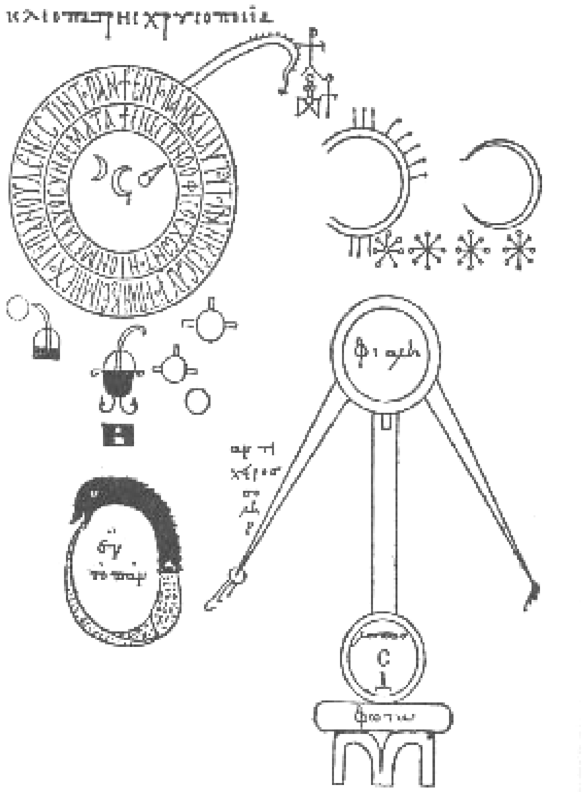
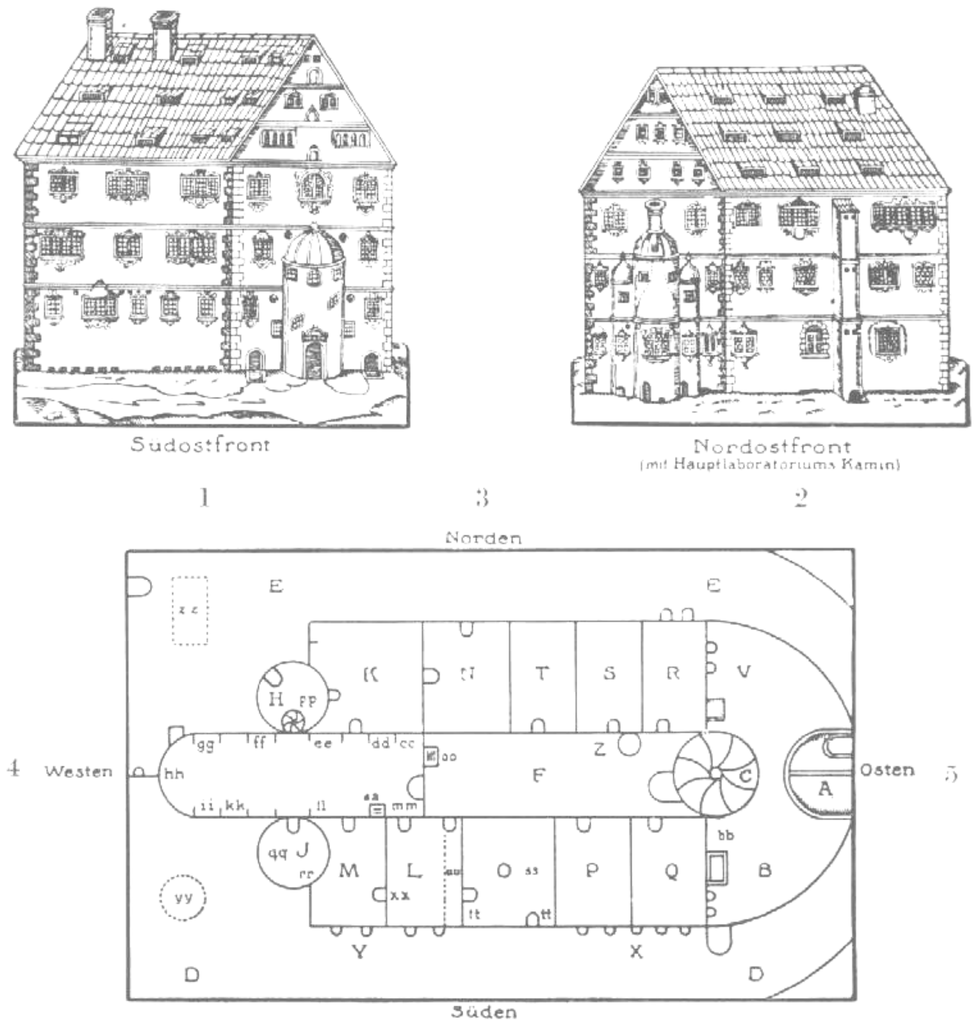
PLENARY LECTURES





Idealised design for a chemical institute by Andreas Libavius,
from Andreas Libavius, *Alchymia,* Frankfurt, 1606.

1. South-east front, 2. North-east front (with the chimney-stack of the main laboratory).

A.	East entrance with small door.
B.	Main room with galleries.
C.	Spiral staircase.
D.	Garden.
E.	Drive.
F.	Vestibule of the laboratory.
G.	Chemical laboratory.
H.	Private laboratory with spiral stairs to the study.
J.	Small analytical laboratory.
K.	Chemical pharmacy.
L.	Preparation room.
M.	Bedroom for the laboratory assistant.
N.	Store room.
O.	Crystallisation room (coagulatotorium)
P.	Wood store.
Q.	South store room.
R.	Fruit store.
S.	Bathroom.
T.	Aphodeuterium (closet).
V.	Vegetable cellar.
X.	Wine cellar.
Y.	Laboratory cellar.
Z.	Water supply
aa	Doors to the laboratory cellar.
bb	Entrance to the wine cellar.
cc	Steam-bath.
dd	Ash-bath furnace.
ee	Water-bath.
ff	Distillation apparatus for upward distillation.
gg	Sublimation apparatus.
pp	Philosophers' furnace in the private laboratory.
qq	Assay furnaces
hh	Ordinary fireplace.
ii	Reverberatory furnace.
kk	Distillation apparatus.
ll	Distillation apparatus with spiral condenser.
mm	Dung bath.
nn	Bellows, which can also be brought into the laboratory.
oo	Coal store.
rr	Analytical balances in cases.
ss	Tubs and vats.
tt	Distillation "per lacinias" (table with vessels).
xx	Equipment and benches for preparations.
zz	Water tanks.

← Previuos page: **Image from Greek manuscript,** The gold making equipment of Cleopatra.

New Directions in the Chemical Design of Materials

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Chemical design of materials is gaining increasing importance in the last few years. This is not only due to the novelty of the methods of synthesis, but also because of the unusual structures and the associated properties of the materials, prepared by chemical methods. A large proportion of the materials obtained by this means are metastable. In this presentation, an attempt will be made to present some of the highlights of chemical design, taking case studies from various areas of interest. These will include open-framework structures and inorganic-organic hybrids. New classes of inorganic nanotubes and other types of nanostructured materials will be discussed.

PL 2

From Genomes to Cellular Mechanisms and Drug Design

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By browsing genomes and analysing the results through bioinformatic tools, it is possible to guess cellular pathways till now unexplored. This is the case of copper homeostasis and assembling of cytochrome c oxidase. The proteins are then produced and structurally characterized. This can be considered structural genomics. From the structure, the transfer pathways are discussed in details. Whenever possible comparison is performed among different living beings.

Extracellular human zinc proteinases are also looked for in the genoma and their validation as pharmacological targets is looked for in the literature. Some of them are produced and inhibitors as candidate drugs are investigated.

Mechanisms of the Formation of Uniform Fine Particles and Their Applications

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Since many properties of particles depend on their size and shape, it is hardly necessary to stress the importance of the uniformity of finely dispersed matter in science, technology, and medicine. While in the recent past the major focus has been on the colloidal matter, presently the interest has expanded to simple and composite nanosized materials. Although some may believe the latter TO represent a new field of science, it will be shown that such systems have been recognized already 150 years ago.

The most versatile technique for the production of many, if not most, well defined dispersions is by precipitation from solutions. It has always been understood that in this process nanosize particles must be intermediates, which were assumed to grow further by attachment of constituent solute species to yield the final larger products. However, it has now been amply documented that in a large number of cases the essential stage in colloid formation is the aggregation of the nanosized precursors. The major task is then to elucidate how this mechanism may produce *monodispersed* colloids. A model defining conditions that result in the size selection will be described, and its application to several experimental test systems will be demonstrated. While the model is capable of explaining the formation of uniform spheres, the next challenge is to resolve the question of different particle shapes, also generated by the aggregation of smaller primary subunits.

The understanding of the underlying processes can be used to design methods for the preparation of dispersions to desired specifications for various applications. Examples will be offered on the effects of uniform nanometer and micrometer size particles, alone and in mixtures, in diverse areas, including the formation of uniform drugs of different morphologies, of pigments, of fluorescent dispersions for medical diagnostics, and of well defined slurries for chemical mechanical polishing of wafers.

Modern Trends in Chemical Education

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What are the present trends in chemical education? In this talk, I examine the trends in education in introductory chemistry and in physical chemistry. I begin by looking at the issues that currently confront us: the decline in mathematical activity, prejudice against the subject (or at least its industrial manifestations), and a variety of aspects of the subject that deter students from it. However, it is possible to regard each of these problems as a challenge, and I explore ways in which we can rebuild our subject. There will be nothing radical, just looking for opportunities to convert pessimism into optimism.

There are many trends afoot. One modern thrust of education is the inclusion of biological examples, and I will explore how that can be done without losing sight of the core ideas of the subject, and warn against certain dangers. Multimedia opens up great opportunities, of course. But there are also dangers in relying to heavily on multimedia rather than the intellectual rigor of books, and I will examine this issue. For introductory chemistry, I identify what I regard as the handful of core ideas that any scientifically aware student should know. In physical chemistry I shall identify the structure of the subject and the core knowledge we expect. In this connection, I attempt to identify the handful of core equations and ask how the mathematical component of chemistry can be rendered palatable.

Beyond the Molecular Frontier — Chemistry Challenges for the Future

Ronald Breslow

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Chemistry has been called the Creative and Useful Science, since the new substances and new reactions and processes invented by chemists have added enormously to human welfare. However, the Challenges and Opportunities for the future are at least as exciting as are chemistry's past achievements. In a recent survey of chemistry and chemical engineering — for which Ronald Breslow and Matthew Tirrell were the co-leaders — these challenges and opportunities have been outlined across the broad range of areas, including in particular those that are the focus of ICOSECS-4. In this talk some of the future advances in chemistry will be described that will let us continue to bring benefits to humanity while increasing our fundamental understanding of the natural world and of its created extensions.

Electrospray Wings for Molecular Elephants

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Small effusive leaks into vacuum systems, as in Knudsen cells and classical molecular beam machines, made many conributions to science in the twentieth century. They have continued to serve both both science and technology in the early years of the twenty first. Beginning in the 1950s, big convective leaks have turned out to be even more powerful and versatile tools. The supersonic free jets produced by these big leaks have greatly extended molecular beam methods, become a corner-stone of cluster science and technology, and rewritten the book on molecular spectroscopy. Thoss jets are now adding new dimensions to the techniques of mass mass spectrometry by making possible the production of intact ions from the large, complex and fragile species that play such vital roles in living systems. The path from the first crude experiments of Dunoyer into the groves of atomic and molecular physics followed along the trail blazed by Otto Stern and his disciples. That trail was then extended into the fertile fields of chemistry, by the likes of Herschbach, Lee, Polanyi, Smalley, Zare and Zewail, five of whom received Nobel Prizes for their contributions. More recently that trail entererd the lush gardens of biology where mass spectrometry is providing bumper crops of information and understanding. This travelogue will describe some of the landmarks along what has been a fascinating journey.

Organic Functionalization of Carbon Nanotubes: Synthesis and Applications

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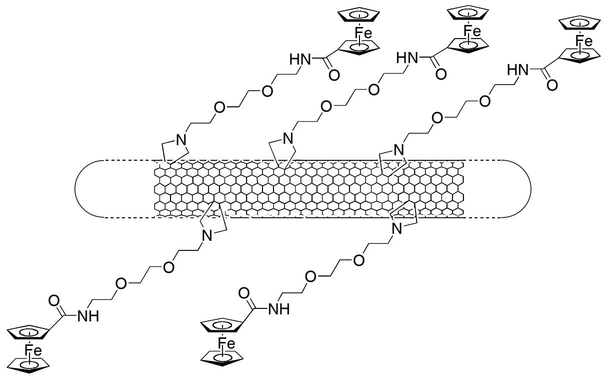
In the bottom-up approach to molecular nanotechnology, fabrication and manipulation takes advantage of innovative materials, which possess novel properties and intriguing potential. Carbon Nanotubes (CNT), effectively long, thin cylinders of graphite, seem to be the ultimate and ideal building blocks in nanotechnology. Extraordinary properties have been attributed to CNT, so that a wide variety of different technological applications are being investigated, ranging from wiring in integrated circuits and nanoscale components to composite materials with improved functional characteristics. Even fantastic scenarios such as space elevators and bullet-proof vests made of CNT have been raised, showing the strong promise that these materials hold, due to their unique mechanical strength.

The progress in the investigation of carbon nanotubes is growing on a nearly daily basis. Advances in production processes have resulted in obtaining CNT with high structural perfection: relatively large amounts can now be produced of either single-walled carbon nanotubes (SWNT), consisting of a single graphite sheet seamlessly wrapped into a cylindrical tube with diameters ranging 0.4 nm - 3 nm, or multi-walled carbon nanotubes (MWNTs) which comprise an array of concentric cylinders with diameter of 1.4 nm – 100 nm. However, high molecular weights and strong intertube forces keep CNT together in bundles, making their manipulation, characterization and analytical investigation very difficult. The organic functionalization offers the great advantage of producing soluble and easy-to-handle CNT. As a consequence, compatibility of CNT with other materials, such as polymers, is expected to improve. In addition, once properly functionalized, CNT become soluble in many solvents, so that their solution properties can be studied. In many cases, the new derivatives retain the main properties of the original carbon form, and many functionalized carbon nanotubes may find useful applications in the field of materials science and technology. Also in medicinal chemistry carbon nanotubes are set to play an important role. Their use as drug delivery scaffolds and substrates for vaccines has been already demonstrated.



Within this contribution, we will review our most recent achievements in the field of synthesis of functionalized carbon nanotubes and their applications in materials science and medicinal chemistry.

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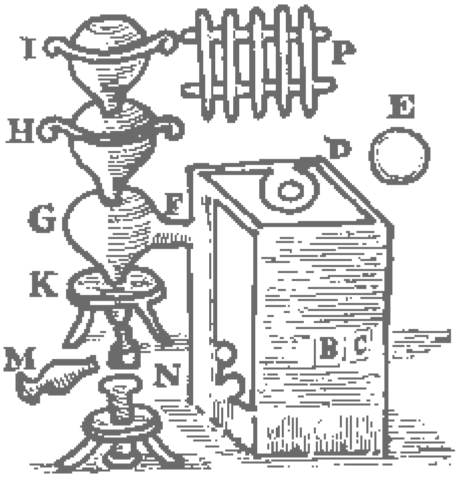
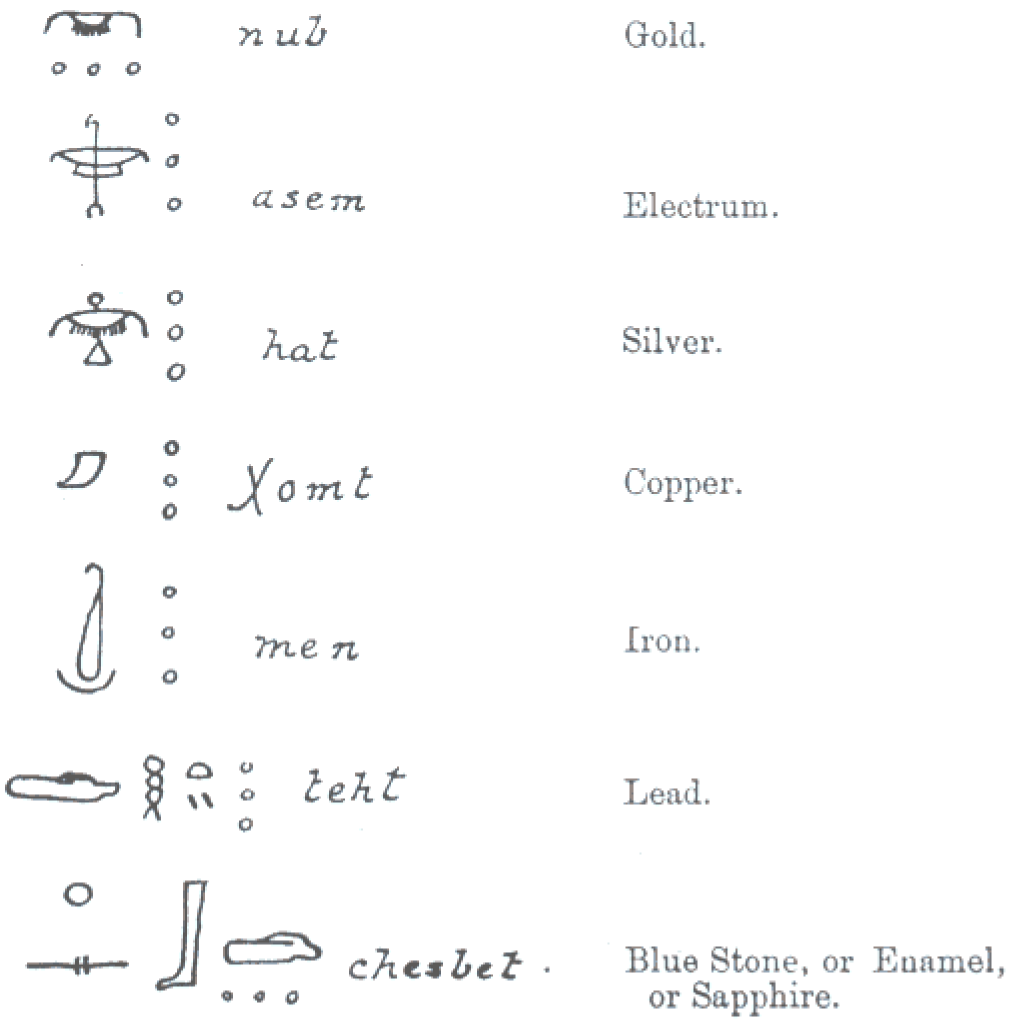
GENERAL TOPICS

INVITED LECTURES





nub	Gold.
asem	Electrum.
hat	Silver.
Xomt	Copper.
men	Iron.
teht	Lead.
chesbet.	Blue Stone, or Enamel, or Sapphire.

Egyptian symbols for metals,
from Lepsius, *Metals in Egyptian Inscriptions*, 1860.

← Previous page: **Distilling apparatus** from John French's *The art of distillation*, London 1651.

Platinum Monolayer Fuel Cell Electrocatalysis

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Fuel cells are soon expected to become one of the major sources of clean energy, and considerable environmental benefits and preservation of fossil fuels could follow should this direct energy-conversion power source become a reality. A high noble metal loading in anode and cathode and a low activity of cathode electrocatalysts are drawbacks of existing technology. Placing atoms of a catalytically active metal by two new deposition methods on nanoparticles of suitable metal substrate facilitates its full utilization and an ultimate reduction of its loading. Most such atoms have low coordination that can maximize their activity. This is the basis of our *monolayer catalyst* concept that can reduce catalysts' noble metal loading and increase their activity as described below.

The Pt submonolayer on Ru nanoparticles electrocatalyst ($PtRu_{20}$) has highly dispersed Pt on top of Ru which provides a high H_2 oxidation activity and better CO tolerance than some commercial PtRu alloy catalysts with a several times higher Pt content. EXAFS data show that the electrocatalyst has a Pt-Ru coordination of 1:4 and distance of 2.69 Å. The Pt-Pt coordination could not be clearly established. This suggests that Pt forms small two-dimensional islands on Ru. The XANES data show the *d*-band vacancy of 0.345 vacancy/atom for $PtRu_{20}$ at 0.40V, which is substantially larger than the 0.30 value for Pt foil. This can cause a decreased back bonding of CO to Pt, thus increasing the CO tolerance. The data indicate that the electronic effect in the Pt-Ru electrocatalysts is larger than previously assumed. A 1000 hour fuel cell test showed an excellent long term performance stability of $PtRu_{20}$ indicating that it is a real electrocatalyst. An important property of this system is a strong Pt segregation which keeps Pt atoms at Ru surface.

The kinetics of O_2 reduction was determined by rotating disk-ring method on a Pt monolayers on Au(111), Pd(111), Rh(111), Ir(111) and Ru(0001) surfaces and on Au and Pd nanoparticles. STM and XANES were used to characterize Pt monolayers on single crystal and nanoparticles, respectively. The plot of the Pt monolayer catalytic activity vs. the d-band partial filling of the substrate has a maximum for the Pt/Pd(111) couple. It indicates that the metals with low *d*-band filling may not be good support for Pt. The kinetics of O_2 reduction is significantly enhanced at Pt monolayers on Pd(111) and Pd nanoparticle surfaces in comparison with the reaction on Pt(111) and Pt nanoparticles, respectively. The observed increase in the catalytic activity appears to be caused partly by decreased formation of PtOH. A delayed oxidation of a Pt monolayer on Pd is indicated by voltammetry and XANES data. For Pt monolayer on carbon-supported Pd nanoparticles, the Pt mass-specific activity is 5-8 times higher than that of the Pt nanoparticle electrocatalyst. The total noble metal (Pt + Pd) mass-specific activity shows a twofold increase.

The results obtained with a Pt monolayer on metal nanoparticle electrocatalysts indicate that this approach can be used to synthesize real electrocatalysts and that it opens up a new research direction for designing electrocatalysts with improved properties and reduced noble metal loadings.

Preparation of Chiral Ferrocene Derivatives for Asymmetric Synthesis

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In recent years, the design of new ferrocene derivatives has been of considerable interest, as a result of their utility in organic synthesis and materials science. Chiral non-racemic ferrocenes, especially 1,2-disubstituted with planar chirality, have achieved an important place in asymmetric metal-catalyzed synthesis since it was shown that they can introduce, when used as chiral ligands, high degrees of enantioselectivity in several chemical transformations, e.g. addition of R_2Zn compounds to aldehydes, hydrogenation, cross-coupling and aldol reactions. For the preparation of planar chiral ferrocene derivatives, chiral N,N-dialkylferrocenylalkylamines play a crucial role because of the possibility of highly diastereoselective *ortho*-lithiation with simple organolithium reagents (e.g. n-BuLi). The further transformation of the lithiated chiral ferrocenes leads to useful functionalized 1,2-disubstituted derivatives (aminoalcohols, aminophosphanes etc.). Chiral non-racemic α-hydroxyalkyl ferrocenes are attracting increased interest as key compounds, which can be converted into N,N-dialkylferrocenylalkylamines with complete retention of the configuration. There are several routes for the synthesis of α-hydroxyalkyl ferrocenes, e.g. enantioselective addition of dialkylzinc compounds to ferrocene carbaldehyde, enantioselective reduction of acylferrocenes, or addition of monolithium ferrocene to chiral carbonyl compounds.

We will describe synthetic strategies and use of readily available sources of chirality (chiral pool), which allowed efficient preparation of chiral α-hydroxyalkyl ferrocenes and 1,2-disubstituted ferrocenes with planar chirality. We will demonstrate the application of NMR spectroscopic methods for determination of the configuration of newly formed stereogenic centers, which is confirmed by X-ray crystallography. We will, finally, demonstrate the application of the new chiral ferrocenes as ligands for enantioselective addition of dialkylzinc compounds to aldehydes.

Combinatorial Chemistry: Past, Present, and Future

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Combinatorial chemistry is undoubtedly the most significant new chemical subdiscipline that has emerged within the last twenty years. Although a precise definition is debatable, combinatorial chemistry embraces a suite of technologies for the parallel synthesis of new compounds, and screening the resulting *library* for a desired property. The biotech and pharmaceutical industry routinely employ combinatorial chemistry for the purposes of lead discovery and optimisation in drug discovery. While this remains the most important application of combinatorial methodology, the principles are translatable to other fields such as catalysis and materials science.

In this presentation, I will discuss some highlights of combinatorial chemistry from both my and other research groups, and finish by suggesting some of the key areas that will be of importance in the future.

Prediction of Regioselectivity in Reactions of Arene-Tricarbonyl-Chromium Complexes

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The large enhancement of reactivity of complexed aromatic ring in the arene-tricarbonyl-chromium complexes is now well documented for both nucleophilic and electrophilic reactions[1].

Taking also into account the high stereoselectivity in reactions of complexes due to the screening of one face of the ring by the bulky $Cr(CO)_3$ moiety, arene metal complexes become attractive synthons for asymmetric syntheses.

However the use of complexes as synthetic tool is confronted with a problem arising from striking differences in regioselectivity of the reactions of substituted complexes as compared to their free arenes counterparts. For example, while *tert*-butylbenzene gives in electrophilic reactions the expected *para*-substitution, the corresponding complex exhibits a quasi total *meta*- directed reactions; in solvolysis of ring-substituted complexes of benzyl chlorides or acetates a *para*-Bu^t or *meta*-NMe_2 substituent is associated with an unexpected decrease in reactivity; some physical characteristics (e.g. ^{1}H- and ^{13}C-NMR shifts for various ring positions) show also important changes by complexation.

Although specific explanations have been proposed for each individual case, a general rationalization of regioselectivity in reactions of arene-tricarbonyl-chromium complexes is still lacking.

Present report is concerned with our efforts to develop a consistent general view on the above problem.

Starting from a substantial volume of NMR data (^{1}H-, ^{13}C-, ^{19}F-, ^{31}P- and ^{15}N-) collected for various substituted complexes and their corresponding free arenes, a semi empirical quantitative relation between the nature of substituent and NMR chemical shifts has been established. Thus became possible to calculate values of chemical shifts for complexes, directly from F (field), R (resonance) and Es (steric) parameters of Swain-Lapton type equation. From these data is possible to calculate populations of the two fundamental conformations of trigonal $Cr(CO)_3$ moiety with respect to substituent from complexed aromatic ring: the eclipsed (with one CO ligand superposed over substituent) and the staggered (CO ligands projected over 2,4,6-positions). Finally, from relative ratios of these conformational populations also associated with conformational dependence of the transition state stability, reliable mechanistic pathes have been devised for various reactions. Calculated regioselectivities on the above mentioned grounds are in very good agreement with experimental data even for - apparently – most striking cases.

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Cytotoxic Metabolites from Red Algae

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Most of the efforts towards the discovery of new bioactive metabolites have focused for many years on the easily accessible higher plants. The last decades though, obscure and rare organisms, because of the scientific advancement in the areas of chromatography, spectroscopy and marine technology, became accessible.

Prior to the development of reliable diving equipment the collection of marine organisms was limited to those easily obtainable at the sublittoral zone. Subsequently, depths from approximately 3 m to 40 m became routinely attainable and the marine environment has been increasingly explored as a source of novel bioactive agents.

If the novelty and complexity of compounds discovered from marine sources were the only criteria, then the success of research in this area would be assured for there are many marine natural products that have no counterpart in the terrestrial world.

Marine organisms have exhibited an impressive spectrum of biological properties and several representatives have been investigated in depth as potential new biotechnological agents with activities including: Cytotoxicity; Antibiotic activity; Anti-inflammatory and antispasmodic activity; AntiViral activity; Cardiotonic and Cardiovascular activity; Antioxidant activity; Enzyme inhibition activity and many others.

Halogenated secondary metabolites, while rare in land plants, are common in marine organisms due to the abundance of chloride and bromide ions in seawater. Of all marine seaweeds, red macro algae possess the highest abundance of unique biosynthetic pathways for organohalogen production.

Many halogenated low molecular weight metabolites have exhibited an impressive array of biological properties ranging from anti-microbial to insecticidal activities. Studies on the natural products chemistry of the red seaweeds were recently stimulated by the discovery of the acyclic monoterpene halomon, which exhibits selective antitumor activity in the National Cancer Institute's human tumor and disease oriented in vitro screen.

Among others, red algae of the genus *Laurencia* have been proven to be an endless source of novel secondary metabolites. The fascinating chemical variation of *Laurencia obtusa* collected from a number of sites in the Greek Seas has exhibited significant levels of cytotoxicity.

