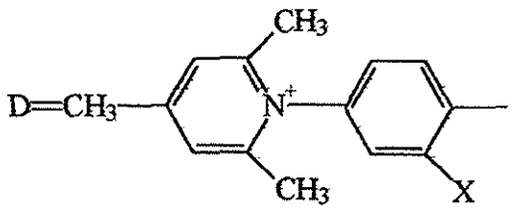
HL2  X = H and

$[ClO_4]^-$

 where

pyrazol-5-one was replaced by

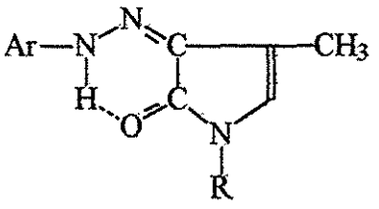
HL[3]



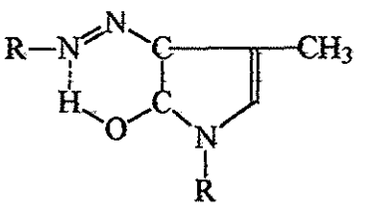
X = H

$[BF_4]^-$

In solution, there is an equilibrium between the hydrazoketo and azoenol forms of pyrazol-5-one azo derivatives[7]

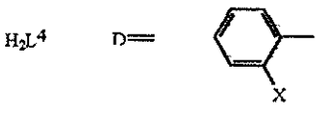


Hydrazoketo form

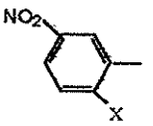


Azoenol form

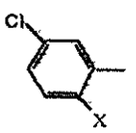
and therefore, these ligands act bidentately and have monobasic properties.
(*ii*) complexes with general formula $[VO(L)(H_2O)]$, in which the vanadium is linked to only one azoderivative and to one water molecule. The L corresponds to the anionic part of the following H_2L ligands



H_2L^4 X - COOH



H_2L^5 X = OH and



H_2L^6 X = OH and

Six compounds of these two series have been prepared and characterized. Their molecular weights, IR, UV-VIS spectra and conductance have been measured and the results were analyzed in order to obtain information on the structure and the stereochemistry of the compounds in solid state.

EXPERIMENTAL PROCEDURE

All compounds and solvents were pure BDH grade chemicals. The ligands used were prepared according to the method previously described[8,9].

Physical Measurements

The electronic spectra of all compounds were obtained by the diffuse-reflectance technique, dispersing the sample in MgO, with a Specord M400 Carl Zeiss Jena Spectrophotometer.

The IR spectra were determined with a Perkin-Elmer FT-IR spectrophotometer in the range of 4000-200 cm^{-1}, in KBr pellets.

Molecular weights were determinated in chloroform at 37°C with a Mechrolab Model 301A vapor pressure osmometer. Concentrations of the solutions were in the range of 10^{-3}-10^{-4} M.

Elementary analysis were determined with a Carlo Erba EA 1108 apparatus. Vanadium was determined by the gravimetric method. Conductance measurements were obtained with a Radelkis conductometer type OK-102/1.

Preparation of the compounds

Complexes of type (1) $[VO(L)_2]$ were synthesized by dissolving (0.004 mol) HL in 50 ml of hot ethanol/acetone mixture (1/1 v/v) and then adding (0.002 mol) of vanadyl sulphate (dissolved in 10 ml H_2O/ethanol 50%). The pH of the reaction medium was adjusted with (0.004 mol) $CH_3COONa.3H_2O$ from 4-4.5 to 8-8.5 followed by stirring the reaction mixture, under reflux on a water bath for about 1.5 hours. The solid complexes were separated by filtration, washed with ether and dried at room temperature.

The complexes were purified by recrystallization, (η = 60%). The general reaction was

$$VOSO_4.2H_2O + 2HL + 2\,CH_3COONa.3H_2O \rightarrow [VO(L)_2] + Na_2SO_4 + 2CH_3COOH + 8H_2O$$

Complexes of type (2) $[VO(L)H_2O]$ were prepared by dissolving (0.004 mol) of the H_2L in 50 ml of hot ethanol and adding an aqueous solution of $VOSO_4.2H_2O$ (0.004 mol). The pH of the reaction was adjusted with (0.004 mol) $CH_3COONa.3H_2O$. The mixture of reaction was heated under reflux on a oil bath at 112°C for 0.5 hr. The solid complexes were filtered off, washed with ether and then dried at room temperature. The complexes were purified by recrystallization, (η = 65%). The general reaction was:

$$VOSO_4.2H_2O + H_2L + 2\,CH_3COONa.3H_2O \rightarrow [VO(L)(H_2O)] + Na_2SO_4 + 2CH_3COOH + 7H_2O$$

