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CONTENTS / CONTEÚDO

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ERNESTO GIESBRECHT, GREAT CHEMICAL EDUCATOR AND FATHER OF BRAZILIAN INORGANIC CHEMISTRY

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ABSTRACT

Ernesto Giesbrecht, Brazil's foremost inorganic chemist and chemical educator was born in Ponta Grossa, Paraná, Brazil in 1921 and passed away in São Paulo in 1996. He obtained the Bachelor Degree in Chemistry from the University of São Paulo in 1943 and was awarded a Doctor of Science Degree by the same institution in 1947. He worked at the University of São Paulo most of his life and published over one hundred and fifty scientific papers dealing with alkaloids, compounds of sulfur, selenium and tellurium, chemical education and the chemistry of lanthanides and actinides. He trained approximately thirty research scientists in inorganic chemistry, that eventually spread chemical education and inorganic chemistry throughout Brazil. Prof. Ernesto Giesbrecht was a great chemical educator and may be considered the father of Brazilian Inorganic Chemistry.

RESUMO

Ernesto Giesbrecht, notável educador e fundador da escola de química inorgânica brasileira, nasceu em Ponta Grossa, Paraná, Brasil em 1921 e faleceu em São Paulo em 1996. Formou-se Bacharel em Química na Universidade de São Paulo em 1943 e obteve o grau de Doutor em Ciências da mesma instituição em 1947. Trabalhou na USP a maioria da sua vida e publicou mais de cento e cinquenta trabalhos científicos sobre alcalóides, compostos de enxofre, selênio e telúrio, educação química e a química dos actinídeos e lantanídeos. Formou aproximadamente trinta pesquisadores que eventualmente espalharam e consolidaram a química inorgânica e a educação química no Brasil. O Prof. Ernesto Giesbrecht foi um grande educador químico e pode ser considerado Pai e Fundador da Química Inorgânica Brasileira.

KEYWORDS: History of Chemistry, Actinides, Lanthanides, Compounds of S, Se, Te.

Ernesto Giesbrecht was born on March 27, 1921 in Ponta Grossa, Paraná, Brazil and died in São Paulo on July 20, 1996. His father Hugo was an employee of the railway company in the State of Paraná and his mother Rosina was originally from Joinville, Santa Catarina. He completed elementary school and began secondary school in his native town, Ponta Grossa.

When Ernesto was eleven years old, his family moved to

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São Paulo where he completed his secondary school studies at the Liceu Coração de Jesus and graduated in 1939. Subsequently, he entered the Faculty of Philosophy, Sciences and Letters of the University of São Paulo where he was awarded the Bachelor of Chemistry Degree in 1943. He received the Doctor of Science Degree from the same university in 1947. His doctoral dissertation dealing with organic compounds of sulfur,selenium and tellurium was done under the scientific supervision of Heinrich Rheinboldt.

In 1952 Ernesto Giesbrecht passed the public contest for Privatdocent (Livre Docência) at the University of São Paulo defending a research thesis dealing with reactions of hydrazine with selenious acid derivatives. In 1953, he went to Zürich, Switzerland where he worked with Paul Karrer (Nobel Prize in Chemistry of 1937)in the area of alkaloids. During 1956, he collaborated with Ludwig Audrieth at the University of Illinois, studying the chemistry of rare earth polyphosphates.

Ernesto Giesbrecht held faculty positions at the University of São Paulo from 1943, when he entered as Assistant Professor of General and Inorganic Chemistry,until his death in 1996. He became a full Professor of Chemistry in 1962 and retired formally in 1991, but continued his work at the Chemistry Institute as an Invited Professor up to the end of his life.

Prof. Ernesto Giesbrecht held many important administrative positions, among them those of Director of the Chemistry Institute of the University of São Paulo (1974-1978), Dean of the Faculty of Philosophy, Sciences and Letters of the University of São Paulo at Ribeirão Preto (1981-1984), Assistant Dean of the School of Cultural Communications and Vice-Director of the Institute of Biological Sciences of the University of São Paulo. He was a member of the Chemistry Advisory Committee of the Brazilian National Research Council (CNPq), Coordinator

ERNESTO GIESBRECHT (1921-1996)

of the Multinational Chemistry Program of the Organization of American States (OAS) and together with Henry Taube acted as Coordinator of the U.S. National Academy of Sciences - Brazilian National Research Council (CNPq) Cooperation Program in Inorganic Chemistry.

Prof. Dr. Ernesto Giesbrecht was also a member of the Executive Committee of the Commission of Chemical Education of the International Union of Pure and Applied Chemistry (IUPAC) from 1980 to 1985, participated at many internatinal symposia and conferences patronized by IUPAC and UNESCO (United Nations Scienctific and Cultural Organization) and presided and organized , among others, the 1st and 5th Latin American Seminars sponsored by the Organization of American States and was Co-President of the Ninth International Conference on Chemical Education held in São Paulo in 1987 and sponsored by IUPAC.

Prof. Ernesto was a member of the Brazilian Academy of Sciences, founding member of the Academy of Sciences of the State of São Paulo and recipient of many prizes, awards and distinctions. Among them we cite the Fritz Feigl Prize in 1969, the Heinrich Rheinboldt Prize in 1971, the Special Recognition of the Brazilian Chemical Society in 1991, the Brasted Award of the American Chemical Society in 1992 and the National Order of Scientific Merit (Comenda da Ordem Nacional do Mérito Científico) of the Brazilian Federal Government in 1995.Dr. Ernesto, as he was sometimes called by his associates at the University of São Paulo,was also Secretary General of the Federation of Latin American Chemical Societies (FLAQ).

Ernesto Giesbrecht continued the great effort and example of Heinrich Rheinboldt and Heinrich Hauptmann, and more than anybody else was the person responsible for the consolidadtion of the Chemistry Institute of the University

of São Paulo. In 1957, after his return from the United States, in collaboration with Madeleine Perrier and Geraldo Vicentini he founded what may be called the Brazilian School of Inorganic Chemistry,concentrating research in the area of actinide and lanthanide coordination chemistry. He trained approximately thirty research scientists in inorganic chemistry, who eventually spread chemical education and inorganic chemistry throughout Brazil. During his tenure as Dean of the Faculty of Philosophy, Sciences and Letters in Ribeirão Preto, he was instrumental in consolidating the Chemistry Department.[1-6]

He published approximately one hundred and fifty papers dealing with alkaloids, compounds of sulfur, selenium and tellurium, chemical education and the chemistry of actinides and lanthanides. A detailed description of rare earth research at the University of São São Paulo that includes 173 references was given by Prof. Ernesto himself in a paper in collaboration with G. Vicentini and Lêa B.Zinner published in Química Nova in 1984.[4] A partial list of Prof. Ernesto's publications was given in an article, published by two of his disciples, Aécio P. Chagas and Henrique E. Toma in 1991.[5]

In the area of chemical education, Prof. Ernesto Giesbrecht participated at all levels, including secondary school students and teachers, undergraduate and graduate programs and chemical instrumentation. In the 1960's he helped implement the Chemical Bond Approach Project and Chem Study throughout Brazil and Latin America. He was responsible for bringing to Brazil many highly qualified foreign faculty members.[7] As we mentioned above, he participated and organized many national and international events on chemical education. Professor Ernesto believed that the great majority of the public and even secondary and university students were not conscious of the educational, social, economic and political importance of

of Chemistry.[8] He spent a lot of his efforts trying to improve the image of chemistry and show its central role in the development of science and a harmonious life.

Prof Ernesto was Editor of the *Revista Iberoamericana de Educaiõn Quimica* (1966-1975) and member of the Editorial Board of various journals including the *Anais da Associação Brasileira de Química* and *Anais da Academia Brasileira de Ciências*. Prof. Ernesto Giesbrecht was a Member of the Editorial Board of the *Southern Brazilian Journal of Chemistry* since its founding and always gave us help and encouragement.

We first met Prof. Ernesto in 1978 in São Paulo, a short time after our arrival in Brazil, coming at the invitation of the Brazilian Ministry of Education and Culture to help establish the Graduate Program in Physical Chemistry at the Federal University of Santa Catarina. Prof. Ernesto was kind, humane, courteous and always ready to help and give advice.

Prior to our coming to Brazil, we asked a famous chemist with whom we had the privilege to collaborate at the University of California about chemists and the state of chemistry in this country of continental dimensions. He told us that he knew of two great and good chemists in Brazil. The name of one of them was Ernesto Giesbrecht.

At our personal invitation, Prof. Ernesto Giesbrecht visited and gave seminars at the Federal University of Santa Catarina and the Federal University of Rio Grande do Sul. During his visit in Florianõpolis, impressed by the exaggerate enthusiasm that some of us (young at the time) had about establishing the graduate program in chemistry, Prof. Ernesto warned us and another young Visiting Professor to proceed more slowly and with care because science and chemistry were still provincial in Brazil. An advice and a lesson of life, that Professor Ernesto gave us because of his friendly and humane character, that unfortunately we understood only many years later!

When the chemical community in Brazil was split by the formation of the Sociedade Brasileira de Quĩmica (SBQ), he tried

to do his best to reunite the two segments and always participated in the events organized by both societies. We last met Prof. Ernesto at the Annual Congress of the Associação Brasileira de Quĩmica (Brazilian Chemial Association) held in Recife, Pernambuco, undoubtedly one of the best chemistry meetings ever held in Brazil. Although his health was already failing, he made special efforts and served up to the end as a judge of research works presented by young scientists.

During the time that Prof. Dr. Ernesto Giesbrecht was Member and President of the Chemistry Advisory Committee of the CNPq (Brazilian National Research Council) all the research projects and research reports were duly evaluated and there was perfect communication between the CNPq and the scientific community. In more recent years, not following the good example, some of the members of the Chemistry Advisory Committee of the CNPq were glorifying themselves at scientific meetings for judging scientific projects and research reports without reading them and the communication between the CNPq and the scientific community was at best precarious, if not absent at all.

Prof. Ernesto leaves behind his wife Astrẽa Mennucci Giesbrecht, who also holds a Doctors Degree and is a Professor at the Chemistry Institute of the University of São Paulo, their daughter Astartẽ and their son Ralph, and above all the legacy of a mission accomplished and well done.

Prof. Dr. Ernesto Giesbrecht was a great and friendly person who respected life and his fellow man and also was an outstanding chemical educator. Like all great teachers, he firmly believed that a teacher can teach best by his example. Prof. Ernesto may be considered the Father of Brazilian Inorganic Chemistry.

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SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY

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GLUCOSE AND LACTATE BIOSENSORS COUPLED WITH MICRODIALYSIS PROBE FOR CONTINUOUS MONITORING

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ABSTRACT: Several microdialysis probes coupled to a microcell, where an amperometric biosensor for glucose or lactate was inserted, have been tested to evaluate the stability of the biosensor response for *in vivo* monitoring of glucose and lactate levels. Microdialysis probes with a molecular weight cut off ranging from 6000 to 20000 Daltons (Da) were compared. A good sensitivity, reproducibility and stability of the signal were noticed for both systems with different biosensors.

RESUMO Várias sondas para microdiálise, acopladas à uma microcélula e contendo biosensores amperométricos para glicose ou lactato, foram testadas para avaliar a resposta *in vivo* para monitoramento de níveis de glicose ou lactato. Foram comparadas várias microsondas com limites de peso molecular entre 6000 e 20000 Daltons (Da). Foi observada uma boa sensitividade, reprodutibilidade e estabilidade do sinal para ambos os sitemas com vários biosensores.

KEYWORDS glucose, lactate, microdialysis probe, flow through analysis

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TABLE 1

CHANGES IN SOME BIOCHEMICAL PARAMETERS OF PATIENTS WITH VARIOUS LIVER DISEASES

Disease	Number of patients	LP	Bilirubin	GPT	TG	GSH	CL
Control	37	8,6 ± 3,8	1,05 ± 0,8	26,5 ± 3,5	136 ± 12	47,4 ± 4,3	53,7 ± 6,1
Alcoholic hepatitis	11	10,8 ± 5,4	5,8 ± 3,7	38,5 ± 4,1	243 ± 62	32,5 ± 1,6	67,4 ± 7,5
Viral hepatitis	35	21,9 ± 3,2 +	9,3 ± 4,1	496,3 ± 24,3 +	315 ± 24	36,9 ± 2,8	74,5 ± 4,8
Acute viral hepatitis	15	66,8 ± 8,4	19,9 ± 2,6 +	532,7 ± 36,5	428 ± 31 +	24,6 ± 3,9 +	85,8 ± 6,4 +
Chronic hepatitis	14	11,3 ± 3,8	3,8 ± 1,6	47,5 ± 5,2	278 ± 21	53,8 ± 6,1	64,7 ± 5,4
Cyrrhosis	8	17,5 ± 4,3	15,7 ± 4,2	36,8 ± 3,6	236 ± 45	29,6 ± 4,9	42,5 ± 5,8
Hepatic coma	10	7 ± 9,5	21,5 ± 8,5	530,2 ± 34,5	410 ± 30	28,5 ± 4,5	84,6 ± 5,4

LP - lipid peroxides **GSH** - glutathione **GPT** - glutamate:pyruvate-transaminase
CL - chemiluminescence **TG** - triglycerides

Parameters have been expressed in this way :

LP - nmole/ml
Bilirubin, TG, GSH - mg %
CL - pulse/minute/0,1 ml ser

+ = significant differences compared to control for $p < 0,01$

INTRODUCTION

Microdialysis is a new technique for continuos monitoring[1-3], based on the principle of dialysis : in a dialysis tube filled with a liquid (carrier flow), chemical substances diffuse in the direction of the lowest concentration due to the gradient concentration.

The technique presumes the continuos removing of chemical substances from any compartment without removing any liquid. Because the dialysis tube is a micro-tube (100-200 μm inner diameter) and the flow rate is very low (25 μL/min) the concentration is not altered by amount taken out.

This technique was first used for measurements of neurotransmitter in the brain and had already been coupled to liquid chromatography[4-6].

Although, the technique had been developed in some laboratories[7-13], several problems unsolved are still remaining.

One of the newest application of microdialysis is for continuos *in vivo* monitoring[14].

In our case the microdialysis technique has been coupled with a glucose or lactate electrochemical biosensors to obtain an instrument for continuous *in vivo* glucose or lactate monitoring[15].

The system works as follows: a buffer solution is pumped at a constant flow rate into a thin dialysis hollow fiber immersed in the sample; the probe retrieves glucose or lactate and other compounds of low molecular weight from the sample. Subsequently, it flows into a wall-jet cell provided with a glucose or lactate biosensor, that will monitor the glucose or lactate level.

We compared *in vitro* several microdialysis probes with different molecular weight cut-off (MWCO) and one sterilized thin dialysis hollow fiber. The main purpose of this study was the control of stability response of biosensor for glucose and lactate, taking into account that this technique can be succesfully used *in vivo* monitoring.

The study was motivated due to several advantages offered by this system: the sensitivity of biosensors can be checked frequently, the hollow fiber used as microdialysis probe can be sterilized, the process of *in vivo* implantation can be controlled and reactions such inflammation and clotting can be monitored and eliminated. Moreover, as was presented in a previous paper[15], the system can be miniaturized as for a wearable glucose or lactate monitor (Glucoday).

We report in this paper our results obtained for *in vitro* measurements for continuous monitoring of glucose and lactate.

EXPERIMENTAL

Materials and apparatus

Glucose oxidase (GOD; EC 1.1.3.4. from Aspergillus niger, type VII, 132000 U/g) was obtained from Sigma Chemical. A GOD-immobilized-nylon net membrane was prepared as described in a previous paper[16].

Lactate oxidase (LOD E.C. 1.1.3.2 from Pediococcus species, 35000 U/g,) was also obtained from Sigma Chemical. The LOD was immobilized by covalently bonding on pre-activated Immobilon-AV affinity membranes (Milipore, Bedford, MA, USA) following the procedure described by Villarta et al[17].

The buffer solution, Dulbecco's physiological buffer (pH=7.4), was prepared in doubly distilled water. All chemicals were of analytical grade.

The glucose stock solution (0.5 M + 0.1% Katon), was prepared with β-D(+) glucose from Farmitalia Carlo Erba (Milano, Italy) in buffer, allowed to equilibrate overnight and suitable diluted. Also, we prepared a stock solution of glucose (0.5 M) in albumin 3%. Stock lactate solution (0.1 M + 0.1% Katon) was prepared with L(+) lactic acid (Li salt) obtained from Sigma Chemical and freshly prepared every three days in Dulbecco's buffer. The solutions were stored at 4°C when not in use.

Cellulose acetate (53% acetyl) and polivinyl acetate of high molecular weight were obtained from Farmitalia Carlo Erba. For casting the cellulose membrane a precision gauge tool was used. This membrane, with about 100 Da MWCO, was prepared as in a previous works[18-20].

The CMA/10 Microdialysis probe (i.d. 400 μm, wall thickness 60 μm and a MWCO 20000 Da) was obtained from CMA/Microdialysis (Stockholm, Sweden). To assemble microdialysis probes manually we used several kinds of hollow fiber: 1) Filtral 12 AN 69 HF polyacrylonitrile sodium methallyl sulphonate (i.d. 200 μm and MWCO approximately 20000 Da) was obtained from Hospal Industrie (Meyziev, France); 2) Spectra/Por Hollow fibers, regenerated cellulose (i.d. 215 μm, wall thickness 18 μm MWCO 6000 Da); 3) Spectra/Por Hollow fibers, regenerated cellulose (i.d. 150 μm, wall thickness 9 μm MWCO 9000 Da); and 4) Spectra/Por *in vivo* Microdialysis Hollow fibers, regenerated cellulose (i.d. 150 μm, wall thickness 15 μm) were obtained from Spectrum Medical Industries Inc (Los Angeles, CA). We inserted into all Spectrum hollow fibers a gold-plated 50 μm-diameter tungsten wire obtained from Goodfellow (Cambridge, UK) to avoid the collapse.

Silicone tubing (i.d. 0.300 mm, o.d., 0.630 mm, wall thickness 0.165 mm) from A-M systems was used to connect hollow fibers to flow system.

Assembling of the sensor

The wall-jet flow cell used in our work[21] included three separates electrodes: The working electrode (platinum disk with diameter of 1.6 mm), the reference (Ag/AgCl) and the auxiliary electrode. A thin (20 μm) membrane of cellulose acetate was stretched over the platinum electrode surface: it removes the electrochemical interference (uric acid, ascorbate etc.) with its nominal MWCO 100; this has the effect that ascorbic and uric acid do not reach the electrode surface while hydrogen peroxide passes through easily. A nylon net (thickness 100 μm), with the immobilized glucose oxidase enzyme or an Immobilon membrane with lactate oxidase immobilized was placed over the electrode area. Sleeve of suitable diameter was used to stretch both the membranes on the Pt electrode surface.

Procedures

The peristaltic pump drives the carrier solution, with a constant flow rate through the microdialysis probe (with 10 mm length), immersed in glucose or lactate standard solutions. A steady-state current is obtained. The standard solutions, where the microdialysis probe was immersed, were manually changed.

The optimization of the functional parameters have been described elsewhere[14,15,22]. The diagram of the flow system for in vitro experiments is shown in Figure 1.

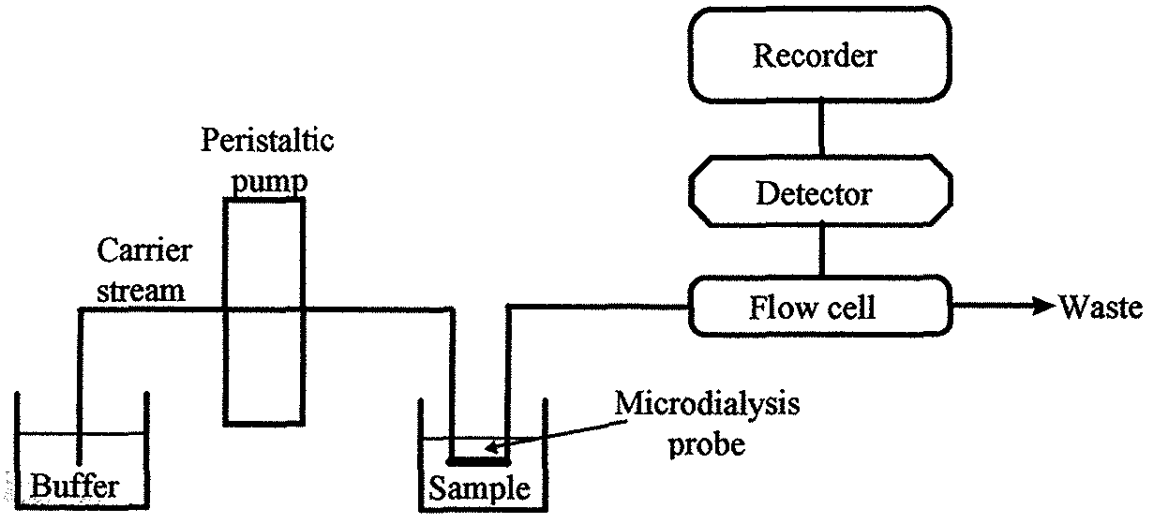

Figure 1. Schematic diagram of the flow system.

RESULTS AND DISCUSSION

The analyte recovery through a microdialysis membrane is a mass transport controlled process. There are three regions were mass transport occurs that must be considered: the sample solution, the dialysis membrane and the solution inside the fiber lumen (i.e. dialysate). Transport in the dialysate is normally considered an important unless the perfusion rate is very low, e.g. < 0.3 μL/min.

At the beginning we checked the performances of the glucose and lactate flow cells without microdialysis probes. For glucose and lactate results are reported in previous papers[14,23]. For lactate we obtained a good linearity (0.1 - 0.5 mM, y=20,7086x+0.72, R=0.9876) and good reproducibility.

The optimum parameters were chosen to be pH=7.4 (Dulbecco's physiological buffer), flow rate 25 μL/min and t=25°C. It had been demonstrated in other studies[14,23,24] that at 37°C the signal (current) obtained with microdialysis probes is about 30% higher and the linearity range is slightly reduced. This is explained by the variation of diffusion coefficient of glucose or lactate through the microdialysis probes.

We compared *in vitro* several microdialysis probes with different MWCO (6000, 9000, 20000 Da) and a microdialysis probe for in vivo measurements.

The dialysis hollow fibers were assembled in laboratory, consisting of a small pieces of a single hollow fiber (1 - 2 cm length) connected with the two ends of Teflon tubes and solded with epoxy glue. We used the manually assembled microdialysis probes which showed better robustness and were easier to handle.

For glucose measurements the fourth microdialysis probe showed almost similar results in spite of different materials and different MWCO. Figure 2a shows the linear response for glucose system with microdialysis probes: 1- MWCO 20000, 1cm length and 2 - microdialysis probe for in vivo experiments. In Figure 2b are presented the linear responses for the same system but for glucose samples prepared in 3% albumin.

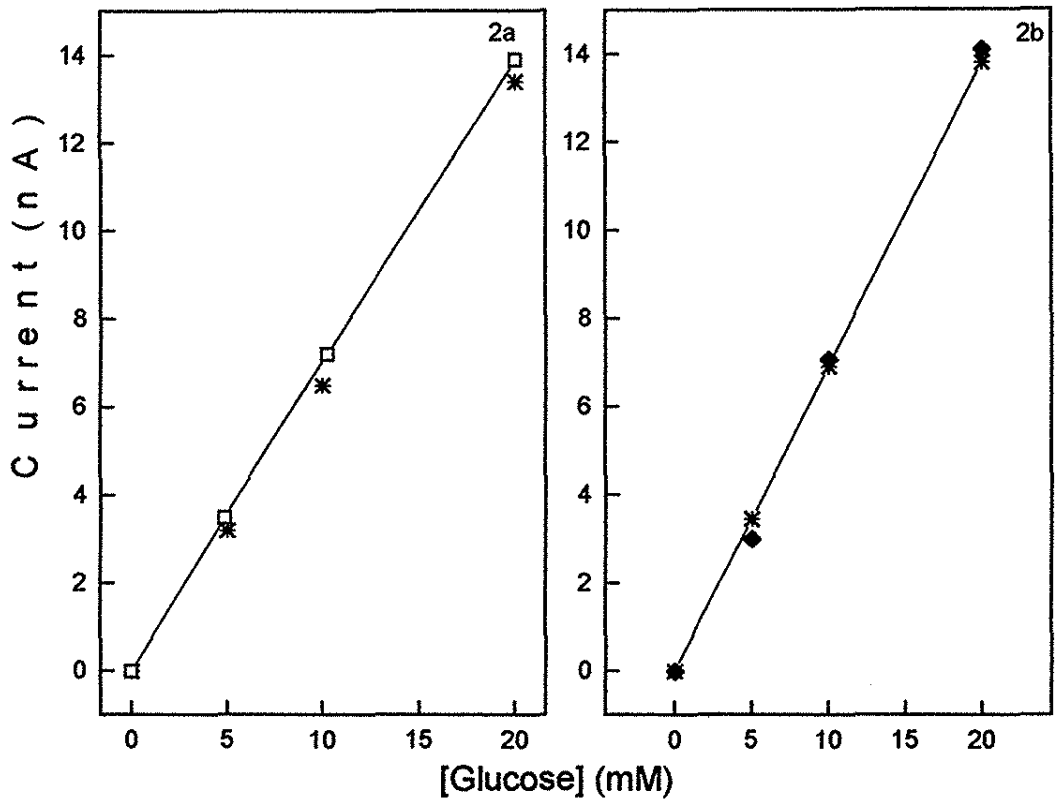

Figure2. The linear response of glucose biosensor coupled with microdialysis probes (1 cm length); **2a** - microdialysis probe with MWCO 20000 Da (□ glucose samples prepared in buffer and * glucose samples prepared in albumin 3%); **2b** - microdialysis probe for *in vivo* measurement (• glucose samples prepared in buffer and * glucose samples prepared in albumin 3%);

As can be observed the results for microdilaysis probe with MWCO 20000 and microdialysis probe for *in vivo* measurements, demonstrate a good linearity for 1 - 20 mM range in both kind of glucose samples (made in buffer and in albumin). The only difference appears for slope values that is higher for system with 20000 MWCO microdialysis probe (0.67) than that for microdialysis probe for *in vivo* (0.47). An explanation of this behavior could be the difference in the geometry or type of materials. For the other microdialysis probes

(6000 and 9000 MWCO) we also obtained, as expected, a good linearity and low differences between the slope values of the calibration curves.

We noticed that for the same concentrations of glucose samples made in albumin 3%, the biosensor gives the values for the current, meaning that albumin does not affect (influence) the response of biosensor (see Fig. 2). The same results were obtained for all kinds of microdialysis probes.

An important study was to check the stability of the biosensor response for a long period as in the case of continuos monitoring. For this reason, the signal (current) was recorded during 15 hours for systems with all four microdialysis probes for both kind of glucose samples. The stability of biosensor response for 10 mM glucose solution prepared in buffer and in albumin 3 % is presented in Figure 3a and 3b respectively. The signals obtained with 20000 MWCO microdialysis probe (Fig. 3a) and microdialysis probe for *in vivo* (Fig. 3b) present small fluctuations due to random variations of the experimental parameters, i.e. stirring conditions.

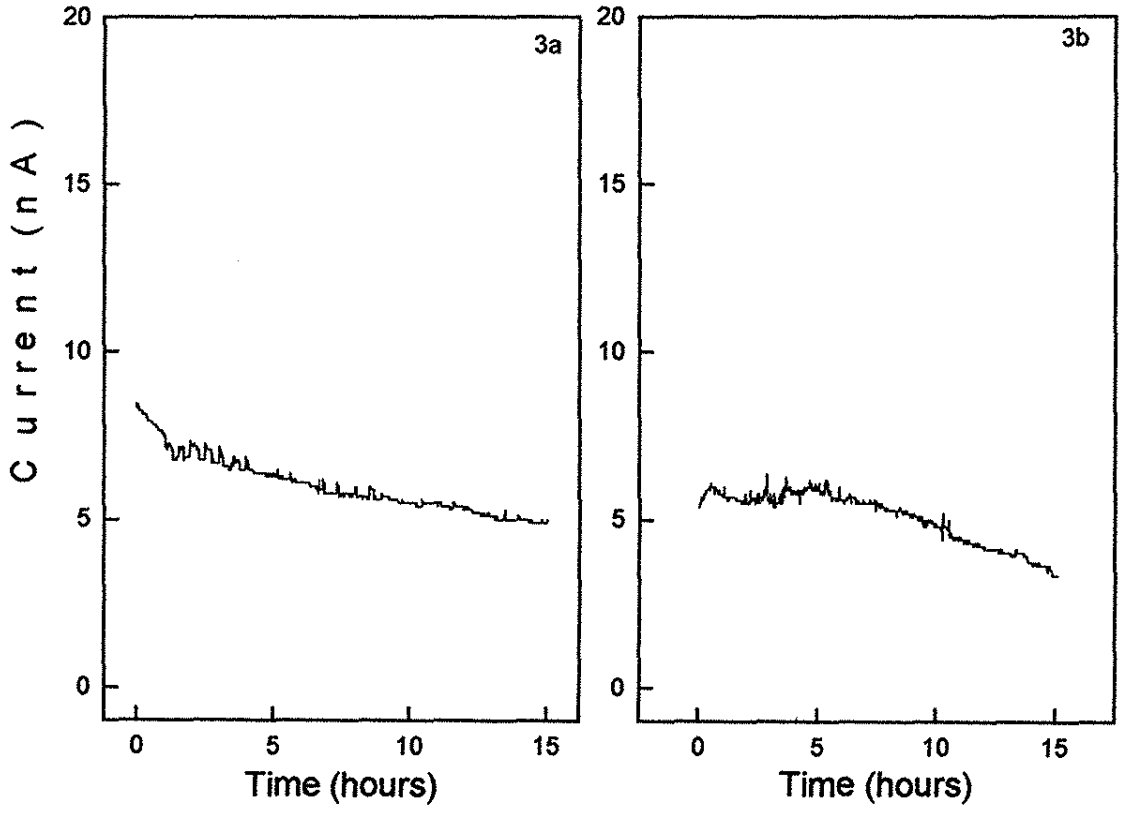

Figure 3. Stability of biosensor response for 10 mM glucose samples; **3a** - glucose sample made in buffer and microdialysis probe with MWCO 20000; **3b** - glucose sample made in albumin 3% and microdialysis probe for *in vivo*.