Insulin-Mimetic Vanadium in Diabetes Mellitus
II. (Bio)chemical Revelations in a Biological Milieu

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Vanadium has been shown to exist in a variety of abiotic as well as biological systems, with prominent activities associated with metalloenzymes, the activation or inhibition of key cellular components, anticarcinogenicity, and others[1]. Outstanding among the plethora of actions exhibited by vanadium is its insulin mimetic ability, as a result of which, keen research interest has been directed toward the aqueous chemistry linked to hyperglycemia in diabetes mellitus II[2]. In an effort to delineate the role(s) of vanadium in insulin mimesis and its future potential therapeutic application in diabetes, we embarked on research targeting the aqueous chemistry of that metal ion V(III,IV,V) in the presence of low molecular mass physiological ligands. Synthetic approaches involving the metal ion with tricarboxylic acids (e.g. citric acid) concentrated on a) the pH-dependence of binary vanadium-carboxylate system reactivity and b) the arising reactivity toward H_2O_2, a physiological agent. Dinuclear complexes like $(NH_4)_2[V_2O_4(C_6H_6O_7)_2] \cdot 2H_2O$ [3], and $(NH_4)_4[V_2O_4(C_6H_5O_7)_2] \cdot 4H_2O$,[4] and vanadium-peroxo-citrate complexes like $(NH_4)_2[V_2O_2(O_2)_2(C_6H_6O_7)_2] \cdot 2H_2O$, and $(NH_4)_6[V_2O_2(O_2)_2(C_6H_4O_7)_2] \cdot 4.5H_2O$, emerged with variable structural attributes and reactivity patterns.[5] Key intermediates were identified, unraveling fundamental mechanistic pathways linking simple starting materials with fully assembled vanadium-citrate complexes. Acid-base pH-dependent chemistry of the arising, complexes, as well as intramolecular redox reactivity associated with the majority of the synthesized and characterized species, supported the rise of diverse vanadium species and the importance of mechanistic insight into a) the stepwise formation of aqueous species in the structural speciation of the vanadium-(peroxo)-citrate system(s) and b) the potential biological significance in insulin mimesis. In vitro biological experiments employing synthetic vanadium complexes shed considerable light onto their potential insulin mimetic activity, complementing the synthetic efforts and the structural speciation of the requisite aqueous binary and ternary systems.

Acknowledgement
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Negative Ion Mass Spectrometry for Environmental Applications

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Introduction

Starting with the development of the electron capture detector for GC, negative ions have been used for Environmental Analytical Applications. In the past decade, Negative Ion Mass Spectrometry, or more closely described as Electron Capture Negative Ion Mass Spectrometry (ECNIMS), has been established as a specific, very sensitive analytical method for the trace level Environmental Applications /1/. It is not conceived as a concurrent method to well established positive ion MS, or to novel, very specific and sensitive Proton Transfer Reaction MS (PTR MS) /2/, but rather as a complementary, or alternative method with some advantages and disadvantages compared to the methods just mentioned above.

Experimental Methods and Results

Our knowledge of Low Energy Electron Molecule Interaction, LEEMI /3,4/, has increased considerably over last half of the century. As a consequence of that fact, the applications of the recognized advantages of ECNIMS has evolved to different methods (Free Electron Beam, Retarded Electron Beam, Bound Electron Transfer Ionization), that are already in the applications /5/ and partly in commercial production /6/. They are going to be reviewed and discussed in respect of their advantages and disadvantages, as well as the ongoing efforts to improve them. Future development of these methods are expected in the form of new ion source geometries that are going to enhance even more the sensitivity, but preserve reproducibility and linearity of response. Also, the preliminary results achieved with the ECNIMS developed at the Faculty of Physics in Belgrade are going to be presented and discussed.

Acknowledgment

Research on this subject has been partly supported through the project ON1249 financed by The Ministry of Science, Technology and Development of Republic Serbia, as well as through the two CEP 2002/2003 of WUS Austria, Office Belgrade.

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DNA-Based Circuits and Automata

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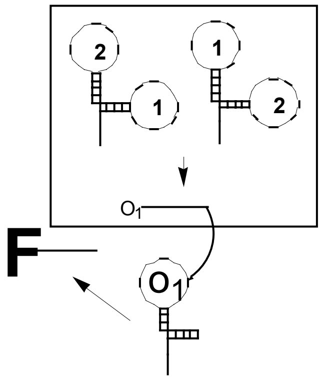
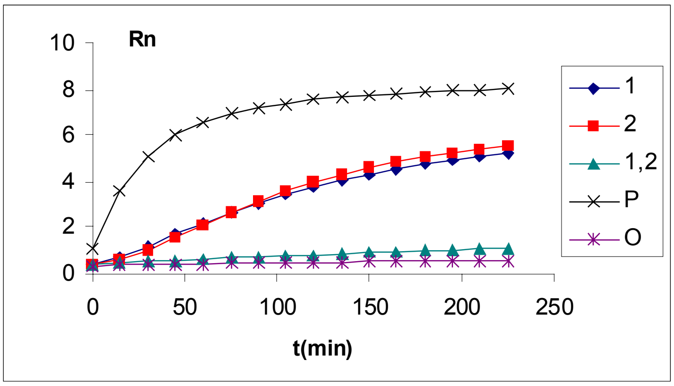
The molecular scale logic gates based on nucleic acid catalysts can be arranged into circuits to perform complex Boolean calculations in solution. I will describe the construction of several molecular circuits, including full adder and tic-tac-toe playing automaton, using single input YESi$_1$ and NOTi$_1$, double input i$_1$ANDi$_2$ and i$_1$ANDNOTi$_2$, and triple input i$_1$ANDi$_2$ANDNOTi$_3$, i$_1$ANDi$_2$ANDi$_3$ and i$_1$ANDNOTi$_2$ANDNOTi$_3$ gates with phosphodiesterase and ligase activity.





Accreditation or Certification for Laboratories?

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This presentation is focused on clarifying the significance of Accreditation and Certification with regard to Laboratories, thus illustrating the usefulness of both terms describing these discrete procedures when implemented for laboratories. Emphasis is given on illustrating both similarities and differences. Reference is made to some recent publications. The discussion reflects the existing experience and gives answers to questions that came out of it.

Accreditation and Certification present both

- similarities related to the audit-based nature of the procedures and
- differences with regard to the tasks and the resulting procedure

Both activities are related to quality assurance policies considered of high importance tools in today's society with regard to the free movement of goods. Main differences refer to the objective and content, the documentation, assessors' competence, the procedure of assessment, the use of the logo, how wide the scope is, etc. Differences in the procedure refer mainly to the validation of test methods, the expression of uncertainty, the calibration of equipment, the competence of personnel. It should be clear that the need to ensure technical competence, accreditation of the laboratory within a detailed description of its scope is the appropriate means to demonstrate it.

Following the established definitions

- Accreditation refers to competence to carry out specific tasks
- Certification refers to assurance of conformity to specified requirements

Laboratories need to demonstrate their technical competence and reliability; to this end they need also to have policies on how to estimate the uncertainty of their measurements. It seems that there is some confusion regarding the significance and the role of Accreditation and Certification within conformity assessment procedures. There is still much more work to be carried out towards a better understanding and homogenisation of the approaches with regard to laboratory work and the use of test and calibration results.

Limiting Factors and Process Strategies for Production of Polyhydroxy Alcohols by Yeasts

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The actual consumer concern for better human health through optimized nutrition increased the interest for polyhydroxy alcohols as sugar substitutes. These sweeteners, in particular xylitol and sorbitol, find a broad application in preparing reduced-energy confectionery products suitable for diabetics and individuals with tendency to obesity. Xylitol can also be used in pharmaceuticals and oral hygiene products designed to reduce and prevent dental carries.

This study focused on the biotechnological production of polyols, as an alternative and environmentally friendly process. Among the yeasts investigated, *Candida boidinii* NRRL Y-17213 was selected as a good polyol producer. Xylose metabolism in this yeast yielded a variety of carbon-containing products which included cell mass, xylitol, glycerol, ribitol, ethanol and carbon dioxide. For xylitol production it was important that the amount of xylose converted to xylitol and the amount of xylitol which was available for further metabolism were well balanced. Critical parameters affecting partitioning of carbon and hence the biosynthesis of polyols were oxygen availability and the initial xylose concentration. *X*ylose was required for the induction of xylose reductase and xylitol dehydrogenase, the key enzymes for xylitol production. In the absence of xylose, xylitol formation did not occur. Initial xylose concentration of 150 g/L induced xylitol formation favoring xylitol at the expense of ethanol production. Above this concentration, a substrate inhibition occurred.

The yeast did not grow under fully anaerobic condition, but anaerobic formations of xylitol, ethanol, ribitol and glycerol were observed as well as xylose assimilation of 11%. Oxygen limited conditions were established in a batch fermentor using 130 g/L xylose and varying the oxygen transfer coefficient, k_La, from 26 to 78 h^{-1}. Biomass yield increased with k_La whereas ethanol, ribitol and glycerol yields exhibited an opposite dependence on the oxygenation level. The most favorable oxygen transfer coefficient for xylitol formation was $k_La=47\ h^{-1}$ when its yield and productivity reached 0.45 g/g and 0.26 g/Lh, respectively.

To determine the specific oxygen uptake rate at which *C. boidinii* starts producing xylitol, the yeast was cultivated in a chemostat under oxygen-limited conditions. Xylitol secretion was triggered at 0.91 mmol O_2/gh. Upon a shift to lower specific oxygen uptake rates, xylitol production rates and yield increased more rapidly than those of ethanol.

In a fed-batch process, xylose concentration was maintained at a suitable level throughout the entire course of fermentation, that is, a level sufficient to induce xylitol formation but not to inhibit yeast growth. The highest xylitol yield was 75% of the theoretical yield, compared to 53% in the batch culture. The volumetric productivity was almost twice as high as the highest obtained under batch conditions.

In mixtures of glucose and xylose, *C. boidinii* first consumed the glucose and only after the glucose was depleted it assimilated the xylose. Faster growth occurred but the xylitol production was lower compared with the process using xylose alone.

Grown only on glucose, the yeast produced not only ethanol, but also sorbitol and glycerol whereas xylitol formation was not observed. By changing some of the environmental conditions, the cell metabolism was shifted towards sorbitol formation. The highest concentration of sorbitol was 31 g/L, or in terms of productivity and yield, 0.32 g/Lh and 0.16 g/g, respectively. The production of glycerol was stimulated by increased osmotic pressure and by addition of a sulfite-steering agent. *C. boidinii* attained a yield of 0.13 g/g, corresponding to 26% of the theoretical glycerol yield.

ORAL PRESENTATIONS

Alchemists at work
from Jean-Jacques Manget's, *Bibliotheca Chemica Curiosa*, Geneva 1702.

← Previous page: **Late mediaeval Indian apparatus**

Synchrotron Infrared Microspectroscopy

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The broadband synchrotron beam of the VUV-IR ring at National Synchrotron Light Source at Brookhaven National Laboratory has brightness that is ca. 1000 times that of thermal (globar) infrared sources in mid-infrared region (800-4000 cm^{-1}). This is because the synchrotron light can be efficiently focused on a small spot since its beam is highly collimated, unlike the globar source that emits radiation in all directions. Furthermore, a synchrotron delivers light in a wide range of infrared wavelengths, making Fourier Transform Infrared spectroscopy possible. Therefore with synchrotron infrared light, samples that are smaller and/or more dilute in concentration can be studied, while the three orders of magnitude increase in brightness translates to data collection times that are ~30 times faster compared to the globar source.

Synchrotron radiation-based FTIR micro-spectroscopy is an advanced analytical technique capable of exploring chemistry within microstructures of samples with a high signal-to-noise ratio at high spatial resolutions without destruction of intrinstic structures of the sample. The technique is able to provide information relating to the quantity, composition, structure and distribution of chemical constituents and functional groups in a sample. An infrared "map" is obtained by sequentially collecting spectrum at a small area (e.g. 10 x 10 μm) and moving the sample to expose adjacent area by a predefined step size (e.g. 10 μm), until the whole area of the specimen has been sampled. By choosing a characteristic infrared band in the obtained spectrum representing the chemical constituent (for instance, amide I at ~1650 cm^{-1} for protein, C=O ester band at ~1740 cm^{-1} for lipid, etc.), spatial distribution of these and other constituents like cellulose and carbohydrate are obtained.

At the Center, infrared imaging of cells, tissues and plant specimens are routinely carried out. Analysis of the chemical constituents of a seed section is used to follow the rate and degradation behavior in ruminants (1). Also, by choosing the benzene ring deformation band at 745 cm^{-1}, the ultimate fate and transport of aromatic compounds within plants can be ascertained (2). Kainic acid-induced epilepsy in rats can be followed by the peak intensity ratio of amide I to lipid bands as an indicator of the disease, demonstrating that the necrosis is the predominant path of cell death as the neurons loose integrity and spread biomaterials towards the surrounding tissue (3). These, as well as a selection of other microscopic measurements will be presented.

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Study of Formic Acid Oxidation at Supported Pt and Pt/Ru Catalysts in Acid Solution

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Fig. 1. illustrates the basic voltammograms of a supported Pt (a) and Pt_2Ru_3 (b) catalysts and the potemtiodynamic curves for formic acid oxidation (c and d) in sulfuric acid solution on Pt and Pt_2Ru_3 catalysts, respectively. The potential region of the hydrogen adsorption/desorption, accompanied with bisulfate desorption/adsorption ($0.05V < E < 0.3V$) is separated from the reversible/irreversible oxide formation by the double layer region at Pt catalysts (a). Consistent with voltammetric feature for bulk Pt/Ru electrode the hydrogen adsoption/desorption region ($0.05V< E < 0.3V$) is first followed by reversible adsorption of OH species and than by irreversible oxide formation at supported Pt_2Ru_3 catalyst (b).

The voltammograms for formic acid oxidation on supported Pt catalyst (c) is very similar to those obtained on bulk polycrystalline Pt electrode. The onset of methanol oxidation coincides with the beginning of reversible oxygen-containing species (OH_{ad}) formation ($E \sim 0.5$ V). The formic acid oxidation is initiated at low potentials ($E \sim 0.25$ V) indicating that OH_{ad} species are not needed for the beginning of the reaction. Pt_2Ru_3 catalyst (d) is approximately as active as pure Pt (c) in formic acid oxidation in the potential region up to $E = 0.5$ V, which is important evidence that OH_{ad} species existing on Ru sites, do not play an important role in formic acid oxidation in this potential region.

The slope of Tafel lines ~120 mV dek^{-1} and the reaction orders of 0.5 for formic acid and 0 for H^+ ion suggest that formic acid follows up to $E \sim 0.5$ V the direct route given by Eqn (1):

$$HCOOH \rightarrow CO_2 + 2H^+ + 2e^- \qquad (1)$$

assuming that breaking H-C bond leading to formate is r.d.s.

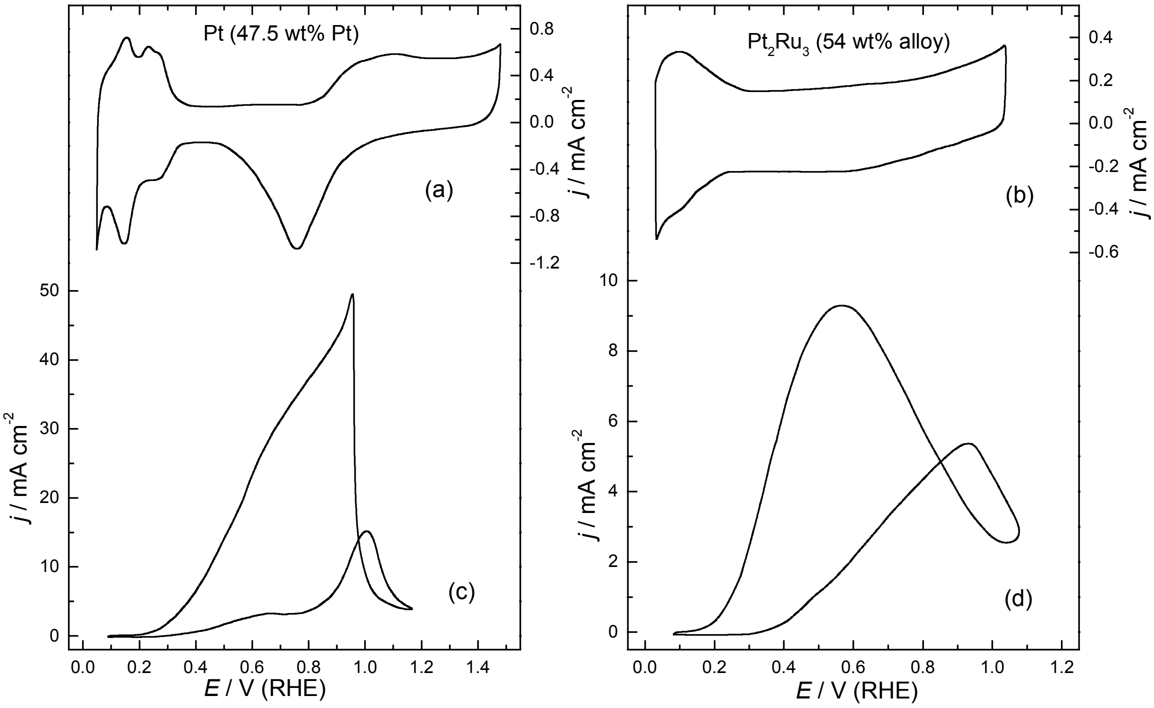

Fig. 1. Basic voltammograms for Pt (a) and Pt_2Ru_3 (b) high surface area catalysts in 0.5 M H_2SO_4. Cyclic voltammograms for the oxidation of 0.5 M formic acid on Pt (c) and Pt_2Ru_3 (d). $T = 295$ K; sweep rate: 50 mV s^{-1}.

New Group VI (Se, Te) Hypervalent Complexes

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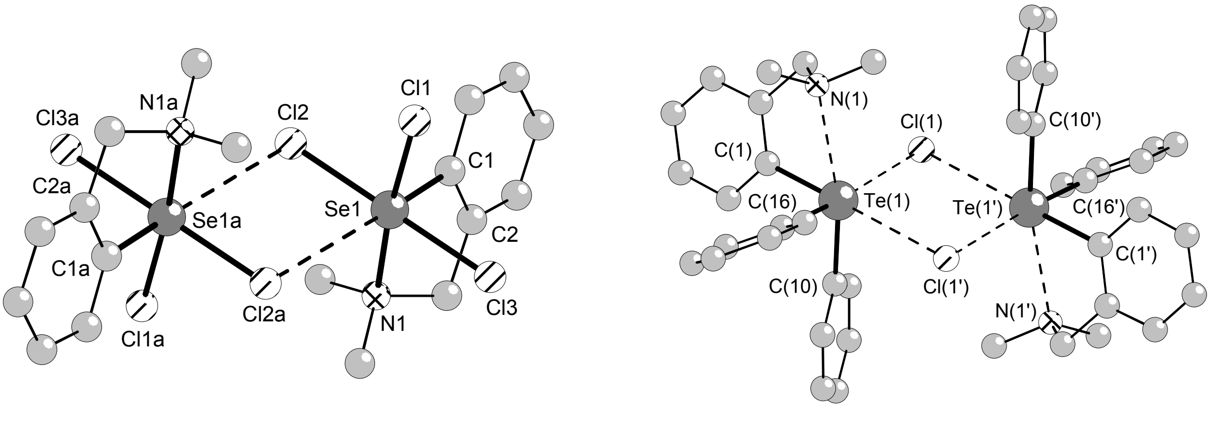
The pendant arm [2-(Me_2NCH_2)C_6H_4] group was observed to stabilise unusual organometallic species, *i.e.* organoantimony[1] or –bismuth[2] derivatives in low oxidation state through intramolecular N→M coordination. Our interests are currently foccused on the synthesis and structural characterization of tellurium(II) and selenium(II) complexes with such pendant arms. Compounds of the type R_2E_2, REX (R = [2-(Me_2NCH_2)C_6H_4], E = Se, Te, X = halogene), as well as complexes of the type REL (L = diorganodichalcogenophophinato, tetraorganodichalcogenoimido-diphosphinato or diorganodithiocarbamato groups) were obtained and structurally characterized.
Selenium(IV) and tellurium(IV) derivatives (*i.e.* [2-(Me_2NCH_2)C_6H_4]$SeCl_3$, [2-(Me_2NCH_2)C_6H_4]$TePh_2Cl$ and [2-(Me_2NCH_2)C_6H_4]$_2$TePhCl·H_2O) are also discussed.
The solution behaviour of these compounds was investigated by multinuclear NMR (^1H, ^{13}C and ^{31}P where appropriate) spectroscopy. The crystal and molecular structure, established by single crystal X-ray diffraction, revealed a strong intramolecular N→E coordination in all cases. While the E(II) derivatives have monomeric structures, dimeric associations were found in all E(IV) compounds.



(a) (b)

Dimeric association in [2-(Me_2NCH_2)C_6H_4]$SeCl_3$ (a) and [2-(Me_2NCH_2)C_6H_4]$TePh_2Cl$ (b)

Synthesis and Characterization of New Complexes with Biological Activity

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The biological activity and role of chemical compounds that can be used as drugs has been focused on their interaction with proteins, enzymes and/or DNA. We have initiated several studies on the interaction of various drugs such as the anticancer drug bleomycin and piroxicam, hydroxamic acids and oximes with various metal ions (VO^{2+}, Cu^{2+}, Ni^{2+}, Co^{2+}, UO_2^{2+}) as well as the interaction of the resulting complexes and the Ru(II)-dicarboxylato complexes with DNA in an attempt to examine the binding mode, possible synergetic effects and their bioactivity.

DNA is the major target of several anticancer agents and their metal ion complexes. Their biological action depends mainly on the DNA-binding mode. Some antibiotics form noncovalent complexes by intercalation and some others form covalent linkages especially with the purine bases. There is also a class of DNA-acting drugs like bleomycins, which cause cleavages at the deoxyribose in the backbone. The interaction on BLM, the major component of the anticancer drug Bleoxane® used for the treatment of Hodgkin's lymphoma, carcinomas of the skin, head, neck and testicular cancers, with Ru(II), Pt(II), Pd(II), Ga(II) and In(III) as well as the interaction of the BLM-complex with DNA has been reported [1-4].

Numerous studies have been devoted on the role of metal ions and their interaction with DNA, with the aim either to understand the modes of action or to design complexes with improved chemotherapeutic and tumor imaging efficacy. In the research field of transition metal anticancer compounds, ruthenium has exhibited a prominent role since its complexes offer potential for the design of new anticancer drugs. Although several antitumor ruthenium compounds have also been shown to bind to DNA and inhibit DNA replication *in vitro*, the pharmacological target for ruthenium compounds and the mechanism underlying its biological effects are not unambiguously known. A small series of complexes whose parent compounds are *cis*- and *trans*-$[RuCl_2(DMSO)_4]$ constitute one class of dimethylsulfoxide Ru(II) complexes exhibiting antitumor activitiy comparable to cisplatin, one of the most effective anticancer drugs used in the clinic. Although a number of Ru-dmso derivatives with various ligands have been synthesized, there are very few examples with carboxylate ligands and none with dicarboxylates.

Piroxicam is an extensively used non-steroidal anti-inflammatory drug (NSAID) and an anti-arthritic drug with a long biological half-life, which acts by inhibiting enzymes involved in the biosynthesis of prostaglandins. The structure of few complexes of piroxicam with Pt(II), Sn(IV), Cu(II) and Cd(II) has been reported. In the literature, the synthesis and the bioactivity of VO^{2+} complexes, a bioelement with interesting biological properties, with NSAIDs has been recently reported.

Hydroxamic acids are involved in numerous biological processes including metal ion transport, e.g. iron(III), and inhibition of metalloproteins such as peroxidases, matrix metalloproteinases (MMPs) and ureases. They can also act as hypotensive, anti-cancer, anti-tuberculous and anti-fungal agents. Oximes are also attractive ligands used in metallurgy, as biochemical models, as analytical reagents and as semi-conducting materials for the detection and determination of metal ions.

The cytotoxic effect of the complexes in two human leukemia cell lines is under investigation.

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Synthesis of Optically Pure Di-and Poly-diarylmethanes *via* Chromium Complexed Benzylic Cations

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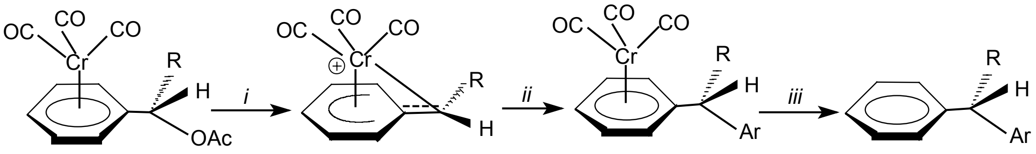
In a previous paper we have reported a facile acid catalyzed condensation of tricarbonyl-chromium complexed benzyl acetates with reactive arenes[1]. We have also showed that the above reaction takes place with total retention of configuration at the benzylic sp^3 –carbon atom from the complex **1** presumable due to the lack of rotation around C-C bond in the relatively stable intermediate, **2**¸ (*Scheme 1*).

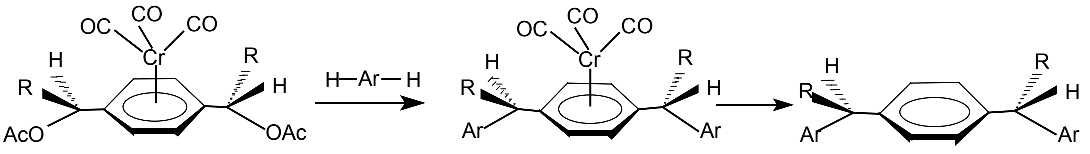


1 **2** **3a** 40% yield **3b** 85% yield **4**

i: BF_3 OEt_2 / $CHCl_3$; *ii*: Ar-H; *iii*: HONO
Ar-H ≡ a: anisole; b: 1,3-dimethoxybenzene

Scheme 1

In view of preparative use of the new reaction for the synthesis of optically pure diarylmethanes a critical point is represented by the large differences in the yields obtained with various arenes. Consequently, the present work is concerned with quantitative determination of reactivities of the suitable arenes. The reactions were performed with complexes **1** (leading to diarylmethanes) but in order to extend the method to the synthesis of poly-diarylmethanes, **7**, the difunctional complexes **5** were also used (*Scheme 2*).



5 **6** **a**: anisole; **b**: 1,3-dimethoxybenzene; **c**: mesitylene; **d**: durene; **e**: diphenylether **7**

Scheme 2

Relative rates of various arenes (see *Schemes 1* and *2*) were determined following the procedure of combinatorial chemistry in reactions of complexes **2** and **5** with an excess of a mixture of arenes **6a-6e** followed by a GS – MS analysis of products after decomplexation.

For the reaction of **1** (R ≡ H) following relative rates were determined: **a** (posn 2)/**a** (posn 4) / **b** (posn 2) **/ b** (posn 4) / c / d / e= 1.1 / 6.7 / 76 / 198 / 10 / 1 / 0 (unreactive). For the reaction of **1** (R ≡ CH_3) the following order of reactivities was established: **6>>a>>c~e** (**c** did not react). For the reaction of **5** (R ≡ H) with a mixture of arenes, **b** and **c**, 7 products (out of 9 possible) were detected in ratios that are in agreement with individual relative rates. The complex **5** (R ≡ Et) gave reliable results only with most reactive arenes **b**>>**a** (posn 4) products showing total retention of configuration.

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Synthesis and Use of Oligonucleotide-Peptide Conjugates

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Immobilization of oligonucleotides onto solid supports is a well established and routine procedure in modern molecular biological research. On the other hand, while the availability of similar technology for proteins would be highly desirable, there is no convenient standard immobilization procedure for this class of biological macromolecules. One possible generic solution to this problem is the use of protein-oligonucleotide conjugates, and several examples of this approach have been reported. However, this has not yet become a routine procedure, one of the reasons for this being the fact that such conjugates have so far not been easily accessible. In a recent contribution, we described the use of PNA-protein conjugates, the rational behind this being that peptide-synthetic techniques could be used to prepare a conjugate between a C-terminal peptide and PNA, which could then be coupled to an expressed protein by native chemical ligation.

We have now developed a convenient procedure for coupling DNA oligonucleotides to proteins. The approach involves incorporation of a 5´-cysteine derivative of thymidine at the 5´-end of an oligonucleotide followed by native chemical ligation with the protein of interest. We have demonstrated the feasibility of this method using the small GTPase Ras, which was expressed as a fusion protein with an intein domain and cleaved from this as a C-terminal thioester to allow the subsequent ligation step.