RESULTS AND DISCUSSION

The solution conductance values in DMF for the solid complexes (Table 1) are in good agreement with the data obtained by previous authors[10] and suggest a non electrolyte behavior of the complexes of both type (1) and type (2). The elementary

Table 1. Analytical data, conductance measurements for Complexes of Oxovanadium (IV)

Complex	Formula	Microanalysis Results				λ^c $\Omega^{-1}cm^2mol^{-1}$	Mol wt	M.p. °C	Powder colour
		% C[a]	% H[a]	% N[a]	% V[a]				
[VO (L^1)$_2$]	$VO(C_{34}H_{22}N_{12}O_6S_2)$	49.45 (50.01)	2.66 (3.00)	20.36 (20.40)	6.17 (6.20)	35.4	824.94	350[b]	green
[VO (L^2)$_2$]	$VO(C_{44}H_{48}N_8O_2)$ $[ClO_4]_2$	53.55 (53.76)	4.86 (5.01)	11.35 (11.44)	5.16 (5.24)	58.6	985.94	357[b]	brown
[VO (L^3)$_2$]	$VO(C_{50}H_{44}N_{12}O_2S_2)$ $[BF_4]_2$	52.23 (52.30)	3.83 (4.00)	14.62 (14.70)	4.43 (4.50)	59	1148.56	431[b]	red - brown
[VO (L^4) (H_2O)]	$VO(C_{18}H_{11}N_5O_3S)$ (H_2O)	46.75 (46.80)	2.81 (2.95)	15.15 (15.30)	11.02 (11.00)	44.2	461.94	275	yelow - green
[VO (L^5) (H_2O)]	$VO(C_{17}H_{10}N_6O_4)$ (H_2O)	45.64 (45.70)	2.68 (2.71)	18.79 (18.80)	11.39 (11.40)	45.3	446.94	271	brown - red
[VO (L^6) (H_2O)]	$VO(C_{17}H_{10}N_5O_2SCl)$ (H_2O)	43.54 (43.55)	2.56 (2.70)	14.94 (15.00)	10.87 (10.95)	44.37	468.44	>300	brown - dark

a Calculated (Experimental) ; b Decomposition temperature ; c 10^{-4} M solution in DMF

Table 2. Assigments of IR Spectral Bands (cm^{-1}) for Complexes of Oxovanadium (IV)

Frequencies	Complexes					
	$VO(L^1)_2$	$VO(L^2)_2$	$VO(L^3)_2$	$VO(L^4)(H_2O)$	$VO(L^5)(H_2O)$	$VO(L^6)(H_2O)$
ν(C=O) pyrazolone	1690 * -	-	1690 * -	~1690 * -	~1690 * -	~1690 * -
ν(C=O) enolic	1280	-	1280	1280	1280	1280
ν(C-O-M)	1540	-	1540	~1545	~1540	~1545
ν(N=N) + ν(C-N-N-C)	1475-1570* +880-900* 1565+910	1560+920	1560+900	1577* 1565+920	1577* 1560+910	1575* 1560+900
δ(OH) phenolic	-	1385* -	-	-	1380* -	1380* -
ν(OH) phenolic	-	3460* -	-	-	3450* -	3450* -
ν(C-O) phenolic	-	1150* 1285	-	-	1140* 1285	1140* 1285
ν(OH...N)	-	1650* -	-	-	1656* -	1656* -
ν(COOH)	-	-	-	2570* -	-	-
ν(OCO)	-	-	-	1425	-	-
ν(C-O-H) of aromaticCOOH	-	-	-	810* -	-	-
δ(OH)+ ν(CO) of aromaticCOOH	-	-	-	1410* -	-	-
ν(CH), δ(CH)	3030*+720* 3030+730	3100+605	3000+720	~3100+730	~3111~720	~3000~730
ν(MN)	410	410	410	405	410	410
ν(MO)	505	500	505	500	500	505
ν(VO)	950	950	950	940	950	952
ν(HO) of H_2O coordinated	-	-	-	3095	3090	3095

* Bands in the free ligands

analysis (Table 1) indicates a ratio VO/HL = ½ for the type (1) complexes and a ratio VO/H_2L = 1/1 for the type (2) complexes. The molecular weights for all complexes correspond to a monomeric structure.

The infrared group frequencies of diagnostic importance are shown in Table 2. Complexes of type (1) $[VO(L)_2]_{sp}$ exhibit a new band corresponding to $\nu(C_{sp}^2\text{-}O)$ enolic at 1280 cm^{-1} while the band corresponding to ν(C=O) pyrazolone dissapears. The band ν(N=N) at around 1475-1570 cm^{-1} in the free ligands is shifted to around 1560 cm^{-1} in the complexes. In the complexes the bands ν(OH) phenolic at around 3460 cm^{-1} and ν(OH...N) at around 1650 cm^{-1} in the free ligand dissapear, while the band ν(C-O) phenolic is shifted from 1150 cm^{-1} in the free ligand to 1285 cm^{-1} in the complex.