The slight decrease in time of the signal comes from the consuming of glucose from the samples and not from the change of enzyme activity.

As regards the decrease of the signal during the monitoring of glucose from albumin, observed for microdialysis for *in vivo* measurements, it can be explained only due to the degradation of albumin with time (the measurement was made *in vitro*) and the covering of the hollow fiber.

For *in vivo* monitoring we have to take into account all the factors that can affect the signal such as: the position and the place of the microdialysis probe, the involuntary muscle contractions near the sampling point and if the patient is affected by another disease e.g. Parkinson's disease.

The linearity of the response of the lactate biosensor coupled with microdialysis probe for *in vivo* is presented in Figure 4. A good linearity for 1 - 10 mM range (y=1.0651x+0.54, R=0.9996) is shown as we expected according to other paper[22].

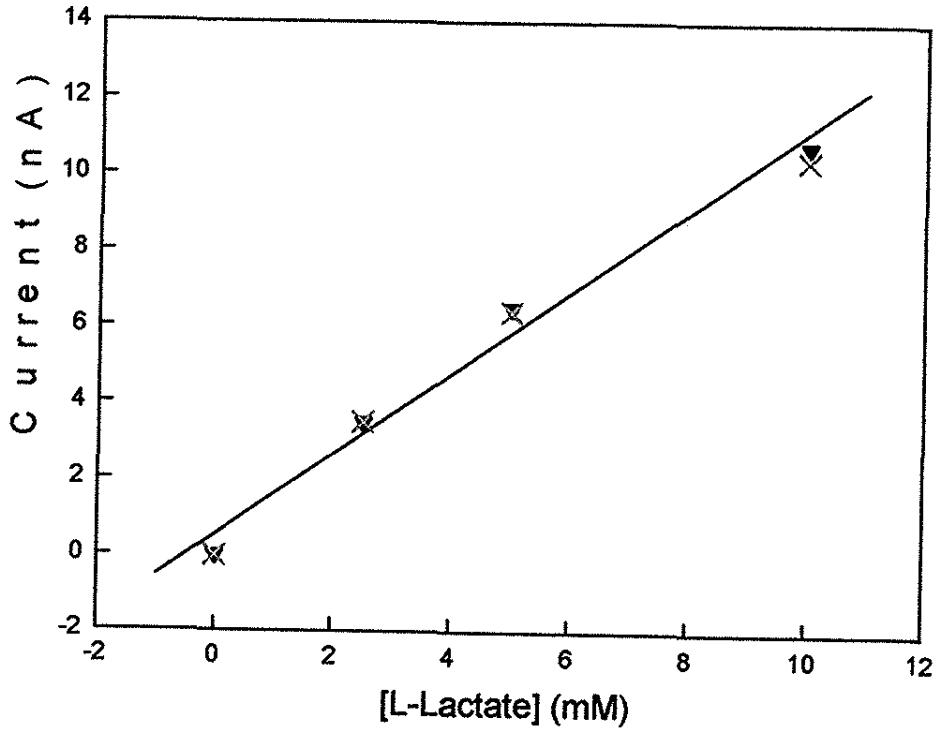

Figure 4. Calibration curve for lactate biosensor coupled with microdialysis probe for *in vivo* monitoring; ▼ values obtained before a continuous monitoring and x values obtained after a period of 12 hours of continuous measurement.

In fact, the main purpose of this research was to check the stability of biosensor response for continuous monitoring. This results from possible applications of this technique in routine clinical chemistry determinations, on-line monitoring of bioprocesses or quality control work.

Figure 5 shows the stability of biosensor response for 5 mM lactate solution with two microdialysis probes monitoring for 10 hours; one of them has MWCO 20000 and the other is used for *in vivo* experiments. As for glucose, all the measurements for lactate were made *in vitro*.

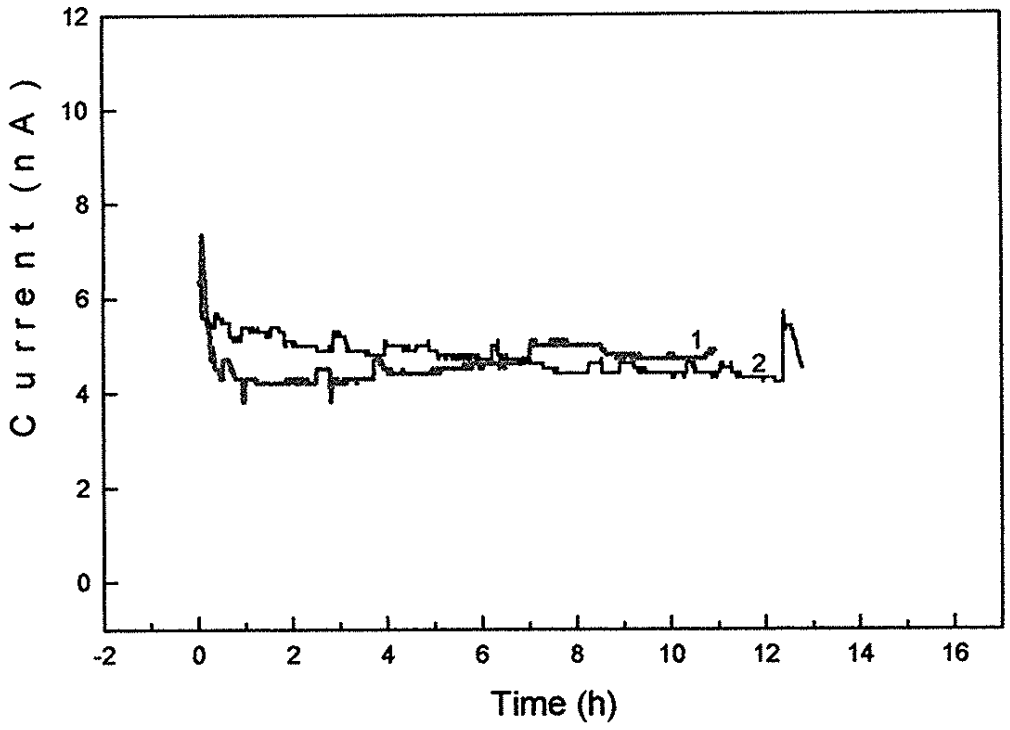

Figure 5. Stability of biosensor response for 5mM lactate with microdialysis probes
1 - for in vivo monitoring and **2** - MWCO 20000 Da

The small variation that we observed in case of glucose system has the same reasons (experimental parameters). After the continuous measurement we checked once again the linearity of the biosensor response which is presented in Figure 4. The same values for the slope obtained in this case proved a good reliability of this system making it suitable for *in vivo* determinations.

CONCLUSIONS

In conclusion, from the stability point of view the coupling of microdialysis with glucose or lactate biosensor in form of wall-jet cell is suitable for measuring glucose and lactate *in vivo*, without any preliminary sample pre-treatment. The glucose system monitors the variations of glucose concentration at the site where the "probe" is inserted. The lactate system

can be used for measurements in sport medicine and in cardiology knowing that lactate is an important metabolite to monitor and control.

The instrument "Glucoday" developed by Ampliscientifica (Milano, Italy) represents a wearable monitor, a sort of metabolic control and it is the first commercial apparatus based on coupling of microdialysis with a biosensor flow cell.

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SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY

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MODELS FOR THE ACTIVE SITE STRUCTURE OF PURPLE ACID PHOSPHATASES

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ABSTRACT

This review article examines the current and most relevant models proposed for purple acid phosphatases (PAPs). It also presents a new possibility for the active site structure of mammalian PAPs based on the work that we and other researchers have done in bioinorganic chemistry.

RESUMO

Este artigo de revisão bibliográfica faz uma análise dos modelos mais relevantes, propostos, para as fosfatases ácidas púrpuras (PAPs). Apresenta também uma nova possibilidade para a estrutura do sítio ativo das PAPs de mamíferos baseada no trabalho que nós e outros pesquisadores tem realizado em química bioinorgânica.

KEYWORDS: purple acid phosphatases, model complexes, active site, bioinorganic chemistry.

INTRODUCTION

"One of the great intellectual challenges presented to Science by Nature is a proper understanding of how enzymes work". This was the introduction to a recent paper[1], in order to establish ideas about enzymes mechanisms. Quite apart from this fascinating challenge, a proper understanding of how enzymes work holds out the promise of obtaining synthetic analogues, capable of closely approach the properties of the natural biomolecules. From a complete characterization of the model compounds, and comparing their properties with the same properties of the enzymes, the scientists should be able to have more precise ideas about the active site structure of the proteins.

Purple acid phosphatases are non-heme metallobiomolecules, so-termed because their pH optimum for enzymatic activity normally lies in the rang 4.9 - 6.0, and their typical intense pink or violet coloration. These enzymes are involved in the hydrolysis of phosphoric acid esters and anhydrides, such as adenosine triphosphate, ATP and others[2].

$$RCH_2O\text{-}PO_3^{2-} + H_2O \rightarrow RCH_2OH + HPO_4^{2-}$$

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PAPs have been isolated from a variety of mammalian tissue , such as , porcine allantoic fluid (referred as uteroferrin), rat bone and spleen, human spleen, bovine spleen (referred to as bovine spleen in the text) and certain plant such as sweet potato, red kidney bean, soybean, and microbial sources. The physiological function(s) on these enzymes has yet to be established[2]. Mammalian PAPs characterized so far are monomeric diiron proteins with molecular weigh of approximately 35 kDa. The plant enzyme from the kidney bean, is in contrast a homodimeric , $[Fe^{III}Zn^{II}]_2$ proteins, of 111 kDa. The most extensively studied PAPs are uteroferrin and bovine spleen. The active site of these last two enzymes consists of a homonuclear diiron complex with two accessible oxidation states[3a] : a catalytically active pink form, $[Fe^{II}\ Fe^{III}]$, λ_{max} = 505-515nm ; $\varepsilon \approx 4000\ M^{-1}\ cm^{-1}/Fe_2$, and an enzymatically inactive purple form, $[Fe^{III}\ Fe^{III}]$, λ_{max} = 550-570 nm; $\varepsilon \approx 4000\ M^{-1}\ cm^{-1}/Fe_2$. The absorptivity of the visible band is roughly additive for successive phenolate coordinated to Fe(III) complexes[3b,c] and model complexes[3d], amounting to $\approx 2 \times 10^3\ M^{-1}cm^{-1}$ per phenolate ligand .This suggests that only one of the iron centers in the active site of uteroferrin and bovine spleen has a visible chromophore. The pink and purple colors of PAPs are due to tyrosinate-to-iron(III) charge transfer transitions [3a]. Therefore, based on the values for the extinction coefficients found in both PAPs, one can speculate about the possibility of two tyrosines residues being coordinated to only one iron center, the non-reducible site . Resonance Raman spectra of the purple and pink forms, using visible excitation, clearly demonstrated the presence of tyrosine ring modes [4]. The presence of histidine imidazole, as a probable ligand to both iron sites, has been demonstrated by NMR[5] and ENDOR[6] studies. Addition of phosphate to the pink form under anaerobic conditions, produces a phosphate complex which is gradually oxidized, in the presence of air, to the purple color[7]. The same purple complex is produced by addition of phosphate directly to the oxidized enzymes, but stronger oxidants such as hydrogen peroxide or ferricyanide, are required for conversion of the reduced pink form to the oxidized purple form in the absence of phosphate[8].

Despite a great deal of characterization of uteroferrin and bovine spleen (absorption spectra[2b,c], circular dichroism spectra[9] , HNMR[5], Mössbauer[10] and EPR[6a] spectra, resonance Raman spectra[4], EXAFS[11], magnetic susceptibility studies[2c,12] , and electrochemical studies[13]) and substantial efforts in several laboratories, crystals suitable for high-resolution X-ray diffraction studies have not been obtained for these PAPs. On the other hand, there exists information about bridging and terminal carboxylato[5b] and hydroxo[13,14] groups coordinated to the dinuclear iron center of uteroferrin and bovine spleen.

More recently, the crystal structure of the enzyme from red kidney bean was determined by the multiple isomorphous replacement method[2d], with resolution of 2.9Å. The iron ion is coordinated by Tyr-167, by the Nε of his-325, and by a monodentate carboxylate, Asp-135. The zinc ion is ligated by the Nε of His-286, the Nδ of His-323, and the amide oxygen of Asn-201. The two metal ions, in the active site structure, are bridged by the monodentate carboxylate group of Asp-164 and the metal-to-metal distance was refined to 3.1Å. Based on the observed coordination geometry, the reaction path and on spectroscopic studies, the researchers[2d] proposed three exogeneus ligands in the coordination sphere of the enzyme, so the active site structure was modeled as shown in Figure1 . The exogenous ligands have to be elucidated better by further studies and synthetic analogues should help to solve this challenge.

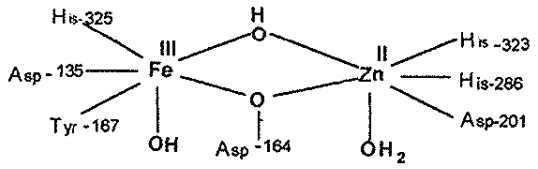


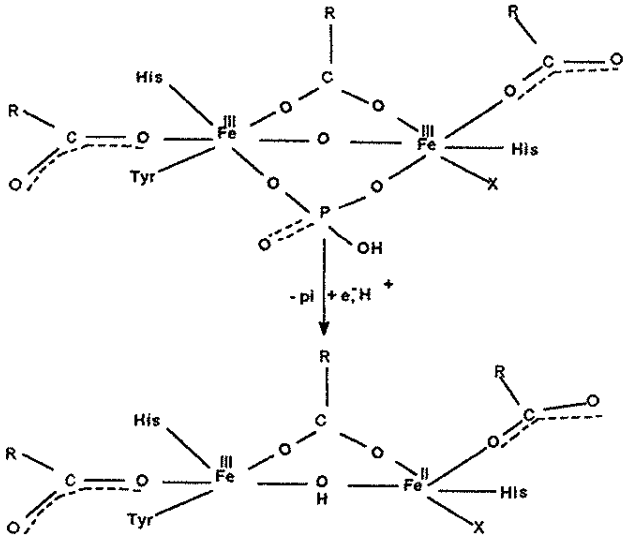
Figure 1. Proposed active site structure of purple acid phosphatases from red kidney bean[2d].

A growing number of dinuclear synthetic analogues of bovine spleen and uteroferrin , containing polypodal ligands having pyridine[15], 1-methylimidazole[16], pyridine-phenolate[17a-d], 1-methylimidazole-phenolate[17c] as pendant arms have been reported. However, most of the model complexes do not exhibit neither the characteristic spectral nor electrochemical properties, $\varepsilon^{o'} = 0.367$ V vs NHE at pH = 5.0 for the redox couple Fe_2^{III} - Fe^{II} Fe^{III}, found in uteroferrin[13]. The coordination environment of the dinuclear iron moieties of PAPs are not yet defined although, the presence of some ligands has already been unequivocally established.

MODELS FOR THE ACTIVE SITE STRUCTURE OF MAMMALIAN PAPs

- Proposals based on enzymatic properties

Based on the properties of Bovine Spleen, B.A . Averill and coworkers[2c] proposed a model for the active site structure of mammalian purple acid phosphatases illustrated in Figure 2.



pi = Inorganic phosphate; His = histidine; Tyr = tyrosinate; X= ?

Figure 2. Active site structure of mammalian PAPs proposed by B.A .Averill and coworkers[2c]

The hypothesis of a μ-oxo bridging group was mainly based on the results from SQUID magnetization measurements[2c], J≈ - 150 cm^{-1}. However, neither EXAFS[11] nor resonance Raman[4] and electrochemical studies[13] have shown any evidence for such a bridge. In addition, a recent magnetic susceptibility study[12] of the oxidized form of bovine spleen reveals an antiferromagnetic coupling constant much smaller, J = -15 cm^{-1}, that indicates the lack of a μ-oxo bridge in the dinuclear iron center of the enzyme. More recently, on the basis of the pH dependence of the activity of the EPR spectra and the visible spectral shifts of the phosphate-saturated reduced and oxidized forms of bovine spleen, a dinuclear iron site bridged by carboxylato and hydroxo groups, was proposed by H. Witzel and collaborators[14].

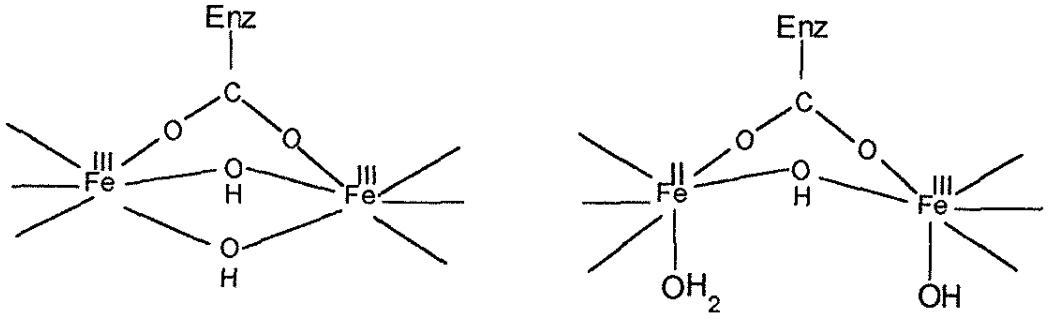


Figure 3. Active site structure of mammalian PAPs proposed by H. Witzel and collaborators[14].

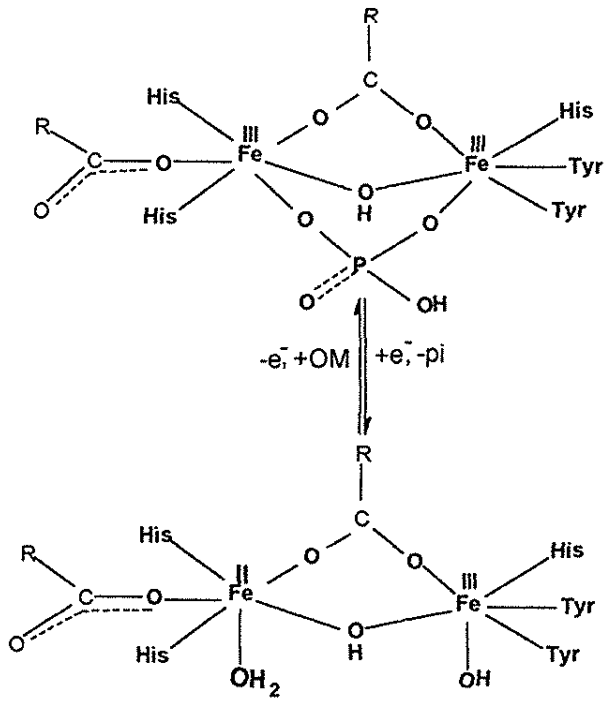
- Proposal based on bioinorganic chemistry approach

The model, illustrated in Figure 3, fails to show the other ligands coordinated to the active site of the enzyme. One can imagine the degree of difficulties that arise when one tries to propose an active site for the enzyme based only on properties. On the other hand, if we take in account the extinction coefficient of bovine spleen and uteroferrin[3a,15b], its is possible to predict[3b-d] the presence of at least one tyrosinate group, as a terminal ligand, in the dinuclear iron center of these PAPs. Taking this into consideration, we synthesized and fully characterized a new complex, $[Fe_2^{III}(BBPMP)(CH_3COO)_2]ClO_4 . H_2O$[17a], where BBPMP is the anion of 2,6-bis [(2-hydroxybenzyl)(2-pyridylmethyl)aminomethyl]-4- methylphenol as a new ligand to obtain synthetic analogues for mammalian PAPs. In the dinucleating ligand, phenolates and pyridines were employed to simulate tyrosinates and histidines respectively, in the enzymes. However, the complex is blue, λ_{max} = 601 nm; ε = 7700 M^{-1}/Fe_2, and the redox potential, $\varepsilon^{o'}$ = -0.71 V vs NHE for the redox couple Fe_2^{III} - Fe^{II} Fe^{III}, is shifted to a more cathodic potential when compared to the value reported for uteroferrin[13]. Fortunately, we realized that it is possible to adjust the chromophore of a precursor complex in order to obtain a suitable model complex for this property in the protein[18,19] .We recently reported a new unsymetrical N_5O_2-donor dinucleating ligand, 2-[((2-pyridylmethyl)amino)methyl]-6-[((2-hydroxybenzyl)(2-pyridylmethyl)amino)methyl]-4-methylphenol -(H_2BPBPMP) - and its first Fe^{II} Fe^{III} complex, $\varepsilon^{o'}$ = 0.38 V vs NHE for the redox couple Fe_2^{III}- Fe^{II} Fe^{III}, as a suitable synthetic analogue that mimics the redox potential of the enzyme. Based on the value found for

the redox potential of the synthetic analogue and of uteroferrin[13] we proposed a ratio of 2:3 for the number of tyrosines and histidines coordinated to the active site of the protein[18,20]. Interestingly, circular dichroism studies[9] also suggest that two tyrosines residues are coordinated to the dinuclear iron center of uteroferrin.

In contrast to the mammalian PAPs, the plant enzymes are insensitive to mild reductants such as ascorbate or dithioerythritol, and no change in the electronic absorption spectrum of oxidized and reduced species is observed[2a,c]. The kidney bean PAP exhibits a visible absorption spectrum, λ_{max}= 560 nm; $\varepsilon \approx 3400$ $M^{-1}cm^{-1}$/dimer. When compared to the chromophoric properties of uteroferrin and bovine spleen this indicates that the reducible site of mammalian PAPs should be similar to the Zn^{II} site of the plant enzyme . However, by the same comparison, this also suggests that the non-reducible site of uteroferrin and bovine spleen must be different from that found [2d] in the enzyme from the red kidney bean. Therefore, based on the active site structure of the kidney bean enzyme and its properties when compared to the corresponding properties of mammalian PAPs and synthetic analogues[18,20] for uteroferrin and bovine spleen it is very reasonable to think about two tyrosines and three histidines residues coordinated to the dinuclear iron site of mammalian purple acid phosphatases. Very recently, we described the synthesis and characterization of a new model complex suitable to mimic the chomophoric properties of the oxidized purple form of mammalian PAPs coordinated to phosphate[21]. The synthetic analogue, $[Fe_2^{III}(BBPMP)(\mu\text{-}OH)(\mu\text{-}O_2P(OPh)_2)].ClO_4$, λ_{max} = 560 nm; ε = 4480 $M^{-1}cm^{-1}$ /Fe_2, presents bridging hydroxo and diphenyl phosphate groups. Taking this into consideration, we can ascribe active site function of mammalian PAPs according to the following ideas: when the organism needs phosphate one of the Fe^{III} site of the oxidized purple form of the enzyme coordinated to this metabolite is reduced by a biological reducing agent, like NADH or NADPH, and the generated pink form free from phosphate is able again to catalyze the hydrolyze of orthophosphate monoesters[2a-c]. Thus, based on a bioinorganic chemistry approach, we present a new possibility for the active site structure of bovine spleen and uteroferrin and the way they could work (Figure 4).

Among the persisting problems which circumvent understanding of the binuclear iron center of uteroferrin and the purple acid phosphatases are the identity of the ligands of each iron atom and how these change in nature or arrangement during redox chemistry[2b]. In this review article we proposed a new possibility to model the dinuclear iron center of mammalian purple acid phosphatases based on their properties when compared to the same properties of some well characterized synthetic analogues and also based on the crystal structure of the enzyme from red kidney bean[2d]. Much more work has to be done in order to solve the challenges of understanding better the structure, the mechanism and the physiological role(s) of PAPs. Enzyme mimics remains an area of definite promise and bioinorganic chemists should be inspired and prepare new synthetic analogues to model the active site structure of purple acid phosphatases.



pi= inorganic phosphate; His= histidine; Tyr= tyrosinate; OM= orthophosphate monoesters.

Figure 4. New proposed active site structure of mammalian PAPs .

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SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY

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HIGH SERUM LIPID PEROXIDES AND THEIR SIGNIFICANCE IN PATIENTS WITH LIVER DEFICIENCY

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ABSTRACT

Various significant levels of lipid peroxides were observed in patients with different liver diseases. The increased values of lipid peroxides might be correlated with the modifications in pathological way of bilirubin, glutamate, pyruvate-transaminase, glutathione, triglycerides and chemiluminescence.

This correlation was observed in the acute hepatic insufficiency such as acute viral hepatitis, hepatic coma, ethylic cyrrhosis. The increase of lipid peroxides in the serum of these patients is related to tissue destructions, cellular membrane lysis and subsequent release of polyunsaturated fatty acids. The determination of lipid peroxides in liver deficiency might indicate an irreversible liver damage and the failure of the antioxidant systems to exert protective role.

RESUMO

Níveis elevados de peróxidos de lipídeos foram observados em pacientes com doenças hepáticas.Os teores altos de peróxidos de lipídeos poderiam ser correlacionados com mudanças patológicas da bilirubina, glutamato, piruvato transaminase, triglicerídeos e quimiluminescência.

Esta correlação foi observada em casos de insufuciência hepática aguda, incluindo hepatite viral, coma hepático e cirrose.O aumento de peróxidos de lipídeos no soro está relacionado com destruição de tecidos, lise da membrana celular e liberação de ácidos graxos poliinsaturados. Teores altos de peróxidos de lipídeos podem indicar dano hepático irreversível e falha dos sistemas antioxidantes.

KEYWORDS: Lipid peroxidation, Liver deficiency, Chemiluminescence, Oxidative stress.

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INTRODUCTION

Formation of peroxides, especially of the lipid ones is a consequence of oxygen activation of the interconversion of the natural defence systems [1-8].

In biological environments, the most favourable substrate of peroxidation is constituted by polyunsaturated fatty acids, important components of cell and subcell membranes.

The continuous formation of lipid peroxides (LP) under normal and pathological conditions has been unanimously accepted [1-8].

The liver seems to be the key organ in oxidative stress. The term "oxidative stress" has been applied to situation when an inbalance arises between the prooxidant and antioxidant equilibrium in favour of the former [4]. A large part of LP are formed in the liver. Likewise, most concentrations of enzymatic and non-enzymatic antioxidants are to be found in the liver [2, 5, 6, 8].

Peroxidation involves direct reaction of active forms of oxygen with formation of free intermediary radicals and semistable peroxides. The most efficient catalysts are the ions of transition metals, haemoproteins, cold, stress, drugs, etc.

Once formed, LP are decomposed leading to the formation of carbonyl compounds. Of these, the most widespread is malondialdehyde (MDA), the determination of which has long constituted the only evidence of LP production in biological systems [1] (Fig.1).

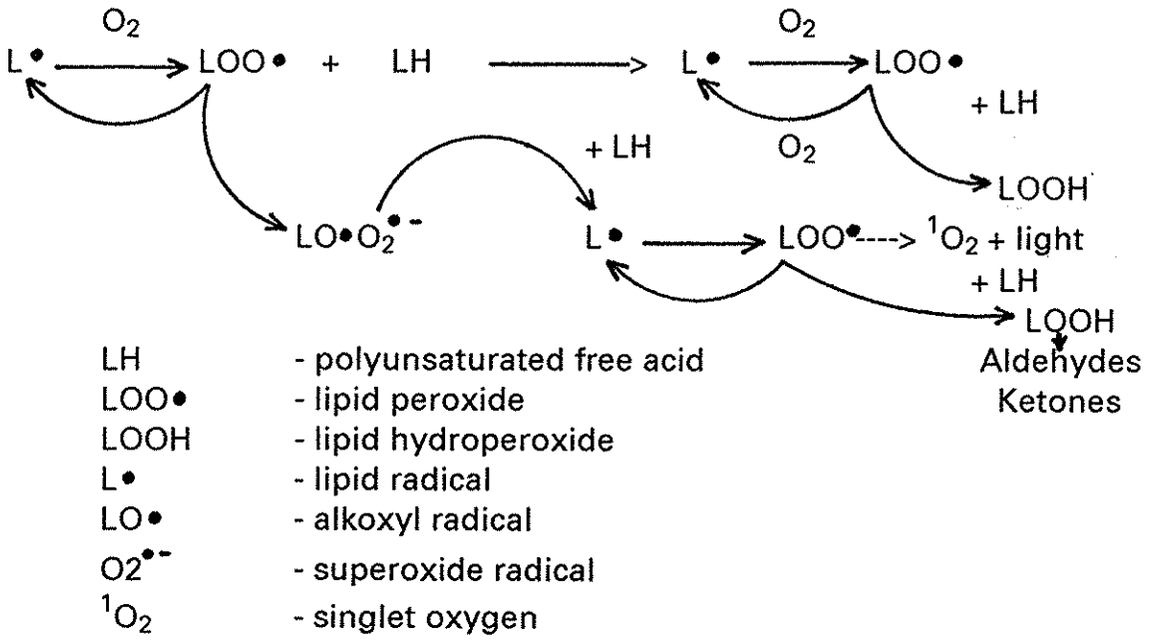

Figure 1. Mechanism of Lipid Peroxides Production

Peroxidation of lipids, at least in the liver, might be a physiological phenomenon, controlled by protective systems, which within certain limits, will not lead to polyunsaturated fatty acids loss.