The procedure developed is potentially applicable to all proteins which can be expressed in such a manner and allows the targeted immobilization of proteins in a specific, sequence-dependent manner to an oligonucleotide-modified surface.

Cross-Linking of Thymine and Tryptophan Radical: Possible Model for Cross-Linking of DNA and Peptides by Ionizing Radiation

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A fast electron (or hydrogen atom) transfer from the DNA to the oxidized tryptophan describes effects of DNA binding on the formation and reactions of tryptophan radicals in peptides, restoring an intact tryptophan residue at the expense of DNA integrity as experimentally observed in γ-irradiated aqueous solutions of tryptophan peptides in presence of DNA. Alternatively, an addition of tryptophan radical to DNA, followed by a consecutive rearrangement, may lead to DNA-peptide cross-linking. We propose the reaction mechanisms for thymine-tryptophan (or indolyl) radical cross-linking as a model for DNA-peptide cross-linking. The initial steps of the proposed reaction mechanisms are: (1) an addition of the indolyl radical to the C_5-hydroxylated thymyl radical, (2) an addition of the indolyl radical to the C_6-hydroxylated thymyl radical, (3) an addition of the indolyl radical to C_5 of thymine, and (4) an addition of the indolyl radical to C_6 of thymine. The B3LYP/6-311G(2df,p) density functional theory method is employed to investigate the feasibility of the complex cross-linking mechanisms. A possible complete reaction mechanism consists of a radical combination (1) forming the initial cross-linked product, a hydrogen transfer within the initial cross-linked product by use of a bridging water molecule, and a dehydration step. Hydrogen-bonding interactions are suggested to play a key role in the hydrogen-transfer reaction step within the initial cross-linked product by way of a bridging water molecule. The overall thermodynamics of the free energy profiles at 0 K and 298 K are similar, but with differences of magnitude for the hydrogen transfer reaction. Due to the entropy contribution to the free energy, temperature may be a key factor influencing the overall mechanism. Although bulk solvation has significant effects on the energetics of the cross-linking mechanisms, the preferred mechanism is suggested to be the same both in the gas phase and in solution. The topological analysis of the electron density at the bond critical point between the indolyl radical (donor) and the thymine (acceptor) moieties in the final cross-linked product shows a more covalent (charge locally concentrated) character of the bonded interaction.

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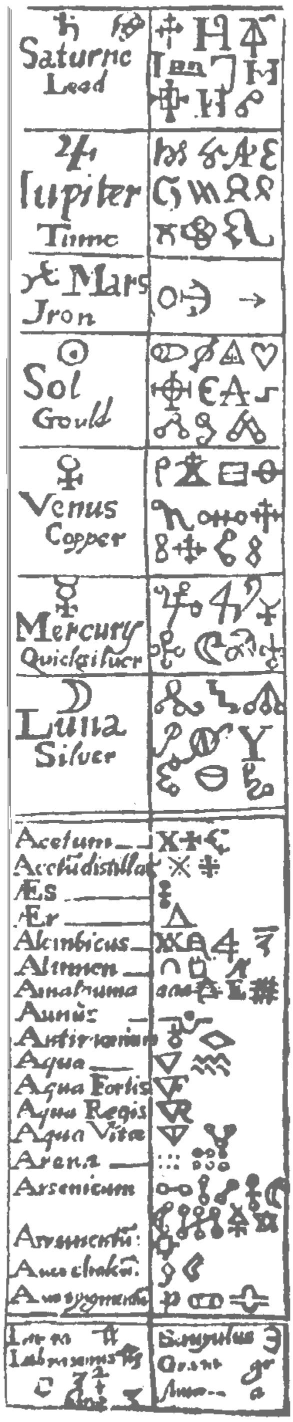

Alchemical symbols used in the 17th century,
from Basil Valentine's *Last Will and Testament*, London, 1671.

← Previous page: **Distilling apparatus**, from John French's *The Art of Distillation*, London 1651.

Usage of the Derivative Spectrophotometric Method for Determination of the Vitamin C Content in Juices

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Fruits, vegetables and most of fruit juices are the main source of vitamin C (ascorbic acid) in human diet. Because of his importance it is usually added in controlled concentrations in many products. Determination of its content in natural and industrial products is very important for the quality control.

In paper [1] the results of for vitamin C determination in some natural products using a second - order derivative spectrophotometric method are demonstrate. The method is based on the measurement of the peak - baseine amplitude in the second order of a spectrum of vitamin C extract from samples at 267.5 nm (${}^2D_{267.5}$). The extraction solution was 1.0 M HCl acid. The following regression equation of a series of standard ascorbic acid solution, within the concentration range from $2\cdot10^{-5}$ - $1\cdot10^{-4}$ M (3.5 - 17.6 μg cm^{-3}), was used for determination vitamin C:

$$ {}^2D_{267.5} = 2.42\cdot10^4 c + 0.025 \qquad R = 0.9992 \qquad (1) $$

The proposed method is simple, fast and reproductive and because of that suitable for routine analysis in determination vitamin C in many natural products.

The aim of this paper has been the investigation of the posibillities of application of second - order derivative spectrophotometric method for determination of vitamin C in complex sistems, without need for previous isolation of supstance or any other prior treatments. The commercial fruit juices, intensively coloured (juices from red fruits) with declared content of vitamin C from different producers, were analysed. On the basis of obtained results it is demonstrated that this method can be used for determination of vitamin C content in these juices, that was not a case with titrimetric method, which has been usually used. Results obtained by using derivative spectrophotometric method show good accordance with declaired values in fresh juices.

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Composition Characterisation of Some Food Fluids by ^{1}H-NMR

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One of the most important problems in the food chemistry regards composition determinations. Although the sensitivity of the NMR method is smaller than for other chemical analyses, it has some important advantages. Thus, this method can provide direct information and a total biochemical profile for the sample. Classical chemical analyses need predetermined analytical conditions, longer time and can give information regarding only specific compounds.[1]

Our current work in composition characterization for food fluids follows two important directions. One direction concerns food fats and the other one Romanian wine studies.

Fats studies consist in characterization of some edible oils. Another aspect of this study concerns computation for determination of characteristically oils indices based on information obtain from ^{1}H-NMR.[2]

In wine studies, the ^{1}H-NMR spectra have been recorded for a group of Romanian wine samples. We made spectral attributions for organic components which can be found in Romanian wines. The compounds identified and quantitatively measured include: carboxylic acids, amino acids, monosaccharide and glycerin.[3]

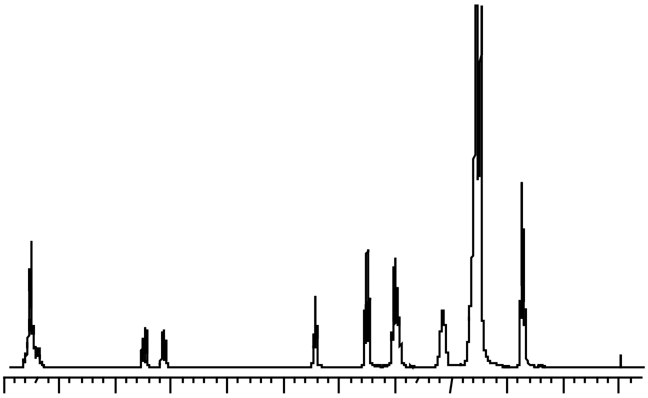

Figure 1. Part of ^{1}H-NMR spectrum for a sun flower oil

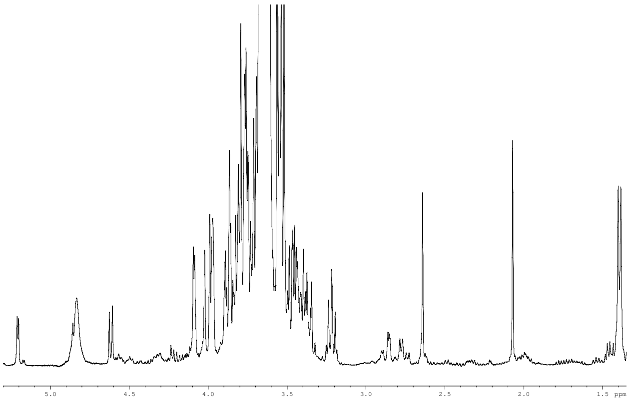

Figure 2. Part of ^{1}H-NMR spectrum for a white Romanian wine

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Determination of Bile Acid Critical Micellar Concentration

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CMC

The critical micellar concentration (CMC) of sodium cholate and sodium 3,7,12-tri-keto-cholate (dehydrocholic acid) was determined by dissolving of color extracted from a waterproof black pen. Measuring of the amount of dissolved color was performed by UV/Vis spectroscopy. This amount is directly related to the concentration of micelles in the solution.

Bile acids

Bile acids are amphiphilic molecules. In aqueous solutions and with a critical micellar concentration, free molecules aggregate, forming micelles. This value (**CMC**) is highly important since it defines the minimal concentration of bile acid required for dissolving a hydrophobic molecule, such as molecules in membranes and some drugs.

Results

The ink extracted with ethanol was deposited in Eppendorf tubes and dried down to form a film. Sodium cholate and sodium 3,7,12-tri-keto-cholate were dissolved in Tris buffer (0.1 M NaCl, pH 8) in following concentrations : 0.025 ; 0.05 , 0,1 ; 0.25 ; 0.5 ; 0.1 ; 2.0 ;2.5 ;4.0 ;5.0 ;6.0 ;7.0 ;8.0 ;9.0 and 10.0 mmol/dm^3. Twenty four hours after depositing the prepared solutions in Eppendorf tubes, the intensity of dissolved color was determined at 383 nm, using UV/Vis spectrophotometer. The CMC values were determined using graph (A/c) plotted from the obtained results. The values were 7±0.5 mmol/dm^3 for sodium cholate and 1.5 ± 0.5 mmol/dm^3 for sodium 3,7,12-tri-keto-cholate.

Conclusion

These experiments showed that 3,7,12-tri-keto-cholate reached CMC at lower amounts than sodium cholate. This results from a stronger hydrogen-bond in 3,7,12-tri-keto-cholatee, formed between keto- and hidroxyl group as well as between 2 hydroxyl groups, compared with sodium cholate, where only two OH groups are involved in forming H-bond.

The Chemical View of Material Culture in the Period From Ancient History to the Classical Period of the Wider Archeological Location of Novi Sad

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The earliest discoveries in the field of the Natural culture in archeological location of south Bachka has come down from later phase of Paleolith. That Material cultur required rich assortiment of stones for production of Artefactas, ovens and sacral objects. The Paleogeographic search had been carried out parallel and found settlements in Virm in this region.The chemical composition of stones and archeological find make possibile to state Hypothesis that Ancient cultures in the Posavina, Potisje, Pomoravlje and Povardarlje, had been linked in each other. The links expressed in motives, customs and also in materials in use. About links testify the Material culture of population in south Bachka from Neolithic and Eneolithic. They had used ceramics, pigments, jewearly, stones on sacral and on other objects. The chemical contnts of searched objects are mainly the origin from the late Bronze age. In that age mixed the material culture of warrior nomads and later the old Slavs. In this paper will be analyses objects from private collection from the view of chemistry. Our investigation scopes with the theritory arround Novi Sad, Petrovaradin and Sremski Karlovci, in connection with disappeared culture from Ancient history to Classical period.

Determination of Selenium by a Kinetic Spectroscopic Method from Bio-Materials

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A kinetic spectrophotometric method from determining of selenium at ng/ml concentration levels was established.
The method is based on the catalytic effect of Se (IV) on the reduction reaction of brillant cresyl blue by sulphide. The reaction was monitored spectrophotometrically by measuring the decrease in absorbance at 613 nm in a fixed time. Under the optimum conditions (ionic strength, temperature, reagent concentrations, time of recation), in the concentration range of 0,45 – 0,75 ppm of selenium, a quite linear regression equation (r = 0,9942), was obtained.
The method is simple, sensitive, selective and precise.
The method has been applied to determination of Se (IV) from biomaterials.

Solution Equilibria Between the Aluminium(III) Ion and Fleroxacin

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The equilibria established in solutions of aluminium(III) ion and quinolone antibacterial fleroxacin were studied by glass electrode potentiometric titrations and UV spectrophotometry. In the concentration range of Al^{3+} between 0.5 and 2.0 mmol/L and fleroksacin 0.8 - 2.5 mmol/L, in the pH interval 2 - 10 the formation of the following complexes was confirmed: $[AlL]^{2+}$ ($\log\beta_{1,1,0} = 11.24 \pm 0.06$); $[AlHL]^{3+}$ ($\log\beta_{1,1,1} = 13.68 \pm 0.14$) and $[Al(OH)_2L]$ ($\log\beta_{1,1,-2} = -1.16 \pm 0.07$). Overall formation constants are given in parenthesis.
The distribution cure of these complexes is shown in Figure 1.

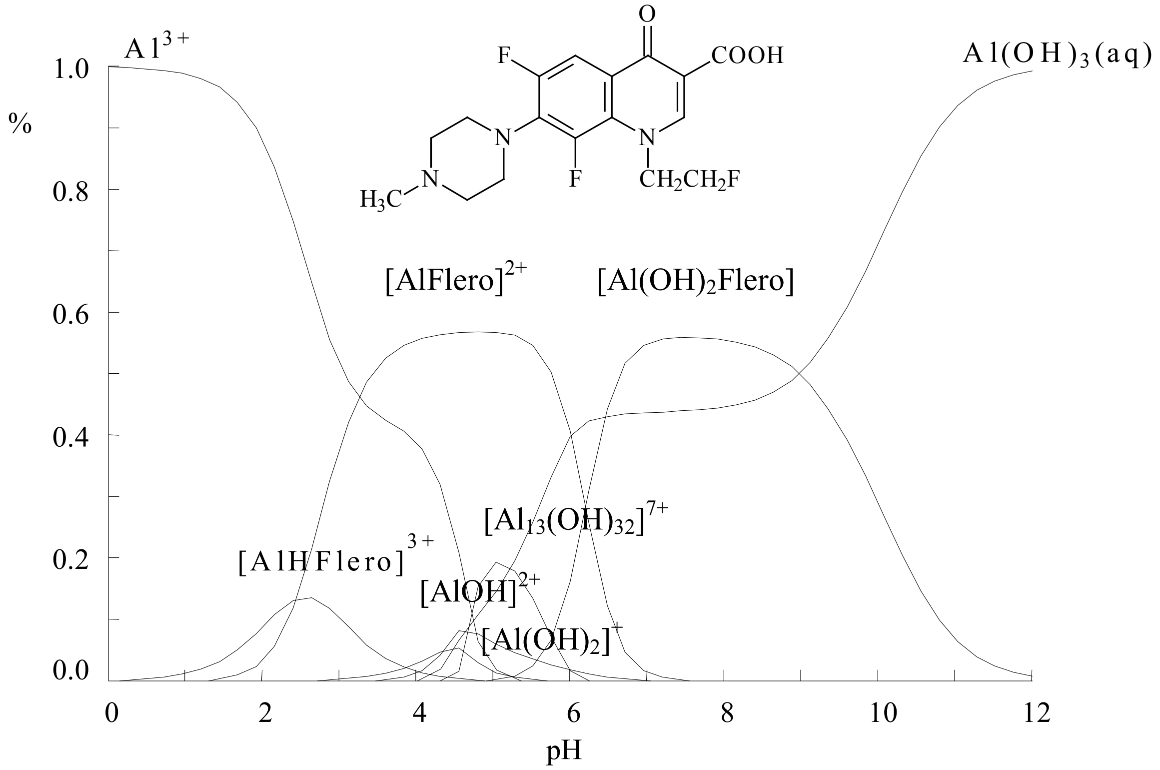

Figure 1. Species distribution of the complexes formed in the Al(III)-fleroxacin system in 0.1mol/L LiCl ionic medium (C_{Al} = 1.4 mmol/L, $C_{Fleroxacin}$ = 0.8 mmol/L)

As can be seen from Figure 1. the neutral complex $[Al(OH)_2L]$ is the dominating one in a physiological range of pH. Thus in case of concomitant ingestion of Al-based antacids and fleroxacin solubilization of Al may occur and its transport across enterocyte membrane. In this way, it may contribute to Al toxicity.

Spectophotometric Method for the Determination of Famotidine in Pharmaceutical Preparations with Cu(II)

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Introduction

Famotidine is effective as an H_2-receptor antagonist in the treatment of gastric and duodenal ulcers. Numerous analytical methods developed for the quantitative assay of this drug in biological fluids and in pharmaceutical dosage forms include spectrophotometric, HPLC, polarographic and potentiometric.

Results and Discussion

The reaction between famotidine and cooper(II) sulphate was investigated over the pH range 2.23 - 5.00 in Britton-Robinson buffer solutions. Absorption curves show that the absorbance of the complex increases from pH 2.23 - 4.30, and then solution become turbid.

The complex gave a absorption peak at 318.5 nm. Since neither Cu(II) nor famotidine absorb at 325 nm all measurements were performed at this wavelength using water as a blank. A Britton-Robinson buffer pH 2.62 was used to provide the working pH. For the complex formation a linear relationship between absorbance and concentration was established over the range 3×10^{-5}-3.6×10^{-4} M, at $\mu = 0{,}2$ and pH = 2.62. The molar absorptivity at 325 nm for the complex was 1.067×10^{3}L $mol^{-1}cm^{-1}$. The regression equation was $y = 0.00258 + 0.3193x$ and the correlation coefficient (r) was 0.9995 (n = 7) indicating excellent linearity. The releability of the method was cheeked at three different pure substance concentrations of famotidine in water. The relative standard deviation varies over the range 2.66 - 1.27 % (N=7) for famotidine concentrations of 0.0304 - 0.0912 mg/ml.

The applicability of the method for the assay of simple dosage forms was examined by analysing Famotidin (20 mg/tabl.) and Lecidil^{R} (20 mg/tabl) tablets. The average percent recovery was found to be from 1.95 - 2.13 %. From the above data it is sugested that the proposed method can be applied with precision for the determination of famotidine in pure substances and in pharmaceutical preparations. The proposed method is rapid, simple and requires the use of inexpencive reagents and apparatus available in every laboratory.

Acknowledgements

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Kinetic Determination of Citric Acid

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A colorless, crystalline organic compound belonging to the family of carboxylic acids, present in practically all plants and in many animal tissues and fluids. It is one of a series of compounds involved in the physiological oxidation of fats, proteins, and carbohydrates to carbon dioxide and water. It is used in confections and soft drinks (as a flavoring agent), in metal-cleaning compositions, and in improving the stability of foods and other organic substances (by suppressing the deleterious action of dissolved metal salts). [1]

A new kinetic spectrophotometric method for determination of citric acid is described in this paper. The oxidation of C_6H_5COONa with hydrogen peroxide in acetic acid solution gives a color product. The reaction is catalyzed by traces of complex Fe (II) with ascorbic acid. [2]. We have observed that small amounts of citric acid strongly inhibited catalysis of this reaction by complex Fe (II) with ascorbic acid. The rate of the reaction decreases proportional with increasing concentration of citric acid. This fact was used as the basis of kinetic method for determination micro amounts of citric acid. A differential variant of the tangent method was used for processing the kinetic data. [3] Optimal reaction condition s for the determination of citric acid in solution were found:

$c_{Fe(II)\text{-}AA} = 2 \cdot 10^{-4}\ mol\ dm^{-3}$, $c_{C_6H_5COONa} = 3.33 \cdot 10^{-4}\ mol\ dm^{-3}$
$c_{CH_3COOH} = 3.33 \cdot 10^{-2}\ mol\ dm^{-3}$ $c_{H_2O_2} = 0{,}0666\ mol\ dm^{-3}$

Under the optimal reaction conditions the citric acid concentration was varied from 1.4 μg cm^{-3} - 14 μg cm^{-3}. The calibration line can be used for determination in the interval mentioned. The relative error ranges from 2.9-6.5% for citric acid concentrations ranging from 1.4 μg cm^{-3} -14 μg cm^{-3}.

The effects of certain ions upon the reaction rate were determined for the assessment of the selectivity of the method.

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Determination of the Protein Content in Wheat Germ Fractions Obtained Using Different Solvents

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A content of Wheat Germs soluble proteins (albumins and globulins, glutamines and prolamines) has been investigated in this paper. The content determination was done in fractions obtained by extraction using different solvents, based on Osborn's method for proteins separation. The method is based on complexation of protein with dye (Commasie Brilliant Blue G-250), resulting in the absorption maximum shift from 465 to 595 nm (the measuring wavelength). The contents of particular proteins have been determined: globulin (63.03 %), glutenine (32.64 %), prolamine (4.33 %), relative to the total content of the soluble proteins, by using different solvents to separate Wheat Germs proteins.

Salting-Out Thin-Layer Chromatography of Several ACE Inhibitors and Their Active Metabolites

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In continuation to our previous chromatographic studies of biological active substances[1,2] in this work we studied retention behavior of certain angiotensin – converting enzyme (ACE) inhibitors and their active metabolites (degradation pruducts) under conditions of salting-out thin-layer chromatography (SOTLC). ACE inhibitors are used in treatment of hypertension and congestive heart failure. Following the administration they are transformed to their active di-acid forms.

The substances investigated were: 1. *Enalapril*, (S)-1-[N-[1-(ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline; 2. *Enalaprilat*, (S)-1-[N-(1-carboxy-3-phenylpropyl)-L-alanyl]-L-proline dihydrate; 3. *Quinapril*, [3S-[2[R*(R*)],3R*]]-2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2, 3,4-tetrahydro-3-isoquinolinecarboxylic acid; 4. *Quinaprilat*, [3S-[2[R*(R*)],3R*]]-2-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid; 5. *Fosinopril*, [1 [S*(R*)],2α,4β]-4-cyclohexyl-1-[[[2-methyl-1-(1-oxopropoxy)propoxy](4-phenylbutyl)phosphinyl]acetyl]-L-proline; 6. *Fosinoprilat*, trans-4-cyclohexyl-1-[[hydroxy(4-phenylbutyl)phosphinyl]acetyl]-L-proline; 7. *Lisinopril*, (S)-1-[N^2-(1-carboxy-3-phenylpropyl)-L-lysyl]-L-proline dihydrate; 8. *Cilazapril*, [1S-[1α,9α(R*)]]-9-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]octahydro-10-oxo-6H-pyridazino[1,2-a][1,2]diazepine-1-carboxylic acid monohydrate; 9. *Cilazaprilat*, [1S-[1α,9α(R*)]]-9-[(1-carboxy-3-phenylpropyl)amino]octahydro-10-oxo-6H-pyridazino[1,2-a][1,2]diazepine-1-carboxylic acid.

The chromatography of investigated compounds was performed on TLC cellulose (Art. 5552, Merck, Germany). The plates were spotted with 2μL aliquots of freshly prepared ethanol solutions of enalapril, quinapril, fosinopril, and cilazapril, aqeous solution of lisinopril and methanol solutions of enalaprilat, quinaprilat, fosinoprilat and cilazaprilat (about 2mg/mL). Ammonium sulphate (Merck, Germany) of analytical grade purity was used for preparation of aqueous solutions with concentrations varying from 0.5 M to 2.5 M. After development, by ascending chromatography, the detection was performed by exposing the plates to iodine vapour. All investigations were performed at room temperature (22 ± 2° C).

In these study it was found that increase of salt concentration in solvent led to increase of R_M values of all investigated substances. The linear dependence between salt concentration and R_M values was established.

On the basis of the results obtained, possible separation mechanisms of investigated substances were proposed.

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The Retention Mechanism of Polar Solutes in Reversed-Phase Liquid Chromatographic Colums

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A clarification of the retention mechanism of small polar solutes in octadecyl reversed-phase chromatographic columns is attempted based on the properties of the special function S, $S = ln\,k_{C_{18}} - ln\,k_{C_2}$, where $k_{C_{18}}$ and k_{C_2} are the retention factors of a solute in C_{18} and C_2 reversed column, respectively. In a recent work we have shown that if the plot of S vs. φ, where φ is the volume fraction of the modifier in the mobile phase, is a straight line parallel to the φ-axis then the adsorption should be the predominant retention mechanism [1]. The application of this criterion to the retention data of ten phenolic compounds from 0.07 M acetic acid aqueous mobile phases modified with methanol, isopropanol, acetonitrile and tetrahydrofuran using C_{18} and C_2 reversed-phase chromatographic columns showed that the retention in C_{18} columns is governed by the adsorption mechanism in all modifiers tested. This conclusion seems reasonable since the polar molecules of the phenol derivatives cannot enter easily into the cavities formed by the non-polar aliphatic chains of the C_{18} stationary phase and consequently the partition mechanism is very unlikely for the retention of these solutes.

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Corrosion Inhibitors Used in Acidic Descaling Solutions: Structure and Concentration - Efficiency Relationships

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To remove the deposits formed on the carbon steel pipes walls are currently used a descaling process executed using some solutions containing citric acid, tetrasodium-EDTA salt, hydrazinhydrate and several types of inhibitors. A method of maintaining of the solutions corrosivity under some limits consists in the use of those inhibitors which can maintain between the reasonable limits the rates of two concurrent processes: the dissolution of deposits and the attack of base metal.

Our experiments were executed on the samples from the following types of carbon steel: SA106, SA508 and SA516 filmed by autoclavization in an environment and at specific parameters of the Nuclear Power Station (NPS) secondary circuit.

The inhibitor types used in above-mentioned descaling solutions were organic substances containing the following specific groups: alcohol, double and triple bonds and simultaneously or not one or more amine groups. These inhibitors have been used in concentrations comprised between $[5.10^{-4}-3.10^{-3}]$M. From the tested inhibitors used in our descaling solutions remember: triethanolamine, ethylendiamine, triethylamine, propargylalcohol, propargylamine and others.

To establish the inhibitors efficiency were used the following two methods: gravimetric and potentiodynamic.

Finally, on the basis of the qualitative structure – activity relationships between the corrosion inhibition efficiency and the molecular structure, we confirmed a reaction mechanism of some inhibitors type amine.

Metals Analysis in Insulating Oils as an Addition in Determination of the Fault Type

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In this paper we present the results obtained from metal analysis of transformer oils. Metals analysis of transformer oil is used to complement dissolved gas analysis (DGA). When a gas-in-oil analysis indicates the presence of a possible fault, metals analysis will help determine the fault type and pinpoint its location. High energy faults not only degrade the transformer's insulation (oil, paper, wood etc...) but can generate metal particles that will disperse in the oil. These particles will be distributed throughout the transformer, mainly due to oil circulation. Certain transformer components produce specific metal particles. These metal particles will be found alone or in different combinations depending on the fault type. Establishing the combinations and concentrations of these metal particles will help to narrow the list of components involved in the fault. The metals that may be found in transformer oil are: aluminum, copper, iron, lead, silver, tin, and zinc. For example, copper would be found in the windings, bronze and brass components. Lead is found in solder joints, connectors and other peripheral components. Iron is located in the transformer core and tank, whereas aluminum can be found in the windings, corona shields and ceramic bushings. Lugs, bolts, connectors and some peripheral components may also contain tin, silver and zinc. Metals analysis is performed using different methods. In our experimental part of work we have used atomic absorption spectroscopy (AA). There are no established threshold levels for metals in oil, nor is there an ASTM approved method. One metal analysis report is not enough to get a true picture of the unit's health. Subsequent tests should be performed to trend the results and look for developing problems. In this paper, the analysis and thorough analysis of the examined transformer is given. As data is being generated and cases documented, metal-in-oil is becoming another tool used to detect transformer faults before they escalate into major problems.

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Reaction of 1,8-Dihydroxy-2-(imidazol-5-ylazo)-naphthalene-3,6-disulphonic Acid Immobilised on a Solid Support with Pd(II)

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The reaction of Pd(II) with 1,8-dihydroxy-2-(imidazol-5-ylazo)-naphthalene-3,6-disulphonic acid (IACA) sorbed onto anion exchange resin Dowex 1-X8 (50-100 mesh) was investigated. The aim of the work was to develop the spectrophotometric method for determination of low Pd(II) concentrations in water, based on the colour reaction of Pd(II) with modified resin. 0.5 g of resin was immersed in 10 ml of 5.1×10^{-5} M IACA solution and left at room temperature until equilibration. The amount of the immobilised dye was 1.02 μmol/g of resin. The complex formation between the modified dye and Pd(II) was followed spectrophotometrically, by recording the absorption spectra of the solid phase in 2 mm cuvette against the unmodified resin. The complex formation induced the batochromic shift of the maximum of the modified dye absorption spectra ($\Delta\lambda$ = 100 nm). The absorption maximum of the resin phase complex was found at 650 nm. The influence of acidity on the complex formation from pH 1 to pH 5 was investigated.