Table 3. The Reflectance Electronic Spectral Data for Oxovanadium (IV) Complexes (cm^{-1}) and the Assigments of their Bands

Complexes	ν_1 (cm^{-1})	ν_2 (cm^{-1})	ν_3 (cm^{-1})	Change transfer bands
$[VO(L^1)_2]$	12 750 $b_2 \rightarrow e^*_\pi$ d(xy) d(xz,yz)	17 100 $b_2 \rightarrow b_1^*$ d(xy) $d(x^2-y^2)$	-	~20 000 ($a_1 \rightarrow b_2$) ~28 000 ($e_\pi \rightarrow b_2$)
$[VO(L^2)_2]$	13 000 $b_2 \rightarrow e^*_\pi$	17 000 $b_2 \rightarrow b_1^*$	-	~20 000 ($a_1 \rightarrow b_2$) ~29 000 ($e_\pi \rightarrow b_2$)
$[VO(L^3)_2]$	13 200 $b_2 \rightarrow e^*_\pi$	18 200 $b_2 \rightarrow b_1^*$	-	~21 500 ($a_1 \rightarrow b_2$) ~27 800 ($e_\pi \rightarrow b_2$)
$[VO(L^4)(H_2O)]$	-	15 873 $b_2 \rightarrow b_1^*$	18 181 $b_2 \rightarrow a_1^*$ d(xy) $d(z^2)$	~30 303 ($a_1 \rightarrow e^*_\pi$) ~23 809 ($a_1 \rightarrow b_2$) ~27 397 ($e_\pi \rightarrow b_2$)
$[VO(L^5)(H_2O)]$	-	16 100 $b_2 \rightarrow b_1^*$	19 100 $b_2 \rightarrow a_1^*$	~31 100 ($a_1 \rightarrow e^*_\pi$) ~24 500 ($a_1 \rightarrow b_2$) ~29 800 ($e_\pi \rightarrow b_2$)
$[VO(L^6)(H_2O)]$	-	16 129 $b_2 \rightarrow b_1^*$	18 867 $b_2 \rightarrow a_1^*$	~33 333 ($a_1 \rightarrow e^*_\pi$) ~24 500 ($a_1 \rightarrow b_2$) ~28 800 ($e_\pi \rightarrow b_2$)

The complexes of type (2) $[VO(L)H_2O]$ exhibit new bands due to ν(OCO) coordinated at 1425 cm^{-1}, and a large band corresponding to the coordinated water molecule appears at 3095 cm^{-1}. In all complexes new bands appear around 505 cm^{-1} and around 410 cm^{-1} corresponding to ν(V-O) and respectively to ν(V-N)[11,12].

Furthermore the presence of the V=O stretching band around 950 cm^{-1} all complexes indicates a monomeric VO unit[13].

The IR spectral data suggest:

(*i*) a coordination through (ON) donor system of the HL ligands after deprotonation of the enolic group.

(*ii*) two HL acting bidentately around a vanadyl unit.

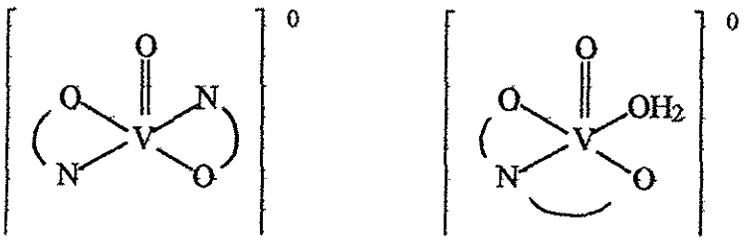
(*iii*) a coordination through (ONO) donor system of the H_2L ligands which act tridentately and dibasic after undergoing the deprotonation of (COOH) group in (H_2L^4) ligand, and (OH) group in (H_2L^5) and (H_2L^6), and the enolic group proceeded from pyrazolone ν(C=O) frequence.

Electronic reflectance spectral data are provided in (Table 3). The complexes $[VO(L)_2]$ exhibit only two bands as shoulders around 13000 cm^{-1} and 17000 cm^{-1}. These bands were assigned to ($b_2 \rightarrow e^*_\pi$) respectively to ($b_2 \rightarrow b^*_1$) transitios [14]. and respectively to ($b_2 \rightarrow a^*_1$) transitions[14].The third band is covered by a charge transfer transition.

The complexes $[VO(L)H_2O]$ exhibit a band beetwin (15873-16129)$cm^{-1}$and a low intensity shoulder beetwin (18181-18867)cm^{-1} assigned to ($b_2 \rightarrow b^*_1$) and respectively to($b_2 \rightarrow a^*_1$) transitions.[14] Charge transfer bands are also observed at (30303-33333) cm^{-1} and (23809-27397) cm^{-1}.