Through a complex process, LP appear in large concentrations in all liver diseases.

As in all stages of peroxidation, electronically excited species are formed, generating chemiluminescence (CL), CL associated to peroxidation has also been studied. A characteristic of CL is that in most reactions involved in this phenomenon, intermediates are reactive species of oxygen, especially singlet oxygen, $^1O_2$ [4, 5, 8, 9 - 12].

MATERIALS AND METHODS

The biochemical determination has been performed according to standard methods[13,14] for bilirubin (BR), glutamate : pyruvate-transaminase (GPT), glutathione (GSH) and triglycerides (TG). Lipid peroxides (PL) have been measured according to Satoh's method[15] and chemiluminescence (CL) by using the H_2O_2 - haemoglobin - luminol system [10].

RESULTS AND DISCUSSION

The results are shown in Table 1 and Figure 2.

Lipid peroxides concentration in plasma becomes statistically increased in severe forms of hepatic insufficiency, varying with bilirubin and GPT levels. On the other hand, GSH concentrations decreases.

Unsignificant increase of lipid peroxides in mild forms of hepatic insufficiency proves the great capacity of resistance and adaptation of the defence systems.

A correlation between the biochemical parameters and the degree of lysis of the hepatic cell and the functionality of the defence systems, has also been noticed.

Thus, triglycerides represent the substrate of peroxidation, bilirubin is the catalyst of peroxidation, favouring HO• formation, LP and CL are the outcome of peroxidation and the glutathione is an indicator of the efficiency of the defence systems against peroxidation. In this respect, an

TABLE 1

CHANGES IN SOME BIOCHEMICAL PARAMETERS OF PATIENTS WITH VARIOUS LIVER DISEASES

Disease	Number of patients	LP	Bilirubin	GPT	TG	GSH	CL
Control	37	8,6 ± 3,8	1,05 ± 0,8	26,5 ± 3,5	136 ± 12	47,4 ± 4,3	53,7 ± 6,1
Alcoholic hepatitis	11	10,8 ± 5,4	5,8 ± 3,7	38,5 ± 4,1	243 ± 62	32,5 ± 1,6	67,4 ± 7,5
Viral hepatitis	35	21,9 ± 3,2 +	9,3 ± 4,1	496,3 ± 24,3 +	315 ± 24	36,9 ± 2,8	74,5 ± 4,8
Acute viral hepatitis	15	66,8 ± 8,4	19,9 ± 2,6 +	532,7 ± 36,5	428 ± 31 +	24,6 ± 3,9 +	85,8 ± 6,4 +
Chronic hepatitis	14	11,3 ± 3,8	3,8 ± 1,6	47,5 ± 5,2	278 ± 21	53,8 ± 6,1	64,7 ± 5,4
Cyrrhosis	8	17,5 ± 4,3	15,7 ± 4,2	36,8 ± 3,6	236 ± 45	29,6 ± 4,9	42,5 ± 5,8
Hepatic coma	10	7 ± 9,5	21,5 ± 8,5	530,2 ± 34,5	410 ± 30	28,5 ± 4,5	84,6 ± 5,4

LP - lipid peroxides **GSH - glutathione** **GPT - glutamate:pyruvate-transaminase**
CL - chemiluminescence **TG - triglycerides**

Parameters have been expressed in this way :

LP - nmole/ml
Bilirubin, TG, GSH - mg %
CL - pulse/minute/0,1 ml ser

+ = significant differences compared to control for $p < 0,01$

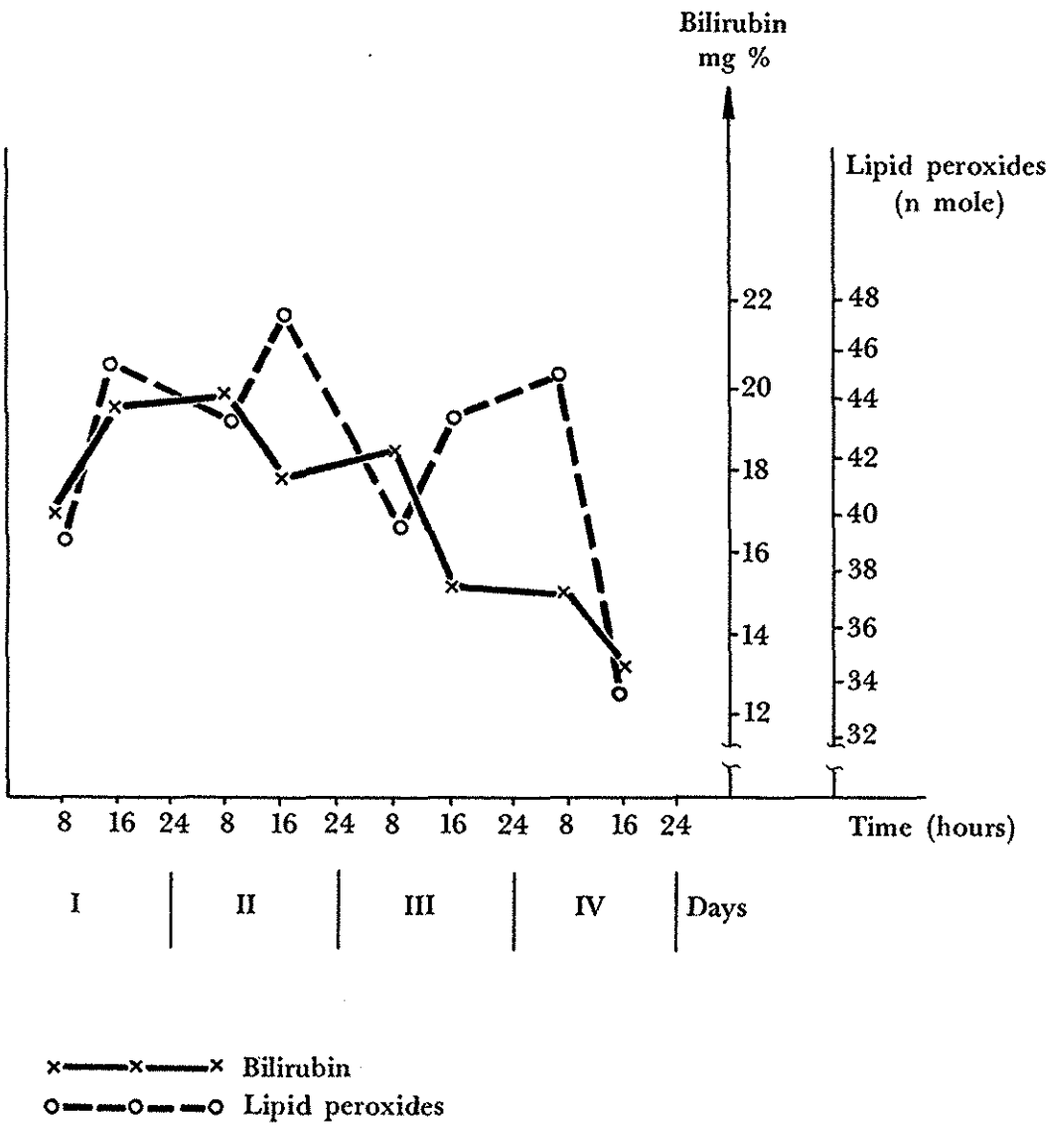

Figure 2 Bilirubin and Lipid Peroxides concentration in Hepatic Coma

increase of PL, TG, BR and CL when GSH is reduced can also be accounted for.

Chemiluminescence of biological systems which undergo peroxidation has a direct relationship with LP concentration and MDA, their product of decomposition, although these parameters of peroxidation are formed by different ways and at different stages (Table 1) [3, 9, 10].

Individual variations of the values under study are greater in mild insufficiencies when, due to prompt and efficient functioning of the defence systems, peroxidation is low.

From the correlation of biochemical parameters and the significance of their values in various hepatic diseases, it results the lipid peroxide level may be a sensitive indicator of the degree of involvement hepatic integrity, as well as of the incapacity and exceeding of antioxidant systems.

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SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY

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USE OF MONTMORILLONITE (SMECTITE) AS CATALYST FOR OLEFIN POLYMERIZATION AND TRANSFORMATION OF SULFUR COMPOUNDS.

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ABSTRACT

Acid activated montmorillonite (smectite) clay was used to eliminate olefins and transform thiophenes and mercaptans present in aromatic BTX (benzene-toluene-xylene) streams from the aromatic extraction unit of COPESUL - Companhia Petroquímica do Sul.

The working temperature of the mineral clay was raised above normally specified values since difficulties were encountered to meet the specification for hydrogen sulfide in xylene and trimethylbenzene. The experimental results showed that montmorillonite (smectite) clay was suitable for olefin elimination and sulfur compounds transformation at higher reaction temperatures (200^{0}C), and that the useful life for catalytic operations could be prolonged by raising the temperature.

KEYWORDS: Montmorillonite (Smectite); clay; olefin polymerization; desulfurization; BTX (benzene-toluene-xylene) streams.

RESUMO

O composto montmorillonita (esmectita) ácido ativado, foi usado na eliminação de compostos olefínicos e transformação de compostos de enxofre, presentes numa corrente de extrato aromático, proveniente da Unidade de Extração de Aromáticos da Companhia Petroquímica do Sul.

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O argilo-mineral teve sua temperatura de operação elevada com objetivo de melhorar sua atividade catalítica, já que vinha apresentando dificuldade de manter o xileno e o trimetilbenzeno especificados em relação a presença de gás sulfídrico. Os resultados mostraram que a montmorillonita (esmectita) possui atividade catalítica para manter os produtos especificados, a temperatura de 200°C e que a vida útil do catalisador poderia ser prolongada elevando-se a temperatura de reação.

INTRODUCTION

The purpose of the present work was to study the properties and conditions under which the clay montmorillonite (smectite) acts in the elimination of unsaturated compounds and the removal of sulfur in the form of hydrogen sulfide from thiophenes and mercaptans. It is important to note that not all cations present in the clay have the same binding energy. The ease with which the cations can be exchanged is in accordance with the following order: Li^+, Na^+, K^+, Rb^+, Cs^+, Mg^{++}, Ca^{++}, Sr^{++}, Ba^{++} and H_3O^+. The mineral clay is used in the Aromatics Fractionation Unit of COPESUL - Companhia Petroquímica do Sul. Its main function is to ensure that the aromatic products meet the bromine index and sulfur specifications. At the present, the unit is having difficulties in meeting the specifications for xylene and trimethylbenzene due to the presence of hydrogen sulfide.

Montmorillonite (smectite) $\{(Al_{1,5}Mg_{0,33})[Si_6O_{10}](OH)_2.nH_2O\}$ is a clay mineral of (t-o-t) smectic dioctaedric structure belonging to the smectic group. According to Klein and Hurbult[1] its principal characteristic is to absorb water molecules between the smectite layers or lamelae, leading to swelling and a pronounced expansion of the structure. The layers consist of tetrahedral SiO_4 units sharing corners with octahedral Al^{+++}, having coordinated oxygen and hydroxyl groups. The structural model of montmorillonite (smectite) in given in Figure 1.

In a slightly acidic solution, cation exchange with protons is possible and because of the layer structure swelling effects occur. The swelling is understandable in terms of ionic strength effects on double layer repulsion.

A typical montmorillonite (smectite) contains a variety of oxides in approximately the following composition: SiO_2 = 57,49%; Al_2O_3 = 20,27%; Fe_2O_3 = 2,92%; FeO = 0,19%; CaO = 0,23%; MgO = 3,18%; K_2O = 0,28%; Na_2O = 1,32%; TiO_2 = 0,12% and H_2O = 14%[3].

Its crystals are of reduced dimensions (average of about 0.15 μm) and their thickness is very small. Organic molecules can be absorbed between the smectite layers usually taking the place or coordinating with exchangeable cations [2-6]. The binding between the smectite layers involves van der Waals forces and considering the isomorphic substitution of the mineral can be used to explain the easy cleavage of montmorillonite (smectite) crystals in liquid medium[2]. Sheets of clay crystal can hold an equilibrium separation distance that may be as large as 100 A° and depends on the concentration of electrolyte in the interlayer aquous phase.

The catalysis of many organic reactions by mineral clays has been known for a long time, it has been applied in many industrial processes and it has been described in detail in the literature[4,5,7].

The present paper will deal only with the use of montmorillonite (smectite) clay as a catalyst in olefin removal (polymerization olefins) and aromatics purification (desulfurization).

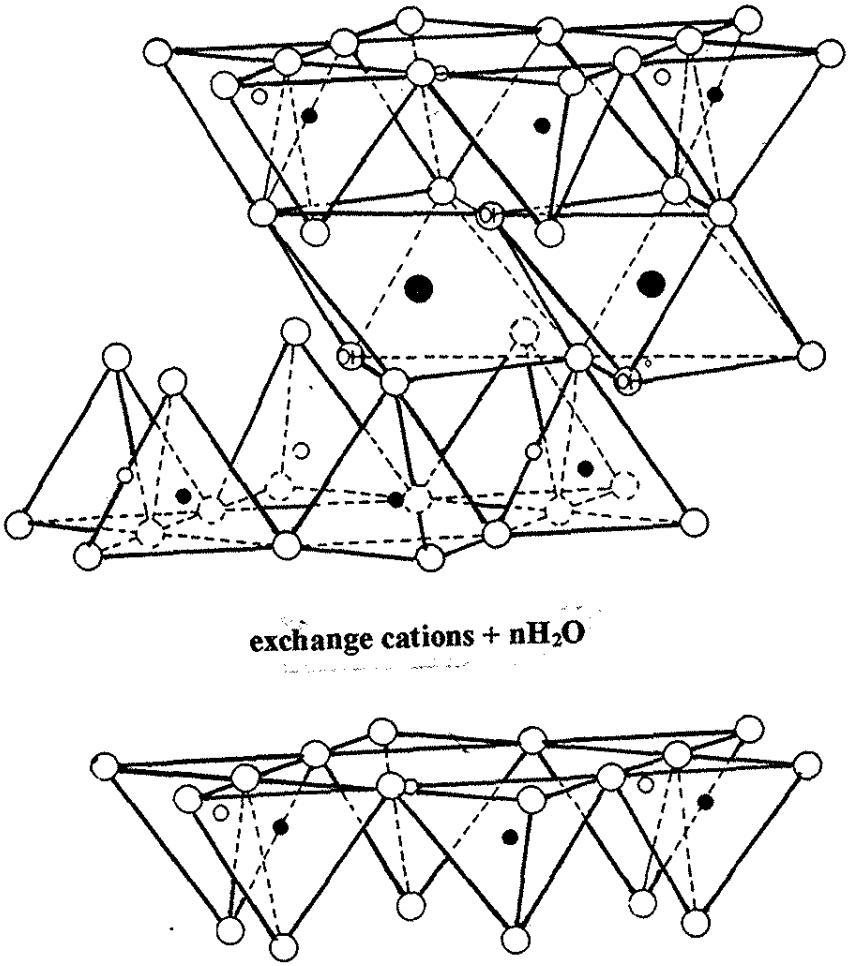


Figure 1. Structural model of montmorillonite (smectite)[2].

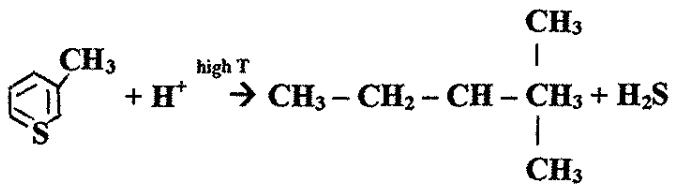
The catalytic properties of montmorillonite (smectite) are essentially related to its ability to absorb organic molecules on the internal surfaces (between the layers). The reactions generally occur at lower temperatures, when compared to clays such as kaolinite and pyrophyllite used in cracking and need time in order to orientate the molecules and introduce the different elements into structures at the correct junctions.

DESCRIPTION OF THE INDUSTRIAL PROCESS

The production of aromatics with high purity specifications involves several unit processes. A block diagram of the aromatics units of COPESUL - Companhia Petroquímica do Sul is given in Figure 2.

U_{21} - Hydrogenation Unit of Pyrolysis Gasoline. This unit was projected in order to hydrogenate in two steps the crude gasoline produced in the Olefins Unit. This gasoline contains an aromatics fraction. The first step involves selective hydrogenation of diolefinic and styrene derivatives. The second step involves the saturation of olefins and the desulfurization of sulfur compounds leading to the formation of hydrogen sulfide. The sulfur, mostly present in thiophenes and mercaptans is not totally removed in the hydrogenation unit and the presence of small amounts (less than 1.0 ppm) leads to failure to meet the required purity specifications. Montmorillonite (smectite) clay promotes this desulfurization process. The reactions under consideration are illustrated bellow:

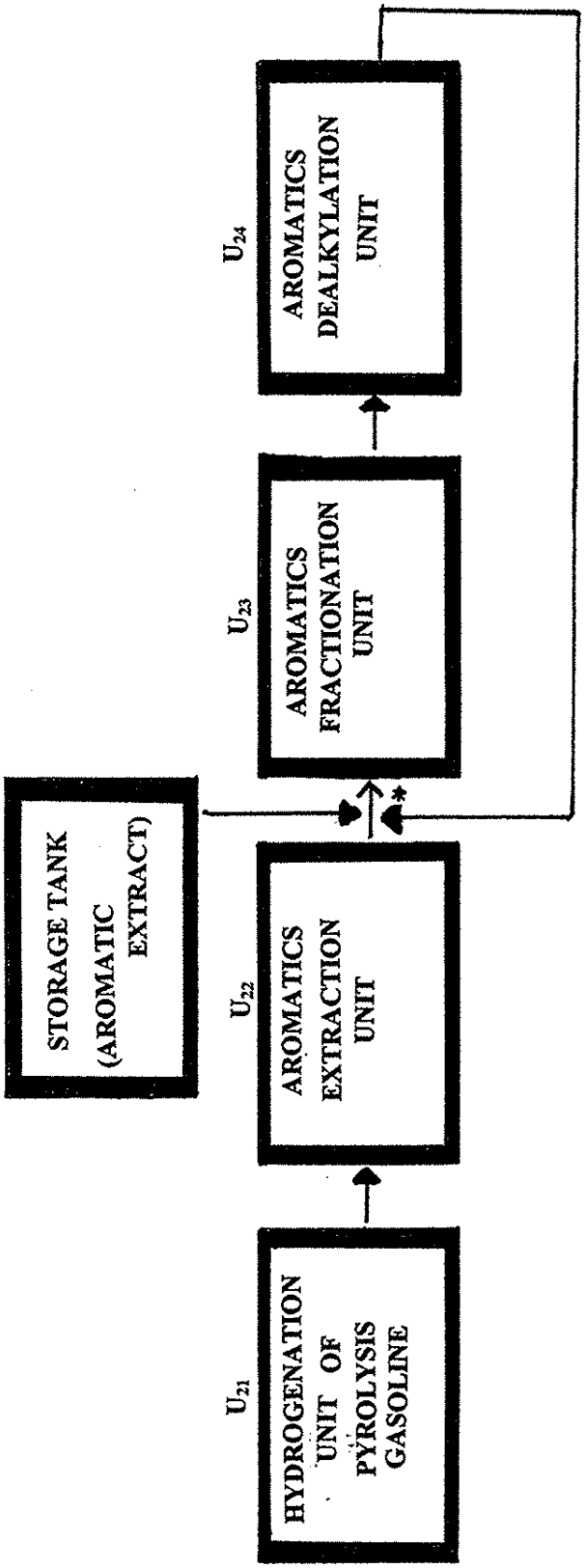
$$Y^+ + H_2C = CH_2 \rightarrow Y - CH_2 - CH_2 + H_2C = CH_2 \rightarrow Y - CH_2 - CH_2 - CH_2 - CH_2^+$$



$$CH_3(CH_2)_2CH_2SH + H^+ \xrightarrow{\text{high T}} CH_3(CH_2)_2CH_3 + H_2S.$$

U_{22} - Aromatics Extraction Unit. The main function of this unit is to extract benzene, toluene and trimethylbenzene from pyrolysis gasoline produced in the Olefins Unit and hydrogenated in two steps in the Hydrogenation Unit (U_{21}) using sulfolane as a solvent. This extract contains undesirable contaminating traces of olefins that have not been hydrogenated in the Gasoline Hydrogenation Unit. Montmorillonite (smectite) clay promotes the polymerization of these defins and leads to acceptable bromine index values in the final product.

U_{23} - Aromatics Fractionation Unit. The purpose of this unit is to produce in high punty grade benzene, toluene, xylene and trimethylbenzene from a feed coming from three streams - the aromatic extract produced in the Aromatics Extraction Unit (U_{22}), aromatic extract from the storage tank and the benzene rich stream produced in the Aromatics Dealkylation Unit (U_{24}). Figure 3 shows a diagram of the BTX (banzene-toluene-xylene) Clay Treatment Towers. The treatment with montmorillonite (smectite) clay is done at the entrance of the Aromatics Fractionation Unit (U_{23}). As previously mentioned, the feed for this unit proceeds from three diferent streams. The first two streams combine and are preheated by the heat exchange with the stream that leaves the clay treatment and subsequently the three streams are heated to the desired operation temperature by using steam under medium or high pressure. The total or final stream is then treated with



* Montmorillonite (smectite) clay treatment.

Figure 2. Block diagram of the aromatic units[7].

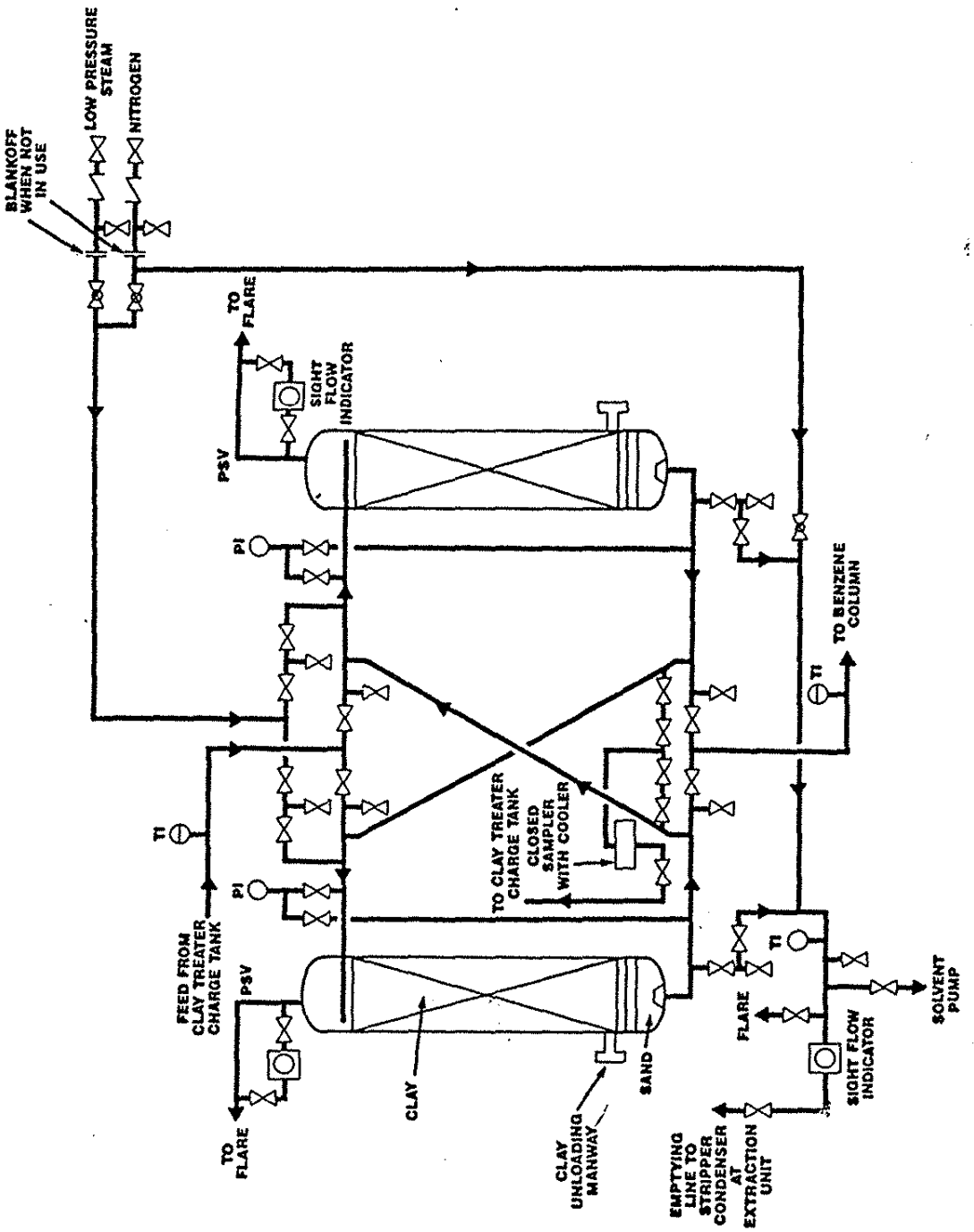


Figure 3. Diagram of the BTX (benzene-toluene-xylene) clay treatment towers[8].

montmorillonite (smectite) clay in one or two clay towers in order to remove the contaminants. The clean stream will then feed the benzene column. Two clay towers are necessary in order to avoid interruptions of the treatment when the clay in one of the towers is saturated. The benzene column also contains water and lighter products such as hydrogen sulfide and sulfur dioxide. The lighter products are removed from the top of the column and burned. Hydrogen sulfide results from reactions of sulfur compounds (thiophenes and mercaptans) from the feed in the presence of montmorillonite (smectite) and sulfur dioxide is the result of degradation of sulfolane used as solvent in the Aromatics Extraction Unit (U_{23}). The degradation of sulfolane, present in small concentration in the clay towers, usually takes place when the temperature reaches 200°C.

U_{24} - Aromatics Dealkylation Unit. The function of this unit is to produce benzene from toluene, xylene or trimethylbenzene streams coming from the Aromatics Fractionation Unit (U_{23}). This unit employs dimethyl disulfide as an eluent in the reaction section (650°C). Reaction of dimethyl disulfide with hydrogen present in the reactor may lead to the formation of hydrogen sulfide and eventual contamination of the product with thiophene.

EXPERIMENTAL PROCEDURE

The experimental work consisted essentially in elevating temperature in the clay towers for a period of operation that lasted over a month. The temperature used was varied from 150°C to 200°C and the pressure range employed was from 12.0 kgf/cm^2 to 15.0 kgf/cm^2. A detailed description of experimental procedure is given in Table I.

Table I. Variation of pressure and temperature in the clay towers.

Date (1995)	Temperature (°C)	Pressão (kgf/cm^2)
10.08	150	12.0
11.08	170	12.0
14.08	200	15.0
19.08	195	15.0
20.08	190	15.0
28.08	200	15.0
14.09	195	14.0

The montmorillonite (smectite) clay used was obtained from Engelhard Exceptional Technologies, Jackson, Mississippi, USA. It was an acid treated clay produced in granular form to facilitate its use in fixed bed applications. It was produced by ion exchange (of Mg, Ca, Na, K and Al ions) in specially selected montmorillonite (smectite) clay and it is characterized by high adsorptive capacity, high catalytic and high surface area. Some typical properties are illustrated in Table II.

The products obtained were analyzed using standard laboratory tests for bromine index in the case of benzene and the presence or absence of traces of H_2S/SO_2 in xylene and trimethylbenzene. The bromine tests verifies the degree of purity with respect to the presence of olefins and the bromine used per g of sample[10].

Table II. Some typical properties of the montmorillonite (smectite) clay used[9].