The stoichiometry of the complex was determined at pH 3 using the specrophotometric titration method. The solid phase was immersed into 10 ml Pd(II) solution containing from 5×10^{-6} to 7×10^{-4} M Pd(II). The results confirmed the formation of 1:1 Pd(II)-IACA complex, as also found in the solution. The calibration graphs using the different volumes of Pd(II) solutions were constructed. The linearity range of absorbance *vs.* Pd(II) concentration extended from 5×10^{-6} - 5×10^{-5}M, 5×10^{-7} - 5×10^{-6} M and 2.5×10^{-8} - 2.5×10^{-7} M for the system of 10, 100 and 200 ml of sample solution, respectively. The relative detection limit (the concentration that produces an absorbance equal to twice the magnitude of the fluctuation in the background absorbance) for the system with 10, 100 and 200 ml sample solution was 5×10^{-6} M, 5×10^{-7}M and 2.5×10^{-7} M Pd(II), respectively. Precision was measured with 10 ml of 5×10^{-5}M Pd(II) sample solution and the relative standard deviation was 10%.

Influence of the Measurement Time on Signal, Noise and Background in Radioisotope X-Ray Fluorescence Spectrometry

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The main advantages of the application of energy dispersive x-ray fluorescence spectrometry (EDXRF) with radioisotope excitation sources in qualitative and quantitative chemical analysis are the non-destruction of the sample, the great depth of information, the accuracy of analysis, the simple operability, and the economic efficiency. One of the important operating EDXRF parameters that most influences the productivity is the measurement time. In order to optimize the measurement time, twelve spectra (see Fig. 1) resulted from varying the measurement time were used in this work to study the signal, noise, and background changes in EDXRF.

The measurements were performed with a Canberra EDXRF system at the Vinča Institute of nuclear sciences. This system consisted of a lithium drifted silicon (Si(Li)) detector, annular ^{109}Cd excitation source, and a multi-channel analyzer. The collected spectra were transferred to a PC computer and analyzed. An amount of 200 mg of NIST 1633b coal fly ash certified reference material was irradiated and measured for different measurement time ranging from 60 to 345600 s.

In each spectrum, eighteen elements (K, Ca, Ti, Cr, Mn, Fe, Cu, Ni, Zn, Ga, Ge, Pb, Se, As, Rb, Sr, Nb, Zr) were identified and their peak areas determined. The signal values linearly increased for all elements, except for Fe where the signal saturation occurred at about 170000 s. However, after an initial increase and reaching a maximum at approximately 6000 s, the signal-to-background ratio for most elements decreased and approached a constant value at longer measurement time. In the event of Fe, a different behavior showing a continuous decrease was observed. The signal-to-noise ratio seems to be a linear function of the measurement time in the studied range.

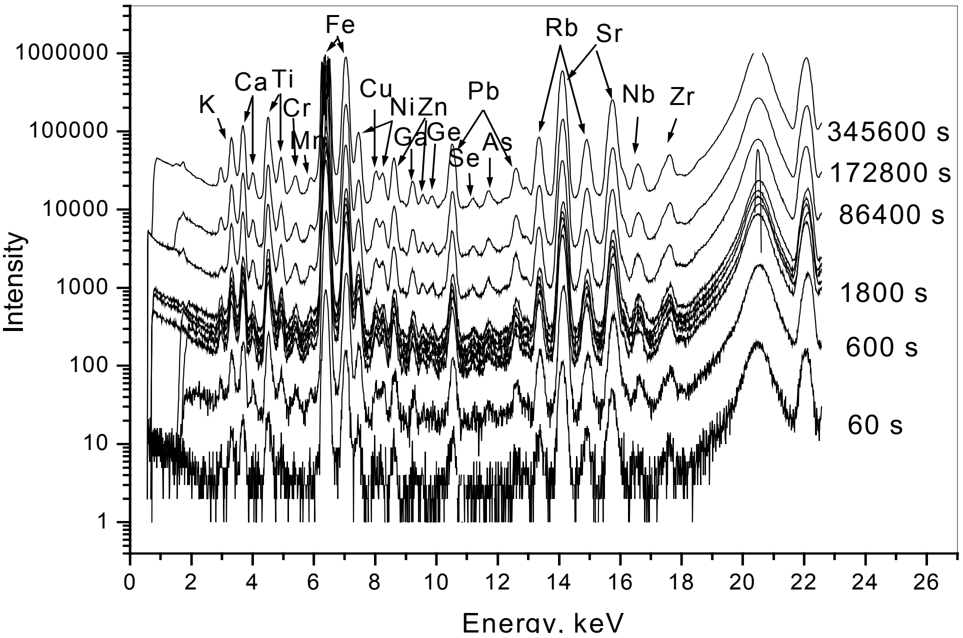

Fig. 1. EDXRF spectra of NIST 1633b coal fly ash sample as a function of the measurement time.

Cadmium Sorption Capacity as a Function of Hydroxyapatite Physico-Chemical Properties

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In this paper, sorption capacities of 10 different synthetic hydroxyapatite (HAP) powders were studied. Eight HAP samples were synthesized from H_3PO_4 and $Ca(OH)_2$, by varying neutralization method parameters (concentration and rate of reactant addition, themperature, aging time, presence of inert athmosphere and mixing speed), according to the Plackett-Burman experimental design. Using statistical software, the effect of each variabile on the sorption capacity was analyzed. In addition, highly crystalline syntetic HAP (HAPc) and comercial Bio-Rad product were also studied, for comparation. The powders were characterized by XR-diffraction and IR analyses. The Ca/P ratios of samples were determined by ICP. Specific surface areas were measured by nitrogen adsorption (B.E.T. method), and the point of zero charge of each sample was determined by batch equilibration technique. Cadmium sorption capacity was determined by batch method. After eqilibration of 0.1000 g HAP samples with 20.00 ml of $Cd(NO_3)_2$ solution containing 1000 ppm of Cd^{2+} ions, for 24 hours, the remained amounts of cadmium were determined by ICP technique.

All samples had the crystalline structure of HAP. Physico-chemical and sorption properties of HAP samples are presented in Table 1.

Table 1. Physico-chemical and sorption properties of HAP powders.

Sample	1	2	3	4	5	6	7	8	HAPc	BioRad
Ca/P ratio	1.59	1.62	1.60	1.62	1.67	1.59	1.55	1.65	1.71	1.53
Point of zero charge pH_{PZC}	6.1	6.4	6.2	10	6.5	6.6	6.5	6.6	6.6	6.6
Crystallite size L_{002} (nm)	48	34	43	31	51	48	31	45	102	39
Fraction of crystalline phase	0.69	0.28	0.36	0.11	0.72	0.63	0.19	0.72	0.90	0.28
Specific surface area (m^2/g)	41	72	67	82	60	58	72	47	24	64
Cd^{2+} sorption capacity (mmol/g)	0.462	0.678	0.654	1.058	0.729	0.592	0.857	0.562	0.199	0.750

Although differences in Ca/P ratios and pH_{PZC} between samples exsists, cadmium sorption capacity could not be related to these properties. On the other hand, there is a good corelation between the amounth of sorbed Cd^{2+} and specific surface area of HAP powders.

Among six selected variables of neutralization preparation method, temperature and aging time were found to be the most significant for sorption characteristics of HAP. Room temperature and no aging of HAP gave a material with the small crystallite size, high specific surface area and the best sorption properties toward Cd^{2+} ion. This makes the synthetic procedure for HAP to be used as a cadmium sorbent - faster and more economic.

Prediction of Polycyclic Aromatic Hydrocarbon Retention Times in Temperature-Programmed Gas Chromatography

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Polycyclic aromatic hydrocarbons (PAHs) are environmental contaminants derived from combustion sources (pyrogenic) or petroleum inputs (petrogenic). PAHs are an important class of environmental contaminants to study because some of these compounds are carcinogenic and/or mutagenic to mammals.

The content of PAHs in the environment is mandated by most regulatory agencies worldwide. PAHs analyses can be accomplished equally well using gas chromatography (GC), gas chromatography/mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), and HPLC-MS. In all cases the chromatographic separation has to be optimized. In this work, the retention behavior of 13 priority pollutant PAHs in temperature-programmed GC was studied.

All measurements were performed on a Spectra-physics model 7100 gas chromatograph with a flame ionization detector. A 1.0 μL aliquot of the mixture containing 13 PAHs in toluene at the concentrations of 0.2 ppm were injected into a Ultra®-1 (crosslinked methyl silicone) capillary column (50 m x 0.32 mm x 0.5 μm). As the initial and the final temperature, 40 and 280 °C were selected, respectively. To make the GC retention model, a non-linear regression fitting approach was employed. This resulted in the following model for retention behavior of PAHs:

$$\log k = A - B \times (\log \text{ramp}) + C \times (\log \text{ramp})^2 \qquad (1)$$

where k is capacity factor, while A, B, and C are estimated model parameters for PAHs (A=1.55-2.13, B=1.095-0.71, C=0.042-0.283). Figure 1 shows both the experimentally obtained and calculated by Eq. (1) capacity factors for PAHs. A good agreement between the obtained and calculated values indicates that the optimization of GC separation can be done in a fast and accurate way by using a computer-added approach.

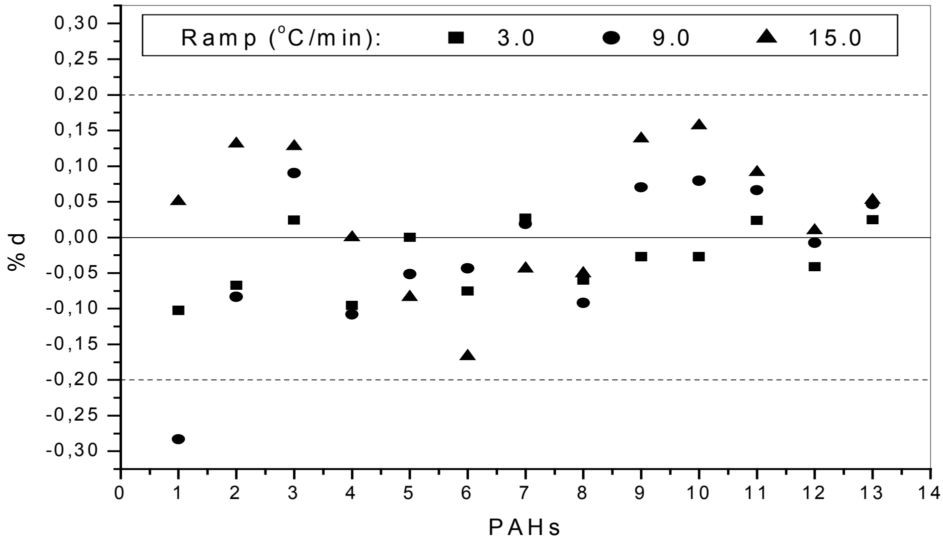

Figure 1. Percentage-normalized difference between the measured and predicted retention times for 13 PAHs (1 - Naphthalene, 2 - Acenaphtene, 3 - Acenaphthene, 4 - Fluorene, 5 - Phenanthrene, 6 - Anthracene, 7 - Fluranthene, 8 - Pyrene, 9 - Benz(a)anthracene, 10 - Chrysene, 11 - Benzo(b)fluoranthene, 12 - Benzo(k)fluoranthene, 13 - Benzo(a)pyrene).

Determination of Heavy Metals by Potentiometric Stripping Analysis in Water and Marine Sediments

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The aim of this work was to determine the content of heavy metals in water, seawater and marine sediments by potentiometric stripping analysis (PSA) method. A study is presented on the characterization, evaluation and optimization of several key operational parameters for a reliable and effective use of the potentiometric stripping measurements for trace heavy metals in real systems.

Optimization of the parameters such as a solution matrix, the effects of solution pH, pre-concentration time and the deposition potential showed an impact on the simultaneous determination of cadmium and lead, i.e. on the reproducibility and sensitivity of the PSA method.

The content of lead and cadmium ions was studied directly in water with mercury film electrode by standard addition in the presence of supporting electrolyte (pH 2.0) and by adjusting [Cl^-] to 1M and pH 5.6 by 1 M NH_4Ac/HCl buffer.

Cadmium and lead were determined in marine sediment samples, after aqua regia digestion, using the same solution matrix and operational parameters and by using GF-AES spectrometry.

The multi elemental composition of the inorganic matrix of the marine sediments was obtained by Energy Dispersive Polarised X-Ray Fluorescence.

Spectrophotometric Determination of Ketoconazole in Tablets

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Ketoconazole, *cis*-1-acetyl-4[4-[[2-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]phenyl]piperazine, is an orally active agent from the class of antimycotics, derivatives of imidazole. Ketoconazole is the only member of this class currently used for the treatment of systemic infections.

As to its chemical characteristics, ketoconazole represents a diprotic base (pK_{a1} 3.2 and pK_{a2} 6.1) and its molecular form is slightly hydrosoluble ($1.4 \cdot 10^{-5}$ M)[1]. This study was aimed at demonstrating that examinations of protolytic equilibria and solubility might be of importance in analytics of ketoconazole, for the choice of methodological approaches for its spectrophotometric determination.

The choice of optimal conditions for ketoconazole determination was done based on the distribution of its equilibrium forms, as well as spectral characteristics. Determinations were performed in 0.1 M HCl at 225 nm which corresponds to the absorption maximum of diprotonated form of ketoconazole. Calibration curve was obtained within the range of ketoconazole concentrations from 3 to 30 μg/ml:

$$A = (-0.0028 \pm 0.0059) + (0.05252 \pm 3.5 \cdot 10^{-4})\, c \qquad (r = 0.9999)$$

where c is the concentration expressed in μg/ml.

The accuracy and precision of the method were checked by analyzing three ketoconazole solutions of different concentration (5, 10 and 20 μg/ml). Recovery (99.2-100.9 %) and low values of relative standard deviation (0.65-0.98 %) point to a satisfactory reproducibility of this method.

The applicability of the method was tested by determining ketoconazole in the following commercial tablets: Mycoseb® (“Zorka Pharma”, Serbia and Montenegro), Nizoral® (Janssen Pharmaceutica, Belgium) and Oronazol® (“Krka”, Slovenia).

The proposed method is precise, rapid and simple. It enables a direct determination of ketoconazole in tablets without previous isolation. In addition, this method does not require the use of expensive equipment and toxic reagents thus fulfilling the concept of Green Chemistry.

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HPLC Methods for the Determination of Econazole Nitrate in Topical Dosage Forms

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Econazole, 1-[2-[(4-chlorophenyl)methoxy]-2-(2,4-dichlorophenyl)ethyl]-1H-imidazole, an imidazole derivative is known by its potent fungicidal and antibacterial action. During the recent years, the application of imidazole derivatives is increasing due to their efficiency in the treatment of mycoses, especially in patients with a decreased immunity (*e.g.* after organ transplantations, AIDS, *etc.*). From the chemical point of view econazole represents a base (pK_a 6) molecular form of which is slightly soluble in water. Pharmaceutical formulations contain econazole as a nitrate salt and it has been determined till present by spectrophotometric, capillary electrophoretic and titrimetric approaches. In addition, econazole was determined by gas chromatography and HPLC using different columns (diol, cyano and C18 columns).

In this work, two HPLC methods for the determination of econazole nitrate using the columns of different polarity (amino and C8) were presented. An acetonitrile-water (30:70 v/v) solvent system (pH 2.5 adjusted with phosphoric acid) was used as the mobile phase. On chromatograms obtained applying these two columns a single econazole (amino column), i.e. nitrate (C8 column) peaks were identified. Calibration curves were obtained on the basis of the relationship between the peak areas (y) and the amount of econazole nitrate (x) in concentration range 0.005-0.05 mg/ml (amino column) and 0.1-1 mg/ml (C8 column). The corresponding equations were evaluated by linear regression functions:

amino column $y = 35.83 + 25210.6\,x$ $(r=0.9994)$

C8 column $y = 13.45 + 1462.7\,x$ $(r=0.9999)$

The proposed methods were applied for the determination of econazole nitrate in Ecalin® vaginal pessaries (each containing 150 mg econazole nitrate) and Ecalin® spray solution (1.0 g econazole nitrate *per* 100 g spray solution), products of "JAKA 80" Pharmaceutical Works (Radoviš, Macedonia). The data listed in the following Table points to a good accordance of the results obtained by these two methods.

Table. The content of econazole nitrate in pharamaceuticals

Ecalin®	Column	Found	RSD, % (n=5)	Percentage of the labelled claim
Vaginal pessaries	Amino	149.0 mg	1.10	99.3
	C8	149.5 mg	1.87	99.6
Spray solution	Amino	1.022 g	0.73	101.6
	C8	1.016 g	1.98	102.2

Based on the results obtained throughout this study it can be concluded that both HPLC methods presented here are reliable and can be successfully applied for routine analyses of pharmaceutical preparations.

Second-Order Derivative Spectrophotometric Method for Determination of the Vitamin C Content in Natural Products

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Vitamin C (ascorbic acid) is very widespread in nature: it can be found in fresh fruits and vegetables, it is added in different food, and also can be found in a large number of pharmaceutical products. Because of its huge importance many analytical methods for its determination have been developed until today, from classical titrimetric to instrumental methods. However, because of the variety of analysed products, none of the methods is universal. Taking that aspect, spectrophotometric methods are especially interesting.

The aim of this paper was to elaborate the method that enables determination of vitamin C content in juices with declared content of this vitamin (HIPP KFT, Hungary) and in different species of fruits and vegetables. It is especially interesting in cases in which it is difficult to use classical spectrophotometry because of the presence of great number of interfering substances and because of intensively coloured solutions. This method is based on the measurement of the peak – baseline amplitude on the wavelength of 267.5 nm in the second order of a spectrum of vitamin C extract ($^2D_{267.5}$) from the investigated samples. As an extractional solution it was used 1.0 M HCl. For determination of vitamin C content it was used regression equation obtained by recording of a series of standard ascorbic acid solutions in concentration range from 3.5 to 17.6 µg/cm^3. Reliability of this method was checked by using already accepted titrimetric method.

The results obtained by investigation of vitamin C content in commercial fruit juices, fruits and vegetables, which are not intensively coloured, using derivative spectrophotometric and titrimetric methods, show that there is a relatively good concordance of obtained values. This is very important considering the fact that these two methods are principally different. Also, the values obtained by using derivative spectrophotometric method demonstrate better concordance with declared values in commercial fruit juices than the ones obtained by using titrimetric method. On the basis of obtained results it is demonstrated that derivative spectrophotometric method is quick, reproductive and universal. This enables the usage of derivative spectrophotometry for routine analysis in determination of vitamin C content in a large number of different products.

Highly Selective Crystallization of Metal(II) Ions with 1,3-pdta Ligand. Crystal Structures of Two Isomorphic Hexadentate $[Mg(H_2O)_6][Zn(1,3\text{-pdta})]\cdot 2H_2O$ and $[Zn(H_2O)_6][Zn(1,3\text{-pdta})]\cdot 2H_2O$ Complexes and the $[Mg(H_2O)_6][Cd(1,3\text{-pdta})(H_2O)]\cdot H_2O$ Complex

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Numerous attempts to obtain crystalline M(II) complexes with 1,3-propanediaminetetraacetate ion (1,3-pdta) and alkaline metals as counter cations have not been successful. The crystalline product obtained from water solutions containing a combination of either Na and Co(II) or Li and Co(II) cations and 1,3-pdta contained solely the hexadentate $[Co^{II}(H_2O)_6][Co^{II}(1,3\text{-pdta})]\cdot 2H_2O$ complex. We have already reported the crystal structure of this complex.[1] However, starting from $Ba[Ba(1,3\text{-pdta})]\cdot 2H_2O$ we were able to obtain crystals containing alkaline earth metals as counter cations. Two such structures have been solved by X-ray crystallography, namely hexadentate: $[Mg(H_2O)_6][Mg(1,3\text{-pdta})]\cdot 2H_2O$, isomorphic with its Co(II) analog, and homometallic $[Ca(H_2O)_3Ca(1,3\text{-pdta})(H_2O)]\cdot 2H_2O$ complex which differs from the two isomorphic complexes in coordination number and geometry, and in coordinative bond distances.[2]

Analogously, we have witnessed frequent occurrence of only one type of crystals obtained from the aqueous solutions containing 1,3-pdta and Mg(II), Zn(II) and Cd(II) cations: from the solution containing Zn(II) and Cd(II) cations we have obtained as the solely crystalline product the $[Zn(H_2O)_6][Zn(1,3\text{-pdta})]\cdot 2H_2O$ complex, isomorphic with the homometallic $[Mg(H_2O)_6][Mg(1,3\text{-pdta})]\cdot 2H_2O$ and $[Co^{II}(H_2O)_6][Co^{II}(1,3\text{-pdta})]\cdot 2H_2O$ complexes, instead of the expected $[Zn(H_2O)_6][Cd(1,3\text{-pdta})]$ complex. Combination of Mg(II) and Zn(II) ions with 1,3-pdta has lead to the $[Mg(H_2O)_6][Zn(1,3\text{-pdta})]\cdot 2H_2O$ complex, again isomorphic with homometalic complexes mentioned above. However, in combination of Cd(II) and Mg(II) with 1,3-pdta we were able to obtain sevencoordinate $[Mg(H_2O)_6][Cd(1,3\text{-pdta})(H_2O)]\cdot H_2O$ complex, different from the homometalic $[Mg(H_2O)_6][Mg(1,3\text{-pdta})]\cdot 2H_2O$ and $[Co^{II}(H_2O)_6][Co^{II}(1,3\text{-pdta})]\cdot 2H_2O$ complexes but isomorphic with the $[Mg(H_2O)_6][Mn^{II}(edta)]$ analog.

The above observations illustrate how the change in the length of the methylene chain in the amino fragment of the edta-type ligand and the type of the charge compensating cations influence the mode of crystallization of edta-type complexes. These can be summarized as follows:

a) 1,3-pdta ligand favours the coordination with metal ions with ionic radii of about 0.8 to 0.9Å with which it forms octahedral complexes by acting as a hexadentate ligand.
b) Complexes of 1,3-pdta with metal(II) ions of the ionic radii of 0.8 to 0.9Å form isomorphic crystals in which the charge compensating cations are the divalent cations in a form of aqua ions.

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New Acrylate Complexes as Precursors for Advanced Polymeric Materials

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The synthesis of polymeric materials containing metals make up a new research field of current interest due to the practical importance of the obtained products, which possess unique properties: high catalytic activity, unusual magnetic or electro-physical activity [1]. One of the methods used in synthesis of metal-containing polymers is the co-polymerisation of a complex bearing a polymerisable group with selected comonomers [2].

The objective of this paper was the synthesis of four new complex compounds of cobalt (II) with mixed ligands having the general formulae $CoLAcr_2 \cdot xH_2O$ and $CoL_2Acr_2 \cdot xH_2O$ (where L is 1,10-phenanthroline or 2,2'-dipyridyl and Acr is acrylate anion). The presence of the acrylate ion into their composition gives us the possibility to use these compounds as monomers in the co-polymerisation reaction with traditional organic monomers. These compounds were characterized on the basis of chemical analyses, IR and electronic spectra. A systematic study of their thermal behavior was also carried out.

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Investigation of the Stability of Some Polyoxometalates in Aqueous Solutions

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Polyoxometalates (POM) of various classes are very interesting compounds with unusual behaviour: they are good catalysts, superionic proton conductors, compounds with photoconductive and magnetic characteristics and biochemically active compunds too [1].

More than 20 years their anticoagulant, antiviral and antitumoral activity [2] are intensively studied. A fundamantal limitation in application and interpretation of results on the behavior of these compounds in physiological media derives from their nature. Namely, many POMs are not stable in water and degrade or rearrange to a complex mixture of inorganic products in dependence of the solutions pH.

In this report the stability of 12-tunstophosphoric (WPA), 12-silicotungstic (SiWA) and 12-molibdenphosphoric (MoPA) acids and Mg salt of WPA (MgHWPA) was investigated by spectroscopical and electrochemical methods.

Our previous investigations of these compunds in buffered aqueous solutions have shown that their stability is primarily pH dependent in complex way. UV/VIS and IR spectra have shown that structure of Kegging anion is decomposed in alcaline solution. Bisedes that in some buffered solutions the reaction between the buffer and POMs is noticed.

The aim of this study is to investigate the way of POMs decomposition and to identify the forming products. Different buffers (acetate, phosphate, bicarbonate and TRIS) in wide range of pH values were applied. The behaviour of POMs aqueous solutions with addition of NaOH was followed too.

The processes of POMs decomposition and identification of the formed components in solutions and their liophilized forms are followed by NMR and IR spectroscopy. The reduction of POMs in buffered aqueous solutions is studied by cyclic voltammetry.

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New Organomercury(II) Derivatives Containing Ligands with Pendant Arms

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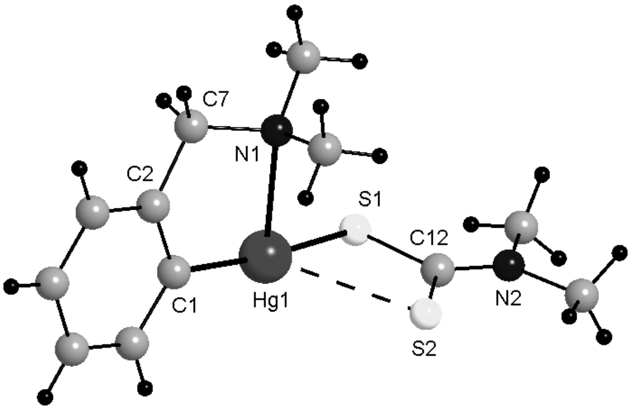
$[2-(Me_2NCH_2)C_6H_4]HgCl$ (**1**) was prepared by reacting $HgCl_2$ with $[2-(Me_2NCH_2)C_6H_4]Li$ in diethyl ether. The compound was investigated by solution NMR (^1H, ^{13}C) spectroscopy and single-crystal X-ray diffraction. Organomercury(II) derivatives containing the $2,6-(Me_2NCH_2)_2C_6H_3$- group, with two pendant arms with N atoms able to coordinate the metal centre, were prepared by reacting $HgCl_2$ with $[2,6-(Me_2NCH_2)_2C_6H_3]Li$ in 1:1 and 1:2 molar ratio, respectively. The solution behavior of $[2,6-(Me_2NCH_2)_2C_6H_3]HgCl$ (**2**) and $[2,6-(Me_2NCH_2)_2C_6H_3]_2Hg$ (**3**) was investigated by NMR (^1H, ^{13}C) spectroscopy. Various complexes of the type $[2-(Me_2NCH_2)C_6H_4]HgL$ or $[2,6-(Me_2NCH_2)_2C_6H_3]HgL$ were prepared by reacting **1** or **2** with the alkali metal salts of potential bidentate ligands (*e.g.* dithiocarbamates, organophosphorus derivatives) and the coordination competition for the metal center between the nitrogen atoms of the pendant arms and the ligand donor atoms was investigated by means of multinuclear (^1H, ^{13}C, ^{31}P) NMR spectroscopy in solution. The assignment of the observed resonances was based on 2D NMR spectra. The molecular structure of $[2-(Me_2NCH_2)C_6H_4]HgS(S)CNMe_2$ (**4**) was determined by single-crystal X-ray diffraction. Its crystals contain discrete monomeric molecules. Due to the strong intramolecular coordination of the N atom of the pendant CH_2NMe_2 arm [Hg(1)-N(1) 2.648(4) Å] the compound exhibit a T-shaped (*C,N*)HgS core in the molecular unit, with an almost linear arrangement of the covalent bonds [C(1)-Hg(1)-S(1) 170.7(1)°]. Weaker intramolecular Hg(1)···S(2) interactions [2.887(2) Å] are also present.



$[2-(Me_2NCH_2)C_6H_4]HgS(S)CNMe_2$

New Aspects of Pyrrhotite Non-Oxidative Dissolution in Acid Conditions

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Effect of acidity

The pyrrhotite non-oxidative dissolution at 60 °C has been studied by two progress variables (i.e., total dissolved iron and formed H_2S) at four different pH values. The dissolution curves show a parabolic shape, and the quantity of formed hydrogen sulfide was always lower than quantity of total dissolved iron. The -log r *vs.* pH curves for both progress variables used are presented in Figure 1. The reaction order of pyrrhotite dissolution with respect to hydrogen ions concentration for both progress variables is virtually equal with unity. The increase of dissolution rate with increase of acidity demonstrates that the protonation of the surface play a crucial role in dissolution process and points to a reaction kinetics controlled by the negatively-charged sulfide groups existing on the mineral surface.