F.A.Cotton[15] noted that the differences in the energy of the third band ν_3 are caused by the nature of the electron-attracting groups around the equatorial atoms.
A strong electron-attracting effect causes a shift of the band ν_3 to a lower wave length. In our paper the value ν_3 =19100 cm^{-1}corresponds to (NO_2) group and the value ν_3 =18867 cm^{-1} corresponds to (Cl) atom. These bands are in good agreement with Cotton's observation.

Based on the above results the following structures are proposed for mononuclear oxovanadium (IV) complexes: structure(I) for $[VO(L)_2]$ complexes and structure (II) for $[VO(L)H_2O]$ complexes.



REFERENCES

1. Y. Kuge, *Bull. Chem. Soc. of Japan*, 45, 799-802 (1972)
2. A. Syamal and K. S. Kale, *Ind. J. Chem.* 19A, 486-488 (1980)
3. R. Seangprasertkij and T. L. Riechel, *Inorg. Chem.*, 24, 1115-1118 (1985)
4. V. V. Zelenstov, *Russ J. Inorg. Chem.*, 7, 670-680 (1962)
5. A. P. Ginsberg, *Inorg. Chem.*, 5, 10, 1656-1662 (1966)
6. L Floru and C. Tărăbăşanu-Mihăilă, Ed., *"Azo Dyes"*, Technique Bucharest (1981) pp.442-443
7. O. D. Gerald and E. P. Dudek, *J. Am. Chem. Soc.*, 86, 20, 4283-4287 (1964)
8. A Emandi and O. Maior, *Rev. Chim.*, 3, 179-181 (1994)
9. A. Emandi and D. Negoiu, *Anal. Univ. Buc.*, II, 19-22 (1993)
10. W. L. Geary, *Coord. Chem. Rev.*, 7, 81-87 (1971)
11. M. F. Abdel-Meyeed and G. B. El-Hevnamy, *Kolorisztikai Ertesio*, 1, 2-3 (1987)
12. M. G. Abd El Waheed and A. Barakat, *Ind. J. Tech.*, 587-591 (1990)
13. L. Sacconi, V. Campigli, *Inorg. Chem.*, 5, 4, 606-611 (1966)
14. L. G. Vanquickenborne and S. P. McGlynn, *Theoret. Chim. Acta*, 9, 390-400 (1968)
15. F. A. Cotton, *Inorg. Chem.*, 2, 97-102 (1967)

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THE REACTION BETWEEN 2,2-DIPHENYL-1-PICRYLHYDRAZYL FREE STABLE RADICAL AND N-BROMOSUCCINIMIDE

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ABSTRACT

The reactions of 2,2-diphenyl-1-picrylhydrazyl (DPPH) or 2,2-diphenyl-1-picrylhidrazine (DPPH-H) with N-bromosuccinimide (NBS) were studied. Two main compounds Br-DPPH and $(Br)_2$DPPH were obtained, by bromination of the starting material in *para*-phenyl position, and also a secondary product, NO_2DPPH. It was shown that the reactions of NBS with DPPH include a substitution at the picryl group of DPPH with liberation *in situ* of NO_2 (*ipso*-substitution of a nitro group with bromine) and subsequently NO_2 is scavenged by DPPH with the formation of NO_2DPPH.

Keywords: DPPH, free radical, bromination, *ipso*-substitution, scavengers

RESUMO

Foram estudadas as reações de 2,2-difenil-1-picrilhidrazila (DPPH) e 2,2-difenil-1-picrilhidrazina (DPPH-H) com N-bromo-sucininimida. Foram obtidos dois produtos principais, Br-DPPH e $(Br)_2$DPPH, através da bromação do reagente inicial na posição p-fenila. Também foi obtido um produto secundário, NO_2DPPH . Foi demonstrado que as reações de n-bromosucinimida (NBS) com DPPH envolvem uma substituição no grupo picrila de DPPH com liberação in situ de NO_2 (substituição ipso de um grupo nitro com bromo). Subsequentemente, o NO_2 reage com DPPH formando NO_2DPPH.