Moisture	
Free @ 105°C, wt. % loss	**14**
Residual Acidity	
mg. KOH/gm. At phenolphtalein end point	**14**
Particle size. Tyler Standard Sieve	
Passing 20 mesh, wt. %	**75**
Passing 60 mesh, wt. %	**5**
Apparent Bulk Density, Packed	
lbs./cu. ft.	**50**
gm./cc.	**0.80**
Surface Area	
B.E.T. Method, m^2/gm.	**400**

The presence of H_2S was tested using lead acetate indicator paper in the presence of vapors of the product. The presence of hydrogen sulfide leads to the formation of lead sulfide, characterized by its black color. The test of SO_2 consists of wetting filter paper with 5% starch solution followed by drying, impregnation with potassium iodate solution and placing in contact with vapors of the sample. The formation of a blue color indicates the presence of sulfur dioxide in the product[10].

EXPERIMENTAL RESULTS

The experimental results obtained are summarized in Table III.

The analysis of the experimental results shows that activity of the clay improved with relation to rise in temperature, as far as the removal of olefins is concerned. In fact the first elevation in the temperature of the catalyst from 150°C to 170°C significantly removed the olefins present in the benzene fraction (from 12 mg to 4 mg of bromine per g of benzene). However, operation of the clay towers at this temperature did not solve the problem of contamination of xylene and trimethylbenzene with hydrogen sulfide. The elevation of temperature to 200°C led to satisfactory results for both olefin and this removal.

Attempts to lower the operating temperature to 190°C lead to unsatisfactory for xylene and trimethylbenzene due to contamination by H_2S. Subsequent experiments showed that the best operating temperature in order to meet the required specifications for xylene and trimethylbenzene was 195°C. The rise in temperature from 150°C to 200°C had no effect on contamination of the aromatics fraction by sulfur dioxide. This may be due to fact that the feed was low in sulfolane content.

The pressure was raised from 12.0 kgf/cm^2 to 15.0 kgf/cm^2 in order to maintain the product in the clay towers in the liquid phase. The liquid promotes a cleansing or washing of the clay, diminishing the deposits of polymers at the acid sites and increasing the useful life of the catalyst. The lowering of the pressure from 15.0 kgf/cm^2 to 14.0 kgf/cm^2 had as a main purpose a reduction of the pressure of the system, alleviating the load on the feeding pump.

Table III. Experimental results obtained by variation of the temperature in the montmorillonite (smectite) clay tower during the period of August 10, 1995 to September 14, 1995.

Date (1995)	Temperature (^{0}C)	Pressure (Kgf/cm^2)	H_2O/SO_2 Xylene	H_2S/SO_2 Aromatics	Br in Benzene (mg/100 g)
10.08	150	12.0	+/-	+/-	12
10.08	150	12.0	+/-		
12.08	170	12.0	+/-	-/-	14*
13.08	170	12.0	+/-	-/-	4
14.08	200	15.0	+/-	-/-	6*
15.08	200	15.0	-/-	-/-	1
16.08	200	15.0	-/-	-/-	<1
17.08	200	15.0	-/-	-/-	<1
18.08	200	15.0	-/-	-/-	<1
19.08	195	15.0	-/-	-/-	<1
20.08	190	15.0	-/-	-/-	1
24.08	190	15.0	+/-	-/-	2
25.08	190	15.0	+/-	+/-	1
28.08	200	15.0	+/-	-/-	<1
29.08	200	15.0	-/-	-/-	2
14.09	195	14.0	-/-	-/-	<1

*** These analyses were performed before raising the temperature.**
+ Positive (indicates presence of traces amonts of H_2S or SO_2.
- Negative (indicates absence of contaminant).

The pressure differential of the clay towers (pressure at entry minus pressure at exit) was essentially constant with the rise in temperature indicating that there was no significant increase of polymer formation over the reaction bed, allowing free flow of the products.

The experimental results showed that the useful life of montmorillonite (smectite) clay for catalytic operations could be prolonged by raising the operating temperature of the clay towers from 150^{0}C to 200^{0}C.

The mechanism of olefin removal takes place by polymerization reactions at the acid centers of the clay. Montmorillonite (smectite) also catalyzes the transformation of thiophenes and mercaptans present in BTX (benzene-toluene-xylene) streams to hydrogen sulfide[7]. Apparently, the rise in temperature of the clay treating towers helps remove polymers and coke from the acid sites. The presence of sulfolane in small amounts (less than 500 ppm) in the feed has little effect on the catalytic activity since it is readily converted to SO_2. At higher concentrations, however, sulfolane in adsorbed on the clay affects catalytic efficiency.

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SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY

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THE ELECTRICAL BEHAVIOUR OF THE M_xHgI_4 INORGANIC COMBINATION AND SOME STRUCTURAL ALTERATIONS VERSUS THE PRESSURE

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ABSTRACT

In this paper the structural changes of the M_xHgI_4 - type combinations (M = Ag^+, Cu^+, Tl^+, Pb^{2+}, Cd^{2+} and x = 1,2) which occur due to pressure (5 - 30 MPa) applied on the powder of these complexes are presented.

These alterations were confirmed by the X - ray diffraction spectra and by electrical conductibility measurements.

RESUMO

Este trabalho trata de mudanças estruturais que acontecem quando pó de complexos do tipo M_xHgI_4 onde (M = Ag^+, Cu^+, Tl^+, Pb^{2+}, Cd^{2+} e x = 1,2) está sujeito a pressões de 5 a 30 MPa.

Estas alterações estruturais foram confirmadas por espectra de difração de raios-X e medidas de condutibilidade elétrica.

KEYWORDS : tetraiodomercurates, electrical conductibility, X-ray diffraction, structural alterations.

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INTRODUCTION

The structure of the α and β crystalline phases of the Ag_2HgI_4 and Cu_2HgI_4 compounds has been known from the papers initiated by Ketelaar in 1931 - 1938[1-5] and studies continued in the fifties and sixties by Frevel[6], Suchov[7], Hahn[8], Otsuba et al.[9]

Some relationships between the structure and the electrical conductibility, versus either the temperature or the pressure or both of them simultaneously, within the inorganic M_xHgI_4 (where $M = Ag^+$, Cu^+)[10,11] combinations class were established in the period of 1964 - 1974.

Between 1974 and 1975, Kasper and Browall[12,13] determined the structure of the Ag_2HgI_4 monocrystals both for the low temperature crystalline phase - β (ordered) and for the high temperature crystalline phase - α(disordered).

Olson and Harris[14] also performed these determinations on polycrystalline species. In 1982, the relationship structure - electrical conductibility versus the temperature and pressure for the inorganic Tl_2ZnI_4 combination was studied using Raman Spectra, by McOmber - et al[15].

Another paper, elaborated by Brightwell and Buckley in 1984[16], presents the equilibrium phase diagram for the AgI-CdI_2 system compared to the Ag_2HgI_4 and Ag_2ZnI_4 compounds.

In this paper the structural modifications of the M_xHgI_4 inorganic combinations versus the nature of the metallic M^{n+} ion, were studied using the X - ray diffraction and electrical conductibility measurements. The paper also established the structural lattice changes of the respective compounds and the effects on the electrical conductibility, when the microcrystalline powders are exposed to some certain pressure (5-30 MPa) for definite periods.

EXPERIMENTAL PART

An X-ray diffraction type TUR-M-62 apparatus equipped with a HZG-3 diffractometer operating with CuK_α radiation was used. The X-ray excitation was performed at 30 kV and 30 mA. The moving rate of the counter arm of the diffractometer was 0.5° Bragg/min; range was 1.5-25° Bragg. The intensity scale expressed in qpm (quants/min) was selected so that the most intense diffraction line was totally included into the diffractogramme. The measuring of the diffraction lines precision was ±0.005° Bragg.

The electrical conductibility measurements were performed through the "four wells" method[17] using a "Coucusai" French type apparatus. The wells used in performing the determination are made of wolfram and they are fixed using some sapphire bearings. The bearings are positioned collinearly, the distance between them being 1mm.

After being obtained through wet synthesis, the M_xHgI_4 compound were filtered, washed with alcohol and then dried with P_2O_5. The microcrystalline powders were used for further determinations, as follows:

- in order to perform the diffractometric study, microcrystalline powders samples and pellets (cylindrical samples), were obtained from the powder, using a DP-36 (D.R.G.) press. at the following values: 1; 5; 10; 15; 20 and 30 MPa;

- in order to study the electrical conductibility, σ , pellets obtained at the above partial pressures were used for all the five M_xHgI_4 compounds studied. X-ray diffraction data and electrical conductibilities were obtained at room temperature.

RESULTS AND DISCUSSION

The results obtained through the determination of the electrical conductibility, σ, for all the M_xHgI_4 compounds studied.

The Figures 1a - 2a present the electrical conductibility, σ, versus the pressure, P. It can be observed that the electrical conductibility for the Ag_2HgI_4, Cu_2HgI_4 compounds exhibits maxima at a 15 MPa and 20 MPa, respectively. These maxima are in accordance with the determinations performed by R. Well and coworkers[10] for Ag_2HgI_4, by S. Shibata et al.[11] for Cu_2HgI_4 and by McOmber et al.[15] for both of these compounds. Moreover, a second maximum of the electrical conductibility was found for the Ag_2HgI_4 compound, at 25 MPa. The Tl_2HgI_4 and $PbHgI_4$ compounds exhibit a decrease of electrical conductibility with increasing pressure (Fig. 3a and 4a), and the Cu_2HgI_4 compound exhibits maximum values of the electrical conductibility at 30 MPa (Fig. 5a).

The diffraction spectra performed on the M_xHgI_4 compounds do not confirm this supposition. Thus, the diffractogrammes obtained on the respective samples (Tables 1-5), at different pressure, did not lead to the conclusion of a phase transformations, with a change of the diffraction spectrum.

All these determinations are in accordance with the observations made by the Omber and coworkers[15] and Greig and collaborators[19]. They didn't observe any changes in the Raman spectra of the Ag_2HgI_4 , Cu_2HgI_4 compounds as a function of pressure in the range of the pressure values mentioned above. This confirmed that a new crystalline phase didn't appear. $d_o$hkl values sets resulted from the diffractogrammes obtained on the powders and $d_p$hkl values sets were obtained from the diffractogrammes on the same compounds pressed under different pressures. The experimental values $|Adhkl| = d_p hkl - d_o hkl$ (axial parameter referring to the distance between two atomic planes) were calculated using these values sets and graphic represented versus the pressing pressure (Fig. 1b-5b).

Figures 1a,b-5a,b.

These Figures are different for different compounds, but are similar for the same compounds and can be compared to the 1a-5a Figures. Therefore, it can be assumed that the electrical conductibility alteration is determined by some order - disorder phenomena, in relation with the reticulate crystalline planes. (i.e. the number of atoms and holes, within the respective planes, without an alteration of the respective cell unit)

The diffraction spectra of the samples at different pressure are presented in Tables 1-5. It can be appreciated that some alterations of the crystalline lattice appear with the increasing pressure, meaning the appearance or the disappeareance of same spaces, towards which the metallic ions can move or not, determining an increase or a decrease of the total conductibility. The qualitative assumptions regarding to the

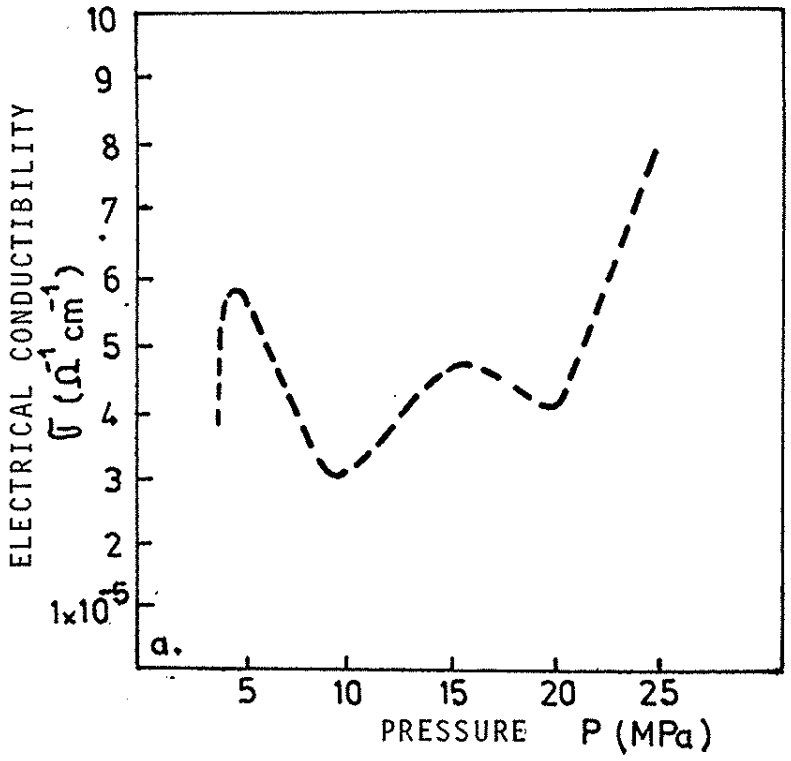

Fig. 1a-The electrical conductibility versus pressure for the Ag_2HgI_4 compound.

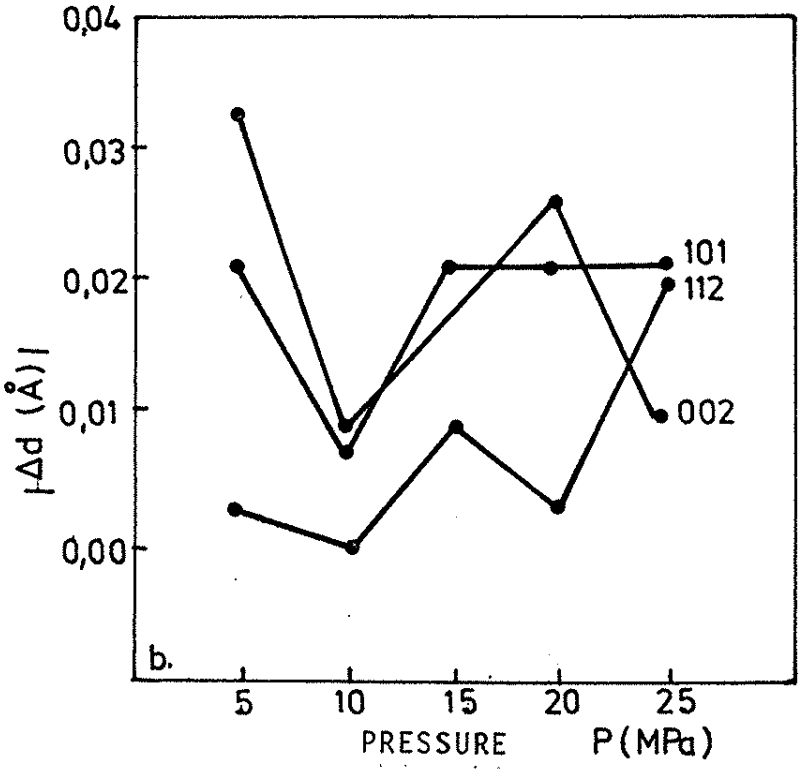

Fig. 1b-The |Δd(A)| parameter versus pressure for the Ag_2HgI_4 compound.

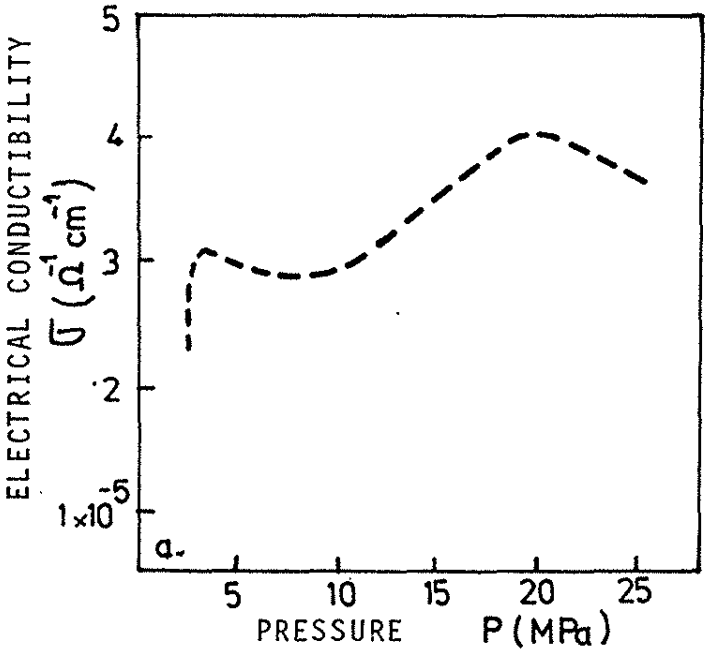

Fig.2a-The electrical conductibility versus pressure for the Cu_2HgI_4 compound.

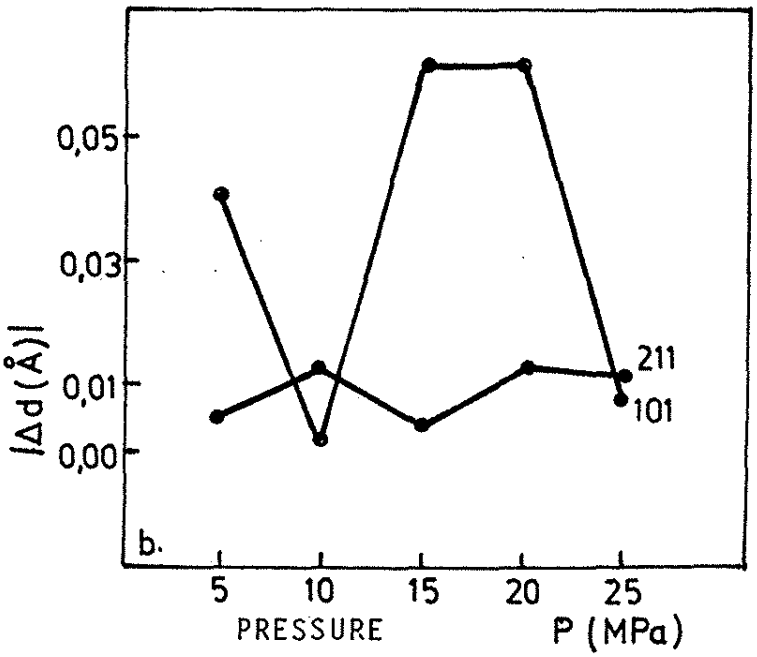

Fig.2b-The |Δd(A)| parameter versus pressure for the Cu_2HgI_4 compound.

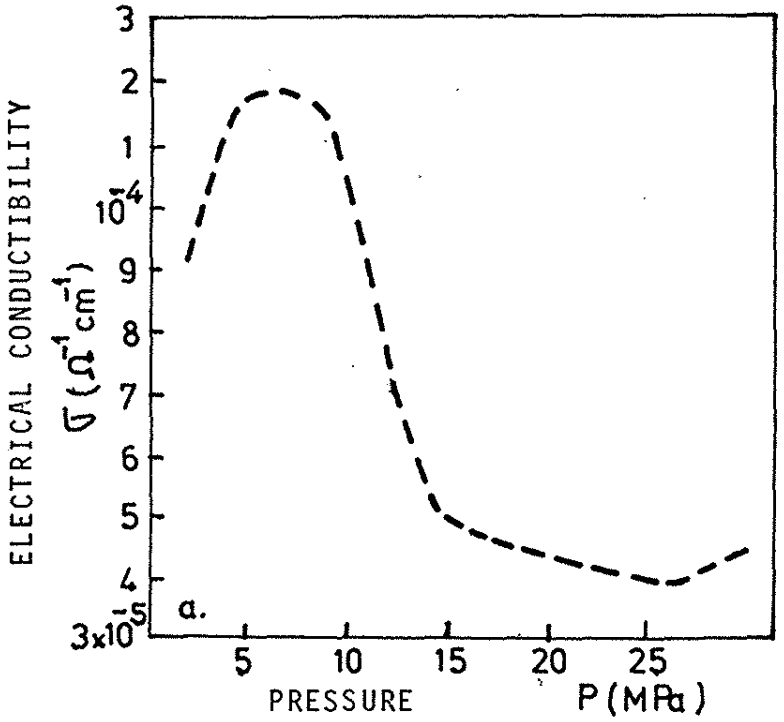

Fig.3a-The electrical conductibility versus pressure for the Tl_2HgI_4 compound.

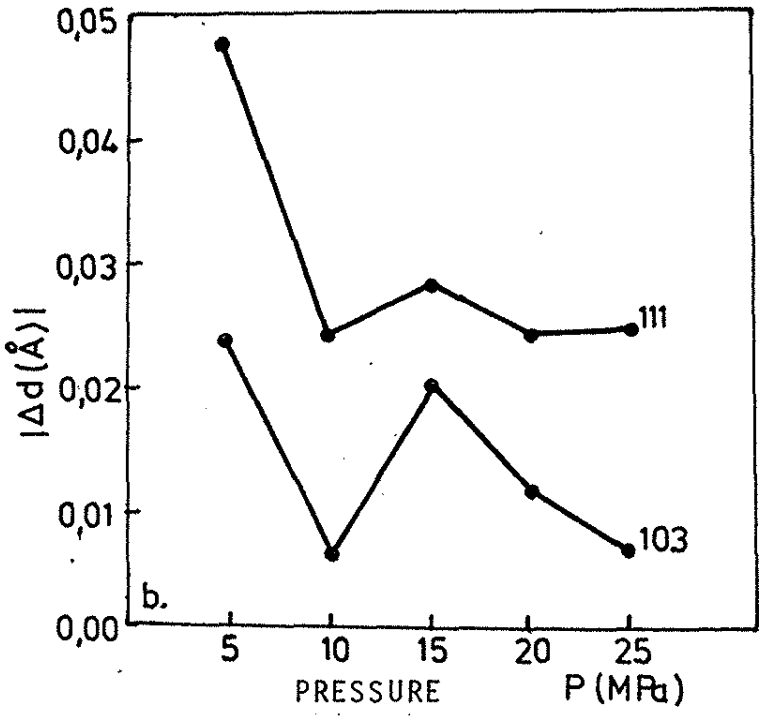

Fig.3b-The |Δd(A)| parameter versus pressure for the Tl_2HgI_4 compound.

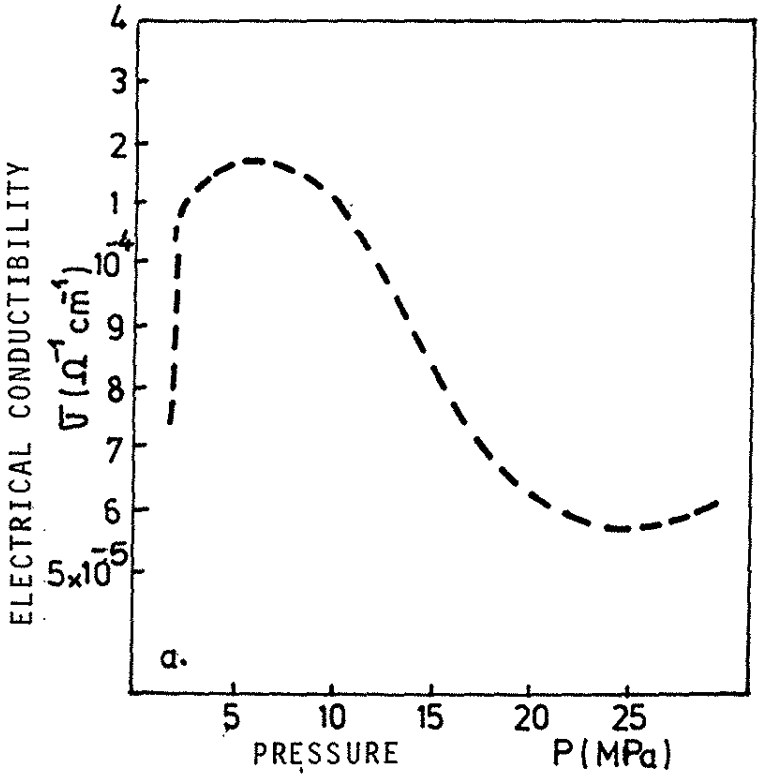

Fig.4a-The electrical conductibility versus pressure for the $PbHgI_4$ compound.

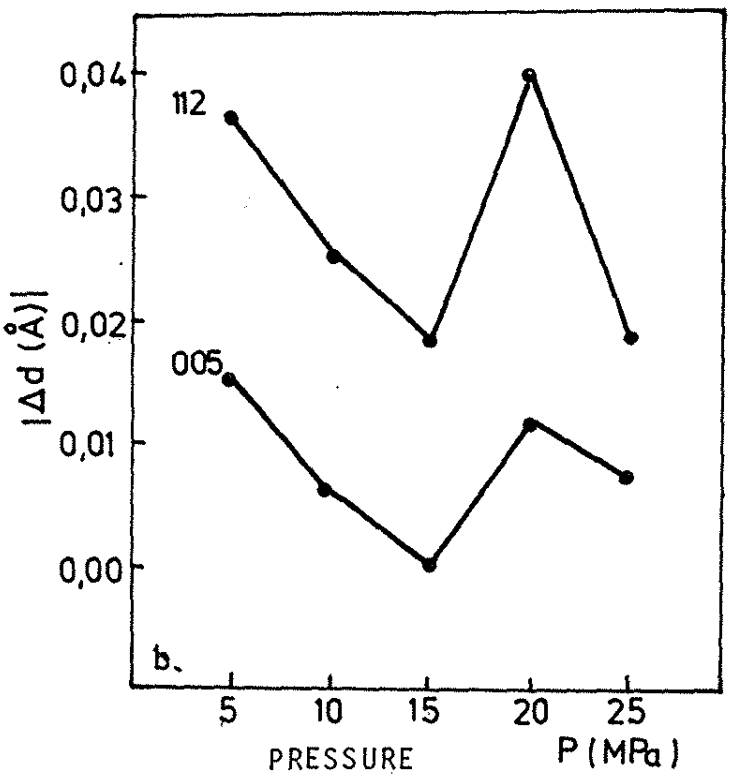

Fig.4b-The |Δd(A)| parameter versus pressure for the $PbHgI_4$ compound.

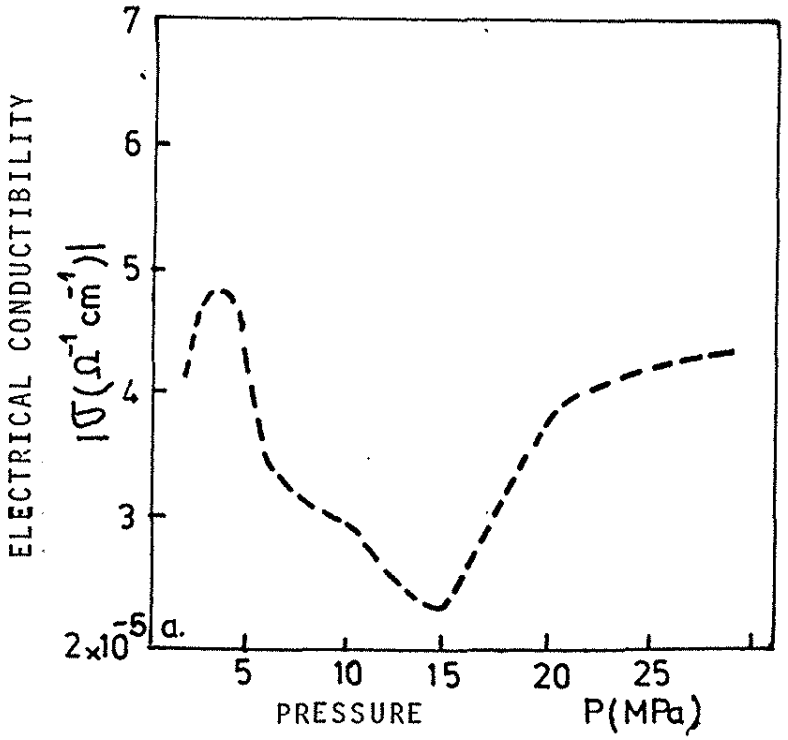

Fig.5a-The electrical conductibility versus pressure for the $CdHgI_4$ compound.

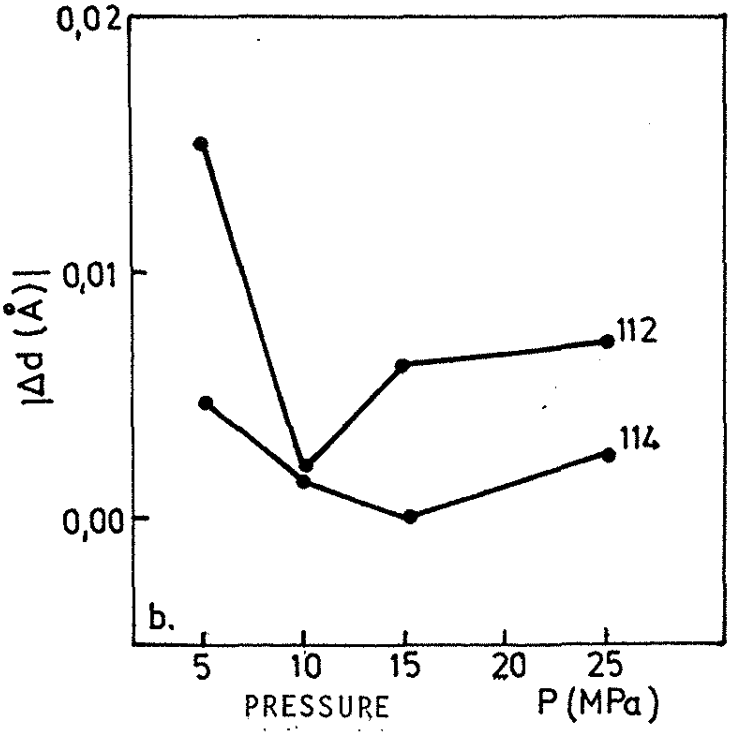

Fig.5b-The |Δd(A)| parameter versus pressure for the $CdHgI_4$ compound.