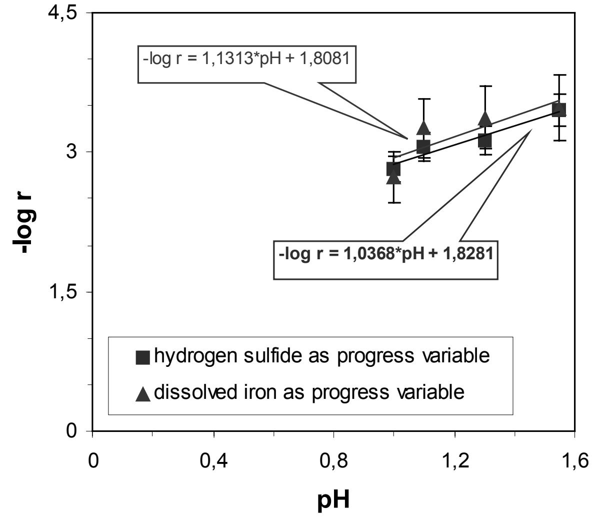

Figure 1. The effect of pH on the pyrrhotite dissolution rate at 60 °C temperature.

Fe/H_2S ratio

Also, the dissolved iron to formed hydrogen sulfide ratio (Fe/H_2S) was calculated at the end of each dissolution experiment. These ratios are: 2.83 (pH=1.00); 2.71 (pH=1.10); 2.66 (pH=1.30) and 2.51 (pH=1.55). As can be observed the pyrrhotite dissolution in nonoxidative conditions is an incongruent process, the ratio of Fe/S from pyrrhotite matrix being quite differently from Fe/S ratio corresponding to dissolution products. Therefore, we can conclude that pyrrhotite dissolution proceeds with sulfur accumulation in its structure. This result is in good agreement with data reported in literature [1-3].

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Advanced Materials: First Row Metal Complexes with Potential Mesogenic Properties. I. Design Synthesis and Characterization of nC-Alkoxy Schiff Base Derivatives

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N,N'-bis(4-decyloxysalicyliden-N-n-propyl)-piperazine (ZOPP) has been obtained by the Schiff condensation of 1,4-bis(3-aminopropyl)-piperazine with 4-decyloxysalicylaldehide respecting the 1:2 molar ratio. Information regarding the nature of ZOPP has been obtained from IR, ^{1}H-NMR and UV data. ZOPP can act as ligand through the two N_2O groups of donor atoms situated on each side of the piperazine bridge. The conformation of the piperazine bridge determines the nature of the complexes. Thus, the *bath* conformation leads to the mononuclear complexes while the chair one leads to dinuclear or polynuclear complexes. Both di- and polynuclear complexes of copper(II) and nickel(II) containing ZOPP as ligand have been obtained and characterized by spectral data and they are discussed in connection with the structural changes, which occur due to complexation.

Kinetics and Mechanism of the Leaching Process of Elementary Bauxite Types

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The process of leaching Al_2O_3 out of bauxite using the solution of NaOH is the subject of many experimental researches, as well as the kinetical studies of the process itself.

This study presents the results of kinetic examinations of the leaching process of different bauxite types (hydrargilite, boehmite and diaspore) using the solution of NaOH.

Characterisation of the starting bauxite and leached samples were caried out with: X-ray analysis, simultaneous DTA-TG-TGA analysis, as well as the methods of the classic chemical analysis. Examinations were performed in laboratory autoclave in isotermic conditions at different temperatures. The selection of kinetics model of isotherms linearization was performed using Sharp's model, introducing the so-colled reduced time $t_{0.5}$ during which rate of reaction of 50 percent is obtained. Dependence α=f (t) at different temperatures made it possible, using this method, to determine important kinetic parameters, the energy of activation and preexponential parameter, which further lead to defining the dependence of the rate of reaction on time and temperature.

Obtained results of energy of activation and depedence of the rate of reaction on time and temperature for listed bauxites are shown in table 1.

Table 1. *Obtained results of energy of activation and depedence of the rate of reaction on time and temperature*

Bauxites type	Ea [kJ/mol]	Depedence of the rate reaction on time and temperature
Hydrargilite	48.460	$-\ln(1-\alpha)=4.39\cdot10^{5}\cdot e^{-5.83/T}\cdot t$
Boehmite	72.590	$-\ln(1-\alpha)=1.67\cdot10^{7}\cdot e^{-8.73/T}\cdot t$
Diaspore	108.813	$-\ln(1-\alpha)=3.81\cdot10^{9}\cdot e^{-13.09/T}\cdot t$

Palladium(II) Complexes with S-Substituted Mercaptooacids

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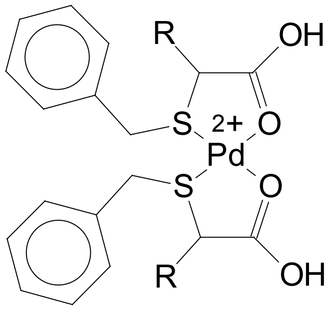
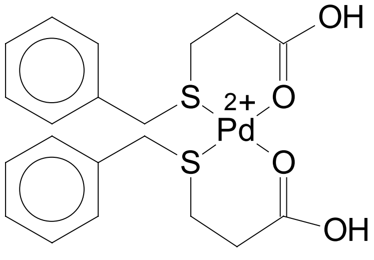
Three S-substituted mercaptocarboxylic acids (benzylthio-acetic, 2-benzylthio-propionic and 3-benzylthio-propyonic acid) were prepared by literature procedure,[1] and subjected to reaction with $PdCl_2$ in a two-phase organic aqueous system. The corresponding palladium(II) complexes of the general formula $[PdL_2]Cl_2$ (where L represents one of the above mentioned benzylthio-carboxylic acids) were isolated. The *cis*-configuration of the square-planar palladium(II) complexes was proposed on the basis of IR, ^1H NMR and ^{13}C NMR spectral data (see the formula).



R = H or CH_3



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Crystal and Molecular Structure of the Dichloroaqua(Pyridoxal Semicarbazone-ONO) iron(III) Chloride Complex

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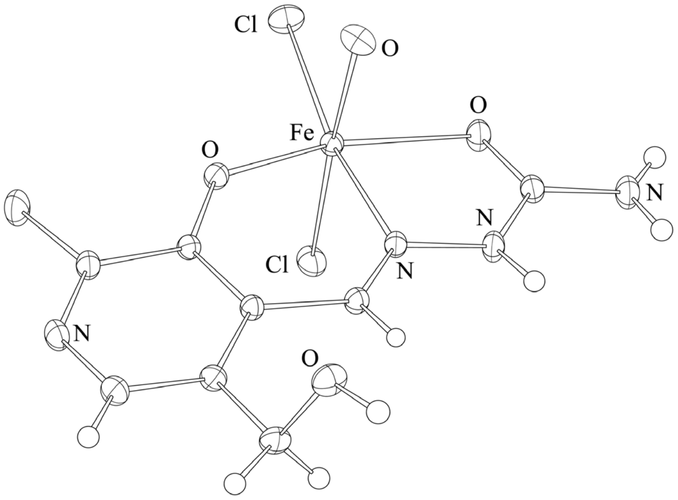
The crystal structure of Dichloroaqua(pyridoxal semicarbazone-ONO)iron(III) chloride consist of discrete complex cations and Cl^- anions. The Fe atom adopts distorted octahedral coordination. The equatorial bonds are formed by deprotonated phenolic oxygen, imino nitrogen and carbonyl oxygen from the organic ligand, and chlorine atom. Octahedral coordination is completed with water molecul and Cl in axial positions. The deviation from the ideal geometry is primarily determined by the rigidity of the chelate rings. The packing of molecules in the unit cell is governed by the presence of free chlorine anions which accept hydrogen bonds from the five surrounding complex molecules. Geometrical parameters of the pyridoxal based ligand in relation to the local enviroment will be disscused by the comparison with the structures of transition metal complexes containing pyridoxal moiety.

Crystal data:
$C_9H_{11}Cl_3$ FeN_4O_4, λ=0.71073 Å, orthorhombic, $P2_12_12_1$, a = 7.073(1)Å, b=8.437(2)Å, c=25.389(5)Å, Z=4, ρ=1.760 Mg/m^3, μ=1.543 mm^{-1}, θ=1.6-36.0°, ref./ par.=6904/191, R(all data) = 0.0335.



Synthesis, Crystal Structure and Analysis of Intermolecular Contacts in the Crystal Structure of Dichloro(2-hydrohy-1-naphtaldehyde-3-methylisothiosemicarbazonato)iron(III)hemiethanol Solvate

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Molecular structure

Black monocrystals of the entitled complex of the formula $[Fe(HL)Cl_2]\cdot 0.5$ EtOH (HL=monoanjon of the 2-hydroxy-1-naphtaldehyde-3-methylisothiosemicarbazone) was prepared by the reaction of a warm ethanolic solution of FeCl3.6H2O and Schiff base ligand in mole ratio 1:1. Ligand is coordinated to the Fe(III) through the hydrazine and imide nitrogen atoms N3 and N1, respectively, and oxygen atom O1. The organic ligand is situated on the mirror plane, with two chlorine atoms positioned on the opposite sides of the plane. Coordinated atoms makes a trigonal bypiramid with N1 nitrogen and oxygen in the axial positions, and the N3 nitrogen and two chlorine atoms in the equatorial plane (Fig. 1a). This molecule posses four strong hydrogen bond acceptors: sulfur, oxygen and two chlorine atoms.Also there are two N-H groups, as a strong hydrogen bond donors. Besides, the extended system of π electrons is situated at the naphtalene fragment. Having in mind that organic ligand is idealy planar, the formation of stacking contacts between the aromatic systems could be expected. The above facts make this molecule an interesting target for analysing how different potentials for intermolecular interactions have been realized, when all posssibilites are forced to be in the same molecular fragment.

Intermolecular contacts

It is intreresting to note that inspite of the planarity of the organic ligand and the presence of extended aromatic system there are no stacking interactions in the crystal, between the naphtalene fragments. Closest complex molecules are oriented so that five and six memebered chelate rings are one above other (Fig. 1b), with centroid's distances ranging from 3.9 to 4.2 Å. However the interatomic distances of the neibhouring rings are above the sum of van der Waals radius. This suggest that electrostatic forces between the two chelate rings are responsible for the assosiation of molecules. These contacts lead to the formation of zig-zag chains. The solvent-containing void is located between the chains, however the role of solvent can not be clearly determined due to disorder.

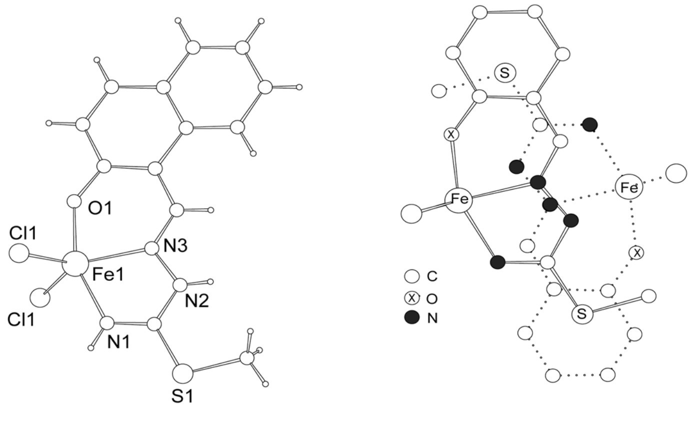

Figure 1. a) Molecular diagram b) Mutual orientation of neighbouring molecules

Synthesis, Characterization and Crystal Structure of a Novel Ni(II) Complex, Ni(L-H)$_2$ (L= 3,5-Dimethyl-1-thiocarboxamide Pyrazole)

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The complex, Ni(L-H)$_2$, L = 3,5-dimethyl-1-thiocarboxamide pyrazole, was synthesised by mixing cold methanolic solution of the ligand (2.5 mmol) and appropriate Ni(II) salts: $NiSO_4 \cdot 7H_2O$, $Ni(OAc)_2$, $Ni(CF_3COO)_2$ and $Ni(SCN)_2$ (1 mmol). The same product is obtained with any of the Ni(II) salts listed. The specific sample used for the measurements described here was made with $NiSO_4 \cdot 7H_2O$.

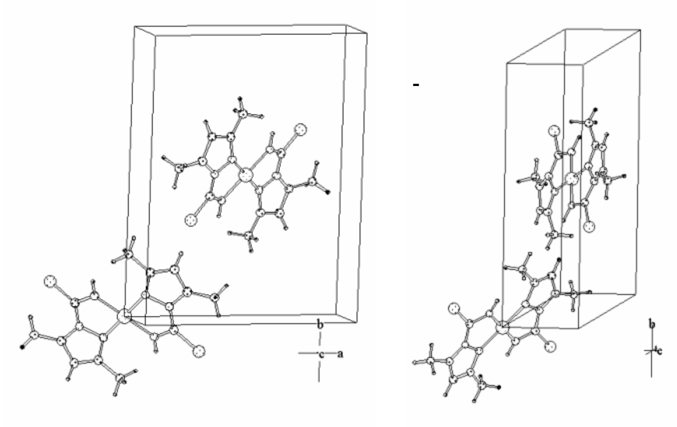

Figure 1. Two views of the unit cell of Ni(L-H)$_2$

A new complex has been characterized by elemental analysis, IR spectroscopy, magnetic and electrical measurements. Its crystal structure was solved from laboratory powder X-ray diffraction data. The compound crystallizes in space group P–1 with two independent half-molecules containing Ni(II) coordinated by four nitrogen atoms in a square-planar geometry. The packing pattern consists of two stacks of parallel molecules mutually tilted at an angle of 118° (Fig1.).

Identification of Some $M_2^{III}Fe^{II}O_4$ and FeOOH (M^{III} = Fe or Cr) Oxide Type Minerals from Macedonia by Powder XRD and AAS and EAS-ICP

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The powder X–ray diffraction (XRD) as well as atomic apsorption spectrometry (AAS) and emission atomic spectrometry with induced coupled plasma (EAS-ICP) are used as powerful techniques in the process of identification of several oxide minerals (magnetite, $Fe_2^{III}Fe^{II}O_4$; chromite, $Cr_2^{III}Fe^{II}O_4$; limonite, FeOOH; goethite, α–FeOOH) collected from various localities in the Republic of Macedonia (Pehčevo, Damjan, Alšar, Raduša, Košino). The content of the main and trace elements in the studied oxides is determined using AAS, EAS-ICP, classical chemical analysis and the results are related to the geological and minerological conditions of their origin localities. As a pattern for mineral identification was the comparison of their X-ray diagrams (peak intensities and 2θ values) with the corresponding literature data for the analogue (natural and synthetic) mineral species. In this context, the powder X-ray patterns were representative for the detection of impurities in some of the studied mineral samples as well.

New Thioderivatives of Selenium and Tellurium with N→E (E = Se, Te) Intramolecular Coordination

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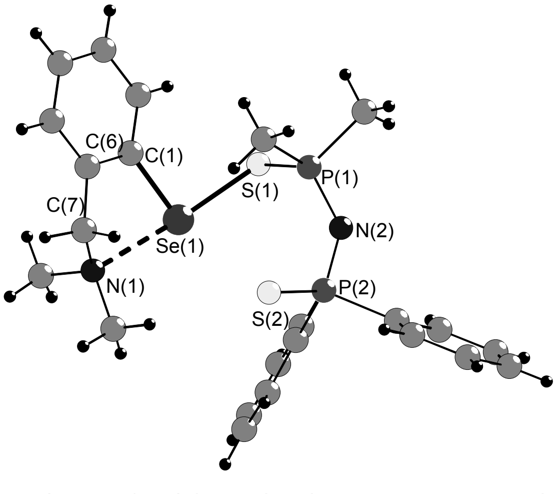
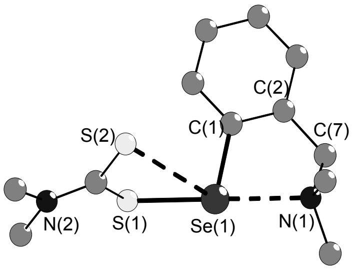
The reaction of elemental selenium with [2-(Me_2NCH_2)C_6H_4]Li resulted in formation of [2-(Me_2NCH_2)C_6H_4]ELi, which after working-up led to [2-(Me_2NCH_2)C_6H_4]$_2$$Se_2$ (**1**). The cleavage of the Se-Se bond in **1** is achieved in the presence of Br_2 to yield [2-(Me_2NCH_2)C_6H_4]SeBr (**2**). **2** was reacted with potassium tetraorganodithioimidodiphosphinates to give [2-(Me_2NCH_2)C_6H_4]Se-S-PR_2=N-PR'_2=S [R = Me (**3**), Ph (**4**); R' = Ph]. Compounds of the type [2-(Me_2NCH_2)C_6H_4]Se-S(S)CNR_2 [R = Me (**5**), Et (**6**)] were prepared by reacting [2-(Me_2NCH_2)C_6H_4]SeBr with $Me_2NCS_2Na\cdot 2H_2O$ and $Et_2NCS_2Na\cdot 3H_2O$, respectively. Similar reactions with tellurium analogs will also be discussed.

All compounds were investigated by multinuclear NMR spectroscopy and the observed resonances were assigned by 2D NMR experiments. The solid-state molecular structures of **3**, **5** and **6** were established by single crystal X-ray diffraction. All compounds are monomeric and the N atom of the pendant CH_2NMe_2 arm is strongly coordinated to the Se atom. This results in a T-shaped coordination geometry for the Se(II) atom in **3**, with a co-linear S-Se-N system. In **5** and **6** the coordination about selenium can be considered essentially as *pseudo*-octahedral, with Se-S and Se···N in axial positions, and Se-C, Se···S (intramolecular interaction) and two lone pair of electrons in ecuatorial positions. The distortion of the coordination geometry from an ideal *pseudo*-octahedron is due to the constraint imposed by the four- and five-membered chelate rings.



2-(Me_2NCH_2)C_6H_4]Se-S-PMe_2=N-PPh_2=S



[2-(Me_2NCH_2)C_6H_4]SeS(S)$CNMe_2$

Spectral Characterization of New Dithiocarbamato Ligands and Complexes with Cu(II), Ni(II), Pt(II) and Pd(II)

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Dithiocarbamates are organosulfur compounds with wide applications. They are used as accelerators in vulcanization, as pesticides, fungicides and as bioactive compounds.

We have recently obtained the N-dithiocarboxy-imino-diacetate in form of an ammonium salt, $(NH_4)_3$*idadtc*. It can be coordinated either as a bidentate or as a tridentate ligand. The anion of the ligand has been used to obtain the corresponding copper(II), nickel(II), platinum(II) and palladium(II) *bis*(ligand) complexes in acidic form. Obtained compounds have been characterized by elemental analysis.

^{1}H NMR spectrum of the ligand exhibits the two signals due to $-CH_2$ and NH_4^+ protons.

^{13}C NMR spectrum of the ligand shows only three signals. A little number of signals suggests symmetrical molecule of ligand.

The three bands at the highest energy that were observed in the electronic spectrum of the solid ligand, could be assigned to the chromophore group NCS_2 [1]. In the spectra of the complexes, beside intraligand bands which were presented in the free ligand, $d \rightarrow d$ bands have been identified too.

In IR spectra, a carboxyl group bands in the 1600-1400 cm^{-1} region were different for the ligands and complexes. While for the ligand two bands were recorded in this range, the copper, nickel, platinum and palladium complexes have showen only one intense band which corresponding to vibration of the free carboxyl group. This behavior indicates that the coordination in the complexes does not take place through the carboxyl group, but only through the sulphur atoms of the ligands. The presence of ν(M-S) band in complexes in 300-400 cm^{-1} region confirms the coordination of the *idadtc*$^{3-}$ ligand to Cu(II), Ni(II), Pt(II) and Pd(II) ions via sulphur atoms.

These experimental data as well as the similarity between the properties of these compounds lead to the conclusion that the coordination of the dithiocarbamato derivative of imino.diacetate in an acidic solution to copper(II), nickel(II), platinum(II) and palladium(II) takes place through the sulphur atoms of the dithiocarbamato moiety, while the carboxyl groups are protonated. The stoichiometry of the compouns as well as the magnetic and UV/VIS data confirm a square-planar geometry.

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Complexes of Pt(II) with Tetradentate Ligand

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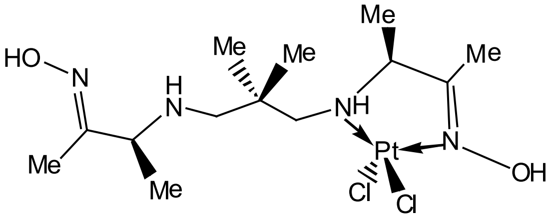
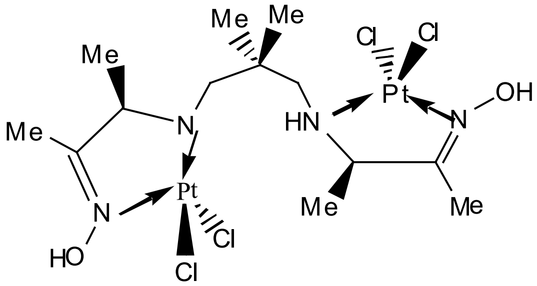
The ability of Pt(II) to form covalent adducts with the base residues in DNA is crucial for the biological activity of various anticancer Pt drugs, so the complexes of platinum with different polyfunctional ligands are of great interest in anticancer research and chemoteraphy [1,2]. Binuclear platinum compounds represent one class of second-generation drugs that have shown significant potential [3]. Exametazine, [4,8-diaza-3,6,6,9-tetramethylundecane-2,10-dione dioxime (HM-PAO)] as tetradentate ligand, with two amine and two oxime groups can form several complex species with Pt(II) ions, so the objective of this work is to investigate complexes formation of Pt(II) with HM-PAO.

Spectrophotometric investigation performed at 14°C and 30°C and at pH~6.4 with I=0.2M, indicated at least successive formation of two types of complexes HM-PAO with $[PtCl_4]^{2-}$ ions under conditions of the excess of metal ion, mononuclear complex HM-PAO to Pt(II) ratio 1:1 and binuclear complex with absorption maximum at 250nm and ratio M:L=2:1. Under conditions of the excess of ligand, also two complex species are formed with λ_{max} at 226nm and 236nm. In these case mole ratio method confirmed stehiometric ratios M:L=1:1 and M:L=1:2 respectively. Probable structures of the complexes in solution are suggested.



Structure of mononuclear complex
$[PtCl_2(meso\text{-}HM\text{-}PAO)]$



Structure of binuclear complex
$[Pt_2\,Cl_4(meso\text{-}HM\text{-}PAO)]$

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Conformational Analysis of Copper(II)-Dextran Complexes by Fourier-Transform IR Spectroscopy

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Deconvoluted IR spectra of dextran and its complexes with copper(II) were analyzed in order to find the most specific spectral peculiarities that allow one to obtain information about the structure and conformation of these macromolecules in solvents that exhibit different influences on the system of intra- and intermolecular interactions. The changes in intensity and width of the IR bands in region 1450-1050 cm^{-1} were related to changes in conformation and short-range interactions of the dextran. The certain band at the 880 cm^{-1} was considered as a characteristic for the conformation change C1-B1 of glucopyranose units. The results of the FTIR spectroscopy study allowed one to suggest a predominant crystalline form of copper(II)-dextran complexes.

Coordination Compounds of Copper (II) with Therapeutically Active Ligands

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It is known that copper complexes can be used to alleviate the inflammation associated with the disease [1].

Synthesis and study of metal complexes with antiinflammatory drugs as ligand, in order to obtain of new compounds which exhibit enhanced activity is a research area of considerable interes [2].

In present paper are presented the study for obtain and characterization of new cooper coordination compounds with oxicams (meloxicam, piroxicam).

The compounds were characterized by elemental analysis, spectrometric and magnetic measurements.

The studies UV, VIS, IR spectra and magnetic measurements allowed to obtain informations about stereochemistry of the metal ion and coordination mode of the ligands, two very important aspects of the structure-activity relationships.

The biological activity of these coordination compunds which depends on their confirmation was confirmed by the experimental pharmacological tests.

The test revealed enhanced antiinflammatory properties of the coordination compounds, comparatively with the ligands.

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Synthesis, Characterization and Superoxide Dismutase Like Activity of Cu(II) and Zn(II) Complexes with a Macrocyclic Ligand Containing Tyrosine Residues

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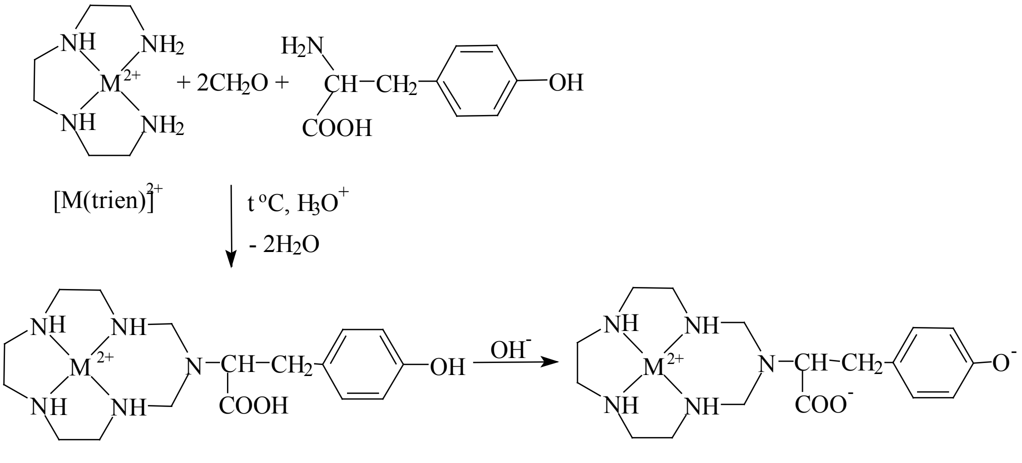
It is well known that the superoxide dismutases control the formation of the toxic subproducts of the respiratory processes of the aerobic organisms. However, the overproduction of superoxide anions is a mediator of reperfusion diseases such as those following acute stroke, shown to be associated with development and continuation of inflammatory processes, involved in diseases such as arthritis and it plays a major role in the initiation of neurological disorders such as Parkinson's disease [1]. Extensive studies have been carried out to find the suitable SOD-mimics because the rational design and synthesis of low molecular weight complexes that mimic these enzymes function has potential for use as a human pharmaceutical in the prevention or treatment of such diseases. Among these, a large variety of polyfunctional ligands have been used to synthesise mononuclear or binuclear copper (II) complexes as structural, spectroscopic or functional model complexes [2].

In order to examine the possibility of Cu(II) complexes to act as superoxide dismutase mimics, a series of new complexes of Cu(II) and Zn(II), with general formula $[M(H_2L)(H_2O)_n](ClO_4)_2\cdot mH_2O$((**1**) M=Cu, n=1, m=3; (**2**) M=Zn, n=2, m=4; H_2L:pentaazamacrocyclic ligand resulted in condensation reaction of tyrosine and 3,7-diazaoctane-1,8-diamine with formaldehyde, respectively $[ML(H_2O)_2]$ ((**3**) M=Cu and (**4**) M=Zn) have been synthesised as it is shown below:



[MH$_2$L]$^{2+}$ (**1**) M: Cu; (**2**) M: Zn [ML] (**3**) M: Cu; (**4**) M: Zn

The methods used in order to characterise the bonding and the stereochemistry of the new complexes were IR, EPR (by dilution in diamagnetic Zn(II) complex as host and in frozen solution at different pH values), ^{1}H NMR and electronic spectroscopy (in solid state and solution). The SOD type activity of $[Cu(H_2L)(H_2O)](ClO_4)_2\cdot 3H_2O$ was established using xanthine-xanthine oxidase system.

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Polynuclear Coordination Compounds as Precursors for Garnets

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Ferrimagnetic garnets are used widely in electronic devices for the microwave region as well as in magnetic bubble domain-type digital memories [1-3].

Rare earth iron garnet nanoparticles ($RE_3Fe_5O_{12}$) where RE = Eu, Gd, Er and $Y_3Fe_{15}O_{12}$ have been prepared by thermal decomposition of polynuclear coordination compund precursors, containing as ligands – anions of polyhydroxicarboxylic acids (tartarate, malate, gluconate):

$(NH_4)_6[Y_3Fe_5(C_4O_5H_4)_6(C_4O_5H_3)_6]\cdot16H_2O$
$(NH_4)_6[Ln_3Fe_5(C_4O_5H_4)_6(C_4O_5H_3)_6]\cdot16H_2O$ (**I**)
where Ln(III) = Eu, Gd, Er

$(NH_4)_6[Ln_3Fe_5(C_4O_6H_4)_6(C_4O_5H_5)_6]\cdot16H_2O$ (**II**)
where Ln(III) = Gd, Er

$(NH_4)_6[Y_3Fe_5(C_6O_7H_{10})_6(C_6O_7H_9)_6]\cdot8H_2O$
$(NH_4)_6[Ln_3Fe_5(C_6O_7H_{10})_6(C_6O_7H_9)_6]\cdot22H_2O$ (**III**)
where Ln(III) = Eu, Er

The complex precursors were characterized by chemical analysis, IR and UV-Vis spectra, magnetic measurements and thermal analysis.