INTRODUCTION

The synthesis of the substituted derivatives of the 2,2-diphenyl-1-picrylhydrazyl free stable radical (DPPH) involves various methods, including radical-radical reactions.[1,2]

The scavenger behavior of DPPH, encountered in many physico-chemical processes, afforded the obtaining of the substituted diphenylpicrylhydrazine R-DPPH-H (R- means a substituent in the *para*-phenyl position, -H a hydrazine and a form without -H a hydrazyl radical).[3] In this way the bromo- and nitro-substituted derivatives of DPPH were obtained.[4,5]

Because of its unusual stability, DPPH has focused special interest for a long time; therefore numerous *mono*- and *di*-substituted compounds have been prepared.[5,6] In particular, the reaction of DPPH with nitrogen dioxide or halogens to form substituted hydrazines has been studied in detail.[1,4]

The 2-(*p*-bromophenyl)-2-phenyl-1-picrylhydrazyl Br-DPPH and 2-*bis*-(*p*-bromophenyl)-1-picrylhydrazyl $(Br)_2$DPPH were obtained by the following reactions: i) the reaction of DPPH with hydrobromic acid in presence of sodium bromide;[7] ii) the reaction of DPPH or DPPH-H with bromine[4] and iii) the synthesis of the bromo-derivatives from substituted diphenyl amine.[5]

The mechanism of the reaction between DPPH and N-bromosuccinimide (NBS) proceeds *via* free radical intermediates, as is shown herein. This paper presents a new method for the synthesis of Br-DPPH and $(Br)_2$DPPH compounds.

EXPERIMENTAL

NBS, DPPH and DPPH-H were Aldrich products. The solvents employed were analytical grade used without purification. In the synthesis, the utilization of DPPH-H instead of DPPH lead to better results.

UV-Vis spectral determinations were performed with a Specord UV-VIS spectrophotometer in methylene chloride. The EPR spectra were recorded at room temperature on a JES-3B (JEOL) spectrometer with 100kHz field modulation using X-band frequency. The parameters of the EPR spectra were measured in comparison with those of Fremy's salt (a_N=13.0 Gauss). The NMR spectra were recorded at ambient temperature (ca. 295K) with a Varian Gemini 300BB instrument; the solvent was deuterated chloroform; internal TMS was used as reference both for ^{1}H-NMR and ^{13}C-NMR spectra.

The NMR and ESR spectra were identical with those in literature.[4,8]

The reaction of DPPH-H with NBS in carbon tetrachloride

Br-DPPH

Five hundred milligrams of DPPH-H (1.25 mmol) dissolved in carbon tetrachloride was allowed to react with 240 mg N-bromosuccinimide (1.3 mmol) at 0-5°C. After 24 hrs. the carbon tetrachloride solution was filtered off, stirred with an aqueous solution of ascorbic acid until the color changed to red-brown, and the organic phase separated; the solvent was removed and the residue chromatographed on silica gel GF 254 (Merck). $(Br)_2$DPPH-H (14%), Br-DPPH-H (39%), DPPH-H (12%), and NO_2-DPPH-H (5%) were obtained. By oxidation of the hydrazine with solid potassium permanganate in methylene chloride the free stable radicals were obtained in 95% yield. Elemental analysis for Br-DPPH-H ($C_{18}H_{12}N_5O_6Br$): calculated (C, H, N, Br %): 45.59; 2.55; 14.77; 16.85; found

45.45; 2.50; 14.90; 16.73. Melting point 181-3°C (literature data 182-4 °C); UV-Vis λ_{max}=320 nm, in basic media λ_{max}=424 nm, for the corresponding free radical λ_{max}=520 nm. TLC analysis on silica gel GF 254 (Merck), toluene eluent, R_f=0.60, for the free radical R_f=0.68.

$(Br)_2$DPPH

Samples of 500 mg DPPH-H (1.25 mmol) was treated with 460 mg NBS (2.6 mmol), and the reaction mixture worked up similarly. $(Br)_2$DPPH-H (32%), Br-DPPH-H (15%), DPPH-H (12%), and NO_2-DPPH-H (11%) were obtained. By oxidation in methylene chloride the corresponding free radicals are obtained with 95% yield. Elemental analysis for Br_2DPPH-H ($C_{18}H_{11}N_5O_6Br_2$): calculated (C, H, N, Br %) 39.09; 2.00; 12.66;28.89; found 38.45; 2.00; 12.70; 28.73. Melting point 158-60°C (literature data 158-62°C); UV-Vis λ_{max}=319 nm, in basic media λ_{max}=432 nm, for the corresponding free radical λ_{max}=520 nm. TLC analysis on silica gel GF 254 (Merck), toluene eluent R_f=0.66, for the free radical R_f=0.78.