TABLE 1 - X-Ray diffraction data for powder - Ag_2HgI_4 compound and powder under pressure effect

P, MPa												
	0		5		10		15		20		25	
d_o Å	I/I_1	hkl	d_p, Å	I/I_1	d_p, Å	I/I_1	d_p, Å	I/I_1	d_p, Å	I/I_1	d_p, Å	I/I_1
6.2668	14	002	6.3000	12	6.2757	14	6.2492	14	6.2405	16	6.2580	13
									5.9644	14		
5.6253	19	101	5.6467	13	5.6182	25	5.6041	19	5.6467	22	5.6041	16
									4.5253	16		
4.4622	16	110	4.4711	15	4.4533	19	4.4533	19	4.4622	16	4.4313	15
3.6390	100	112	3.6419	100	3.6390	100	3.6302	100	3.6419	100	3.6186	100
3.4981	16	103	3.4954	12	3.4954	17	3.4847	18	3.5036	19	3.4740	14
2.8184	16	202	2.8236	13	2.8219	19	2.8167	24	2.8289	19	2.8115	14
2.7525	15	211	2.7542	13	2.7608	19	2.7378	24	2.7592	18	2.7460	14
2.5728	14	212	2.5771	11	2.5743	17	2.5671	19	2.5786	16	2.5671	13
2.3433	14	213	2.3480	11	2.3374	17	2.3386	19	2.3456	15	2.3386	14
2.2317	49	220	2.2328	38	2.2338	54	2.2275	73	2.2349	50	2.2222	48
2.1040	16	222, 300	2.1007	11	2.1010	16	2.1000	17	2.1100	15	2.1000	14
1.9239	28	312	1.9079	16	1.9087	29	1.9004	38	1.9095	30	1.9012	34
1.9034	28	116	1.9004	16	1.9034	31	1.8952	38	1.9034	29	1.8959	34

TABLE 2 - X-Ray diffraction data for the powder - Cu_2HgI_4 compound and powder under pressure effect

P, MPa												
0			5		10		15		20		25	
d_o, Å	III_1	hkl	d_p, Å	III_1	d_p, Å	III_1	d_p, Å	III_1	d_p, Å	III_1	d_p, Å	III_1
5.4399	14	101	5.4800	5	5.4399	22	5.5003	25	5.5003	24	5.4433	34
3.5172	100	112	3.5282	100	3.5036	100	3.5227	100	3.5309	100	3.4700	100
3.3857	14	103	3.4035	6	—	—	3.3907	28	3.3984	24	3.3756	31
—	—	—	3.2452	7	—	—	—	—	—	—	—	—
—	—	—	3.1728	8	—	—	—	—	—	—	—	—
—	—	—	3.1099	7	—	—	—	—	—	—	—	—
—	—	—	3.0659	7	—	—	—	—	—	—	—	—
3.0500	16	200, 004	3.0475	6	—	—	—	—	—	—	—	—
2.7592	10	104, 202	2.8030	5	—	—	2.7708	25	—	—	—	—
2.6542	12	211	2.6588	5	2.6420	28	2.6526	25	2.6649	24	2.6450	30
2.2618	10	105, 213	—	—	—	—	—	—	—	—	2.2275	30
2.1562	24	220, 204	2.1581	10	2.1532	40	2.1552	45	2.1611	39	2.1522	47
2.1454	20	115, 221	—	—	2.1493	35	2.1445	40	2.1450	35	2.1480	47
2.0651	8	224, 006	2.0777	8	2.0696	25	2.0768	25	2.0777	21	—	—

TABLE 3 - X-Ray diffraction data for the powder - Tl_2HgI_4 compound and powder under pressure effect

P, MPa												
0			5		10		15		20		25	
d_o, Å	I/I_1	hkl	d_p, Å	I/I_1	d_p, Å	I/I_1	d_p, Å	I/I_1	d_p, Å	I/I_1	d_p, Å	I/I_1
6,5823	19	002	6.6810	18	6,5726	18	6,6019	22	6,6019	20	6,6019	20
4,6091	15	102	4,6571	12	4,6187	18	4,6474	24	6,6474	18	4,6474	15
4,1990	15	111	4,2466	20	4,2227	18	4,2267	24	4,2227	22	4,2227	18
3,5643	41	103	3,5785	12	3,5699	14	3,5841	38	3,5756	37	3,5699	33
3,3309	20	004	3,3581	36	3,3334	26	3,3432	38	3,3309	35	3,3309	22
3,1120	100	201	3,1356	100	3,1184	100	3,1227	100	3,1163	100	3,1163	100
2,9838	61	104	2,9994	107	2,9818	79	2,9955	81	2.9818	90	2,9838	69
2,9227	15	202	2,9434	16	2,9302	16	2,9377	22	2,9321	18	2,9265	20
2.7625	19	211	—	—	—	—	2,7661	24	2,7658	22	2,7625	20
2,6110	13	203	2,6300	15	—	—	—	—	2,6121	14	—	—
2,4870	13	105	2,4952	15	2,4806	12	—	—	—	—	—	—
2,3563	19	213	2,3659	18	2,3539	16	2,3622	22	2,3587	17	2.3575	18
2,3120	22	204	2,3200	18	2,3109	19	2,3212	22	2,3109	18	2.3120	22
2,2727	17	115	2,2849	18	2,2749	16	2,2838	19	2,2716	16	2.2750	18
2,2222	17	221	2,2328	22	2,2201	21	2,2296	27	2,2212	20	2,2222	20
2,1920	24	006	—	—	2,1902	19	2,1943	30	2,1902	41	2,1902	27
2.1100	17	301	2,1176	25	2,1110	19	2,1157	24	2,1100	20	2.1100	22
2,0650	32	302	2,0561	24	2,0482	19	2,0535	24	2,0499	22	2,0490	21

TABLE 4 - X-Ray diffraction data for the powder - $PbHgI_4$ compound and powder under pressure effect

	P, MPa											
	0		5		10		15		20		25	
d_o, Å	I/I_1	hkl	d_p, Å	I/I_1	d_p, Å	I/I_1	d_p, Å	I/I_1	d_p, Å	I/I_1	d_p, Å	I/I_1
6,964*	100	—	7,0303*	100	7,0081*	100	6,9971*	100	7,0415*	100	7.0192*	100
6.553	10	002	6,6019	12	6,5824	18	6,6216	13	6.6414	14	6.6414	16
4,2913	10	003	4,3078	12	4,2910	20	4.2954	13	4.3161	16	4,3078	16
4.0220	8	112	4,0586	12	4,0476	20	4,0404	13	4.0623	14	4.0404	16
3,3330	15	201	3,3482	19	3,3482	29	3,3408	18	3,3556	23	3.3432	25
3,2804	13	044	3,2995	16	3,2971	25	3,3019	17	3,2971	20	3.2932	22
2,6992	10	203	2,7120	13	2,7104	20	2,6992	11	2.7071	14	2.7104	17
2,6345	8	005	2,6496	12	2,6405	20	2,6345	13	2.6465	16	2.6420	17
2,4012	7	221	2,5033	10	2,4979	16	—	—	—	—	—	—
2,1415	9	311	2,1490	12	2,1434	14	2,1466	11	2.1434	11	2.1450	16

* The most intense spectral line belongs to the PbI_2 compound (JCPDS 7-235) and not to $PbHgI_4$ compound

TABLE 5 - X-Ray diffraction data for the powder - $CdHgI_4$ compound and powder under pressure effect

P, MPa										
0			10		15		20		30	
d, Å	III_1	hkl	d_p, Å	III_1	d_p, Å	III_1	d_p, Å	III_1	d_p, Å	III_1
6,2317	83	002	6,2143	188	6,2317	118	6,2230	124	6,1712	90
4,1106	76	101	4,1257	54	4,1409	61	4,1219	64	4,1031	57
3,5756	100	102	3,5756	100	3,5756	100	3,5784	100	3,5587	100
3,1120	21	004	3,1120	11	3,1099	9	3,1099	11	3,0867	10
3,0014	48	103	3,0113	56	3,0073	46	3,0093	49	2,9955	47
		111								
2,7625	41	112	2,7741	17	2,7641	13	2,7675	19	2,7558	17
2,5265	24	104	2,5334	15	2,5320	9	2,5334	13	2,5224	13
2,1902	55	114	2,1953	33	2,1922	21	2,1902	36	2,1871	28
2,1871	29	200	2,1892	33	2,1861	25	2,1851	34	2,1780	30
2,1581	28	105	2,1601	25	2,1591	22	2,1611	17	2,1571	17
2,0695	31	202,	2,0741	35	2,0750	28	2,0741	29	2,0677	24
		006								
1,9285	28	211	1,9324	12	1,9324	9	1,9309	10	1,9247	12
		203								
1,8732	31	106	1,8717	12	1,8725	12	1,8753	14	1,8695	13
1,8609	31	212	1,8660	12	1,8645	9	1,8631	11	1,8568	15

explanation of the electrical conduction within the inorganic type M_xHgI_4 combinations consider the metallic ion mobility[18] and also the preferential tendency of increasing of the crystalline cell-unit reticulate parameters, both on "a" or "c" direction.

β-Ag_2HgI_4 and β- Cu_2HgI_4 phases are structurally identical in accordance with the literature data. A similarity between the shapes of the electrical conductibility versus pressure diagrams and the shapes of the $|\Delta d(hkl)|$ diagrams can be noticed. The diagrams in Figures 1a,b-5a,b show a correlation between the electrical conductibility and the $|\Delta d(hkl)|$ values, leading to the conclusions that the appearance or disappearance of some spaces within the crystalline lattice can contribute to the alteration of the electrical conductibility.

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SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY
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MICELLAR CATALYZED HYDROLYSIS OF LITHIUM *p*-NITROPHENYL ETHYL PHOSPHATE (LiPNEF) AND THE PSEUDO PHASE ION EXCHANGE MODEL

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ABSTRACT

The hydrolysis of lithium p-nitrophenyl ethyl phosphate (LiPNEF) was studied at 25º, 35º and 45ºC by spectrophotometric techniques in the presence of micelles of cetyltrimethylammonium bromide (CTAB), sodium hydroxide and salt. The concentraion of NaOH used varied from 0,050 to 5,00M and the NaCl ranged from 0,0050 to 0,030 M. Pseudo-first order rate constants (k_ψ) and second order rate constants (k_2) and activation parameters such as E_a, $\Delta H^{\neq}$, $\Delta G^{\neq}$ and $\Delta S^{\neq}$ were measured. The system was also studied by tensiometric, viscosity and quasi-elastic light scattering methods. At low concentrations of NaOH (below 0,55 M), the reaction can be explained in terms of conventional models of micellar catalysis, including the pseudo-phase ion exchange model. For higher concentration of NaOH, conventional models of micellar catalysis are not applicable. In fact, at high hydroxide concentration, the system no longer contains micelles but liquid crystalline mesophases and a model analogous to phase transfer catalysis appears to be more appropriate.

RESUMO

A hidrólise do lítio p-nitrofenil etil fosfato (LiPNEF) foi estudada a 25º, 35º e 45ºC por métodos espectroscópicos na presença de micelas de brometo de cetiltrimetilamônio (CTAB), hidróxido de sódio e sal. A concentração de NaOH variou entre 0,050 e 5,00 M e de NaCl entre 0,0050 e 0,030 M. Foram medidas constantes de velocidade de pseudo-primeira ordem (k_ψ) e segunda ordem (k_2) e parâmetros de ativação tais como E_a, $\Delta H^{\neq}$, $\Delta G^{\neq}$ e $\Delta S^{\neq}$. O sistema também foi estudado por métodos de tensiometria, viscosidade e espalhamento quase-elástico de luz. À concentrações baixas de NaOH (menos de 0,55M) a reação pode ser explicada em termos termos de modelos convencionais de catálise micelar, inclusive o modelo de troca iônica. Para concentrações mais elevadas de NaOH, os modelos convencionais não são aplicáveis. De fato, a concentrações elevadas de NaOH, o sistema não contém mais micelas, mas mesofases líquido-cristalinas e um modelo análogo à catálise por transferência de fase parece mais adequado.

KEYWORDS: Micellar Catalysis, Phosphate Esters, Pseudo Phase Ion Exchange Model, Cetyltrimethylammonium Bromide-CTAB.

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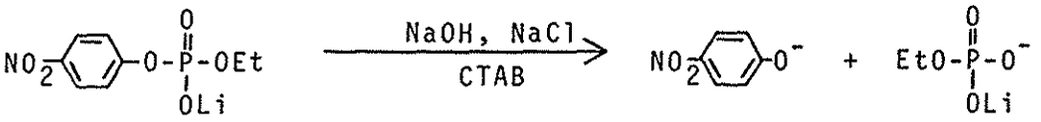
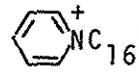
INTRODUCTION

The present paper deals with the hydrolysis of lithium p-nitrophenyl ethyl phosphate (LiPNEF) in aqueous solutions in the presence of micelles or other aggregates of cetyltrimethylammonium bromide (CTAB) and varying concentraions of NaOH and NaCl. The reaction under consideration is illustrated below.



The organophosphorus compound under consideration (LiPNEF) is a common pesticide related to Paroxon and Parathion that have a wide use in agriculture.[1,2]

In previous studies we have shown that the hydrolysis of di- and tri-substituted phosphate esters is catalyzed by micelles of cetyltrimethylammonium bromide [$C_{16}H_{33}\overset{+}{N}(CH_3)_3\ Br^-$, CTAB] and also by micelles of N,N-dimethyl-N-hydroxyethyl-dodecylammonium bromide, [DHEDAB, $n\text{-}C_{12}H_{25}\overset{+}{N}(CH_3)_2CH_2CH_2OH\ Br^-$] and N,N-dimethyl-N-hydroxyethylcetylammonium bromide, [CHEDAB, $n\text{-}C_{16}H_{33}\overset{+}{N}(CH_3)_2CH_2CH_2OH\ Br^-$].[3] Micelles of DHEDAB and CHEDAB are excellent catalysts for the hydrolysis of both LiPNEF and p-nitrophenyl diphenyl phosphate in the presence of OH^-, with over 300-fold rate enhancement for

the hydrolysis of the triaryl phosphate in the presence of CHEDAB. The catalytic effect and the dependence of the reaction rate on hydroxide ion concentration has been explained in terms of nucelophilic participation of the alkoxide ion of DHEDAB and CHEDAB, with pK_a of 12.4 and 12.9, respectively for the ionization of the hydroxyl group. For reactions with fluoride ion, the hydroxy-substituted surfactants are no better catalysts than the corresponding alkyltrimethyl-ammonium bromides, suggesting that electrophilic catalysis is relatively unimportant. Cetylpyridinium bromide [CPBr, ] has approximately the same effect as CTAB at low hydroxide concentration and a slightly more pronounced effect with fluoride ion. Zwitterionic surfactants such as lauryl carnitine chloride (LCCl) and palmityl carnitine chloride (PCCl) have little effect on the rate of hydrolysis of LiPNEF. [4,5]

The addition of primary amines increased the rate of reaction in the presence of CTAB and CHEDAB for the triaryl-phosphate, but much of the increase was due to attack by amine on the aryl group. In the absence of micelles, amines increased the overall rate of the reaction by attacking the aryl group without markedly catalyzing hydrolysis.[6]

The micellar catalyzed oxidative cleavage of a carbon-carbon bond in Dicofol[7] and the micellar catalyzed dehydro-chlorination of 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane (DDT) and some of its derivatives have also been the subject of our investigations.[8,9]

In more recent studies we have reported results obtained for the hydrolysis of *p*-nitrophenyl diphenyl phosphate in aqueous solutions in the presence of micelles of diethylheptadecylimidazolinium ethyl sulfate (DEHIES) and CTAB, sodium hydroxide and dimethyl sulfoxide (DMSO) and analyzed the effect of internal pressure of the medium, dielectric constant, donor number and polarity of the solvent and the effect of DMSO on micellization.[10-12]

EXPERIMENTAL PROCEDURE

Materials. Lithium p-nitrophenyl ethyl phosphate (LiPNEF) was prepared from diethyl phosphate and sodium p-nitrophenoxide using LiCl in dry acetone, followed by precipitation with diethyl ether.[13,14]

The surfactant cetyltrimethylammonium bromide (CTAB) was purchased from Aldrich Chemical Company, Milwaukee, Wisconsin, USA. It was recrystallized from ethanol three times and dried under vacuum. NaOH and NaCl were supplied by Merck do Brasil, S.A., Rio de Janeiro and were of analytical reagent grade. The water was deionized and distilled.

Kinetics. The hydrolysis of LiPNEF was studied spectrophotometrically measuring the rate of appearance of the p-nitrophenoxide ion at 4030 $\AA$. A Varian 634 spectrophotometer, equipped with a water-jacketted cell compartment was used. The pseudo-first order rate constant (k_ψ) was determined at 25°, 35° and 45° C by graphical methods using the integrated form of the rate equation. The second order

rate constant (k_2) was calculated from k_ψ and the hydroxide ion concentration. The activation parameters were determined from measurements of the reaction rate at three different temperatures using appropriate equations.[10]

The experimental procedures for quasi-elastic light scattering and viscosity measurements have been described elsewhere in the literature.[15,16]

RESULTS AND DISCUSSION

Some typical experimental results obtained for the pseudo first order rate constant (k_ψ) for the hydrolysis of LiPNEF at 25ºC are illustrated in Figure 1. The values of k_ψ for low concentrations of NaOH (less then 0,55 M) decrease as a function of concentration of NaCl, an observation typical of micellar catalyzed reactions.[3] At higher concentrations of NaOH (more than 1,00 M), however, the experimental values of k_ψ are essentially constant and are not affected by the addition of salt, illustrating the more pronounced electrolyte effect of the hydroxide ion.

Figure 2 shows some typical results obtained for the second order rate constant k_2 $\left[k_2=k_\psi/(OH^-)\right]$ as a function of NaCl concentration for fixed low concentrations of sodium hydroxide. It can be seen that the second order rate constant is highly dependent and decreases in the presence of salt.

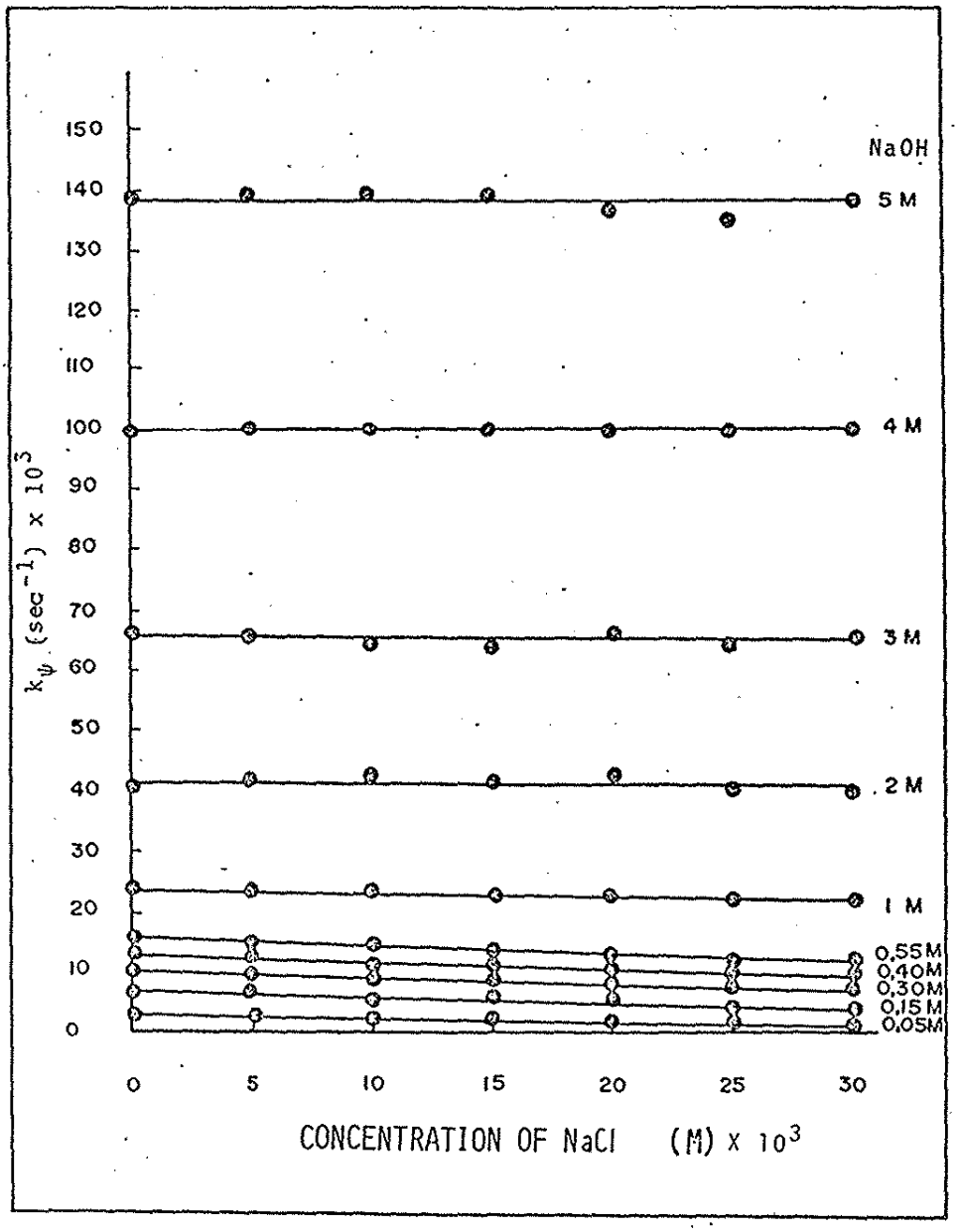


FIG. 1. PLOT OF THE PSEUDO-FIRST ORDER RATE CONSTANT (k_ψ) VERSUS THE CONCENTRATION OF SALT FOR THE HYDROLYSIS OF LiPNEF AT 25°C IN THE PRESENCE OF 0.0088 M CTAB AND DIFFERENT CONCENTRATIONS OF SODIUM HYDROXIDE.

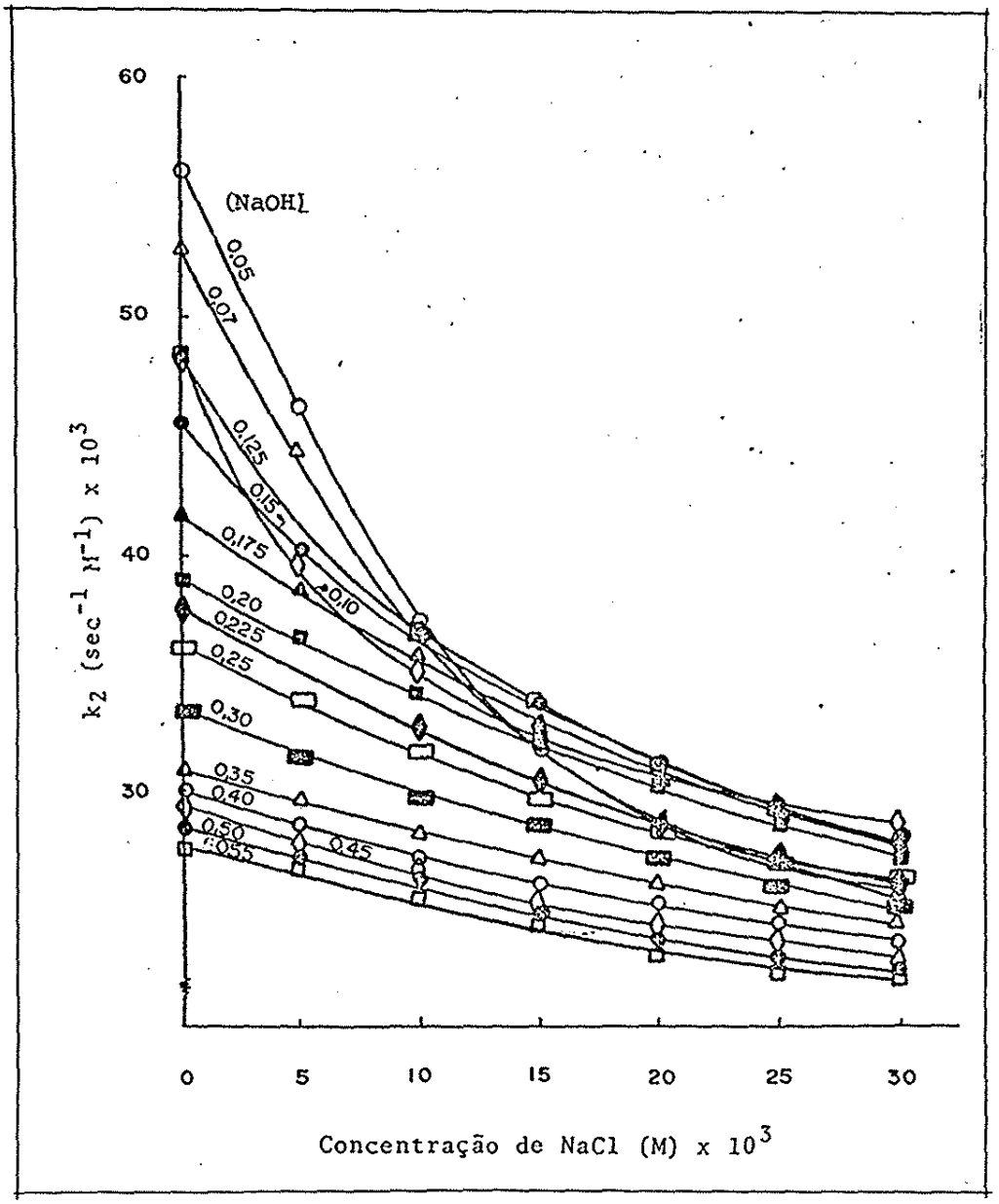


FIG. 2. VARIATION OF THE SECOND ORDER RATE CONSTANT (k_2) VERSUS THE CONCENTRATION OF SALT FOR THE HYDROLYSIS OF LiPNEF AT 25ºC IN THE PRESENCE OF 0,0088 M CTAB AND LOW CONCENTRATIONS OF SODIUM HYDROXIDE.

Figure 3 illustrates the variation of the second order rate constant k_2 as a function of NaCl concentration for fixed high and low concentrations of NaOH. It can be clearly noted that for high concentrations of NaOH (above 1,00 M) the values of k_2 are practically constant and do not depend on the presence of salt.

Figure 4 shows the dependence of the second order rate constant k_2 on the hydroxide ion concentration in the absence of salt and the presence 0,0088 M CTAB. The experimental values of k_2 decrease exponentially at low concentrations of NaOH (0,010 to 2,00 M), reach a minimum at 2,00 M and increase at higher concentrations of NaOH (2,00 to 5,00 M).

Figure 5 illustrates some typical results obtained for the diffusion coefficient (D) of the CTAB-H_2O-NaOH ternary system at 25ºC by means of quasi-elastic light scattering. It is interesting to note the presence of three different types of behavior of the diffusion coefficient D , indicating the presence of spherical micelles (positive slope part), elliptical micelles (zero slope) and stepladder growth with gelatinous and liquid crystalline mesophases (negative slope part). This observation is consistent with viscosity and surface tension measurements for the same system.

The activation parameters were determined from experimental values of k_ψ at 25º, 35º and 45ºC in the presence and absence of salt at different concentrations of NaOH. Some representative are summarized in Tables I and II.