Single phase rare earth iron garnets obtained were characterized by XRD, IR spectra, magnetic measurements. The average particle size of these garnets ranged between 26 – 35 nm.

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Kinetics and Mechanism of the Reactions Between Pt(II) and Pd(II) Complexes with Sulfur-Bonding Ligands

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The aqueous solution chemistry of Pt(II) complexes has been extensively studied during recent decades, owing to the anti-cancerous activity of cisplatin and related compounds.[1,2] The interactions of Pt(II) with sulfur-bonding ligands are very important from biological and medical point of view. Although the platinum interactions with DNA are held responsible for their antitumor activity, there are many other potential biomolecules that can react with Pt(II) complexes. The sulfur containing molecules play a significant role in the metabolism of platinum-based antitumor complexes. Binding of cisplatin to intracellular thiols is known to be the reason for its renal toxicity and other side effects.[1]

To study these interactions, a very suitable compound appeared to be monofunctional $[Pt(dien)Cl]^+$ (dien = 1,5-diamin-3-azapentane). However, Pd(II) complexes are very useful models for studying the kinetics of Pt(II) complexes, because their behavior in the solutions is very similar.[3]

In order to get more information about the interactions between Pt(II) complexes and S-bonding ligands, we were studied the substitution reactions between monofunctional $[Pt(dien)OH_2]^{2+}$ and $[Pd(dien)OH_2]^{2+}$ with L-cysteine and S-methyl-L-cysteine as a function of temperature and pH. All kinetic measurements were performed under pseudo-first-order conditions with large excess of the nucleophiles. The significantly negative activation entropies suggest that the activation process in the studied systems seems to be strongly dominated by bond making and the mechanism is associative A or I_a. These reactions were followed at different pH values (0.5 -1.5) as well.

Comparing the rate constants it can be seen that the Pd(II) complexes is about 10^3-10^4 times more reactive than corresponding Pt(II) complex. It has been found that the rate constants, k_1, of the substitution processes increased with the increasing of pH.

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Influence of the Nature and Textural Properties of Different Supports on the Thermal Behavior of Keggin Type Heteropolyacids

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In order to obtain highly dispersed heteropolyacids (HPA) species, $H_3PMo_{12}O_{40}$ and $H_4PVMo_{11}O_{40}$ were supported on various supports: silica (Aerosil- Degussa and Romsil types), TiO_2, SiC.
The thermal decomposition of supported and unsupported HPA has been followed by different techniques (TGA-DTA, FT-IR, UV-VIS-DRS, XRD, low temperature nitrogen adsorption, scanning electron microscopy).
All supported HPA were prepared by impregnation using the incipient wetness techniques with a mixture water: ethanol = 1:1. Samples were prepared with different concentration to examine the effect of loading on the thermal behavior of supported acid catalysts. The thermal stability was evaluated in reference to the bulk solid acids and mechanical mixtures.
By deposition on silica types supports an important decrease of thermal stability was observed on Romsil types and a small decrease on Aerosil type. The stability of the heteropolyacids supported on titania increases due to the anion-support interaction as the thermal decomposition proceeds in two steps. The structure of HPA is not totally destroyed at 723K as some IR bands are still preserved.
A relatively uniform distribution of HPA on the support surface is observed for all compositions of active phase. No separate crystallites of the bulk phase of HPA were found in the SEM images.
The UV-VIS-DRS spectra exhibit a single maximum of LMCT at 320 nm, as HPA's protons are connected to oxygen atoms of silica surface and do not exert their strong polarisation action on electron shell of KU.

Lanthanide Complexes of Propanediaminetetramethylenephosphonic Acid

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Propanediaminetetramethylenephosphonic acid (PDTMP, H_8L) was prepared and its complexes with some lanthanide ions (La, Eu, Gd and Sm) have been isolated under various conditions. IR spectra and thermal stabilities of PDTMP and its complexes were studied in order to get compounds as potential contrast agents in magnetic resonance imaging.

Synthesis and Characterization of a Mononuclear Vanadyl Complex with the Non-Steroidal Anti-Inflammatory Drug Piroxicam

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Piroxicam, H_2*pir*, (figure 1) is a potent and extensively used non-steroidal anti-inflammatory drug (NSAID), and an anti-arthritic drug with a long biological half-life, which acts by inhibiting enzymes involved in the biosynthesis of prostaglandins [1]. Piroxicam, a potentially tetradentate ligand, is known to react as a monodentate ligand through the pyridyl nitrogen towards Pt(II) [2], as a bidentate chelating ligand via the pyridyl nitrogen and the amide oxygen, towards Cu(II) and Cd(II) [3] and as a singly deprotonated tridentate ligand through the enolic oxygen, the pyridyl and the amide nitrogen atoms in the tin(IV) complex [4]. Vanadium is an ultramicrotrace bioelement with interesting biological properties [5]. In the literature, the synthesis and the bioactivity of VO^{2+} complexes with the NSAIDs tolmetin, ibuprofen, naproxen [6] and aspirin [7] has been recently reported.

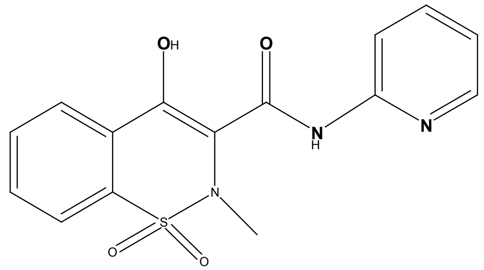

Figure 1. Piroxicam, H_2pir. (in bold the potential coordination sites)

We have initiated studies on the piroxicam-metal interaction in an attempt to examine their mode of binding and possible synergetic effects. In this paper we report the synthesis and study of the mononuclear VO^{2+} complex with piroxicam.

The reaction of vanadyl sulfate with the simply deprotonated piroxicam in methanol has led to the green microcrystalline complex VO(H*pir*)$_2$(H_2O) (**1**). The complex has been characterized with elemental analysis, IR, UV-Vis and EPR spectroscopy. The existing data suggest that the geometry round V can be described as octahedral with two bidentate piroxicam ligands bound to VO^{2+} via the pyridyl nitrogen and the amide oxygen occupying the base of the octahedron and the water oxygen lying in trans-position to the vanadyl oxygen. The EPR spectrum (figure 2) of the complex in *dmso* at 17K is typical of a mononuclear octahedral VO^{2+} complex with $A_{||}$=172(1)x10^{-4} cm^{-1} supporting an N_2O_2 base [8].

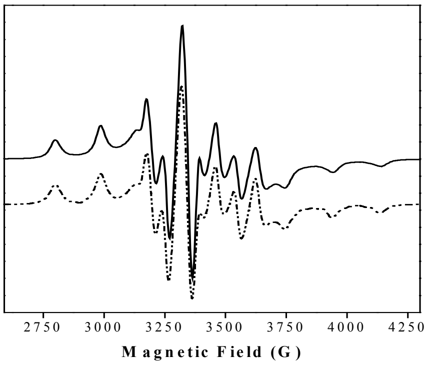

*Figure 2. Experimental (–) and theoretical (˙ ˉ ˙) EPR spectrum for (**1**) in dmso.*

The development of crystals suitable for the determination of the crystal structure with X-ray analysis as well as the biological study of the complex are still under research.

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Structure of a New Nickel(II) Complex Containing the Pyromellitate Ion and 2,2'-Bipyridine, $[Ni_2(C_{10}H_2O_8)(C_{10}H_8N_2)_2(H_2O)_6]\cdot 2H_2O$

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The title binuclear complex is obtained as a part of our studies on ternary transition metal complexes containing tetraanion of pyromellitic (1,2,4,5-benzenetetracarboxylic) acid, pyr, and some aromatic diamines, as 2,2'-bipyridine, bipy [1–3]. Due to presence of four carboxylate groups, pyr can coordinate in numerous ways, acting as a bis-monodentate [3,4] or polydentate [5] ligand having a bridging, chelating or combined function.

The blue single crystals were obtained by slow diffusion of two, A and B, solutions through a glass filter. The solution A contained $5.0\cdot10^{-4}$ mol of each $Ni(NO_3)_2\cdot6H_2O$ and bipy in a H_2O–EtOH mixture, whereas B was solution of Na_4pyr ($c = 0.01$ mol dm^{-3}) in water. The first crystals appeared within a 24 h period, but the single crystals of a suitable size were filtered off after about 10 days.

Crystal data: $C_{30}H_{34}Ni_2N_4O_{16}$, $M_r = 824.04$, triclinic, space group P–1, $a = 7.5784(1)$, $b = 9.712(2)$, $c = 11.968(2)$ Å, $\alpha = 76.89(2)$, $\beta = 87.32(1)$, $\gamma = 79.85(2)$ °, $V = 844.4(3)$ Å^3, $Z = 1$, $F(000) = 426$, $\rho_x = 1.620$ g cm^{-3}, μ(Mo Kα) = 1.197 mm^{-1}, $R_1 = 2.93$ % for 2926 observed reflections [$I > 2\sigma(I)$], $R_{w2} = 7.77$ % (refinement on F^2) for 3303 independent reflections and 235 refined parameters, with $\Delta\rho_{max} = 0.347$ and $\Delta\rho_{min} = -0.423$ e Å^{-3}.

In described compound, pyr acts as a bridge and it is coordinated as bis-monodentate ligand with two uncoordinated COO groups. The centre of symmetry is coinciding with the centre of pyr aromatic ring. Ni(II) ions are in distorted octahedral environment consisting of two N atoms (from bipy) and four O atoms (three from H_2O molecules and one from COO group). The bond distances [2.0510(1) – 2.0841(2) Å] and angles [79.72(7) – 92.00(7) °] are in accordance with similar complexes. Beside three coordinated H_2O molecules per one Ni(II) atom, two lattice H_2O molecules are also present in the structure.

The binuclear coordination unit of the title compound is very similar to the recently described complexes with different aromatic diamine ligands: $[Co_2(pyr)(phen)_2(H_2O)_6]\cdot2H_2O$, phen = 1,10-phenanthroline [1] and $[Ni_2(pyr)(dipya)_2(H_2O)_6]\cdot4H_2O$, dipya = 2,2'-dipyridylamine [2].

Crystal packing is governed by a 3-D network of intermolecular hydrogen bonds, which are in the range of 2.672(3) – 2.777(3) Å, and with O–H…O angles between 156.8(1) and 177.3(1) °. All coordinated H_2O, as well as the lattice H_2O molecules are double H bond donors, while the lattice H_2O molecules are acceptors, too. There are four intramolecular H bonds between coordinated H_2O and free O atoms from COO groups [2.695(2)×2 and 2.983(3)×2 Å]. Two H bonds between lattice H_2O and O atoms from coordinated COO groups also exist [2.672(2)×2 Å].

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Design of New Mono- and Polynuclear Squarate-Complexes

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The squarate dianion, $C_4O_4^{2-}$, is an interesting aromatic moiety with structural particularities (a set of four oxygen donors, planar stereochemistry, *p*-electron delocalization) that can act as a μ-bridging ligand between metals and serve as a pathway for magnetic superexchange interaction between paramagnetic ions. Several metal squarates have indeed been reported in the literature and in the light of the structures of squarate-metal complexes reported so far it is clear that *chelation* by this ligand is limited to some alkaline- and rare-earth metal cations[1]; for the squarate coordination chemistry with 3*d* ions, a wide variety of binding modes[2,3] has been found: monodentate, μ-1,2-bis(monodentate), μ-1,3-bis(monodentate) and tetrakis(monodentate).

We synthesised a new series of the mono- and polynuclear complex compounds of Cu(II), Mn(II), Fe(III) and Cr(III), where the bridging ligand is squarate, coordinated in μ-1,3- or μ- 1,2- bis(monodentate) manner.

1,10-phenantroline and *p*-chloro-benzene-pyridazyl-hydrazine (L) have been used as blocking ligands to control the polymerisation process and to make possible the isolation of homo- and heterodinuclear complexes of Cu(II), Mn(II), Fe(III) and Cr(III).

Magnetism and Mössbauer, IR, and electronic spectroscopic studies support the structures of the synthesised squarate complexes.

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Substitution Reactions of $[Pt(terpy)X]^{2+}$ with Some Biologically Relevant Ligands

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The anti-tumour activity of cisplatin, is ascribed to interactions between the complex and DNA.[1] There are many other potential biomolecules that can also react with Pt(II) antitumor active complexes, such as proteins and enzymes. Sulfur-containing molecules have a high affinity for platinum and could form very stable bonds. Moreover, the interaction of Pt complexes with sulphur-containing biomolecules has been associated with negative phenomena, such as neprotoxicity, gastrointestinal toxicity, ototoxicity and neurotoxicity.[1]

There has been much interest in studying the interaction of platinum complexes with sulfur containing biomolecules.[1,2] With the aim to get more information about these interactions, we have now performed and report here a detailed study on the complex-formation kinetics of substitution reactions of the complexes $[Pt(terpy)H_2O]^{2+}$, $[Pt(terpy)(cyst\text{-}S)]^{2+}$ and $[Pt(terpy)(guo\text{-}N7)]^{2+}$, where terpy = 2,2':6',2''-terpyridine, cyst-S = L-cysteine and guo-N7 = guanosine, with some biologically relevant ligands such as inosine, inosine-5'-monophosphate, guanosine-5'-monophosphate, L-cysteine, glutathione, thiourea, thiosulfate and diethyldithiocarbamate. These reactions were studied in aqueous solutions, 0.10 M Bis-Tris at pH 7.2 using variable-temperature spectrophotometry. The reactions of $[Pt(terpy)H_2O]^{2+}$ with INO, 5'-IMP and 5'-GMP showed that these ligands are very good nucleophiles. The second order rate constants varied between 5×10^2 and 7×10^2 $M^{-1} s^{-1}$ at 25 °C. The $[Pt(terpy)(cyst\text{-}S)]^{2+}$ complex is unreactive towards nitrogen donor nucleophiles, and cysteine cannot be replaced by N7 from INO, 5'-IMP and 5'-GMP. However, sulfur donor nucleophiles such as thiourea, thiosulfate and diethyldithiocarbamate could displace the Pt-cysteine bond. Diethyldithiocarbamate is the best nucleophile and the order of reactivity is: thiourea $<$ thiosulfate $<$ DEDTC. The reactions of $[Pt(terpy)(guo\text{-}N7)]^{2+}$ with sulfur donor ligands showed that these nucleophiles could substitute guanosine from the Pt(II) complex, of which diethyldithiocarbamate and thiosulfate are the strongest nucleophiles.

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Synthesis and Characterization of 3d Metal Complexes with 2,6-Diacetylpyridine Bis(selenosemicarbazone)

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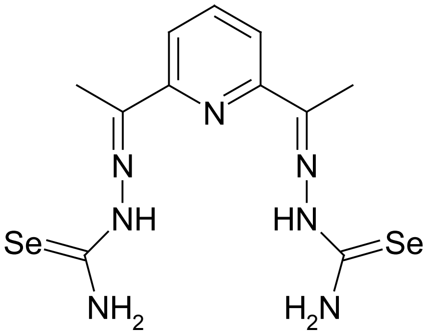
Selenosemicarbazones and their complexes where found to have antimalarical and antifungal activities.

The subject of this work is synthesis of 2,6-diacetylpyridine bis(selenosemicarbazone) and its complexes with 3d metals.

Acetone selenosemicarbazone was synthesized starting from acetone, hydrazine hydrate and KSeCN[1], and was transformed to selenosemicarbazide by reaction with hydrazine hydrate in methanol[2]. 2,6-Diacetylpyridine bis(selenosemicarbazone) (*Scheme 1*) was obtained by reaction of selenosemicarbazide with 2,6-diacetylpyridine (mole ratio 2 : 1) in 5% acetic acid, and recrystallized from chloroform.

2,6-Diacetylpyridine bis(selenosemicarbazone) was used as a ligand for synthesis of complexes with 3d metals (Fe(II), Ni(II), Co(II) and Cu(II)). The complexes were characterized by elemental analysis, IR and UV/VIS spectroscopy, magnetic and conductivity measurements.



Scheme 1

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Barbituric Derivatives: Synthetic and Spectral Aspects of Mono- and Dinuclear Copper(II), Cobalt(II) and Nickel(II) Complexes

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The synthesis and characterization of the Mannich base N,N'-bis-(5,5'-diethyl-barbituryl-1-methyl)-piperazine, (VEP), is reported. VEP can act as a mono- or dinucleating ligand depending on the conformation of the piperazine bridge. Mono- and dinuclear copper(II), cobalt(II) and nickel(II) complexes have been obtained by metal – ligand direct synthesis, by varying the solvent and counterion nature, temperature and metal to ligand molar ratio. The complexes have been characterized by elemental analysis, electric conductivities, Uv-Vis and IR spectroscopy in order to obtain information regarding their structure.

Hypervalent Organotin(IV) Compounds with Intramolecular Coordination

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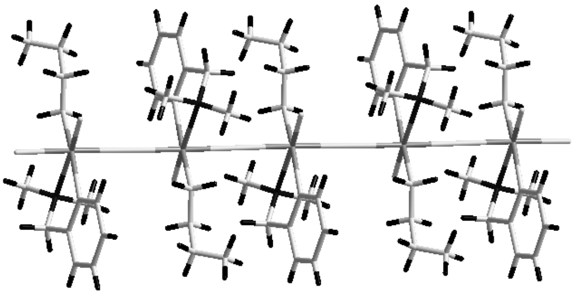
$[2\text{-}(Me_2NCH_2)C_6H_4]SnBuCl_2$ (**1**) was prepared by reacting $BuSnCl_3$ with $[2\text{-}(Me_2NCH_2)C_6H_4]Li$ in hexane. Reactions of (**1**) with excess of potassium fluoride afford isolation of $[2\text{-}(Me_2NCH_2)C_6H_4]SnBuF_2$ (**2**) as a white crystalline solid. Compounds containing a bridging sulfur atom or a carbonato group, $[\{2\text{-}(Me_2NCH_2)C_6H_4\}SnMe_2]_2S$ (**3**) and $[\{2\text{-}(Me_2NCH_2)C_6H_4\}SnMe_2]_2(CO_3)$ (**4**), were isolated after the reaction of $[2\text{-}(Me_2NCH_2)C_6H_4]SnMe_2Cl$ with excess of Na_2S or Na_2CO_3 All compounds were investigated in solution by multinuclear NMR spectroscopy. The molecular structure of **1** - **4** was determined by single-crystal X-ray diffraction. The crystals of **1** contain monomeric units with the metal atom exhibiting a distorted trigonal bipyramidal coordination environment. The monomeric units form a supramolecular architecture through Cl···H intermolecular interactions. Compound **2** is polymeric, with an octahedral coordination geometry around the central tin atom. The structures of **3** and **4** consist of two $[2\text{-}(Me_2NCH_2)C_6H_4]SnMe_2$ linked by a bridging sulfur or carbonato fragments. In both cases the tin atom is pentacoordinated. The N atom of the pending CH_2NMe_2 arm is strongly coordinated to the metal centre [Sn-N 2.458(5) Å for **1**, 2.494(4) Å for **2**, 2.805(3) and 2.786(5) Å for **3**, 2.636(4) and 2.551(3) Å for **4**, respectively], *trans* to Cl, F, S or O atoms [N(1)-Sn(1)-Cl(1) 171.61(15)° for **1**, N(1)-Sn(1)-F(1) 170.57(11)° for **2**, N(1)-Sn(1)-S(1) 168.45(8) and N(2)-Sn(2)-S(2) 172.49(11)° for **3**, N(1)-Sn(1)-O(1) 164.24(9) and N(2)-Sn(2)-O(2) 169.21(9)° for **4**, respectively].



$[2\text{-}(Me_2NCH_2)C_6H_4]SnBuF_2$ (2)

Complexes of Mg(II), Zn(II) and Cd(II) with N-Carbobenzyloxyglycine

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Structure-anticonvulsant activity studies of glycine derivates have shown that in the case of mono-supstitution, N-supstitution is more important than amidation or esterification of the carboxylate group and that the N-carbobenzyloxyglycine is the most interesting compound tested [1]. In spite of that, in the literature there are no data about the complexes with N-carbobenzyloxyglycinato ligand. Because of that we have undertaken in first instances a syntheses of these complexes exploring Mg(II), Zn(II) and Cd(II)-ions. Magnesium and zinc take part in the function of human body, but cadmium is toxic.

In this paper we have described syntheses of new complexes with N-carbobenzyloxyglycine and Mg(II), Zn(II) and Cd(II)-ions. The complexes are characterized with elemental analysis, IC, ^{1}H and ^{13}C NMR spectroscopy. The structure of these complexes is proposed, and investigation of biological activity of these complexes are in progress.

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Synthesis and Crystal Structure of $[Cu(3,5\text{-}Me_2Pz)_2Cl_2]_2$

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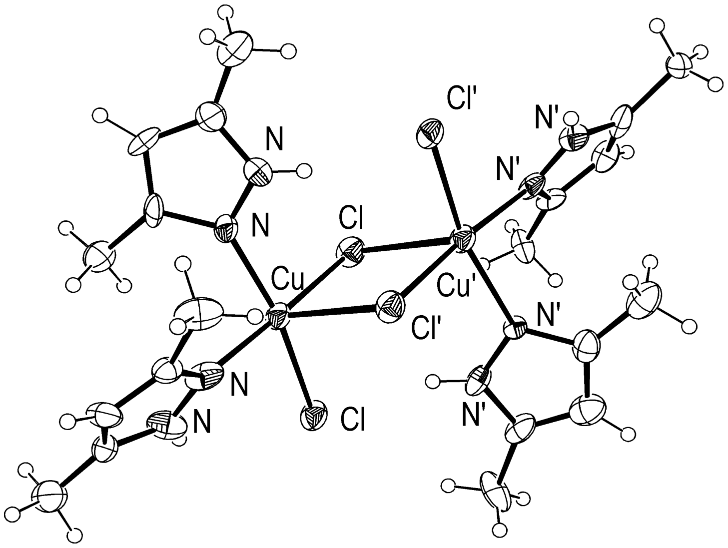
In a attempt to prepare a Cu(II) complex with Schiff base derivative if Girar-T reagent and acetylacetone we unexpectedly obtained the green monocrystals of title complex $[Cu(3,5\text{-}Me_2Pz)_2Cl_2]_2$, where $3,5\text{-}Me_2Pz$=3,5-dimethylpyrazol.

Binuclear Cu(II) complex has a centrosymmetric structure where center of symmetry is located at the mid-point of the Cu…Cu' line. Two mononuclear halves are slightly different what was the reason that the $P2_1/c$ space group was unappropriate for crystal structure refinement. Each Cu atom has square-pyramidal surroundings with the apical position being taken by bridging Cl atom. Orientation of monodentate pyrazol ligands are caused by the intramolecular N-H…Cl hydrogen bonds with an H…Cl distance of about 2.36 Å.

The X-ray data were collected on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated Mo-$K\alpha$ radiation. This experiment was performed at a room temperature using $\omega/2\theta$ technique to a maximum 2θ values of 52 °. Based on statistical analysis of intensity distributions (and systematic absences) it was established that the complex crystallizes in the $P2_1$ space group instead of $P2_1/c$ space group previously indicated for low-temperature X-ray data [1]. The structure was solved by direct methods and difference-Fourier methods, and refined by full matrix least-squares using SHELXL97 program to a final R1 = 0.0972 for 2741 reflections with $I > 2\sigma_I$.

Crystallographic data: $Cu_2\ C_{20}\ H_{32}\ Cl_4\ N_8$, Mr = 653.42, monoclinic, space group $P\ 2_1$, a = 8.741(3)Å, b = 13.780(4) Å, c = 11.846(3) Å, β = 106.42(2) °, V = 1368.7(7) Å^3, Z = 2, D_c = 1.585 Mg/m^3, $\mu(MoK\alpha)$ = 1.970 mm^{-1}, Mo $K\alpha$ radiation, λ = 0.71073 Å, GooF = 1.115.



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Brass Corrosion Inhibitors

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The aim of this investigation is following the corrosion potential of brass with various deformation degrees in acidic sulphatic solution without and with addition of corrosion inhibitors. Due to the influnce of copper and chloride ions on corrosion damages of devices and equipment made of brass, the obtained investigation results were, besides contribution to knowing of corrosion mechanisms and reaction rate, also important to the major interest for metal protection in practice.
Investigations were carried out with CuZn-42 brass, with five deformation degrees (0%, 20%, 40%, 60% and 80%), in 0.1M solution of Na_2SO_4, at pH-value 2, with addition of copper and chloride ions. The followings were used as corrosion inhibitors:benzothiazole (BTA), thiourea, ethylene diamino tetra acetate (EDTA), hydrazine sulphate (HS) and 2-butyn-1.4 diol (DS-3), in concentrations of $1 \cdot 10^{-2}$% and $1 \cdot 10^{-1}$%. BTA, thiourea, hydrazine sulphate, DS-3 and EDTA, have been used as effective acid corrosion inhibitors [1,2,3,4,5]. Based on recorded anode polarisation curves, the values of corrosion potentials were determined as well as corrosion current densities. Protection degreee of inhibitors was discussed by degreee of inhibitor efficiency.
Previous scientific investigations in the field of copper and copper alloys corrosion, have given the certain results and pointed out what matters and under what circumstances have an inhibiting influence regard to corrosion. Very often used inhibitor of copper corrosion in acidic and alkaline media is BTA. BTA forms protective Cu-BTA film [1] on copper and brass surface. Sayed at al. [2,3] studying the effect of BTA on α-brass exposed to a nitrate solution concluded that the presence of BTA inhibited the dissolution of brass due to the formation of a copper oxide layer on the brass surface. Evaluation of the effect of BTA on copper and zinc alloys exposed to H_2SO_4 suggested that BTA is a good inhibitor for copper and copper-zinc alloy, but not for pure zinc [4]. Brass is widely used in various industrial operations and the study of corrosion of brass and inhibition is a subject of practical importance.
In solution of 0.1 M Na_2SO_4, with addition of copper ions, the all analyzed corrosion inhibitors in concentration of $1 \cdot 10^{-2}$% show the inhibiting effect. BTA has the highest inhibiting degree (from 88% to 95%), where inhibiting degree drops in a range: BTA > thiourea > DS-3 > EDTA > HS.
In solution of 0.1 M Na_2SO_4, with addition of chloride ions and in inhibitor concentration of $1 \cdot 10^{-2}$%, only thiourea shows the inhibiting effect, with inhibiting degrees from 53% to 63%. The other inhibitors show the activation influence on corrosion process.
In solution of 0.1 M Na_2SO_4, with addition of chloride ions and in inhibitor concentration of $1 \cdot 10^{-1}$%, BTA inhibitors show the inhibiting effect (with inhibiting degrees from 94% to 97%) and thiourea (with inhibiting degrees from 5% to 59%). The other inhibitors show the activation influence on corrosion process. Deformation degree of brass samples has no important influence on inhibiting degree of corrosion process.

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Electrochemical Deposition of Pb Across the TiO_2 Layer on a Titanium Surface

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Titanium belongs to a group of valve metals and may be covered either spontaneously or electrochemically by a passivating oxide layer. This layer is mainly TiO_2 which is semiconductor in nature: i.e. it permits reduction reactions, but suppress the oxidation reactions(1,2). If covered by noble metals or oxides, it serves for important industrial sytheses, for instance for either chlorine or oxyhalogenide salts production(3,4). Electrocatalyst layer, for instance ruthenium dioxide(3,4), is deposited usually by thermal decomposition of noble metal salts.

In this work the cathodic deposition of lead on Ti surface was examined, followed by conversion of metallic to lead dioxide. As an electroplating solution, diluted lead nitrate in 0.1 M $KClO_4$ was used. Prior to titanium electroplating, lead electrodeposition procedure was proven using platinum electrode. When platinum was polarized in the lead nitrate solution used, lead evolution was observed at -0.4 V vs. SCE and limiting diffusion current was attained. If polarized in opposite direction, anodic dissolution occured at the potential identical to the one of cathodic deposition, thanks to the high solubility of lead perchlorate. However, when the electrode covered by Pb layer was treasferred into 1M Na_2SO_4 solution, and polarization cycle was done, starting with the cathodic one, conversion of lead firstly to insoluble sulphate and then to insoluble dioxide layer was observed.