The reaction of DPPH-H with NBS in DMF

Br-DPPH

Samples of 500 mg DPPH-H (1.25 mmol) and 230 mg NBS (1.3 mmol) were dissolved at 0-5°C in DMF. After 1 hr. water and ascorcic acid were added until a yellow-red precipitate appeared, which was filtered off, dried and cromatographed under the same conditions as described above. The products were isolated with the following yields: $(Br)_2$DPPH-H (12%), Br-DPPH-H (42%), DPPH-H (10%), and NO_2-DPPH-H (5%). Oxidation in methylene chloride give the corresponding free radicals with 95% yield. Elemental analysis for Br-DPPH-H ($C_{18}H_{12}N_5O_6Br$): calculated (C, H, N, Br %) 45.59; 2.55; 14.77;16.85; found 45.55; 2.50; 14.92; 16.83. Melting point 183°C (literature data 182-4 °C); UV-Vis λ_{max}=320 nm, in basic media λ_{max}=424 nm, for the corresponding free radical λ_{max}=520 nm. TLC analysis on silica gel GF 254 (Merck), toluene eluent R_f=0.60, for the free radical R_f=0.68.

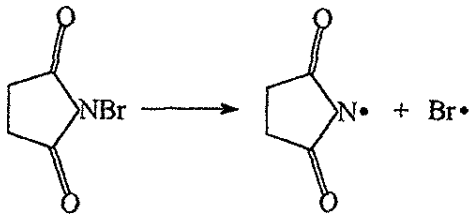
$(Br)_2$DPPH

Samples of 500 mg DPPH-H (1.25 mmol) and 460 mg NBS (2.6 mmol) were processed similarly as described above. $(Br)_2$DPPH-H (37%), Br-DPPH-H (14%), DPPH-H (8%), and NO_2-DPPH-H (10%) were obtained. By oxidation in methylene chloride the corresponding free radicals are obtained in 95% yield. Elemental analysis of Br_2DPPH-H ($C_{18}H_{11}N_5O_6Br_2$): calculated (C, H, N, Br %) 39.09; 2.00; 12.66; 28.89; found 38.65; 2.10; 12.70; 28.75. Melting point 161°C (literature data 158-162°C); UV-Vis λ_{max}=319 nm, in basic media λ_{max}=432 nm, for the corresponding free radical λ_{max}=520 nm. TLC analysis on silica gel GF 254 (Merck), toluene eluent R_f=0.66, for the free radical R_f=0.78.

The compound NO_2-DPPH-H was isolated in the same conditions at R_f=0.26 (λ_{max}=352 nm), for free radical R_f=0.46 (λ_{max}=505 nm).

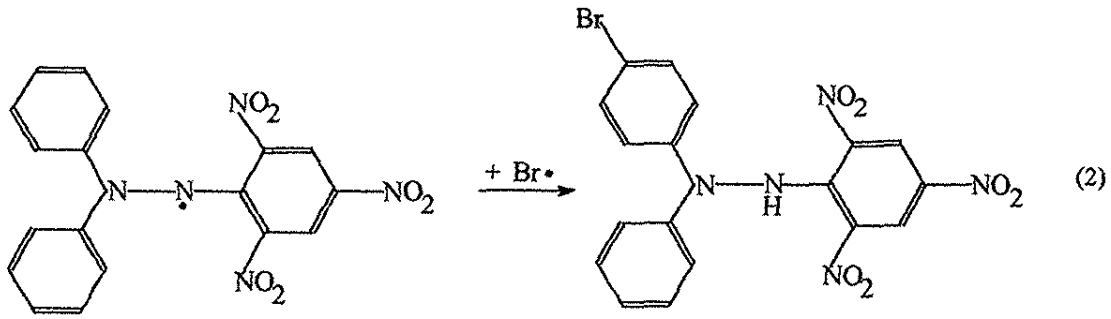
RESULTS AND DISCUSSION

NBS is widely used in the preparation of a bromoderivatives originating in active substrates, the bromination occuring by a radical mechanism (Eq. 1).



(1)

Both free radicals generated may interact with DPPH, but only the bromine radical yields the compound shown in the next equation (the bromine radical is scavanged by DPPH, which requires both combination and H-transfer, Eq. 2):

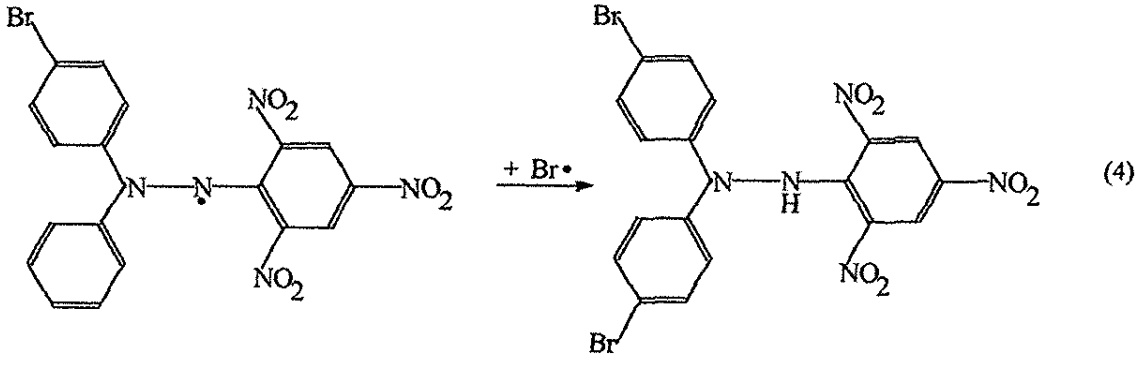


(2)