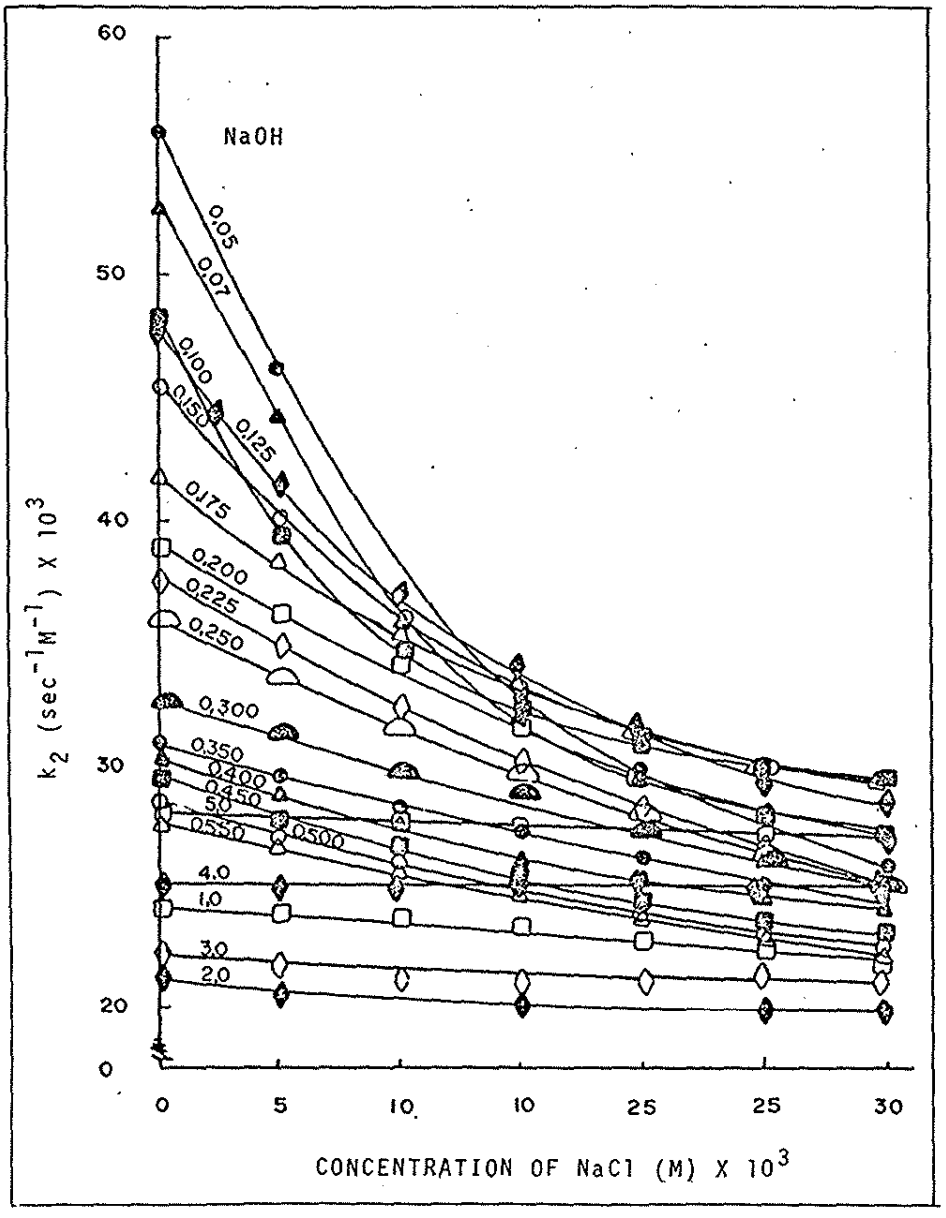


FIG. 3. VARIATION OF THE SECOND ORDER RATE CONSTANT (k_2) VERSUS THE CONCENTRATION OF SALT FOR THE HYDROLYSIS OF LiPNEF AT 25ºC IN THE PRESENCE OF 0,0088 M CTAB AND DIFFERENT FIXED CONCENTRATIONS OF SODIUM HYDROXIDE.

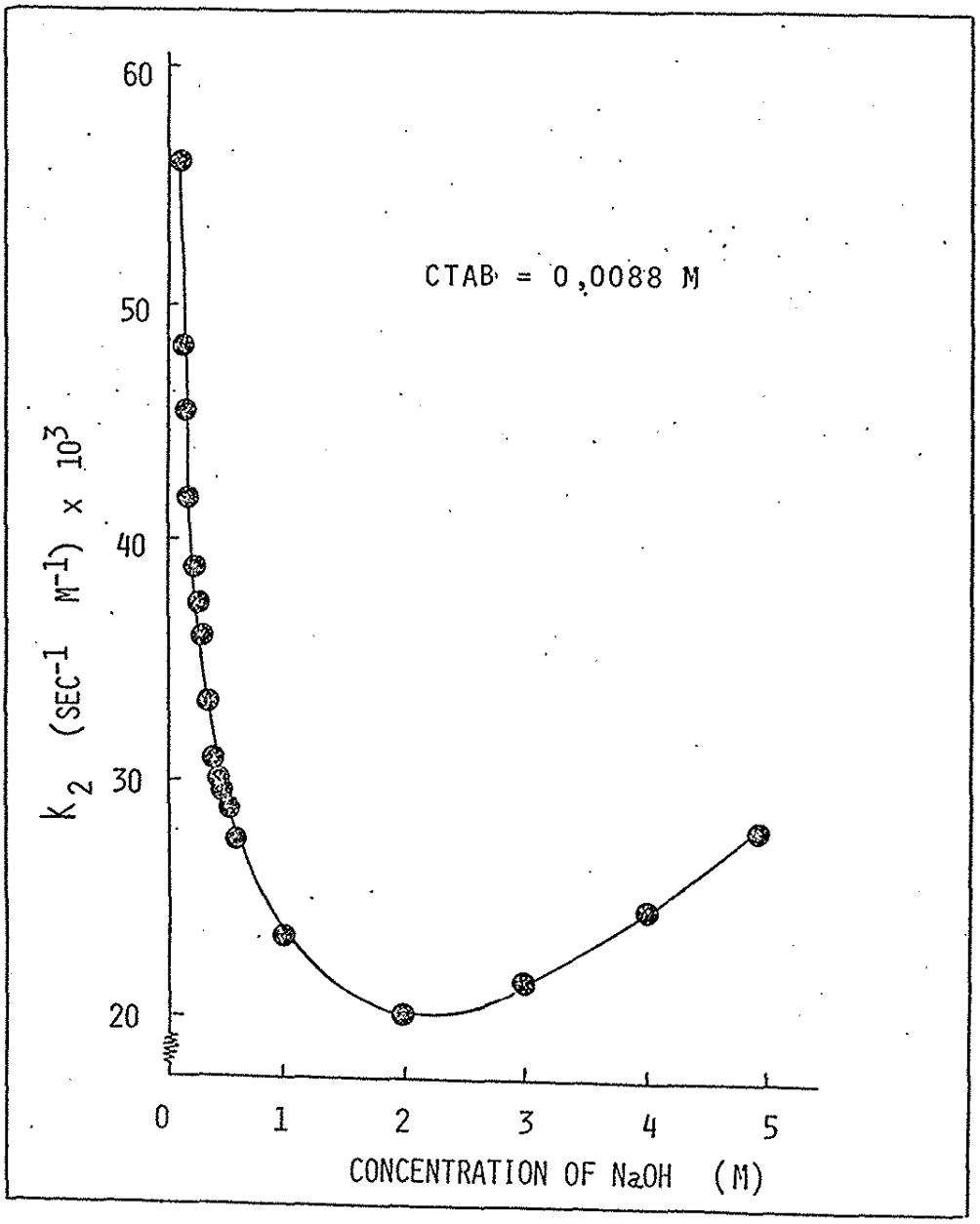


FIG. 4. VARIATION OF THE SECOND ORDER RATE CONSTANT (k_2) AS A FUNCTION OF SODIUM HYDROXIDE CONCENTRATION FOR THE HYDROLYSIS OF LiPNEF AT 25°C IN THE ABSENCE OF SALT.

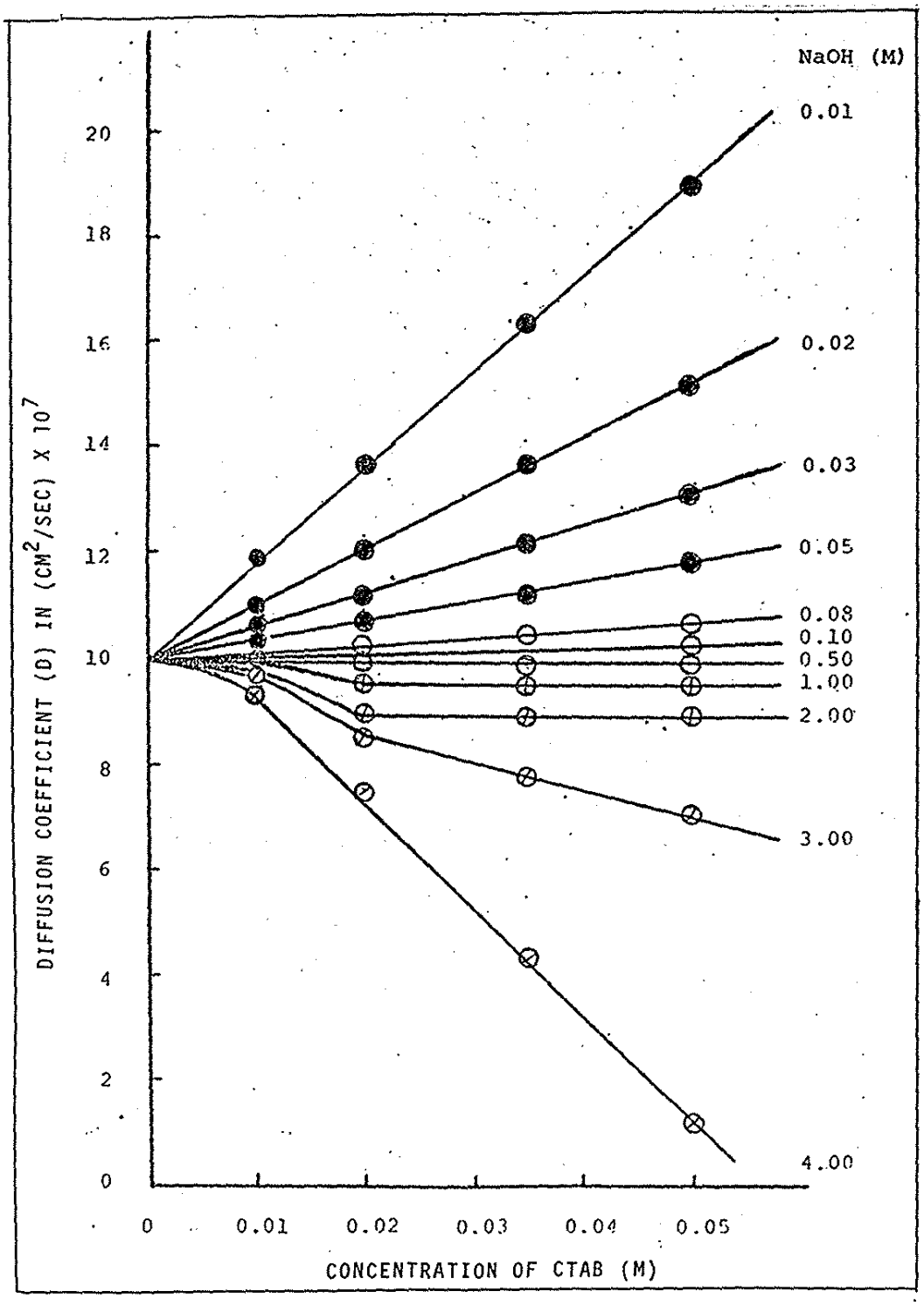


FIGURE 5. DIFFUSION COEFFICIENT (D) FOR THE CETYLTRIMETHYL-AMMONIUM BROMIDE-WATER-SODIUM HYDROXIDE TERNARY SYSTEM AT 25°C.

TABLE I. ACTIVATION PARAMETERS FOR THE HYDROLYSIS OF LiPNEF IN THE PRESENCE OF 0,0088 M CTAB, 0,030M NaCl AND DIFFERENT CONCENTRATIONS OF NaOH.

NaOH (M)	E_a (kcal/mole)	$\Delta H^{\neq}$ (kcal/mole)	$\Delta G^{\neq}$ (kcal/mol)	$\Delta S^{\neq}$ (e.u.)
0,05	14,7	14,1	21,4	- 24,4
0,10	13,4	12,8	20,9	- 27,2
0,50	10,2	9,58	20,1	- 35,3
1,00	9,32	8,73	19,7	- 36,7

TABLE II. ACTIVATION PARAMETERS FOR THE HYDROLYSIS OF LiPNEF IN THE PRESENCE OF 0,0088 M CTAB, THE ABSENCE OF SALT AND DIFFERENT CONCENTRATIONS OF NaOH.

NaOH (M)	E_a (kcal/mole)	$\Delta H^{\neq}$ (kcal/mole)	$\Delta G^{\neq}$ (kcal/mole)	$\Delta S^{\neq}$ (e.u.)
0,05	14,2	13,6	21,5	-26,4
0,10	13,6	13,0	20,6	-25,6
0,50	11,8	11,2	19,9	-29,4
1,00	11,2	10,6	19,6	-30,4

In general, for low concentrations of sodium hydroxide, the activation parameters are comparable to others obtained for similar reactions catalyzed by micelles[11] and they decrease as a function of NaOH. The addition of NaCl also causes a decrease. It thus appears that the presence of NaOH and NaCl lead to a more structured or ordered transition state.

Most of the models proposed for micellar catalysis[17-22] consider the partition coefficient for the substrate between the micellar and aqueous phase and the distribution of the reagents between the two phases. The hydrolysis of LiPNEF with hydroxide ion in the presence of CTAB may be considered a bimolecular reaction between OH^- and the substrate. Since the concentration of OH^- in the micellar phase is dependent on the concentration of bromide ion and surfactant, a quantitative treatment of the reaction rate must consider ion exchange on or near the micellar surface. For the reaction under consideration, the model proposed by Quina and Chaimovich[21] reduces to Equation (I) that gives the theoretical dependence of the pseudo first order rate constant, k_ψ, as a function of the total hydroxide ion concentration, $(OH)_T$.

$$k_\psi = \frac{\left[k_{2m/\overline{V}}\, K_s K_{OH/Br}\, (Br)_m/(Br)_w + k_2^o\right](OH)_T}{(1 + K_s C_D)\left[1 + K_{OH/Br}(Br)_m(Br)_w\right]} \quad (I)$$

where

C_D = concentration of micellized detergent

k_ψ = pseudo first order rate constant

k_{2m} = second order rate constant in the micellar phase

k_2^o = second order rate constant in the aqueous phase

$K_{OH/Br}$ = ion exchange constant

K_s = binding constant for the substrate

$(Br)_m$ = concentration of Br^- in micellar phase

$(Br)_w$ = concentration of Br^- in aqueous phase

$(OH)_T$ = total OH^- concentration

$\bar{V}$ = molar volume of the surfactant

With substrates such as lithium *p*-nitrophenyl ethyl phosphate that are very insoluble in water and are solubilized by CTAB the expression for k_ψ can be reduced to a simpler form given by Equation (II).

$$k_\psi = \frac{k_{2m}}{C_D\bar{V}} \quad (OH)_T \frac{K_{OH/Br}\,(Br)_m/(Br)_w}{1 + K_{OH/Br}(Br)_m/(Br)_w} \qquad (II)$$

The concentration of Br^- in the micellar phase can be obtained using the following equations.(Eq. III-VII)[23]

$$A_1 = C_D + CMC + K_{OH/Br}(OH)_T + (1-\alpha)C_D K_{OH/Br} \qquad (III)$$

where

CMC = critical micellar concentration of CTAB

α = degree of ionization of the micelle

$$(OH)_m = \frac{(-A_1) + \left[(A_1)^2 + 4(1-K_{OH/Br})OH_T K_{OH/Br}(1-\alpha)C\right]^{1/2}}{2(1-K_{OH/Br})} \qquad (IV)$$

where $(OH)_m$ = concentration of OH^- in micellar phase

$$(Br)_m = (1 - \alpha)C_D - (OH)_m \qquad (VI)$$

$$(Br)_w = \alpha C_D + CMC + (OH)_m \qquad (VII)$$

We have calculated the theoretical values of k_ψ for the reaction discussed above using various concentrations of OH^-, $\bar{V}$ = 0,37 l/mole; $K_{OH/Br}$ = 0,08; α = 0,20 and CTAB = 0,0088 M.

Table III summarizes some parameters used for the calcuation of the pseudo first order rate constant (k_ψ) and Table IV presents the experimental values of k_ψ and values calculated for k_ψ using the ion exchange model and different fixed concentrations of k_{2m}.

Figure 6 illustrates plots of the experimental pseudo first order rate constant k_ψ for the hydrolysis of LiPNEF at 25ºC versus the hydroxide ion concentration and calculated k_ψ values using the ion exchange model and different values of k_{2m}. As can be seen, there is some agreement between the experimental data and the theoretically calculated results only at lower concentrations of hydroxide ion.

Figure 7 illustrates the same results using an expanded scale for the hydroxide ion concentration in the range of 0,00 to 0,55 M , where there is good agreement between the experimental and calculated values of k_ψ.

Figure 8 shows a plot of the experimental pseudo first order rate constant k_ψ for the hydrolysis of LiPNEF at 25ºC versus hydroxide ion concentration giving the best fit of the experimental data with the pseudo phase ion exchange model and using a value of 0,0035 s^{-1} M^{-1} for k_{2m}.

TABLE III. SOME PARAMETERS USED FOR THE CALCULATION OF THE PSEUDO FIRST ORDER RATE CONSTANT (k_ψ) USING THE ION EXCHANGE MODEL.

$(OH)_T$	Exp. k_ψ	A_1	$(OH)_m$	$(Br)_m$	$(Br)_w$	$(Br)_m/(Br)_w$
0,05	0,00280	0,01428	0,001770	0,005630	0,004450	1,264939
0,08	0,00370	0,01628	0,002297	0,005103	0,004977	1,025329
0,10	0,00482	0,01828	0,002712	0,004688	0,005392	0,869591
0,13	0,00600	0,02028	0,003050	0,004350	0,005730	0,759137
0,15	0,00683	0,02228	0,003334	0,004066	0,006014	0,676193
0,18	0,00730	0,02428	0,003576	0,003824	0,006256	0,611336
0,20	0,00845	0,02628	0,003785	0,003615	0,006465	0,559070
0,25	0,00900	0,03028	0,004132	0,003268	0,006812	0,479717
0,30	0,01000	0,03428	0,004408	0,002992	0,007088	0,422064
0,35	0,01080	0,03828	0,004634	0,002766	0,007314	0,378119
0,40	0,01200	0,04228	0,004823	0,002577	0,007503	0,343430
0,45	0,01330	0,04628	0,004984	0,002416	0,007664	0,315304
0,50	0,01420	0,05028	0,005122	0,002278	0,007802	0,292011
0,55	0,01520	0,05428	0,005242	0,002158	0,007922	0,272388
1,00	0,02350	0,09028	0,005887	0,001513	0,008567	0,176672
2,00	0,04020	0,17028	0,006395	0,001005	0,009075	0,110700
3,00	0,06530	0,25028	0,006592	0,000808	0,009272	0,087090
4,00	0,09940	0,33028	0,006697	0,000703	0,009377	0,074933
5,00	0,13800	0,41028	0,006762	0,000638	0,009442	0,067518

* All parameters are defined within the text.

TABLE IV. CALCULATED PSEUDO FIRST ORDER RATE CONSTANTS ($k\psi$) FOR DIFFERENT FIXED VALUES OF k_{2m} USING THE ION EXCHANGE MODEL.

		Calculated k_ψ for different fixed values of k_{2m}			
$(OH)_T$	Exp. k_ψ	0,0025	0,0030	0,0035	0,0040
0,05	0,00280	0,003528	0,004234	0,004939	0,005645
0,08	0,00370	0,004365	0,005239	0,006112	0,006985
0,10	0,00482	0,004994	0,005993	0,006992	0,007990
0,13	0,00600	0,005495	0,006594	0,007693	0,008792
0,15	0,00683	0,005911	0,007093	0,008275	0,009457
0,18	0,00730	0,006265	0,007518	0,008771	0,010024
0,20	0,00845	0,006574	0,007889	0,009204	0,010519
0,25	0,00900	0,007094	0,008513	0,009932	0,011351
0,30	0,01000	0,007524	0,009028	0,010533	0,012038
0,35	0,01080	0,007890	0,009468	0,011047	0,012625
0,40	0,01200	0,008212	0,009855	0,011497	0,013140
0,45	0,01330	0,008501	0,010201	0,011901	0,013602
0,50	0,01420	0,008764	0,010516	0,012269	0,014022
0,55	0,01520	0,009006	0,010807	0,012608	0,014410
1,00	0,02350	0,010701	0,012841	0,014981	0,017121
2,00	0,04020	0,013480	0,016176	0,018872	0,021568
3,00	0,06530	0,015937	0,019125	0,022312	0,025500
4,00	0,09940	0,018301	0,021961	0,025622	0,029282
5,00	0,13800	0,020625	0,024750	0,028875	0,033000

* All parameters are defined within the text.

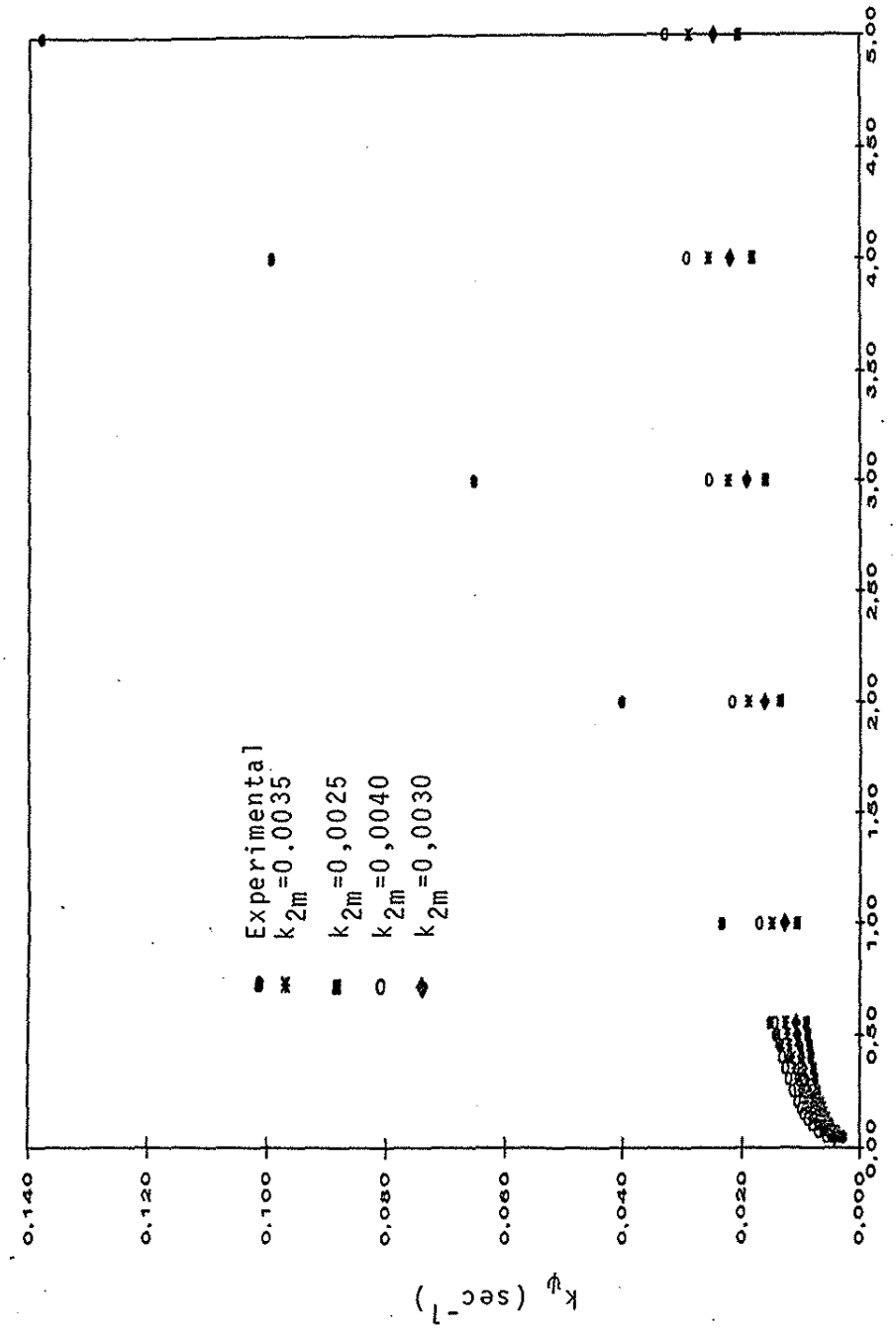


FIGURE 6. PLOTS OF THE EXPERIMENTAL PSEUDO FIRST ORDER RATE CONSTANT k_ψ FOR THE HYDROLYSIS OF LiPNEF AT 25ºC VERSUS HYDROXIDE ION CONCENTRATION AND FITS OF THE EXPERIMENTAL DATA WITH THE ION EXCHANGE MODEL USING DIFFERENT VALUES OF k_{2m}.

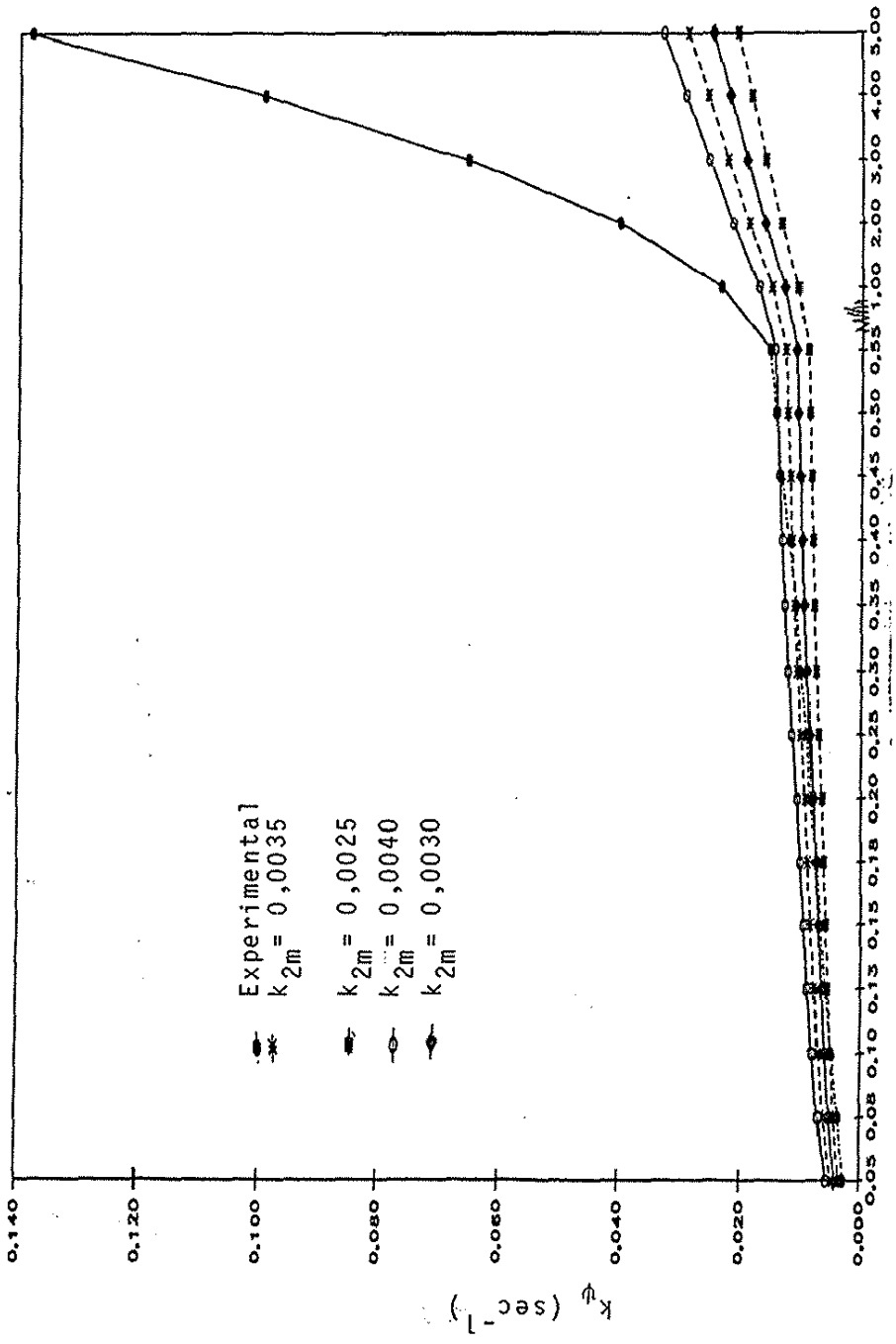


FIGURE 7. PLOTS OF THE EXPERIMENTAL PSEUDO FIRST ORDER RATE CONSTANT k_ψ FOR THE HYDROLYSIS OF LiPNEF AT 25ºC VERSUS HYDROXIDE ION CONCENTRATION AND FITS OF THE EXPERIMENTAL DATA WITH THE ION EXCHANGE MODEL USING DIFFERENT VALUES OF k_{2m} WITH AN EXPANDED SCALE AT LOW HYDROXIDE CONCENTRATION.