When titanium was used, to suppress fast selfpassivation, freshly dry-polished Ti electrode was dipped into plating perchlorate solution under cathodic polarization of -1 V vs.. SCE, at which the self-formation of TiO_2 is very slow(1) , and after sufficient time of lead electrodeposition, the plating solution was replaced by sulphate solution. In sulphate solution, polarization cycle was carried out in anodic direction, starting from the cathodic potential at which lead was deposited. During polarization in the anodic direction, conversion of metallic lead to sulphate and further to dioxide was observed on the basis of corresponding current peaks. Simultaneously, TiO_2 layer was thickened around the PbO_2 particles, on the basis of anodic oxidation. In this manner, conductance of the Ti/TiO_2-PbO_2/electrolyte surface was provided in anodic polarization region, based on the electronic conductivity of lead dioxide. This enabling the oxidation (iodides, bromides, hexacianoferrates) reactions on its surface, during of which, thanks to the particulate nature of PbO_2, the surface displayed the behaviour of microelectrode arrays(5)..

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Mechanisms of Chromium Dissolution Processes in Sulfate Solutions in the Acid to Neutral pH Range

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It has been shown elsewhere [1] that metallic chromium in deaerated aqueous sulfuric acid solutions behaves either as a passive metal, when introduced into the solution after being previously in contact with air, or as an active metal, if activated by a short cathodic pulse. In the passive state Cr attains an open circuit (or corrosion) potential, $E_{corr,1}$, while in activated state more negative open circuit potential, $E_{corr,2}$, was obtained. They were in the range of –0.4 V to –0.7 V (vs. SCE) for pH ~ 1 , and pH dependent. In the active state Cr dissolves with the simultaneous formation of Cr(II) and Cr(III) ions in the ratio 7:1.

Anodic Tafel lines in the active dissolution region have slopes $b_{a,a}$ ~ 120 mV dec^{-1} and reaction order $n_{H^+} = 0$, i.e., anodic reaction is pH independent (process **I**). Simultaneously, Cr dissolves by a non-electrochemical process, in a direct chemical reaction of Cr with H_2O molecules of the solvent, which is potential independent, but include H^+ ions, as proposed by Kolotyrkin et al. [2](process **II**). Active dissolution state of Cr cannot be achieved in solution with pH > 3, when Cr is always in the passive state, with stable hydrogen evolution during cathodic polarization but on the oxidized Cr surface, similarly to the case when Al was cathodically polarized [3]. Anodic polarizations of passive Cr starting from the $E_{corr,1}$ potential show the Tafel dependence with $b_{a,p}$ ~ 240 mV dec^{-1}, with an independence of the anodic process on the solution pH (process **III**).

Summarizing the experimentally obtained kinetic data and diagnostic criteria for the dissolution of Cr in sulfate solutions in the pH range 0.5 – 6, **three** Cr dissolution mechanisms are proposed:

- For the dissolution of Cr in an **active state** in solutions with pH < 3 simultaneous occurring of processes **I** and **II** :

  Process **I** :
  $Cr + H_2O \rightarrow CrOH_{ads} + H^+ + e^-$ (1)
  $CrOH_{ads} \leftrightarrow Cr^{2+} + OH^- + e^-$ (2)
  $Cr^{2+} \leftrightarrow Cr^{3+} + e^-$ (only 1/8) (3)

  Process **II**
  $Cr + H_2O \leftrightarrow CrOH_{ads} + H$ (4)
  $CrOH_{ads} + H^+ \rightarrow Cr^{2+} + H + OH^-$ (5)
  $2H \rightarrow H_2$ (6)

- For the dissolution of Cr in **passive state** (pH 0.5 – 6)

  Process **III**:
  $2Cr + 3H_2O = Cr_2O_3 + 6H^+ + 6e^-$ (7)

with the detailed mechanism not clear as yet, but reaction controlled by the charge transfer step through the oxide layer, similar to the dissolution of Al in passive state [3].

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Kinetic Analysis of Hydrogen Evolution at Fe-Mo Alloys in Alkaline Solution

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The hydrogen evolution reaction (HER) on Fe-Mo alloys was investigated by using electrochemical impedance spectroscopy and dc polarization measurements in 1.0 mol dm^{-3} NaOH solution at 25 ^{0}C.

Fe-Mo alloys of different composition were deposited at the constant current density, on mild steel substrate, from pyrophosphate bath, at 60 ^{0}C. The rate constants of the forward and backward reaction of Volmer, Tafel and Heyrovsky steps were estimated by a nonlinear fitting method. It was found that at the lower overpotentials Tafel step is rate determining. At the higher overpotentials Heyrovski and Volmer steps were found as rate determining. Fe-Mo alloy deposited at the constant current density of 100 mA cm^{-2} exhibits the best catalytic activity for HER as a consequence of both, alloy composition and increased electrode surface area.

Voltammetric Behavior and Study of N, N'-Bis-(phenyl cynnamaldehyde) Pheneylenediimine at a Glassy Carbon Electrode in Dimethylformamide (DMF)

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The electrochemicals reduction of diimine compounds and their Schiff bases complexes has, during four decades, been the subject of many investigations. Their complexes play an important role in many electrocatalytic processes [1-4].

In the present study the electroreduction of N,N'-Bis(phenyl cynnamaldehyd) pheneylenediimine at glassy carbon electrode in DMF by classical voltammetry (DC), differential pulse voltammetry (DP) ,cyclic voltammetry (CV) and controlled potential electrolysis was investigated.b In DMF this compound is reduced in two cathodic processes at -1.45 to -1.65 and -2.4 to -2.6 Volt. Both of these cathodic peaks are irreversible and due to linearity of their current with concentration, are diffusion controlled. The cyclic voltammetry and chronoamperometry has been employed to study the mechanism of this cathodic processe. The influence of scan rate on the current function ($i_p/v^{1/2}$) shows an EC mechanism. The ratio of I_f/I_b in chronoamperometry was also confirmed EC mechanism.

Finally, the mechanism of these cathodic peaks and some electrochemical parameters such as diffusion coefficient, transfer coefficient and protonation constant were reported.

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Corrosion Rate Measurements of Carbon Steel in CO_2/H_2S Saturated Aqueous Brine Solutions

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Considerable work had been done to define effects of CO_2 and H_2S on corrosion rates of pipelines[1-3]. However, little effort has been spent on the subject of CO_2 contaminated with small amount of H_2S[4].

Research has put more light on the effect of temperature, PH, flow and other parameters that have an impact on corrosion processes[5-10] trying to understand the mechanisms through which CO_2 and H_2S act upon metallic surfaces[11]. Advances in the area of corrosion research have provided a greater understanding of the phenomena of corrosion. These efforts have led to different models, correlations or charts[12,13]. On the other hand, current corrosion models and mathematical correlations used for the prediction of corrosion rate consider essentially the presence of CO_2 on the steels, neglecting the effect of H_2S, despite a number of efforts made towards learning about the corrosion processes in the complex systems CO_2 / H_2S / H_2O. This is basically due to the incomplete knowledge of the synergistic relationship between CO_2 and H_2S.

CO_2/H_2S corrosion in oil and gas production environments represent one of the most important areas of corrosion in Albania. Pipelines used for transmission of natural gas and crude oil tank are exposed to the action of the contaminating agents diluted in liquid water. CO_2 and H_2S are the contaminants that worries the most to the pipeline operator, mainly due to the variety of damages (localized corrosion, cracking and hydrogen embrittlement among others) they may cause. Low cost carbon steel is generally used as construction material in these facilities. This is why the corrosion coupons used throughout this investigation were from the same carbon steel. This work was developed using weight loss experiments of samples in a CO_2, H_2S and CO_2/H_2S saturated, stirred brine solution. The tests were performed at 20°C.

Scanning electron microscope (SEM) and EDX methods were used to analyse corrosion products and to study surface morphology. The following conclusions can be drawn from the present work:

1. Hydrogen sulfide strongly effects the corrosion rate of carbon steel.
2. Carbon dioxide effects the corrosion rate of carbon steel to a lesser degree than H_2S.
3. The combination of CO_2 and H_2S did yield the lowest corrosion rate.

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On the Reaction Paths in Methanol Oxidation on Polycrystalline Pt

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Methanol oxidation is an important electrochemical reaction from both practical and fundamental aspects because it is anodic reaction in the direct methanol fuel cell (DMFC) and a prototype of the oxidation of small organic molecule. Although the reaction has been extensively investigated over the decades, there is still no consensus in the literature whether methanol oxidizes through one serial path or two parallel paths are operative. In this communication an influence of the convection of the electrolyte on the kinetics of the methanol oxidation was used as a criterion for the occurrence of the different reaction paths.

Methanol oxidation was investigated on a stationary and a rotating disk electrode with smooth polycrystalline Pt as the electrode material. Quasi steady-state polarization curves were recorded by linear potential sweep of 1 mV/s in 0.02 M to 1 M $HClO_4$ solution with 10^{-4} M to 1 M CH_3OH at 30 °C. The methanol oxidation rate was found to be about ten times lower on the rotating electrode than on the stationary one in all electrolytes examined. No significant influence of the rotation rate of the electrode was found, *i.e.* the current densities on the electrode rotating between 500 and 2000 rpm were the same within experimental error. The Tafel slopes were ~90 mV/dec on the stationary and ~120 mV/dec on the rotating electrode. Influence of the methanol concentration on the reaction rate is presented in Fig.1. On the stationary electrode the reaction order with respect to methanol was found to be 0.23 over four decades of the methanol concentration. However, a curved line fitted through the data for the rotating electrode is a transition of the reaction order of 0.5 to the reaction order of zero. On both stationary and rotating electrode the reaction order with respect to H^+ was -0.7. Comparing these results with the recent DEMS [1] and HPLC [2] studies of methanol oxidation on smooth Pt surface, it can be proposed that two parallel pathways are operative: one via strongly adsorbed CO and the other via soluble intermediates like formaldehyde and/or formic acid. On the rotating electrode formaldehyde diffuses away from the electrode and the path via strongly adsorbed CO is predominant. In the quiescent electrolyte formaldehyde is further oxidized to formic acid and CO_2. Much higher reaction rate in the quiescent electrolyte indicates that the reaction path via formaldehyde is significantly faster than the path via strongly adsorbed CO. Thus, strongly adsorbed CO is not a poison, but a reactive intermediate which oxidation rate is rather low.

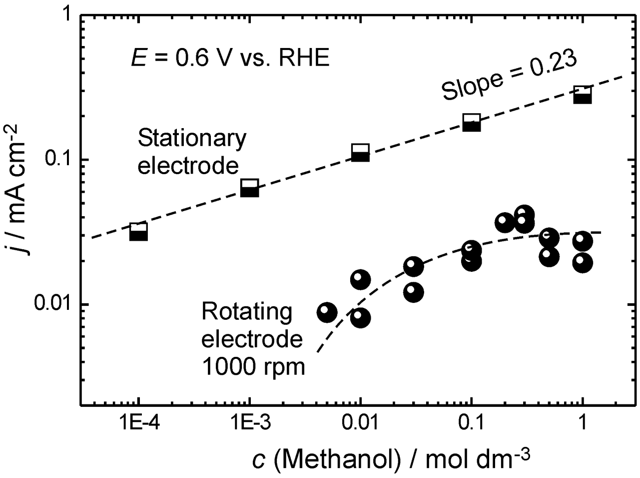

Fig.1.
Reaction rate of methanol oxidation as a function of the methanol concentration at the constant potential of 0.6 V (middle of the linear Tafel region) in 0.1 M $HClO_4$.

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Hydrogen Evolution and Oxygen Reduction on Gold-Platinum, Platinum-Gold Modified Surfaces in Acid Solution

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Hydrogen evolution (HER) and oxygen reduction reactions (ORR) on platinum modified gold electrode (Au–Pt) and gold modified platinum electrode (Pt–Au) in sulfuric acid solutions have been investigated and compared with pure metals. Surface modification of the electrodes has been conducted from sulfuric acid solutions containing corresponding metal-chloride complexes using cyclic voltammetry. Comparing the charges of hydrogen underpotential deposition region, and corresponding oxide reduction regions, it has been concluded that platinum overlayer on gold forms 3D islands, while gold on platinum forms 2D islands. Platinum overlayer on gold substrate increases activities for HER and ORR, comparing with pure gold, with the same mechanism as on pure platinum. On the contrary, gold layer on platinum slightly decreases activity for both reactions comparing with pure platinum. Mechanism for HER is more platinum like, while mechanism for ORR is combination of two and four electrons paths depending on the electrode potentials.

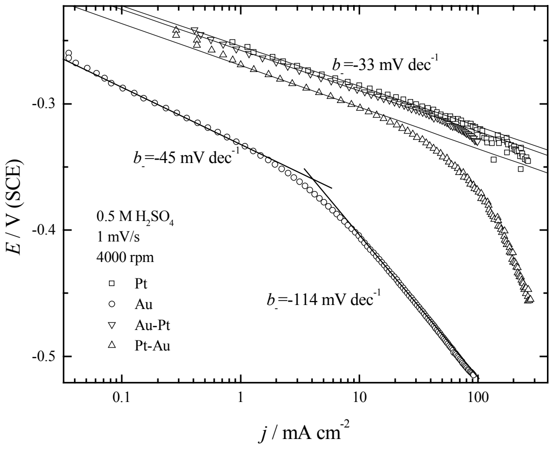

Figure 1. Polarization curves (IR corrected) for hydrogen evolution reaction on Pt, Au, Pt–Au and Au–Pt electrodes.

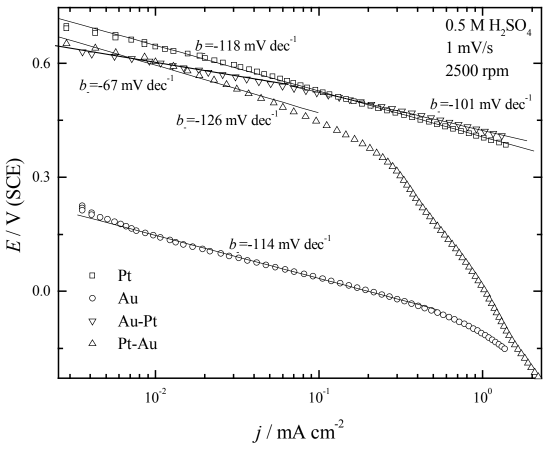

Figure 2. Polarization curves for oxygen reduction reaction on Pt, Au, Pt–Au and Au-Pt electrodes. Data for Pt, Au and Au–Pt were corrected for diffusion effects.

Voltammetric Characteristics of Some Novel Fe(III) Complexes with Ligands Based on Pyridoxal Semicarbazones

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Electrochemical behaviour of numerous Fe(III) complexes with semicarbazone-based ligands has been a subject of our research for many years. Our new interest is focused on the carbazone derivatives of pyridoxal, their redox characteristics and reactivity in non-aqueous media. Although the complexes of certain metal ions with pyridoxal thiosemicarbazones have been known for some time [1,2], the syntheses of new analogous ligands, pyridoxal semi- and isothiosemi- carbazones and of their Cu(II) and Fe(III) complexes being described only recently [3]. Physico-chemical characteristics of Fe(III) complexes with neutral (H_2L) and monodeprotonated (HL^-) forms of all three ligands were reported in our previous article [4].
In this contribution we present the results of voltammetric and spectrophotometric investigations of new Fe(III) compounds with HL^- and L^{2-} of cationic and non-electrolyte type. Voltammetric study was carried out at a glassy carbon electrode in DMF solutions containing several supporting electrolytes. The obtained results revealed the complexity of electrochemical behaviour of these complexes: multiple redox processes localized mainly at ligand moieties are registered, accompanied by chemical reactions and adsorption.
In comparison with rich voltammetry of previously described analogous Fe(III) complexes with semicarbazone-based derivatives of salicylaldehyde, the present complexes behave even in a more complex manner [5]. This could be partly ascribed to the existence of tautomeric equilibria in ligand solutions, as observed also in their UV-vis spectra.

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Oxygen Reduction on Some Macrocycle Co(III) Complexes in Acid

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Complexes of transition metals (like Co or Fe) of MN_4 chromophore appear to be promising class of materials for the reduction of oxygen[1,2]. According to Chang et al.[3], *cis* and *trans* complex configurations favour different paths of the oxygen reduction. Complexes with *cyclam* as macrocycle that can exists in both of these configurations can be interesting from this point of view. Therefore we were interested to study the influence of different Co(III) macrocyclic complexes on the oxygen reduction in acidic solution.

Mixed-ligand cobalt(III) complexes with macrocyclic amine 1,4,8,11-tetraazacyclotetradecane (cyclam) and heterocyclic dithocarbamates ($Rdtc^-$), with heteroatom (O, S or N) in the heterocyclic ring, or with methyl group on piperidine ring of $Rdtc^-$ ligand as well as with β-diketonato ligands have been used. The reduction of oxygen was examined at GC rotating electrode in O_2 saturated 0.1 M $HClO_4$ in the potential range from 0.2 V to – 1.1 V at the sweep rate of 5 mV/s and different rotation rates.

The results obtained exhibit that complexes influence oxygen reduction by shifting the potential in anodic direction and by increasing its current in some extent. Also, the curves for O_2 reduction at GC in the presence and in the absence of complexes are without the plateau for limiting current density. However, the curve recorded for GC electrode is similar to the one presented by Sundberg et al.[4] for the same material in 0.1 M HCl and according to the authors shows the reduction of O_2 to H_2O_2 as major final product. Thus, as the examined complexes are in *cis* conformation this is contrary to Chang et al.[3] conclusion that *cis* conformation rather than *trans* favours 4-electron path in oxygen reduction.

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Corrosion of Iron in Bicarbonate Solutions

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Carbon dioxide induced corrosion of iron in the salt free and 0.2 M Na_2SO_4 added aqueous solutions free of oxygen in the pH range 4-7 was studied by the slow sweep potentiodynamic technique using Puratronic iron rotating disc electrode. Anodic dissolution reaction with a slope of b_a ~ 30 mV/dec and reaction order n_{OH^-} ~ 1 or 2 is the same as earlier established [1] for this pH range and seems not to be affected by the presence of carbon dioxide in shorter period of time. There are experimental data that during longer anodic polarization (and corrosion as well) in higher pHs iron carbonates form at the surface. Cathodic polarization curves exhibit two limiting current density waves, with limiting currents depending on pH, electrode rotation speed and, when added, concentration of sodium bicarbonate. Limiting currents are of the type of the mixed diffusion-homogeneous reaction control. The corrosive electrolyte contains dissolved free CO_2, H_2CO_3, H_3O^+, HCO_3^- and to some extent CO_3^{2-} species, each of them being potentially reacting species (one or more simultaneously) of the cathodic reaction in the corrosion process. In the relevant literature [2,3] limiting reaction current controlling the rate of corrosion in the pH range 4-5 was ascribed to the slow reaction of hydration of dissolved carbon dioxide into carbonic acid. Our data indicate, however that the first limiting current density wave affecting and controlling the corrosion rate is due to the slow carbonic acid first dissociation rate and hydrogen evolution reaction due to the discharge of the so formed H_3O^+ formed ions. Second cathodic wave is also a slow chemical reaction wave dependent on the stirring rate and bicarbonate ion concentration and is probably due to the electrochemical reaction of the bicarbonate ions, that are dominant in this pH range. These two reaction mechanisms are compared and discussed.

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The Effect of Fast Reversible Primary Oxide Growth on Anodic Aldehyde Oxidation

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Fast reversible electrode reactions draw less attention than the slow rate determining steps and there imposes the main question: Are reversible peaks for the primary oxide growth,

$$M + 2\ H_2O \Leftrightarrow M\text{-}OH + H_3O^+ + e^- \qquad (1)$$

associated with a fixed or narrow potential range, or can be shifted to other values along the scanning axis? Potentiodynamic experiments with a broad issues of aldehydes and monosaccherides show that anodic oxidation of –CHO-group starts at its reversible potential, that for formaldehyde means 0.032 V *vs. RHE,* and depending on concentration of reacting species, proceeds all along the anodic scans close to the oxygen evolving limits. Even more so, since the reaction is mass-transfer limited, in particular at higher aldehyde contents, surface oxide growth arises mostly or almost suppressed, and as the result, immediately after its desorption, there appears sudden hysteretic current jump and repeated peak of aldehyde oxidation continues during the cathodic scans close to the hydrogen evolving limits. Formaldehyde, in particular, enables all ratios with water mixing and thereby, unusually high limiting currents, or the charge capacity of its anodic oxidation within quite unusually broad potential range, starting within the H-adatoms desorption and extending all along, even together with anodic oxygen evolution. All holds at or along such peaks immediately lead to the steady state currents and after reestablished scans, straight proceed with the previous cyclic voltammogram shape. Such state of experimental evidence is clearly associated with two typical rather fast reversible reactions of primary oxide growth (Eq. (1)), and subsequent fast anodic aldehyde oxidation,

$$M\text{-}OH + H\text{-}CHO + H_2O \Rightarrow H\text{-}COOH + H_3O^+ + M + e^- \qquad (2)$$

Potentiodynamic experiments have been carried out on polycrystalline Pt, characterized with stable monolayer surface oxide growth, Au featuring rather loose oxide chemisorption bonds, and Pd behaving multilayer oxide deposits and at the same time both adsorption and absorption of hydrogen. Correspondingly, anodic peaks and charge capacities are much more pronounced on Au, little less so on Pt, and appear much suppressed on Pd.

Due to dissociative water adsorption, rather facilitated spillover in the M-OH transfer and ionic exchange membrane properties, anatase titania and similar catalytic hypo-*d*-electronic oxides (ceria, hafnia, zirconia, tungstenia, or their mixtures), taken as the support of nanostructured metallic part of catalysts, even enhance further above discussed aldehyde oxidation rates [1].

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Reversible UPD/UPO Peaks as Decisive Precursors of CO Tolerance for Anodic Hydrogen Oxidation

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Potentiodynamic investigation of acidic (0.1 M H_2SO_4) and alkaline (0.1 M KOH) solutions of molybdate, tungstenate, vanadate and chromate on polycrystalline Pt, Au and Pd electrodes have clearly revealed the presence of reversible peaks of their primary oxide formation and oxidation, that take place within the peak of hydrogen adsorption and close to the hydrogen desorption, respectively. These typical reversible oxides (MoO_2, WO_2, VO_2, Cr_2O_3), which anodic and cathodic peaks grow symmetric ones above another along potential axis, behave electronic conductive properties and feature pronounced catalytic activity. Their growing peaks are clearly delineated and lead to erroneous conclusion that there occurs UPD metal deposition, while longer cathodic H-adatom adsorption along with hydrogen evolution finally results in corresponding metallic deposits. All these oxides at more positive potentials turn into the higher valence irreversible oxides (MoO_3, WO_3, VO_3, CrO_3), characterized with corresponding anodic oxidation peaks. However, the latter are nonconductive and easy soluble, so that voltammograms are missing their reduction peaks, or in other words, anodic oxidation of the primary into higher oxides takes place all the way, back and forth broad anodic and cathodic scans. Such behavior corresponds to the shift of the first reversible peak for primary oxide growth,

$$M + 2H_2O \Leftrightarrow M\text{-}OH + H_3O^+ + e^- \qquad (1)$$

upon submonolayer Ru deposit on Pt substrate from 0.6V *vs* RHE, characterized for plane Pt, to the potential range of H-adatom desorption [1]. Similarly, $MoPt_3$ and $MoPt_4$ characterizes anodic CO oxidation at about 0.2 V. Primary oxides of Mo, W, Cr, V are cites for almost reversible CO oxidation, while higher oxides are totally inactive in such a respect both for hydrogen and CO oxidation, and their appearance upon catalytic surface reduces its otherwise rather high active properties. CO tolerance is usually associated with so called oxophilicity of some elements (Ru, Mo, Os, Ir) [2]. However, some hypo-*d*-electronic elements (affording the bonding *d*-band) in combination with hyper-*d*-electronic transition metals (characterized by the anti-bonding *d*-band), are able to shift the reversible peak of primary oxide growth and enable CO anodic oxidation (and thereby remarkable CO tolerance) close to or even within the H-adatoms potential desorption range [3],

$$CO + M\text{-}OH + H_2O \Rightarrow CO_2 + H_3O^+ + e^- \qquad (2)$$

This paper has intention to show physical basis for CO tolerance and even for possible simultaneous anodic CO and H-adatoms oxidation.

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Electrorefining Copper Anodes Obtained from $Cu_{65\text{-}72}Zn$

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Copper and its alloys have found use in many areas of common living conditions due to its good mechanical and physical properties, such as electrical conductance, toughness, flexibility, corrosion resistance etc. The required copper quality could be produced by the use of various raw material sources and technological treatment processes. Electrolytic refining process of anodic copper, obtained from copper concentrate, could produce chemical copper content which enables good mechanical and physical properties

Presented results in this work are related to discovery ability of electrolytic refining of anodic copper obtained from residue $Cu_{65\text{-}72}Zn$ and characterization of the obtained cathode copper. Those investigations were carried out by the use of apparatus with semi-industrial diameters. Acidic sulphate solution was used, with constant volume of 150 dm^3. The horizontal centrifugal pump has ensured desirable electrolyte circulation, and the system heating was performed by two electrical heaters with automatically control. The electrochemical system was consisted of 5 anodes and 6 cathodes. The interaxile distance between the two samenamed electrodes was 100 mm. The anodes chemical content, obtained from brass by suitable process was: Cu–99.52 %, Zn-260 ppm, Si-22 ppm, Sb<2 ppm, As<3 ppm, Fe<5 ppm, Ni<5 ppm, Pb-19 ppm, Cd<4 ppm, Te<12 ppm, O_2-980 ppm, Ag-7 ppm.

The copper content was determined by the use of electro-gravimetric method, zinc content was determined by method of atomic emission spectrophotometry and impurities content was determined by optical emission spectrographia method. Titanium was used as cathode material.

The results of number experiments showed a possibility for obtaining the cathode copper with suitable purities by using electrochemical process. Based on number experiments, the following parameters were determined as technological conditions: copper content was in range from 38 to 42 g/dm^3; sulphuric acid concentration was from 160 to 180 g/dm^3; electrolyte temperature was conducted between 55 and 60°C; electrolyte flow was adjusted to be one change of cell volume in two hours. Each experiment was carried out for 24h what was suitable for obtaining the starting sheet in classic electrolysis. The obtained copper was very brittle, so further investigations were carried out for obtaining deposits with suitable toughness. The new experiments serie was conducted under said technological parameters with addition of surface-active agent such as thiourea and gelatin. The investigations were conducted with thiourea and gelatin concentrations in range: 7-28 g/dm^3. The experimental results were shown that increasing concentrations of surface-active agent leads to an increase of copper deposit brittleness. By increasing surface-active agent concentration over the said value, the obtained deposits were fragile like glass. The chemical analysis has showed lower impurities content than content according to the issued standard BS 6017.

The mechanical-physical analysis of the obtained copper characterization has showed a possibility of waste brass usage for anodic copper production.

Electrochemical Decomposition of Alkaline Borohydride Solutions

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Alkaline borohydrides such as $LiBH_4$, $NaBH_4$, KBH_4 are very promising hydrogen storage and releasing reagents as they contain 18.4, 10.5 and 7.4 wt.% of hydrogen, respectively. Their aqueous solutions are very unstable, but they can be stabilized if the alkaline borohydrides are dissolved in concentrated solutions of NaOH or KOH. By using different catalysts, the rate of alkaline borohydride hydrolysis from such solutions can be controlled and hydrogen can be produced via the following reaction:

$$MBH_4 + 2H_2O \xrightarrow{cat.} MBO_2 + 4H_2 \qquad (1)$$

Recently, the electrochemical decomposition of alkaline borohydrides has attracted attention as it proceeds with an exchange of up to eight electrons:

$$MBH_4 + 8OH^- \rightarrow MBO_2 + 6H_2O + 8e^- \qquad (2)$$

The present study aims to investigate the electrochemical conversion of stabilized $NaBH_4$ solutions on metal hydride electrodes prepared from AB_5 type alloys.

Probes of $Mm(NiCoAlMn)_5$ alloys (Mm=mischmetal), produced by inductive melting, were immersed for 12 hours into $NaBH_4$ aqueous solution. This treatment leads to formation of metal hydrides, detected by XRD analysis.