The free radicals involved in the processes (R may be the free radicals derived from succinimide, bromine or nitrogen dioxide free radical) allowed the oxidation of hydrazine species to the hydrazyl free radical (Eq.3):

(3)

If an excess of NBS is employed $(Br)_2$DPPH is expected to form (Eq. 4):



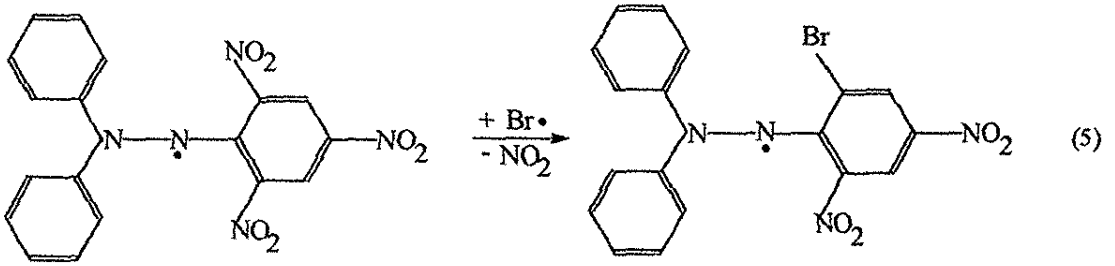
(4)

The study showed that for the DPPH, Br-DPPH and $(Br)_2$DPPH compounds, the relative ease of oxidation of the hydrazines to the corresponding free radical decreases as the bromo groups are added (Weil observed the same behaviour for the nitrocompounds NO_2-DPPH and $(NO_2)_2$DPPH).[1]

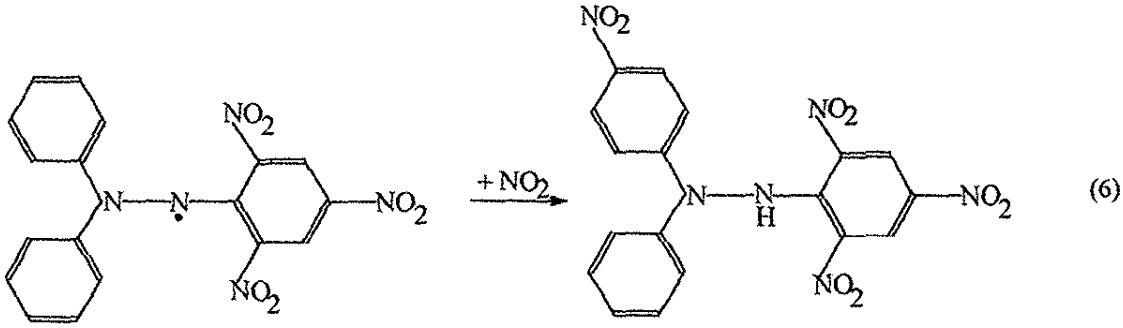
The reactions were carried out in carbon tetrachloride or dimethylformamide (DMF). Although bromination with NBS takes place in carbon tetrachloride, utilization of DMF offers some advantages, because the process is faster, occurs in homogeneous phase and one can easily separate the reaction products by water addition.

An attempt was made to increase the yield and the selectivity of the reaction for one or the other product (Br-DPPH and $(Br)_2$DPPH); the reaction was carried out at low temperature (0-5° C). This processes favoured the obtention of brominated compounds and decreased the yield of the *ipso*-substituted derivatives.[4] The average yield of brominated derivatives increases about 10% when the reaction occurs at low temperature.

All the experiments have shown the formation of NO_2-DPPH, by *ipso*-substitution process (bromine radical *ipso*-substitued one *ortho*-nitro group), followed by NO_2 radical scavanged by DPPH (Eqs. 5 and 6).[3,4,6,8]



(5)



(6)

After the isolation of the bromoderivatives, elementary analysis, melting point and the UV-Vis, NMR and ESR spectra were identical with the literature data.[1-3,9] In basic media the hydrazinic hydrogen is removed (because it has an acidic character),[10,11] and the anion formed exhibits a different absorption spectrum (see experimental part).

The use of the corresponding hydrazine DPPH-H instead of DPPH gave better results as far as the reduction of secondary compounds concerned, as shown by TLC analysis.

In conclusion, although the reaction between DPPH-H and NBS is quite complex, the proposed method is a viable alternative for the DPPH bromination. The reaction involves the generation of bromine radical which is scavenged by DPPH or Br-DPPH. The *ipso*-substitution of a nitro group from picryl moiety with bromine yields NO_2DPPH.