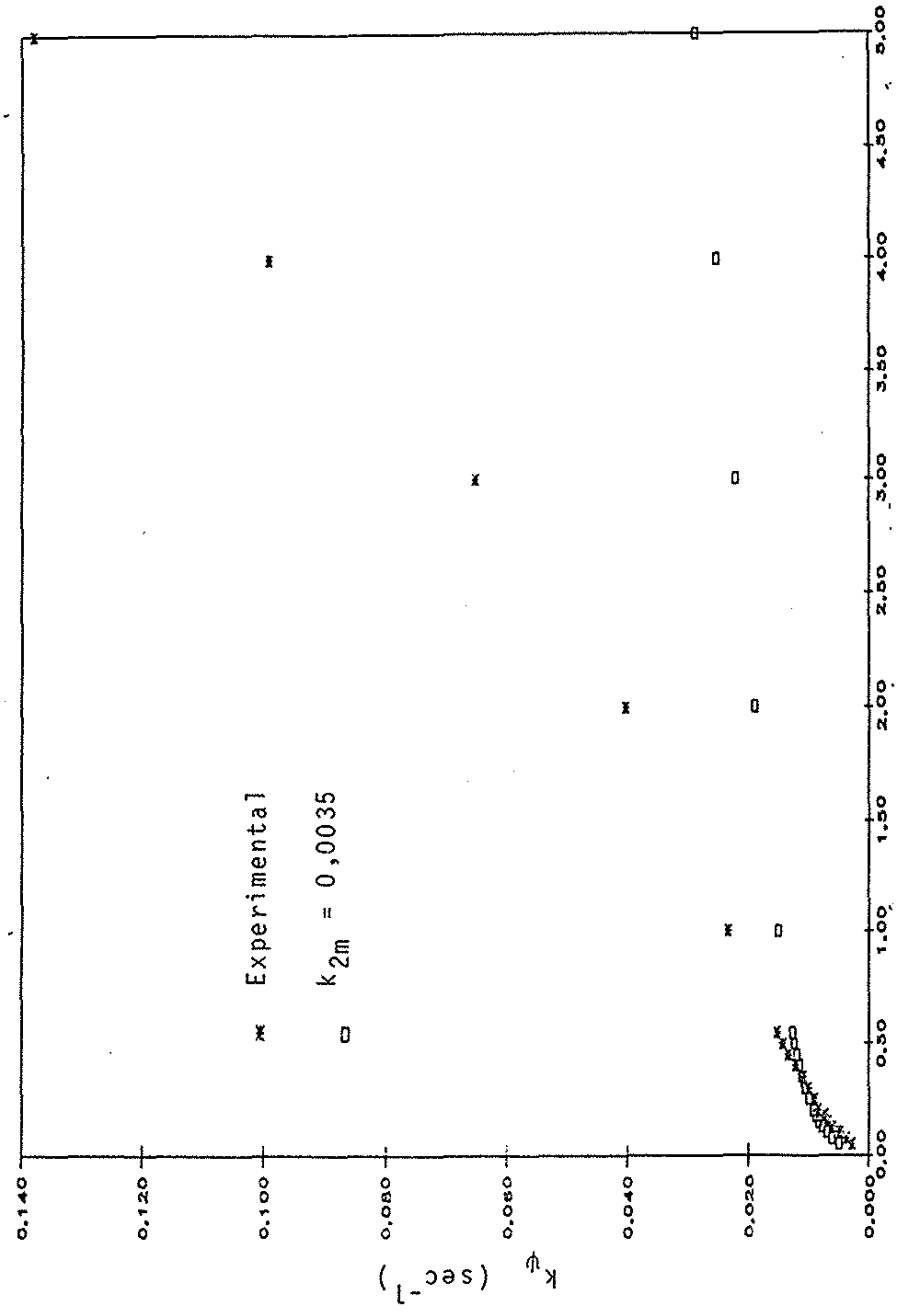


FIGURE 8. PLOT OF THE EXPERIMENTAL PSEUDO FIRST ORDER RATE CONSTANT k_ψ FOR THE HYDROLYSIS OF LiPNEF AT 25ºC VERSUS HYDROXIDE ION CONCENTRATION AND BEST FIT OF THE EXPERIMENTAL DATA WITH THE ION EXCHANGE MODEL USIG A VALUE OF k_{2m} OF 0,0035 s^{-1} M^{-1}.

Attempts to explain the experimental results obtained for the hydrolysis of LiPNEF using the pseudo phase ion exchange models presented in the literature[18-23] lead to failure of the models at higher hydroxide concentrations. Such failure at high hydroxide ion concentration has first been observed by Bunton, Romsted and Savelli[24] and by Lapinte and Viout[25]. The limitation of these models is not surprising, since they assume a constant micellar structure and involve partitioning of the substrate and the reactant between the aqueous and micellar phases and a fixed number of sites. All of them assume a closed thermodynamic system for a case when the kinetics under consideration may be more similar to flow kinetics, particularly when the micelles change in form, size and shape or undergo transitions to liquid crystalline mesophases.

More recent models, such as those proposed by D.G. Hall[26] that considers the transition state and by Bunton and Moffatt[27,28] that suggest a Coulombic Model and use the Poisson-Boltzmann Equation take into considerations some of shortcomings mentioned above.

Bunton, Romsted and Savelli[24] in their paper that may be considered a major breakthrough im micellar catalysis, explained the discrepancy between the theoretical models and the experimental results by considering an additional reaction pathway across the micellar boundary at the shear surface between the Stern and the Gouy-Chapmnan layers of the micelle. We have

suggested that conceptually this interfacial boundary or micelle-water interface, as it has been called, should not be very different from the interface present in systems where phase transfer catalysis is taking place.[8,9,29,30]

Quasi elastic light scattering, viscosity and surface tension studies of the CTAB-H_2O-NaOH (See Figure 5) and CTAB-H_2O-NaCl [15,16] systems clearly indicate changes in size and shape of the CTAB micelles and formation of liquid crystalline mesophases as a function of electrolyte concentration.

Consideration of the kinetic results presented above in light of the structural changes occuring in the system excludes the theoretical pseudo phase ion exchange models presented in the literature [18-23] for concentration of OH^- above 0,55 M. Changes in size, form, shape of the CTAB micelle and formation of lamellar and liquid crystalline mesophases are not taken into account in any of these models.[18-23]

For solutions of surfactants containing higher concentrations of electrolyte, serious consideration should be given to models more akin to phase transfer catalysis or liquid crystalline catalysis. Samori and his collaborators have described liquid crystalline catalysis by smectic B solvents [31,32] and Ramesh and Labes have investigated the control of reaction kinetics by manipulation of micellar size and shape [33,34] and the influence of disc-rod-sphere transitions in nematic lyotropics on a unimolecular isomerization reaction.

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SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY

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SYNTHESIS OF SOME THEOPHYLLINE DERIVATIVES

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ABSTRACT *Eight new theophyllines derived from the methyl esters of chlorosulphonyl-aryloxyalkylcarboxylic acids, with a possible action on the vascular system have been prepared. Their structures have been elucidated by IR, ^{1}H- NMR and elementary analysis.*

RESUMO *Foram sintetizados oito novos derivados da teofilina a partir de ácidos clorosulfonil ariloxialquil-carboxílicos. Eles tem uma possível ação sobre o sistem vascular. As suas estruturas foram elucidadas por infra-vermelho, ^{1}H-RMN e análise elementar.*

KEYWORDS 8-substituted theophyllines, theophyllinyl-sulphonyl-phenoxyacetats, phenoxyacetic esters, esters of sulphonamidated aryloxyalkylcarboxylic acids.

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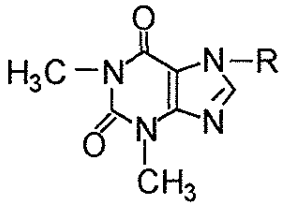
INTRODUCTION

In recent years theophyllines have become particularly important among the agents for vascular diseases.

Numerous studies are to be found in the literature on theophylline derivatives that are aimed to obtain products with hypotensive or antihypertensive, vasodilatory, coronarodilatory or antiarrhythmic properties and with low toxicity [1-6].



R = various substituents

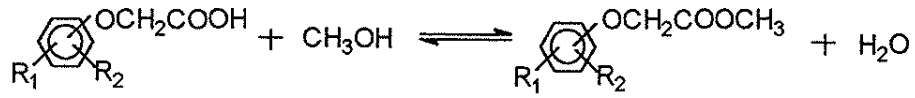
Since more selective compounds in this area are still a challenge, new theophylline derivatives continue to be synthesized and screened for their cardiovascular activities.

In the present paper we report the results of new studies obtained for some theophyllines derived from methyl chlorosulphonylphenoxyacetates, with possible hypotensive and vasodilatory actions, of low toxicity and a prolonged time of action.

RESULTS AND DISCUSSION

The method of synthesis used for obtaining the above mentioned theophylline derivatives is based on the condensation reaction of the esters of chlorosulphonyl aryloxycarboxylic acids in acetone, in the presence of triethylamine[7].

The reactions carried out are shown below. The aryloxyalkylcarboxylic acids were submitted successively to esterification, chlorosulphonation and condensation with theophylline[8-13].



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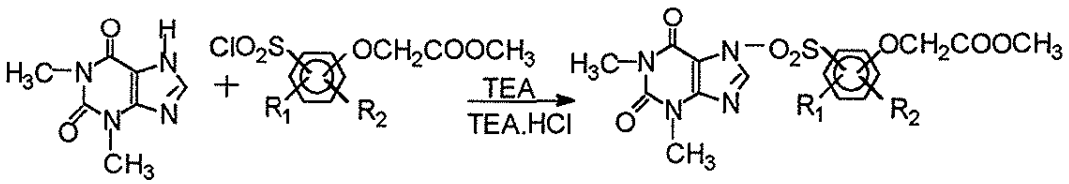

(3)

where: R_1 = H,CH_3,Cl,OCH_3;

R_2 = H,CH_3.

The final products have been purified by washing with acetone and hot water and recrystallization from acetic acid-water.

The theophylline derivatives obtained are solid, amorphous substances, with characteristic melting points. The compounds obtained were characterized by means of elementary analysis and IR and ^{1}H-NMR spectral measurements. (Table 1.)

Infrared spectra were recorded as KBr pellets using a UNICAM SP.100 apparatus (infrared spectrophotometer).

The ^{1}H-NMR spectra were determined with JEOL- 60 MHz spectrometer using dimethylsulfoxide as solvent.

Table 1. Theophyllines derived from methyl esters of chlorosulphonyl-phenoxyacetic acids

No	Compound	Formula	%N		M.p.
			calc.	found	°C
1.	methyl 4-teophyllinylsulphonyl phenoxyacetate	$C_{16}H_{16}N_4O_7S$	13.7	13.7	200
2.	methyl 2-cloro-4-teophyllinylsulphonyl phenoxyacetate	$C_{16}H_{15}N_4O_7ClS$	12.6	12.4	212-214
3.	methyl 4-chloro-2-teophyllinylsulphonyl phenoxyacetate	$C_{16}H_{15}N_4O_7ClS$	12.6	12.5	247-249
4.	methyl 2-methyl-4-teophyllinylsulphonyl phenoxyacetate	$C_{17}H_{18}N_4O_7S$	13.2	13.1	215-216
5.	methyl 3-methyl-4-teophyllinylsulphonyl phenoxyacetate	$C_{17}H_{18}N_4O_7S$	13.2	13.0	209-211
6.	methyl 2-methoxy-4-teophyllinylsulphonyl phenoxyacetate	$C_{17}H_{18}N_4O_8S$	12.7	12.5	170
7.	methyl 2,3-dimethyl-4-teophyllinylsulphonyl phenoxyacetate	$C_{18}H_{20}N_4O_7S$	12.8	12.47	188-190
8.	methyl 4,6-dimethyl-2-teophyllinylsulphonyl phenoxyacetate	$C_{18}H_{20}N_4O_7S$	12.8	12.6	177-178

The IR spectral analysis allowed us to reach conclusions on both the substituient positions in the aromatic ring as well as on the new bonds formed by synthesis. (Table 2.)

The main informations on the substituent position in the aromatic ring are given by the out-of-plane deformation vibration of the C-H bond. The vibration frequency is dependent on the substituent number and position and practically independent of their nature. Thus, the $\gamma_{C\text{-}H}$ absorption band within the 805 - 825 cm^{-1} range indicates the presence of two adjacent hydrogen atoms in the ring, while the deformation band of the single hydrogen is to be found within the 870-885 cm^{-1} range and is less intensive. Consequently, these two absorption bands in the IR spectrum are indicative of the 1,4-; 1,2,4-; 1,3,4-; 1,2,3,4- or 1,2,4,6- substitutions which confirm the presence of the sulphonamidated group in the position para to the ether oxygen or in the ortho position when the para is not free.

The aryloxyalkylcarboxylic derivatives have an extended conjugation between the ether oxygen, aromatic ring and sulphonamide group. As a consequence, the IR spectra show absorption bands that can be attributed to the C — S, S — N and S — O bonds.

The band of the C — S bond is to be found between 1080-1100 cm^{-1} being characteristic to all aromatic compounds containing a S atom directly bound to the ring.

The absorption bands characteristic to the S — O and S — N bonds appear within the 1020-1040 cm^{-1} and 1040-1080 cm^{-1} ranges, respectively.

The SO_2 group shows two intense bands corresponding to the symmetric and nonsymmetric vibration within the 1120-1180 cm^{-1} and 1300-1360 cm^{-1} regions, respectively.

Table 2. IR and ^{1}H- NMR data of the new substances.

Compound	IR (cm^{-1})	^{1}H-NMR (ppm)
1.	1130, 1340 (SO_2); 1735 (C=O), 1180 (C-O); 1090 (C-S) ; 1260 (C-O-C_{aryl});1670(CON_{amidic});1620(C=N);2910(NCH_3);1430(CH_2); 825(1,4-disubstituted benzene)	3.22(3H,s,$CH_{3teophylline}$);3.41(3H,s,CH_{3ester});3.68(3H,s, $CH_{3teophylline}$);4.8(2H,s,CH_2);6.8(2H,d,aryl);7.6(2H,d,aryl); 8.04(1H,s,teophylline)
2.	1120,1330 (SO_2);1750 (C=O),1180(C-O);1080(C-S);1260 (C-O-Caryl);1670(CON_{amidic});1610(C=N);2900(N-CH_3),1440(CH_2); 850,880(1,2,4-trisubstituted benzene)	3.24(3H,s,$CH_{3teophylline}$);3.48(3H,s,CH_{3ester});3.78(3H,s, $CH_{3teophylline}$);5.08(2H,s,CH_2);7.4(1H,d,aryl);8.2(1H,d,aryl); 8.68(1H,s,teophylline)
3.	1120,1320(SO_2);1720(C=O),1180(C-O);1080(C-S);1260(C-O-C_{aryl});1680(CON_{amidic});1610(C=N);2900(N-CH_3);1430(CH_2); 850,880(1,2,4-trisubstituted benzene)	3.2(3H,s,$CH_{3teophylline}$);3.47(3H,s,CH_{3ester});3.76(3H,s, $CH_{3teophylline}$);5.04(2H,s,CH_2);7.36(1H,d,aryl);8.15(1H,d,aryl); 8.64(1H,s,teophylline)
4.	1120,1330(SO_2);1735(C=O),1180(C-O);1090(C-S);1260(C-O-C_{aryl});1670(CON_{amidic});1610(C=N);2900(N-CH_3),1450(CH_2); 845,880(1,2,4-trisubstituted benzebe)	2.25(3H,s,CH_{3aryl});3.22(3H,s,$CH_{3teophylline}$);3.48(3H,s,CH_{3ester}); 3.75(3H,s,$CH_{3teophylline}$);4.98(2H,s,CH_2);7.1(1H,d,aryl); 8.02(1H,d,aryl);8.62(1H,s,teophylline)
5.	1120,1330(SO_2);1730(C=O);1180(C-O);1090(C-S);1260(C-O-C_{aryl});1670(CON_{amidic});1610(C=N);2900(N-CH_3),1450(CH_2)	2.3(3H,s,CH_{3aryl});3.25(3H,s,$CH_{3teophylline}$);3.5(3H,s,CH_{3ester}); 3.8(3H,s,$CH_{3teophylline}$);5.0(2H,s,CH_2);7.1(1H,d,aryl); 8.1(1H,d,aryl);8.65(1H,s,teophylline)
6.	1120,1330(SO_2);1720(C=O);1170(C-O);1090(C-S);1280(C-O-C_{aryl});1670(CON_{amidic});1610(C=N);2900(N-CH_3),1445(CH_2); 1010,2850(CH_3O-C_{aryl})	3.25(3H,s,$CH_{3teophylline}$);3.45(3H,s,CH_{3ester});3.7(3H,s, $CH_{3teophylline}$);3.82(3H,s,OCH_3);4.82(2H,s,CH_2);7.3 (1H,d,aryl);7.9(1H,d,aryl);8.7(1H,s,teophylline)
7.	1130,1340(SO_2);1720(C=O);1180(C-O);1090(C-S);1270(C-O-C_{aryl});1670(CON_{amidic});1610(C=N);2900(N-CH_3),1450(CH_2)	2.15(3H,s,CH_{3aryl});2.5(3H,s,CH_{3aryl});3.25(3H,s,$CH_{3teophylline}$); 3.45(3H,s,CH_{3ester});3.7(3H,s,$CH_{3teophylline}$);4.75(2H,s,CH_2); 6.7(1H,d,aryl);7.65(1H,d,aryl);8.8(1H,s,teophylline)
8.	1120,1390(SO_2);1730(C=O);1190(C-O);1080(C-S);1260(C-O-C_{aryl});1680(CON_{amidic});1610(C=N);2900(N-CH_3),1450(CH_2)	2.18(3H,s,CH_{3aryl});2.5(3H,s,CH_{3aryl});3.22(3H,s,$CH_{3teophylline}$); 3.43(3H,s,$CH_{3esther}$);3.7(3H,s,$CH_{3teophylline}$);4.7(2H,s,CH_2); 6.85(1H,s,aryl);7.2(1H,s,aryl);8.7(1H,s,teophylline)

The frequency of the C — O ether bond in the aromatic compounds is to be found between 1200-1260 cm^{-1} and the ester group shows two bands within 1735-1750 cm^{-1} and 1050-1300 cm^{-1} ranges, respectively.

The IR spectrum of the theophylline derivatives under study also show bands characteristic of the CO-N((1650-1680 cm^{-1}, 2890-2910 cm^{-1}) and C — N (1600-1620 cm^{-1}) vibration.

The ^{1}H-NMR spectra of the compounds show singlets at about 2.15-3.8 ppm that may be attributed to methyl protons. The CH_2 protons are seen at 4.7- 5.08 ppm as a singlet. Phenyl protons are seen at expected values. In addition the theophylline proton is seen at 8.04-8.8 ppm as a singlet. The elementary analysis of the compounds gave further support for the reported structure [14,15].

EXPERIMENTAL

Methyl 4-theophyllynyl-sulphonyl phenoxyacetate

A sample of 2.645 g (0,01 mole) of the methyl ester of 4-chlorosulphonyl phenoxyacetic acid was dissolved in 30 ml acetone. Subsequently, 1.8 g (0,01 mole) theophylline and 1,5 ml triethylamine were then added. The reaction mixture was refluxed 2 hours. After filtering the product it was washed with 10 ml of acetone and 15 ml of hot water and than recrystallized from 30 ml acetic acid, washed with 15 ml methyl alcohol and dried. The pure product was finally obtained in a 75 % yield. (M.p. = 200° C).

CONCLUSIONS

Eight new theophyllines with possible hypotensive and vasodilating actions have been prepared by the reaction of some esters of chlorosulphonylaryloxyalkylcarboxylic acids with theophylline in the presence of triethylamine. The structures of the compounds obtained have been elucidated by means of elementary analysis and IR and ^{1}H-NMR spectral measurements.

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SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY

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CARBON-13 NMR OF ALIPHATIC TERTIARY AMIDES

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ABSTRACT

This work presents unpublished Carbon-13 NMR data for eight aliphatic tertiary amides. The substituent chemical shifts of the **$CONMe_2$** and **$CONEt_2$** groups were determined and can be useful in correlation analysis.

RESUMO

O presente trabalho apresenta dados inéditos de deslocamentos químicos para oito amidas alifáticas terciárias. Os deslocamentos químicos do substituinte para os grupos $CONMe_2$ e $CONEt_2$ foram determinados e podem ser úteis em análise correlacional.

KEY WORDS: Carbon-13 NMR, chemical shifts, aliphatic tertiary amides.

INTRODUCTION

Recently, we have studied aliphatic compounds by Carbon-13 NMR spectroscopy[1,2]. Although aliphatic tertiary amides are easy to synthesize, there is a lack of NMR data in the literature[3]. We have synthesized several aliphatic tertiary amides of the type **R-Z** where **R** is a alkyl group containing two to six carbon atoms (Ethyl, propyl, butyl, amyl and hexyl groups), and **Z** represents the **$CONMe_2$** or **$CONEt_2$** groups. The purpose of this work was to sinthesize eight non-branched aliphatic tertiary amides with sp^3 hibridization, to record their Carbon-13 NMR data for their full characterization, and to determine the substituent chemical shifts (**SCS**) of the **$CONMe_2$** and **$CONEt_2$** groups. The chemical shifts are inedited and the **SCS** can be useful in correlation analysis.

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EXPERIMENTAL PROCEDURE

Materials: All compounds were prepared according to literature procedures[5]. The physical and spectral data are shown in Tables 1-3. Solvents were of spectroscopic quality and were used without further purification.

Spectra: the C-13 NMR spectra of 1,0 M solutions in CCl_4 with 5 % TMS as an internal reference in 10 mm o.d. sample tubes, were recorded at 25,2 MHz using a Varian XL-100 spectrometer in the FT mode. The conditions were as follows: pulse width, 20 μs; acquisition time, 0,67 s; spectral width, 6150 Hz; pulse repetition time, 0,4 s; temperature, 30 °C; internal lock, D_20; angle tumbling, 45°; number of transients, 6000; and number of data point, 8192. The C-13 NMR spectra were recorded in both the proton-noise decoupled and coupled modes. The H-1 NMR spectra of the solutions investigated, in 5 mm o.d. sample tubes, were recorded at 80 MHz using a Bruker AW-80 spectrometer in the FT mode.

RESULTS AND DISCUSSION

Table 1 shows the physical constants of these compounds. They agree whith published data. The H-1 NMR data are shown in Table 2 and Table 3 shows the C-13 NMR data. Table 4 shows the SCS of the dialkylamide groups. The synthesis of eight tertiary amides allow to amplify the C-13 NMR data of these amides and to estimate directly form the SCS of these groups. The four SCS α, β, γ and δ for the $\mathbf{CONMe_2}$ and $\mathbf{CONEt_2}$ groups are defined as follow: $R\text{-}^{\delta}CH_2\text{-}^{\gamma}CH_2\text{-}^{\beta}CH_2\text{-}^{\alpha}CH_2\text{-}Z$ where Z = $\mathbf{CONMe_2}$ or $\mathbf{CONEt_2}$, and were estimated from the chemical shifts of the unsubstituted compounds [where Z = H]. The signals of aliphatic carbons were assigned by single-frequency off-resonance decoupling (SFORD) and proton noise decoupled (DFL) spectra and known chemical shifts rules[3]. We have determined the SCS of the $\mathbf{CONMe_2}$ and $\mathbf{CONEt_2}$ groups, wich were not been previously reported in the literature. These values can be useful in correlation analysis.

Table 1. Physical Constants of Aliphatic Tertiary Amides[4]

	Compounds	b.p (°C/Torr)	Yield (%)
1	N,N-Dimethyl-N-propanamide	70/20	90.0
2	N,N-Dimethyl-N-butanamide	80/20	93.8
3	N,N-Dimethyl-N-pentanamide	100/20	90.0
4	N,N-Dimethyl-N-hexanamide	115/20	80.0
5	N,N-Dimethyl-N-heptanamide	130/20	92.6
6	N,N-Diethyl-N-pentanamide	110/20	95.4
7	N,N-Diethyl-N-hexanamide	130/20	96.7
8	N,N-Diethyl-N-heptanamide	140/20	86.8

Table 2. H-1 NMR Chemical Shifts of Aliphatic Tertiary Amides in ppm Relative to TMS[4] (Solvent CCl_4)

Compounds	H-2	H-3	H-4	H-5	H-6	H-7	H-1'E	H-1'Z	H-1'	H-2'
1	2.20	1.00					2.90	2.80		
2	2.20	1.60	0.90				2.90	2.80		
3	2.20	1.10 to 1.80		0.90			2.90	2.80		
4	2.20	1.10	to	1.80	0.90		2.90	2.80		
5	2.20	1.10	to		1.80	0.90	2.90	2.80		
6	2.20	0.80 to 1.80		0.90					3.20	a
7	2.20	0.80	to	1.80	0.90				3.20	a
8	2.20	0.80	to		1.80	0.90			3.20	a

a: multiplet in 0,80-1.80 ppm. **E** (entgegen): NR_2 group *anti* to carbonyl oxygen. **Z** (zusammen): NR_2 group *syn* to carbonyl oxygen.

Table 3. C-13 NMR Chemical Shifts of Aliphatic Tertiary Amides in ppm Relative to TMS[4] (Solvent CCl_4)

Compounds	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-1'E	C-2'E	C-1'Z	C-2'Z
1	171.8	26.0	9.2					36.6		34.8	
2	171.0	34.7	18.3	13.9				36.7		35.2	
3	171.0	32.5	27.1	22.5	13.9			36.8		34.8	
4	171.1	32.7	24.6	31.6	22.5	14.0		36.7		34.8	
5	171.0	32.8	24.8	29.1	31.7	22.5	14.0	36.8		34.8	
6	170.1	32.3	27.3	22.5	14.0			41.6	14.6	39.7	13.2
7	170.1	32.6	24.9	31.6	22.5	14.0		41.5	14.6	39.7	13.2
8	170.0	32.6	25.1	29.1	31.7	22.5	14.1	41.5	14.6	39.7	13.2

E (entgegen): NR_2 group *anti* to carbonyl oxygen. **Z** (zusammen): NR_2 group *syn* to carbonyl oxygen.

Table 4. Substituent Chemical Shifts of Aliphatic Tertiary Amides in ppm[4]

group	α	β	γ	δ
$CONMe_2$	19.2	2.3	-2.7	-0.1
$CONEt_2$	19.2	2.3	-2.7	-0.1

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SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY
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DUNCAN ARTHUR MACINNES, FOREMOST AMERICAN ELECTROCHEMIST

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ABSTRACT

Duncan Arthur MacInnes, one of the world's outstanding electrochemists was born in Salt Lake City, Utah on March 31, 1885 and died on September 23, 1965. He graduated from the University of Utah with a bachelor of science degree in chemical engineering in 1907 and obtained a Ph.D. degree in chemistry from the University of Illinois in 1911. He held positions mainly at M.I.T and the Rockefeller Institute for Medical Research. His most important contributions deal with the determination of transference numbers by the moving boundary method, development of the glass electrode and experimental confirmation of the Debye-Hückel Theory.

RESUMO

Duncan Arthur MacInnes, um eletroquímico mundialmente reconhecido, nasceu em Salt Lake City, Utah, USA em 31 de Março de 1885 e faleceu em 23 de Setembro de 1965. Formou-se como engenheiro químico na Universidade do Utah em 1907 e obteve o grau de Ph.D. em Química da Universidade de Illinois em 1911. Trabalhou principalmente no Instituto de Tecnologia do Massachusetts e no Instituto Rockefeller de Pesquisas Médicas. As suas contribuições mais importantes incluem a determinação de números de transferência usando o método da fronteira móvel, o desenvolvimento do eletrodo de vidro e a confirmação experimental da Teoria Debye-Hückel.

One of the world's outstanding chemists, Duncan Arthur MacInnes published over a hundred scientific papers in his special field, electrochemistry, and "Principles Of Electrochemistry", a textbook that was widely adopted for classes in this subject. His scientific work extended over an active period of nearly half a century.

He was born on March 31, 1885, to Duncan MacInnes and his wife, Frances Charlotte (Sayers) MacInnes, in Salt Lake City, Utah. He suffered a nearly fatal accident in a streetcar that resulted in a badly injured leg and the loss of two fingers from his left hand, when he was only thirteen years old, which made it impossible for him to engage in any activity such as sports for a few years. He was not discouraged however by this disability, and perhaps because of it, he undertook a typical life-long program of exercise which eventually resulted in his becoming skilled in hiking, skiing, and mountain climbing.

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While a student at a preparatory school of the University of Utah at the age of sixteen he boarded at the same boarding house as Solomon Farley Acree, who was later to become the chief of a division of the National Bureau of Standards in Washington, D.C. Acree, ten years older than MacInnes, was then an active research chemist, having received his B.S. and M.S. degrees from the University of Texas, and his Ph.D. from the University of Chicago in 1902, and had done postgraduate work at the University of Berlin in Germany. Acree was an assistant professor of chemistry at the University of Utah from 1901 until 1904, and undoubtedly encouraged the young MacInnes to enroll there, which he did in 1903 at the age of eighteen. His first class in chemistry was conducted by an excellent teacher, Dr. William C. Ebaugh. Four years later he was graduated from the University of Utah with a bachelor of science degree in chemical engineering.

Because the country was in the depths of another depression at the time MacInnes was graduated from the University of Utah, he had trouble finding a job locally, and he finally took a job with the Phelps-Stokes Company (forerunner of the Phelps-Dodge Copper Company) in Berlin, Nevada. This job did not suit him however, so by 1908 he was back with his parents in Utah, where his father was in business in American Falls.

MacInnes had applied for a fellowship at a number of eastern universities, and in 1908 he received an offer from the University of Illinois where William A. Noyes was professor of chemistry and director of the chemical laboratories from 1907 to 1926. He studied and did research with Dr. Edward Wight Washburn, who had received his Ph.D. in chemistry from the Massachusetts Institute of Technology (M.I.T.) in 1908. Thus MacInnes was one of Washburn's first research students. He wrote a thesis on "The Laws of 'Concentrated' Solutions. The Ionization and Hydration Relations of Electrolytes in Aqueous Solutions at Zero Degrees", for which he was awarded the degree of doctor of philosophy in chemistry in 1911. After graduation he accepted a position as instructor at Illinois, teaching physical chemistry. He became active in research immediately, and published five papers on electrochemistry at Illinois. Arthur A. Noyes, director of the Research Laboratory in Physical Chemistry at M.I.T., invited MacInnes to join him there in 1917, and MacInnes did outstanding work there in electrochemistry, with the collaboration of other well-known scientists such as A.A. Noyes, Theodore Shedlovsky, James A. Beattie, and Edgar Reynolds Smith, publishing fourteen papers in electrochemistry, and also several in the field of x-rays.

Among MacInnes' most important contributions to science was his work, with Edgar R. Smith, on the determination of transference numbers by the moving boundary method, a spectacular method still described in some laboratory manuals for physical chemistry. Other work of his included that on the development of the glass electrode, work in potentiometric methods of chemical analysis, measurement of acidity (pH) (his early friend Acree was chief of the Division of pH Standards of the National Bureau of Standards), and the determination of ionization constants and activity coefficients.

He took a sabbatical leave from M.I.T. in Paris in 1925 devoted to study and travel in Europe. He wanted to work with Peter Debye, whose theory of interionic attraction had been published with Walter Huckel, but Debye was in the U.S. in 1925. In Paris he visited museums and improved his abilities in the French language. He also visited Holland, Switzerland and Italy, and made his most extended visit to England, about two months. In England he visited Dr. Frederick George Donnan, F.R.S., who proposed the theory of the Donnan Membrane Equilibrium, as well as other workers in physical chemistry.

On his return to M.I.T. he was asked to teach a course in colloid chemistry, which he considered an imprecise field, and his lack of enthusiasm for this topic may have led to his decision to move to the Rockefeller Institute for Medical Research in New York City in 1926 where he did research for the rest of his life, becoming a member in 1940, and Emeritus Member in 1950. MacInnes said that he considered his experiments to confirm the interionic attraction theory of Peter Debye, sometimes called the Debye-Huckel Theory, to be his most important work. He was convinced that strong electrolytes in aqueous solution were completely ionized and that Debye's theory offered the best explanation of their behavior.

The New York Academy of Sciences elected him its president in 1944. He played an important role in starting the Academy's Conferences at Rams Head Inn, Shelter Island, Long Island, New York. These were to be small conferences on topics in which actual work was in progress and that participants were to be limited to investigators who were actively working in the fields under consideration. In MacInnes' view these conferences were needed because the meetings of regular scientific societies, such as the American Chemical Society, had become so large that workers in a specific field were having difficulty getting together for serious discussions about their work.

The Electrochemical Society awarded him its Acheson Medal in 1948, and elected him its president in 1935. MacInnes worked for the Chemical Warfare Service, U.S. Army, in World War II, as director of a group at the Rockefeller

Institute working on topics of interest to the war effort, and was awarded the President's Certificate of Merit for this work in 1948. He was awarded the Nichols Medal by the American Chemical Society's New York Section in 1942, which indicated that his chemical interests included areas of physical chemistry other than electrochemistry. He was elected to the National Academy of Sciences in 1937, and the American Philosophical Society in 1942.

MacInnes became somewhat skilled as a mountain climber, and on one occasion these skills helped him save his party from a serious accident. He was a member of the American Alpine Club and the Appalachian Mountain Club, and was considered to have made significant contributions to the preservation of the environment and the national park system. He died on September 23, 1965.

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Note:

(This biography is an example of the 18,000 entries being prepared for the "American National Biography", sponsored by the American Council of Learned Societies, and to be published in October 1998, by the Oxford University Press.)

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SYNTHESIS OF NEW BENZO[e]DIBENZOFURO[2,3-b]-OXEPIN-5(14H)-ONES.

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ABSTRACT

The new ring systems, benzo[e]dibenzofuro[2,3-b]oxepin-5(14H)-one and benzo[e]dibenzofuro[2,1-b]oxepin-5(14H)-one were obtained by cyclizing of 2-(2'-dibenzofuryloxymethyl)benzoic acid in the presence of polyphosphoric acid ester.By cyclization of the 2-(1'-methoxy-2'-dibenzofuryloxymethyl) benzoic acid was obtained benzo[e]dibenzofuro[2,3-b]-oxepin-12-methoxy-5-one with a indubitable structure. The structure of the new compounds was proved by means of ^{1}H-and ^{13}C-NMR spectra.

RESUMO

Os novos sistemas cíclcos benzo(e)dibenzofuro(2,3-b)oxepin-5(14H)-ona e benzo(e)dibenzofuro(2,1-b)oxepin-5(14H)-ona foram obtidos através de ciclização do ácido dibenzofuriloximetilbenzóico na presença do éster do ácido polifosfórico. O composto benzo(e)dibenzofuro(2,3-b)-oxepin-12-metoxi-5-ona foi obtido com estrutura inequivocável através da ciclização do ácido 2-(1'-metoxi-2'-dibenzofuriloximetil)benzóico. A estrutura dos novos compostos foi comprovada com espectros de RMN de ^{1}H e ^{13}C.

KEYWORDS : Polycyclic heterocycles/Benzodibenzofuro-oxepinones

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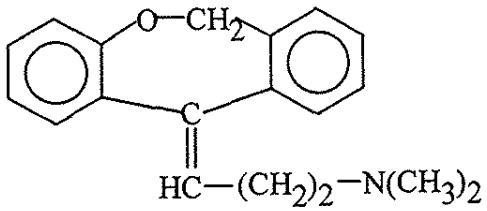
INTRODUCTION

Doxepin **(1)**, a well-known antidepressant agent[1] can be prepared by reacting the corresponding oxepinone with 3-(N,N-dimethylamino)propylmagnesium chloride[2] or with phosphorane ylides[3].



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As an important aspect of the structure-activity studies, we were interested in preparing new benzodibenzofurano-oxepinones with a view to their reaction with a Grignard compound or phosphorane ylide.

This paper reports syntheses of these new ring systems and their UV, IR, ^{1}H, ^{13}C - NMR spectra.

EXPERIMENTAL

Melting points (uncorrected) were recorded on a Büchi apparatus.The UV spectra (methanol) were recorded on a Hewlett Packard-8452A spectrophotometer.The IR spectra were obtained on a Bruker IFS-25 apparatus in KBr pellet. The NMR spectra were taken on a Bruker AM spectrometer (400 MHz and 100.6 MHz for ^{1}H and ^{13}C NMR , respectively). The spectra were recorded in DMSO-d_6 or $CDCl_3$ with Me_4Si as internal standard.

2-(2'-Dibenzofuryloxymethyl) benzoic acid (4).

An amount of 10.0 g (0.054 mol) 2-hydroxydibenzofuran was added to a solution of 0.056 mole of sodium methoxide in 40 ml of dry methanol. The solvent was removed in vacuo and the resultant light brown powder **(2)** was treated with 7.60 g (0.056 mol) phthalide **(3)**. The mixture was stirred at 150 - 160^{0}C for two hours, cooled and treated with warm water. The clear solution was acidified with 4N HCl and the precipitate was removed by filtration,washed with water and dried. The crude product (13.5 g) was recrystallized from ethanol 80% to give colourless crystals, 10.5 g (60% yield) of product **4**, with m.p. 178-179^{0}C. IR (KBr): 1692 (carboxyl, C = O), 3100-2560 (carboxyl, OH) cm^{-1}. UV (methanol): λ_{max} (lg e) : 208 (4.46), 252 (4.15), 290 (4.23), 310 (3.72), 332 (3.71) nm. ^{1}H-NMR (DMSO-d_6): 8.14 (d, 1 H, H-9', J = 7.5 Hz), 7.95 (d, 1 H, H-6, J = 7.7 Hz), 7.80 (s, 1 H, H-1'), 7.33-7.78 (m, 7 H, aromatic H), 7.17 (d, 1 H, H-3', J = 8.8 Hz), 5.7 (s, 2 H, CH_2) ppm. Anal.Calcd for $C_{20}H_{14}O_4$ (318.3): C, 75.46, H 4.43; found C, 75.29, H,4.35.

Benzo(e)dibenzofuro[2,3-b]oxepin-5(14H)-one **(5a)** and benzo(e)dibenzofuro-[2,1-b] oxepin-5(14H)-one **(5b)**

A mixture of 6 g (0.042 mol) phosphorpentoxide, 12 ml dry chloroform and 8 ml dry diethyl ether was refluxed under stirring and in dry atmosphere until the mixture became clear. A quantity of 1.5 g (0.04 mol) of the compound **4** was added to this clear solution of polyphosphoric acid esther and was refluxed for two hours. The mixture was poured into ice,then extracted with chloroform.The organic layer was washed with water, 2N NaOH, water and then dried over Na_2SO_4. The chloroform was evaporated in vacuo and the crude material (1.2 g, 95% yield) was chromatographied on silicagel column. The elution of the column was realised with petrol ether (30 - 50 ^{0}C)/diethyl ether, 10/1. The first to get is **5b**. The isomere **5b** was recrystallized from diethyl ether (30% yield) and **5a** from acetic acid (50% yield). R_f value determined by TLC are 0.70 for **5a** and o.82 for **5b**.

Compound **5a:** orange crystals, m.p. 185-186^{0}C. IR (KBr): 3064, 2950 (CH), 1646 (C = O), 1232, 1025 (COC), 894, 878, 850, 828 and 807 (CH) cm^{-1}.UV (methanol): λ_{max}(lg e) = 216 (4.46), 274 (3.88), 324 (4.30) nm. ^{1}H-NMR ($CDCl_3$): 8.46 (s, 1 H, H-6), 8.05 (d, 1 H, H-11, J = 7.6 Hz), 7.95 (d, 1 H, H-4, J = 7.6 Hz), 7.59 (s, 1 H, H-12), 7.51-7.59 (m, 4 H, aromatic H), 7.35-7.46 (m, 2 H, aromatic H), 5.25 (s, 2 H, CH_2) ppm. ^{13}C-NMR ($CDCl_3$): 189.93 (C = O), 74.5 (CH_2) ppm.Anal.Calcd. for $C_{20}H_{12}O_3$ (300.3): C, 80.00, H, 4.03; found C, 79.80, H, 3.95.

Compound **5b:** pale-yellow crystals, m.p. 134-136 ^{0}C. IR (KBr): 3067, 2967, 2862(CH), 1652 (C = O), 1225, 1023 (COC), 900, 850, 823, 816 (CH) cm^{-1}.UV (methanol): λ_{max}(lg e): 214 (4.42), 258 (3.94), 324 (3.91) nm. ^{1}H-NMR ($CDCl_3$): 8.58 (d, 1 H, H-6, J = 8.2 Hz), 8.23 (d, 1 H, H-4, J = 7.5 Hz), 7.66 (d, 1 H, H-11, J = 8.8 Hz), 7.28 - 7.59 (m, 6 H, aromatic H), 7.22 (d, 1 H, H-12, J = 8.8 Hz), 5.35 (s, 2 H, CH_2) ppm. ^{13}C-NMR ($CDCl_3$) : 191.54 (C = O), 75.0 (CH_2) ppm.Anal.Calcd. for $C_{20}H_{12}O_3$ (300.3) : C,80.00; H,4.03.found: C,79.6 : H,3.80

1-Bromo-2-hydroxydibenzofuran **(6)**

This compound was obtained as colourless needles from 2-hydroxydibenzofuran with the bromine : dioxane complex (93% yield) and separated by fractional cristallization from ethanol-water, m.p. 126-127^{0}C (lit. 9, m.p. 122 - 123^{0}C).

1-Methoxy-2-hydroxydibenzofuran (7)

To a solution of 0.4 g (0.017 mol) of sodium in dry methanol (8 ml) was added 1 g (0.004 mol) of 6 and 0.3 g (0.002 mol) $CuCl_2 \circ 2H_2O$ in 4 ml DMF. The reaction mixture was heated at 110 - 115 ^{0}C for one hour. In this time 6.5 ml methanol was distilled. After heating for 5 min. at 130 ^{0}C, the mixture was cooled, treated with 10 ml water, acidified with 2N HCl to pH = 3 and extracted with diethyl ether. The extracte was then washed with water and dried on $MgSO_4$. The evaporation of solvent afforded 0.6 g (75% yield) of crude product, m.p. 120-122 ^{0}C. After recrystallization from diethyl ether-petrol ether, m.p. = 124 - 125 ^{0}C. IR(KBr): 3550 (OH), 2940, 2840 (aliphatic CH), 1220, 1012 (COC), 805, 771, 760 (CH) cm^{-1}. ^{1}H-NMR (DMSO-d_6): 9.40 (s, 1 H, OH), 8.10 (d, 1 H, H-9, J = 7.6 Hz), 7.65 (d, 1 H, H-6, J = 8.1 Hz), 7.51 (t, 1 H, H-7), 7.40 (t, 1 H, H-8), 7.29 (d, 1 H, H-4, J = 8.7 Hz), 7.11 (d, 1 H, H-3, J = 8.7 Hz), 4.07 (s, 3 H, CH_3),ppm. MS (70 ev); m/z (%) = 214 (92) [M^+], 199 (100), [M^+-15].Anal.Calcd.for $C_{13}H_{10}O_3$ (214.2): C, 72.89, H, 4.71; found C, 73.20, H, 4.60.

2-(1'-Methoxy-2'-dibenzofuryloxymethyl)benzoic acid (8)

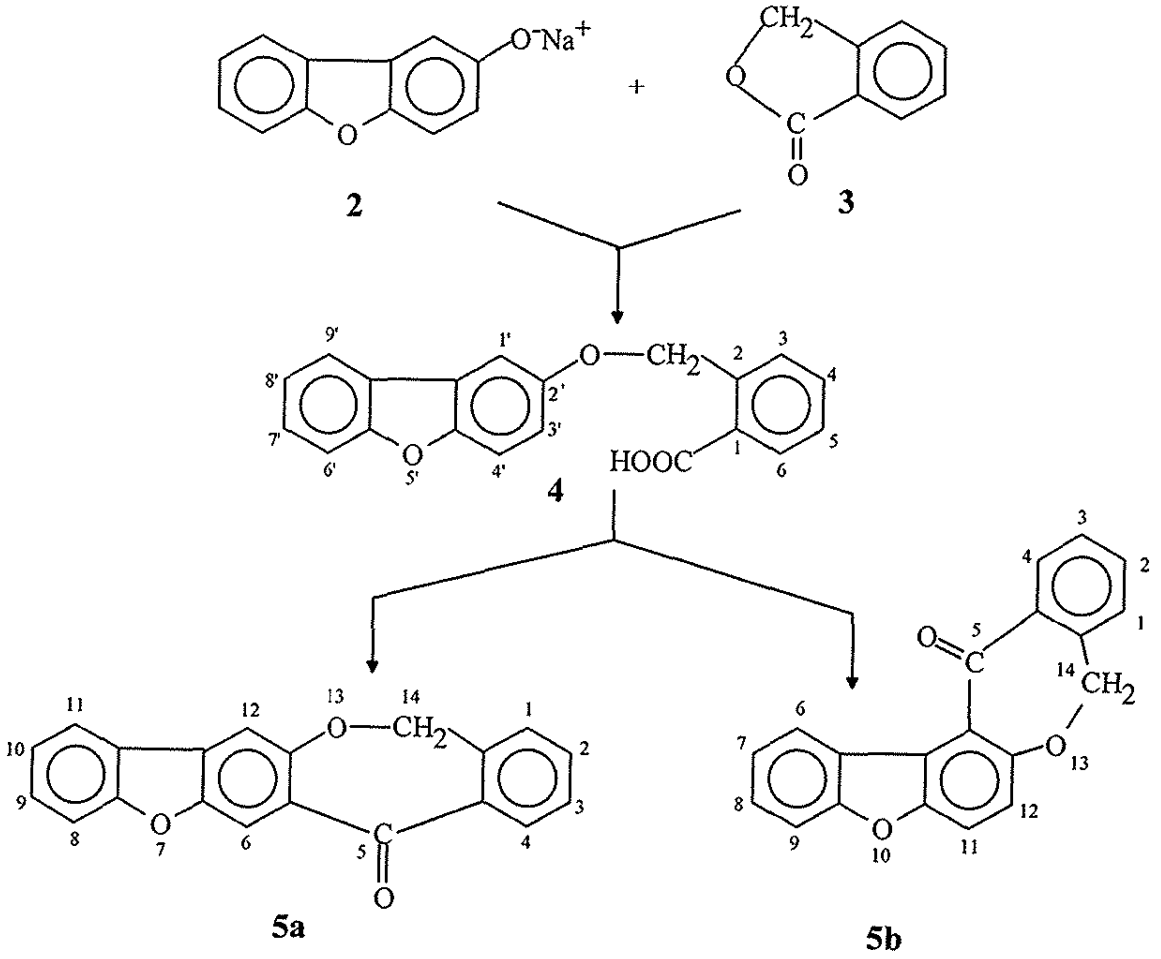
Starting from 3.2 g (0.015 mol) of 7 under the circumstances described above for **4** , but heating at 160 - 165^{0}C for 3 - 3.5 hours, we obtained 2 g (38.5%, yield) of crude product with m.p. 173 - 174^{0}C. After recrystallization from ethanol the pure **8** was obtained (colourless crystals, m.p.= 179 - 180^{0}C). ^{1}H-NMR (DMSO-d_6): 13.1 (s, 1 H, COOH), 8.10 (d, 1 H, H-9', J = 7.4 Hz), 7.98 (d, 1 H, H-6, J = 7.8 Hz), 7.80 (d, 1 H, H-6', J = 7.6 Hz), 7.40 - 7.70 (m, 5 H, aromatic H), 7.39 (d, 1 H, H-4', J = 8.8 Hz), 7.28 (d, 1 H, H-3', J = 8.8 Hz), 5.54 (s, 2 H, CH_2),ppm.^{13}C-NMR (DMSO-d_6): 168.48 (COOH), 70.42 (CH_2), 60.87 (CH_3) ppm.Anal.Calcd.for $C_{21}H_{16}O_5$ (348.4): C, 72.40, H, 4.63; found C, 72.65, H, 4.58.

12-Methoxybenzo(e)dibenzofuro[2,3-b]-oxepin-5(14H)-one (9)

Starting from 1.5 g (0.004 mol) of 8 in conditions shown by the preparation of 5, the crude product (1.3 g, 91% yield, m.p. = 165 - 175 ^{0}C) was obtained. After recrystallization from ethanol, the methoxyoxepinone 9 was obtained (m.p. = 188 - 189 ^{0}C). IR (KBr): 1645 cm^{-1} (C = O). UV (methanol):λ_{max}(lg e) : 207 (4.52), 224 (4.62), 268 (3.92), 324 (4.42) nm. ^{1}H-NMR (DMSO-d_6): 8.16 (d, 1 H, H-11, J = 7.5 Hz), 8.07 (s, 1 H, H-6), 7.96 (d, 1 H, H-4, J = 8.0 Hz), 7.27 - 7.46 (m, 6 H, aromatic H), 5.46 (s, 2 H, CH_2), 4.07 (s, 3 H, CH_3) ppm. ^{13}C-NMR (DMSO-d_6): 188.58 (C = O), 74.20 (CH_2), 60.75 (CH_3) ppm. MS (70 ev); m/z (%): 330.4 (100) [M^+], 315.4 (20) [M^+-15]. Anal.Calcd. for $C_{21}H_{14}O_4$ (330.4): C, 76.35, H, 4.27; found C, 76.10, H, 4.35.

RESULTS AND DISCUSSION

The pathway to benzodibenzofuro-oxepinones begins with 2-hydroxy-dibenzofuran (sodium salt) (**2**). (Scheme 1).



5a **5b**

SCHEME 1

The acid **4** was prepared by the condensation of sodium salt of **2** with phthalide (**3**)[4] and the structure of the product was established through elemental analysis, IR and ^{1}H-NMR spectra. The IR spectrum of the compound **4** shows absorption bands at 1692 (carboxyl, C = O) and 3000-2560 cm^{-1} (carboxyl, OH).The ^{1}H-NMR spectrum exhibits the signal of the methylene = 5.56 ppm and also of the carboxyl group (δ = 13.1 ppm) .

The ring closure of the compound **4** was made according to Maior and Wolff[5] with polyphosphoric acid ester (prepared cf. ref. 6) in chloroform. Compounds **5a** and **5b** were obtained in almost equal percentage and were separated by column chromatography (silicagel).

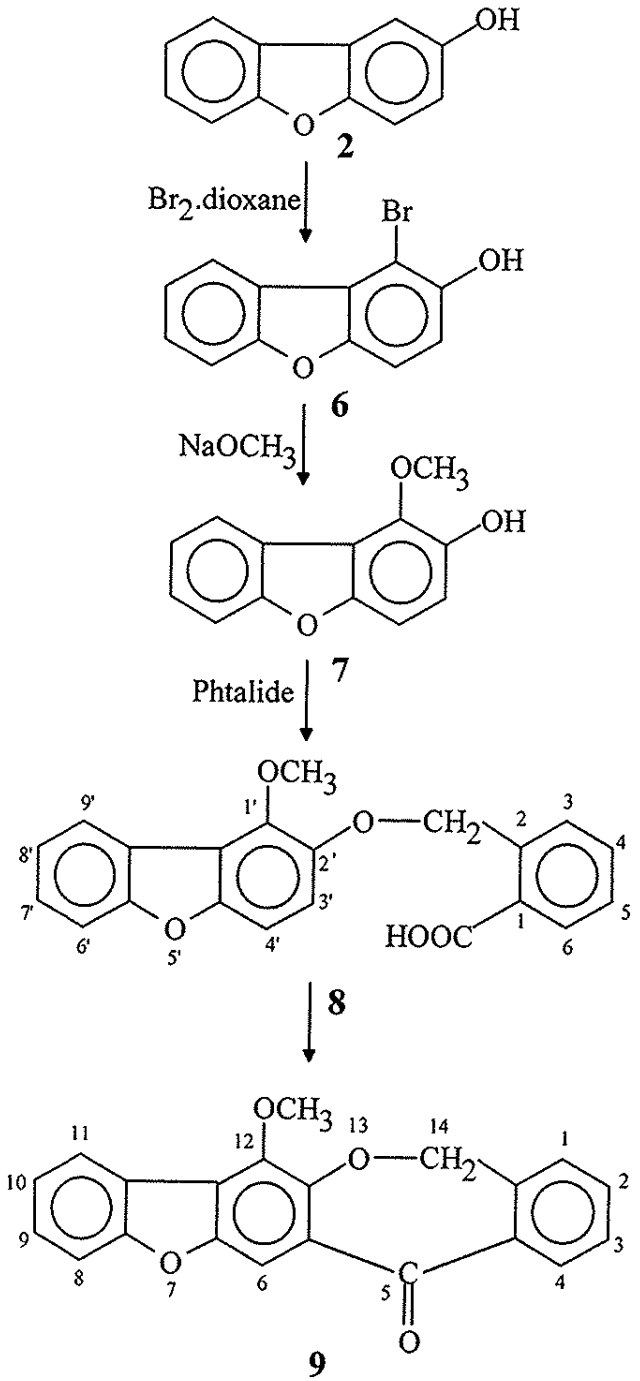
The unequivocable structure of **5a** and **5b** was established by means of ^{1}H-NMR spectrum. The inspection of the spectrum of the compound **5a** allows the assignment of the resonance singlets at d = 8.46 and 7.59 to the proton H-6, (deshielded by carbonyl group) and H-12, respectively. The doublets signals from the spectrum of the compound **5b** at d = 7.66 and 7.22 ppm were assigned to the protons H-11 and H-12, respectively. These chemical shift assignments are in agreement with the data of the parents compounds, dibenzofuran[7] and dibenzo[b,e]oxepin-11(6H)-one[8].

In order to have another benzodibenzofuro-oxepinone with linear structure, we have utilized the reactions from Scheme 2.

The compound **6**, prepared for the first time by Gilman et all[9] from **2** by reaction with bromine in acetic acid, was obtained by us more conveniently by using the Br_2-dioxane complex. The IR spectrum of **6** showed absorption bands for hydroxyl group at $\tilde{\upsilon}$ = 3540 cm^{-1} and at 750 , 810 cm^{-1} assigned to γ_{4CH} , γ_{2CH} ,respectively.

Treatment of **6** with sodium methoxide in the presence of $CuCl_2 \cdot 2H_2O$ in DMF leads to 1-methoxy-2-hydroxydibenzofuran (**7**). The IR spectrum of **7** exhibits two absorption bands located at 1226 and 1015 cm^{-1} assigned to the methoxyl group and mass spectrum shows the molecular ion at m/z = 214 and the [M^+- CH_3] peak at 199 (base peak). We have observed that due to the very strong magnetic field (400 MHz) as well as to the methoxy and hydroxyl groups, the ^{1}H-NMR spectrum of **7** exhibits 4 doublets corresponding to the protons H-3, H-4, H-6 and H-9, two triplet signals assignable to the protons H-7 and H-8 and one singlet due to the hydroxyl group (first order spectrum).

The phenoxide of **7** was then condensed whith phthalide and from mixture the acid **8** was separated. This was characterized by IR, ^{1}H-NMR and Mass spectra. The IR spectrum displays absorbtion at 1695 and 3100-2650 cm^{-1} (large band) assigned to the stretching vibrations of the carboxyl group. The band assigned to the hydroxyl group is absent. The ^{1}H-NMR spectrum of **8** shows signals corresponding to the carboxyl (δ = 13.1 ppm), aromatic protons (δ = 8.1 - 7.2 ppm), methylene (δ = 5.54 ppm) and methyl (δ = 4.07 ppm).


OH
O
2
Br2.dioxane
Br
OH
O
6
NaOCH3
OCH3
OH
O
7
Phtalide
OCH3
O—CH2
HOOC
8
OCH3
O—CH2
O
C
O
9

SCHEME 2

The ring closure of **8** has also been carried out with polyphosphoric acid ester in chloroform. Infrared spectrum of **9** shows no absorption band due to the carboxyl, but displays a band at 1650 cm^{-1} assigned to the carbonyl group. The ^{1}H-NMR spectrum exhibits multiplet corresponding to the aromatic protons and also two singlet signals assigned to the methylene (= 5.46 ppm) and methyl group (= 4.07 ppm). The mass spectrum shows the molecular ion at m/z = 330 (base peak).

Generally, linear polycyclic aromatic compounds absorb at longer wave-lengths than the corresponding angular one[10]. Except for the band at longest wave-length (λ =324 nm) the other absorption bands from the UV spectrum of the oxepinone **5b** (angular) are slightly hypsochromic shifted in comparison with the correspoding bands of the oxepinone **5a** and **9** (linear). The UV spectra of 5a and **9** are similar, but the expected bathochromic shift induced by the presence of the methoxyl group cannot be observed.

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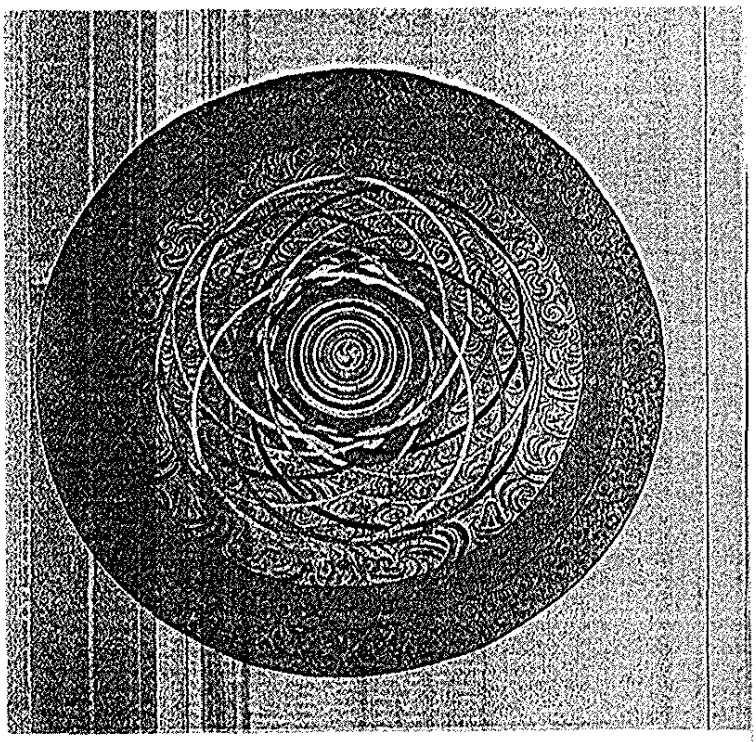

MANDALA CÓSMICA DO TEMPLO PARO DZONG, BUTÃO OCCIDENTAL

COSMIC MANDALA OF PARO DZONG TEMPLE, WESTERN BHUTAN

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