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REFERENCES

1. J. A. Weil, K. V. Sane and M. Kinkade, *J. Phys. Chem., 65*, 710-712 (1961).
2. C. Luca, P. Ionita, M. T. Caproiu, H. Caldararu and T. Constantinescu, *Rev. Roum. Chim., 43*, 000-000 (1998).
3. L. Gille, U. Prosch and R. Stoesser, *Radiat. Phys. Chem., 40*, 461-468 (1992).
4. P. F. Currie, W. Quail and J. A. Weil, *Can. J. Chem., 58*, 723-726 (1980).
5. M.M. Chen, A. F. D'Adamo, R. I. Walter, *J. Org. Chem., 26*, 2721-2727 (1961).
6. P. Ionita, T. Constantinescu, C. Luca, H. Caldararu, M. T. Caproiu and A. T. Balaban, *New J. Chem., 21*, 511-515 (1997).
7. D. H. Solomon and J. D. Swift, *J. Pol. Sci.* A, 3, 3107-3116 (1965).
8. P. F. Currie, J. W. Quail, A. C. M. Rusk and J. A. Weil, *Can. J. Chem., 61*, 1760-1764 (1983).
9. M. M. Chen, K. V. Sane, R. I. Walter and J. A. Weil, *J. Am. Chem. Soc., 65*, 713-717 (1961).
10. C. Luca, P. Ionita and T. Constantinescu, *Rev. Roum. Chim., 39*, 1141-1149 (1994).
11. J. A. Weil and G. A. Janusonis, *J. Org. Chem., 27*, 1248-1250 (1962).

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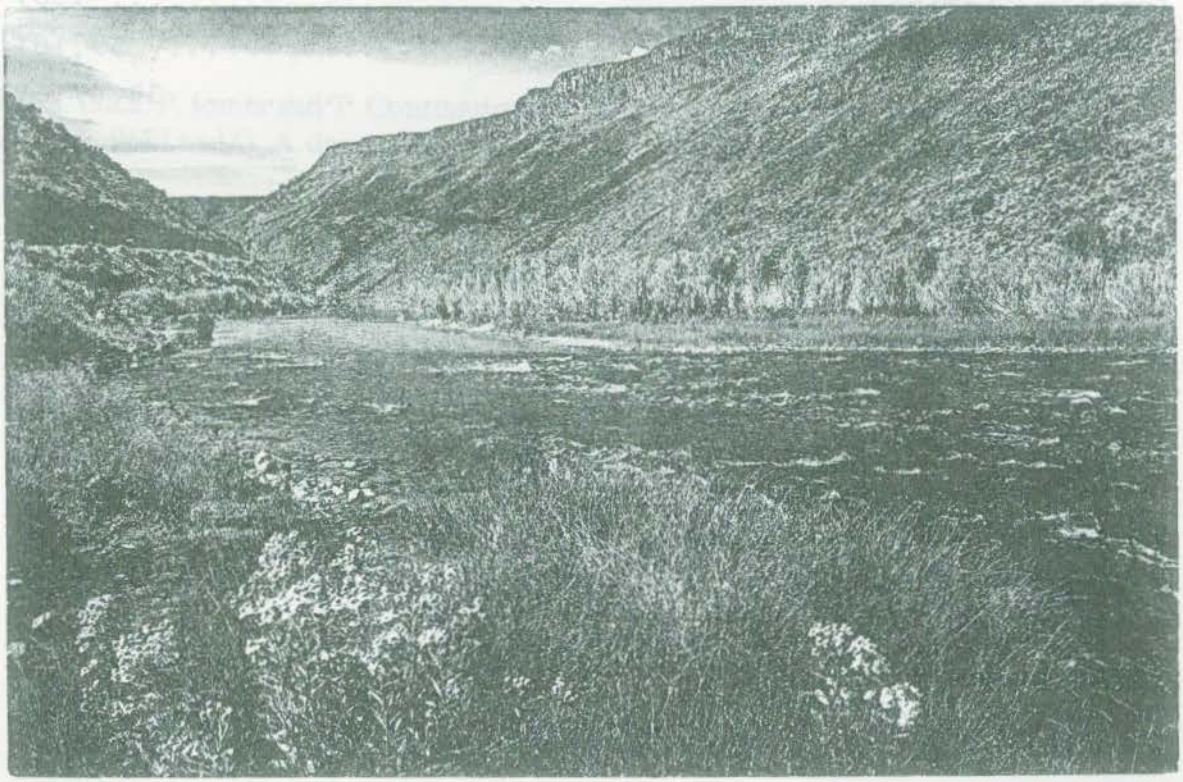

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