Electrodes were prepared by pressing a mixture of metal hydride powder and some additives on Ni-foam, used as a current collector. After preparation, the electrodes were treated with NaF/HF solution, rinsed with distilled water and immersed in 6M KOH electrolyte containing $NaBH_4$ with different concentrations. They were connected as working electrodes in three-electrode electrochemical cell and large area Ni-mesh was used as a counter electrode. All potentials were measured against Hg/HgO reference electrode. Open circuit potential was monitored until stable value was achieved. After that, the working electrode was anodically polarized by constant current up to a cut-off potential of -0.5 V vs Hg/HgO. The electrochemical experiments were performed using *PJT 35-2 potentiostat-galvanostat* (Radiometer-Tacussel, France) with an *IMT 101 electrochemical interface* and *Volta Master 2 software*.

Discharge capacity values were calculated from the obtained *potential-time* plots. These values exceed several times those obtained with the same electrodes in pure KOH solutions. Additionally, the open circuit potential values, obtained in $NaBH_4$ containing electrolytes, are approximately with 100 mV more negative than those measured with electrochemically charged electrodes in 6M KOH electrolyte. These results may be associated with a direct oxidation of $NaBH_4$ dissolved in the electrolyte (reaction 2). The advantage of used metal hydride electrodes is that they can absorb and store part of the hydrogen, produced by reaction 1.

The results of this study reveals the promising features of sodium borohydride as a fuel and of hydrogen storage alloys as negative electrode material for application in direct borohydride fuel cells. Optimization of fuel concentration, electrode material composition and activation treatment should be performed for practical purposes.

The Time Dependent Resistance of Anodically Formed Oxide Film on Titanium in Concentrated Alkaline Solutions

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Having in mind that titanium dioxide undergoes chemical dissolution in strong alkalies, one could expect that the oxide film underwent to a stationary anodic polarization, after a certain time of equilibration, reaches a stationary thickness and displays a stationary value of polarization resistance, independent on the initial thickness. To prove this assumption, polarization resistance measurements were carried out in the following way: freshly polished titanium electrodes were covered by oxide film either by potentiodynamic polarization at a scan rate of 20 mV s^{-1}, between the initial and final potential -1.5 and 1.0 V vs. SCE, respectively, or galvanostatically, using the current density of 0.9 mA cm^{-2} in 1M NaOH. It is noteworthy that, prior than the breakdown occurs, the oxide layers formed galvanostatically consume much more electricity than those formed by potentiodynamic polarization, and their thickness amounts to roughly 60 and 3 nm, respectively. The electrodes were then held in NaOH solution at a constant potential of 0.8 V vs. SCE until a stationary value of polarization resistance was attained. The polarization resistance was measured as the slope of I-E curve in the small voltage range ±10 mV around 0.8 V. In the solutions the concentration of which does not exceed 2 M, the films formed in each way show the increase in polarization resistance in each solution. In the solutions 3M and 5 M, under a constant anodic polarization of 0.8 V, relatively thin films formed by potentiodynamic polarization, show an additional recuperation, while relatively thick films formed galvanostatically, show initially a decrease in polarization resistance and then it attains a stationary value. For the films formed galvanostatically, the stationary value of polarization resistance is always remarkably higher than that of the film formed potentiodynamically. This shows unequivocally that the thicker films, synthesized by consumption more current and time, show a more expressed resistance to the dissolution in alkaline solutions.

By reading the current corresponding to a stationary polarization resistance, the Table I was formed. Having in mind that a part of this current may be the electronic one, these values depict the maximum corrosion rates at a fixed anodic polarization of 0.8 V.

The dissolution of TiO_2 in alkaline solution produces titanates, for example:

$$TiO_2 + 2\,NaOH = Na_2TiO_3 + H_2O$$

To proceed at a suitable rate, this reaction requires high temperature of the order of several hundred degrees. In the experiments in this study, the more sensitive electrochemical methods evidence that the dissolution proceeds at 25 ^{0}C, and furthermore that the two in sity prepared oxide film show a distinct dissolution rate. That may be interrelated to the usual behavior of slightly soluble precipitates, which, upon aging, show a reduced rate of dissolution as well as a reduced solubility.

Table
Steady state corrosion currents (μA cm^{-2}) of potentiodynamically and galvanostatically oxidized titanium, at fixed anodic potential of 0.8 V vs. SCE, in different NaOH solution concentrations.

	2 M	3M	5M
Potentiodynamic.	2.1	3.5	6.0
Galvanostatic.	0.35	1.1	1.7

Comparison of Methanol Oxidation at a Supported Pt Catalyst and at Pt Single Crystal Electrodes in Alkaline Solution

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The methanol oxidation was studied at two differently prepared supported Pt electrodes (Pt-C/GC and Pt/GC), polycrystalline Pt and single crystal Pt electrodes (Pt(111), Pt(110) and Pt(332)) in 0.1 M NaOH.

Pt-C/GC electrode was formed by chemical deposition of commercially available 47.5 wt% Pt catalyst on glassy carbon. Pt/C electrode was obtained by electrochemical deposition of Pt on glassy carbon. Both supported Pt electrodes were characterized by STM in air.

Despite the same metal loading of 20 μg_{Pt} cm^{-2} cross-section analysis of various STM images revealed the different Pt particle size distribution in the catalyst layers (3 – 6 nm at Pt-C/GC and agglomerates consisting of 4 – 20 nm at Pt/GC).

The electrocatalytical activity of the electrode studied increased in a sequence Pt(332) > polycrystalline Pt > Pt-C/GC ~ Pt(110) > Pt/GC ~ Pt(111). Pt-C/GC is more active than Pt/GC. Both supported catalysts were less active than polycrystalline Pt. Negligible differences in the kinetics observed between Pt-C/GC and Pt(110) as well as between Pt/GC and Pt(111) clearly suggested that the activity of supported Pt electrodes can be correlated with the activity of corresponding single crystal electrodes oriented as the sites dominating in the Pt particles in catalyst deposits.

For the average Pt particle diameter of 4 nm in catalyst deposit at Pt-C/GC, average surface distribution amounts ~22% corner and edge low coordinated sites, which may be correlated with (110) sites. For the larger Pt particles consisting in the deposit of Pt/GC electrode the average surface distribution changes in favor of the increasing contribution of (111) sites, while the amount of (110) sites decreases.

The most active electrode appeared to be Pt(332), most likely due to well balanced coverage by methanol and OH_{ad} species and the ability of adsorbed methanol on the terraces to reach easily OH_{ad} species at the step sites.

Chemical reaction between HCO_{ad}, formed by methanol dehydrogenation and OH_{ad}, generated by OH^- anion discharged, giving formate was suggested as r.d.s. of methanol oxidation in alkaline media at the electrodes studied. The slope of Tafel lines ~120 mV dek^{-1} and reaction orders of 0.5 for methanol and OH_{ad} fit well with mechanism proposed.

Kinetics of Hydrogen Electrode Reactions on a $LaMmNi_{3.55}Co_{0.75}$ $Mn_{0.4}Al_{0.3}$ Alloy in Aqueous 1 M KOH Solution

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The exchange current density (j_0) and energy of activation ($\Delta G^{\#}$) for the hydrogen electrode reaction (HER) are important parameters for understanding electrode kinetics and are the measure of electrocatalytic activity of negative electrode of hydride batteries. Senoh et al. [1] investigated the dependence of j_0 for HER in the low depth of charge (DOC) region on $MmNi_{3.9-x}Mn_{0.4}Al_xCo_{0.7}$ hydrogen storage alloy electrodes at constant temperature. Wu et al. [2] investigated the temperature dependence of j_0 for HER on Ni-Co-$LaNi_5$ composite electrodes. In the same paper $\Delta G^{\#}$ was calculated for HER on the investigated electrodes.

The aim of our work was to determine j_0 at various DOC and at different temperatures, and to calculate $\Delta G^{\#}$, for the HER on a commercial hydrogen storage electrode with the composition $LaMmNi_{3.55}Co_{0.75}Mn_{0.4}Al_{0.3}$. The mentioned parameters were obtained by a potential sweep voltammetry in a thermostated three-electrode electrochemical cell. The alloy prepared as a working electrode, Pt-foil as a counter electrode, and saturated calomel electrode as a reference electrode, immersed in 1M KOH solution.

From the obtained voltammograms j_0 was calculated from the slope of the linear polarization curves, at zero current [1]. The depth of charge was calculated from the surface area under the observed anodic peak.

The obtained results (Fig. 1) indicate that j_0 depends linearly on DOC at the low DOC values, as well as that j_0 increased with increasing temperature at the selected DOC.

According to the Arrehenius relation [2] the apparent $\Delta G^{\#}$ for HER was determinate from the slope of log j_0 versus T^{-1} plot (Fig. 2). The obtained $\Delta G^{\#}$ values were of 28.0, 28.6 and 29.4 kJ mol^{-1} at the DOC of 10.0 12.5 and 15.0 mA h g^{-1}, respectively. The corresponding value for HER on Ni amounts to 57.0 kJ mol^{-1} [1], indicating better electrocatalytic activity of the investigated alloy.

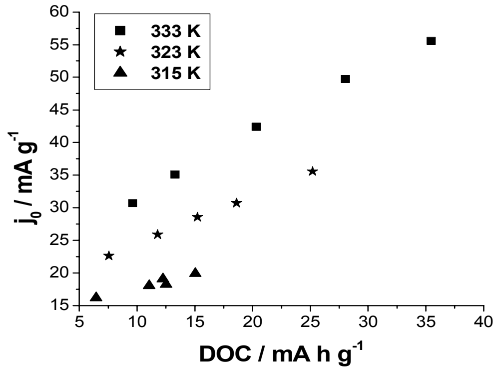

Fig. 1. Exchange current density vs. depth of charge at different temperatures.

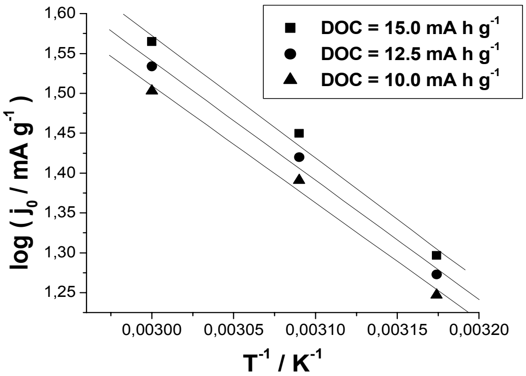

Fig. 2. Logarithm of exchange current density vs. T^{-1}, at selected depths of charge

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The Electrochemical Study of the Reduction Behavior of Some 3,5-R-Ditiazolium Derivatives

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The object of the present paper is the study of the behavior of some 3,5-R-ditiazolium perchlorates at electrochemical reduction in aprotic media (DMSO), by electrochemical coupled with spectral (UV-VIS, EPR) methods using *in-situ* techniques. Cyclic voltammetry (stationary electrode) and linear voltammetry (rotating disc electrode RDE) were employed to characterize the electron transfer steps (electron transfer rates k_s, transfer coefficients α, diffusion coefficients D_O).

The cyclic voltammetry data point out two or three reduction processes, in function of the substituent on the heterocyclic ring, assigned respectively to the successive reduction steps of the ditiazolinium moiety.The peak potentials of these waves vary in function of the nature of the substituent group R, being less negative in the order: R = phenyl, R = styryl, R = *p* -methoxy styryl and R = *p* - NO_2 styryl. The anodic wave observed in the positive potential range was assigned to the oxidation of the substituted ditiazole moiety to its positive ion. The anodic peak is shifted towards more positive potential values with the increasing electron acceptor character of the substituent. The decrease of the intensity ratio i_{pa}/i_{pc} for the first redox couple with the increasing electron acceptor character of the substituent attests for the increased reactivity of the intermediate species resulting from the first electron transfer. The electrochemical data attest a complex behavior, the reactivity of the intermediate species depending on the substituent group R in the ditiazole ring. The linear voltammetry results are in agreement with the cyclic voltammetry results.

The semiempirical AM1 calculations of the electronic structural features implied in the redox processes of the investigated compounds account reasonably for the substituent effects outlined by the experimental results.

The Effects of Chemical Composition on the Corrosion Behavior of Aluminum Alloys

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This work as the appendix of our recent property investigation and characterization of aluminum alloys, is concerned with investigation of chemical composition effects on corrosion behavior of aluminum alloys.

The parameters that define the corrosion stability and mechanical properties of the aluminum alloys are determined on the base of performed experimental procedure and obtained results. The investigation aim was the characterization of examined alloys from the standpoint of their application.

The Al-Mg alloys with different alloying element contents were studied. The investigation of chemical composition, mechanical characteristics and structure was performed for certain cast alloys. The corrosion behavior of the alloys in chloride solutions of various concentrations was studied too.

In order to achieve the alloys with small grain size, the modification procedure was employed by titanium that was added as pre-alloy AlTiB with 5% Ti and 1% B.

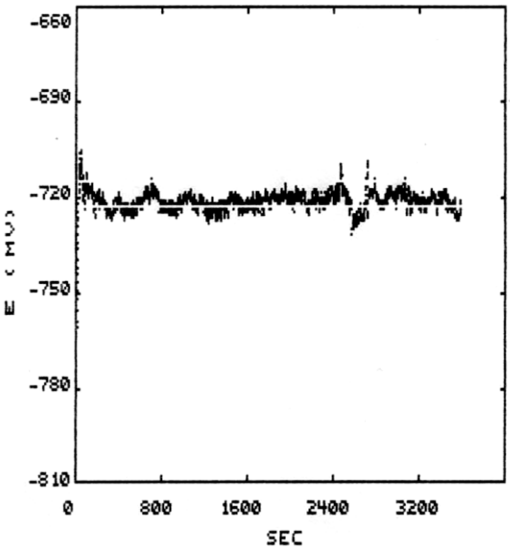

Figure 1. E_{corr} vs. Time Equilibrium of AlMg Alloy

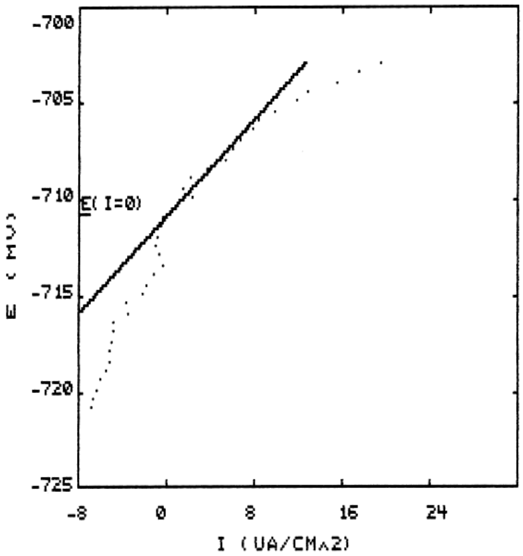

Figure 2. Polarization Resistance Curve of AlMg alloy

Study of the Corrosion Inhibition of Carbon Steel in Diluted Ammonia Media by Ethylenthioure and N-Cyclohexyl-benzthiazole-sulphenamide

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Numerous advanced treatments using organic compounds have been proposed in order to improve the corrosion protection [1-4]. The inhibition efficiency of the organic compounds is closely related to the structure and the properties of the layer formed on the metal surface.

The inhibiting effect of N-cyclohexayl benzthiazol sulfenamide (NCBSA) and ethylenthiouree (ETU) on the corrosion of the carbon steel in diluted ammonia solution at room temperature has been studied by electrochemical measurements and Mossbauer spectroscopy.

In the electrochemical measurements the anodic polarisation of steel electrodes in the inhibitor containing 10^{-3} M ammonia solutions is shifted to less negative values, while the chatodic polarisation shifts to more negative values with increasing current density. The presence of organic inhibitors in corrosive medium increases the anodic and chatodic overpotentials and decreases the corrosion current.

The concentration of the inhibitors in a 10^{-3} M ammonia solution was 200 ppm. In the presence of NCBSA and ETU in corrosive medium the corrosion current decreases. The inhibition efficiency was 71% in the presence of ETU in corrosive medium, respectively 95 % in the presence of NCBSA in the 10^{-3} M ammoniac solution, which proves a very good adsorbability of these substances on the carbon steel surface.

The electrochemical corroded carbon steel samples in 10^{-3} M ammonia solution without NCBSA and ETU and in a 10^{-3} M ammonia solution with these inhibitors were also tested using Mossbauer surface analysis.

The parameters of CEMS spectrum show the presence of Fe^{3+} and are similar to those shown by amorphous Fe^{3+} oxihydroxides super paramagnetic α-FeOOH and/or γ-FeOOH and $Fe(OH)_3$, for the sample which was corroded in absence of NCBSA and ETU. The Mossbauer spectrometry indicates the formation of the superficial layer on the surface of the corroded electrode in the presence of NCBSA and ETU, which provides a very good adsorbability of these inhibitors on the metal surface.

This is consistent with the interpretation of the electrochemical measurements data in terms of the formation of the complexes between NCBSA or ETU and metal cations found in the carbon steel structure.

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Role of the Substrate on the Electrocatalytic Activity of Platinum Deposited on Glassy Carbon Electrodes for Methanol Oxidation

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Although widely studied, deposition of platinum particles on glassy carbon (GC) and catalytic properties of such electrodes have been disscused mostly through the effect of the particle size and Pt loading[1,2]. Properties of (GC) are determined not only by pretreatment but also by the temperature of thermal treatment applied during the production of the material. Application of different temperatures (higher or lower) results in different porosity (lower or higher respectively), structure (highly ordered or lower ordered respectively) and activity. Electrochemical pretreatment either by anodic or by cathodic polarisation in alkali or in acid, results not only in changes of double layer charge and morphology of the surface but also in changes of fraction of different functional groups[3]. We were interested in how these changes in properties of GC influence electrocatalytic activity of platinum deposited on GC electrode for the oxidation of methanol in acidic and alkaline solutions.

Two GC samples were used: K – thermally treated at 1000°C and G - thermally treated at 2500°C. Samples were polished, anodically polarised in H_2SO_4, or NaOH and cathodically polarised in H_2SO_4. Pt was deposited from H_2SO_4 + H_2PtCl_6 solution under the same conditions but with to different loadings. The electrocatalytic activity of the electrodes prepared was studied for methanol oxidation in 0.5 M $H_2SO_4$and in 0.1 M NaOH.

The results obtained show that the activity of the electrodes differs depending on the GC treatment. Electrochemical treatment of GC support might not influence real Pt surface area and Pt loading but has enhanced effect on the specific activity. The extent of the activity depends on the treatment applied indicating the pronounced role of organic residues of GC support. Despite of more pronounced scattereing of the data of GC_K/Pt electrodes with GC support thermally treated at lower temperature the results obtained at both samples are following the same tendency.

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Adsorption and Corrosion Inhibitive Properties of Some Thiazole Derivatives on Copper Surface in Acidic Solutions

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The inhibition charachteristics and adsorption properties of some thiazole derivatives against copper corrosion in acidic sulphate containg media have been investigated. This kind of organic molecules can be adsorbed at the metal-solution interface as a result of reducing the metal corrosive attack in acidic media[1,2].

Adsorption and corrosion inhibitive properties of four organic molecules: 5-benzylidene-2,4-dioxotetrahydro-1,3-thiazole(5-BDT), 5-(4′-isopropylbenzylidene)-2,4-dioxotetrahydro-1,3-thiazole (5-IPBDT), 5-(3′-thenylidene)-2,4-dioxotetrahydro-1,3-thiazole (5-TDT), 5-(3′,4′-dimetoxybenzylidene)-2,4-dioxotetrahydro-1,3-thiazole (5-MBDT), were investigated on copper electrode in 0.1 M Na_2SO_4 solution at pH=2.95.

Using electrochemical methods the corrosion and adsorption parameters were studied at different inhibitor concentrations in temperature range of 288-308K. The results showed that the corrosion inhibition efficiency increased with inhibitor concentration and temperature.

The experimentally obtained results showed that the investigated organic molecules adsorptions followed the Bockris-Swinkel′s isotherm, by replacing one (in case of 5-IPBDT, 5-TDT), three (in case of 5-BDT) and four (in case of 5-MBDT) water molecules from the copper surface. All investigated organic molecules gave high values for equilibrium constant of the adsorption process (K) and positive values of standard free energy of the adsorption ($-\Delta G_{ads}$), which suggested fast and spontaneity of the adsorption reaction on copper surface.

The $-\Delta G_{ads}$ values indicated that during the temperature increase the type of adsorption change from the physical adsorption to the chemisorption.

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Voltammetric Measurement of Kinetics of the Dimethylsulphoxide Bromination

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Bromine in dimethylsulphoxide (DMSO) + 0.5 M $KClO_4$ supporting solution was studied by voltammetry on rotating Pt disc electrode. In even freshly prepared solution, considerable anodic wave was observed, indicating the presence of reduced bromine species, i.e. fast reaction of bromine with the solvent. This is in accordance with the paper of Martin et al. [1], where bromination of DMSO was studied by the methods of organic chemistry. With negatively charged species, the bromine in excess forms the tribromide complex ions. As a consequence of the formation of a stable intermediate tribromide ions, the voltammetric curve in the observed solution shows two steps: one due to the bromine-tribromide process, and the other due to the tribromide-bromide process. The total difference between the limiting anodic and cathodic currents corresponds to the amount of bromine introduced in the solution, however, the reduction wave corresponding to the bromine reduction is reduced in height and decreases continuously with increasing time. Using the height of this wave as a measure of the unreacted bromine concentration, the kinetics of DMSO bromination was measured. The current-to-concentration conversion was done using the fact that one third of the difference between the heights of final cathodic and anodic current plateaus correspond to the initial bromine concentration of 3.25 mM. The reaction between bromine and DMSO must be of the second order, however, the solvent is in high excess and therefore, the reaction rate may be expressed by a first order law:

$$-\frac{dc_{\mathrm{Br_2}}}{dt} = k \cdot c_{\mathrm{Br_2}}.$$

Fig 1. shows the dependence of bromine concentration on time, and its initial slope enabled to estimate the rate constant of DMSO bromination, to amount to k = $3.4 \cdot 10^{-2}$ min^{-1}.

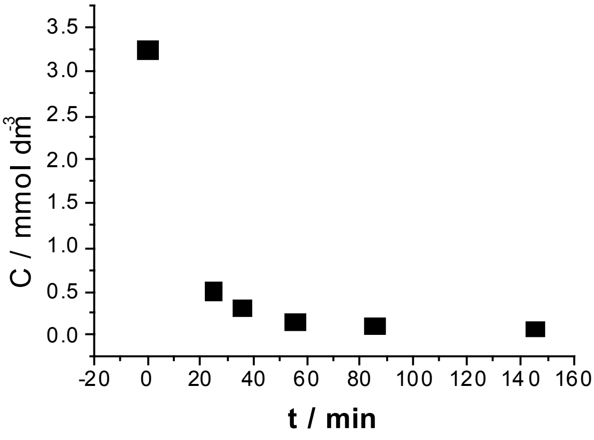

Fig 1. The dependence of bromine concentration (C) on time, based on the measurements of limiting current of bromine reduction in the solution DMSO + 0,5 M $KClO_4$ + 0,00325 M Br_2.

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Characterization of $[Zn(\mu\text{-}L)(HL)(OAc)]_2$ by Cyclic Voltammetry

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The reaction of warm MeOH-DMF solution of $Zn(OAc)_2 \cdot 2H_2O$ and 4-acetyl-3(5)-amino-5(3)methyl-pyrazole (HL) in a stoichiometric ratio 1:2 yielded binuclear complex $[Zn(\mu\text{-}L)(HL)(OAc)]_2$ [1].

In this paper the investigation of electrochemical behaviour of $[Zn(\mu\text{-}L)(HL)(OAc)]_2$ by cyclic voltammetry method in deaerated dimethylsulphoxide (DMSO) solution is carried out. The investigation is done in the potential range of +0,10 V to –0,75 V on Pt electrode as the working electrode vs. SCE.

When $[Zn(\mu\text{-}L)(HL)(OAc)]_2$ complex is dissolved in DMSO catodic and anodic current peaks on recorded voltammetric curves are well defined. The potential wave peak in anodic area is in on +0.25 V and its corresponding wave peak in anodic area is on –0.30 V (SCE).

The investigation of the influence of the polarization speed showed that with the enhancement of polarization speed from 10 to 100 mV/s the height of the wave peaks is constant both in cathodic and anodic area of voltammogram. It also showed that kinetics of catodic deposition and anodic dissolution of zinc in solution of $[Zn(\mu\text{-}L)(HL)(OAc)]_2$ + DMSO proves a lot of similarities with kinetics in watery solutions [2].

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HNO_3/Silica Gel Supported CAN. Oxidative Deprotection of Benzylic Tetrahedropyranyl Ethers Under Solvent-Free Conditions Using Microwaves

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The protection – deprotection of alcohol functionalities is of paramount importance in organic chemistry as testified by the plethora of imaginative reagents and methods that have been devised to accomplish this key functional interconversion. Although several methods have been appeared in the literature concerning the deprotection of THP ethers, there are only few reports dealing with the direct oxidation of tetrahydropyranyl ethers to the corresponding carbonyl compounds. Consequently, there is a demand to develop and introduce more selective and milder methods and reagents for this transformation.

During the past few years, cerium ammonium nitrate (CAN) have become synthetic reagents and catalysts of growing importance. It has recently been used for the protection of THP and THF ethers under neutral conditions.

The use of supported reagents has attracted much attention, because of improved selectivity, reactivity and associated ease of manipulation. Since polar reactants adsorbed on the surfaces of various mineral carries absorb microwave energy, a variety of reagents supported on such surfaces can be utilized for the enhancement of organic reactions using a simple microwave oven. Recently, microwave enhanced chemical reactions especially on inorganic solid supports and under solvent-free conditions have attracted much attention. They offer several advantages over conventional homogeneous and heterogeneous reactions with respect to high reaction rates and yields.

In continuation of our recent work on microwave-assisted reaction under solvent-free conditions, herein, we report our results for a solvent free microwave protocol that leads to a facile selective oxidative deprotection on benzylic THP ethers using CAN irradiation.

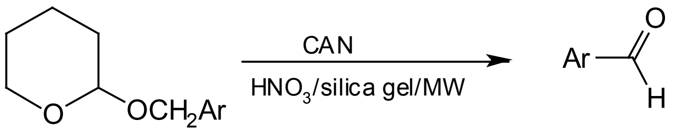
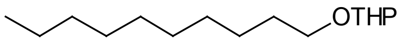
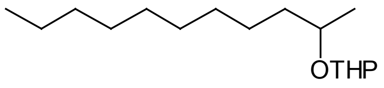


Table 1. Oxidative deprotection of THP ethers with CAN supported onto HNO_3/silica gel

Entry	Substrate	Time, min	Product	[a]Yield, %
1	$PhCH_2OTHP$	6	PhCHO	90
2	*m*-O_2N-$C_6H_4CH_2OTHP$	4	*m*-O_2N-C_6H_4CHO	91
3	*p*-$O_2NC_6H_4CH_2OTHP$	4	*p*-$O_2NC_6H_4CHO$	92
4	*p*-Me-$C_6H_4CH_2OTHP$	5	*p*-Me-C_6H_4CHO	90
5	2-O_2N-5-Me-$C_6H_3CH_2OTHP$	5	2-O_2N-5-Me-C_6H_3CHO	90
6	PhCH(Me)OTHP	10	PhCO(Me)	Trace
7	CyclohexanolTHP	10	--	--
8	 OTHP	10	--	--
9	 OTHP	10	--	--

[a]*Yields refer to isolated products.*

Synthesis, Structure and Properties of Heteroconjugated Alkenes
I. Methods for Obtaining of 4-Arylsulphonyl-2-Butenenitriles

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We take a keen interest in heteroconjugated alkenes due not only to the availability of some reactive centers in them, but also to the possibilities of obtaining new substances with potential biological activity. With respect to this 4-arylsulphonyl-2-butenenitriles deserve special consideration. Reference analysis shows that up to the recent days only a unique representative of these substances has been obtained, synthesized as a result of multistage reactions, without separation and purification of the intermediate products.

The investigations carried out by us show that 4-arylsulphonyl-2-butenenitriles can be obtained by two independent methods.

The first one consists in interaction of 3, 4-dibromobutyronitrile with arylsulphinic acids sodium salts in the presence of sodium acetate and acetic acid:

$$BrCH_2-CH-CH_2-CN + ArSO_2Na \xrightarrow[CH_3COONa]{CH_3COOH} ArSO_2CH_2-CH=CH-CN + 2\,NaBr$$

Ar=C_6H_5, p-$CH_3C_6H_4$, p-ClC_6H_4, p-BrC_6H_4, p-IC_6H_4, p-$NO_2C_6H_4$, α-$C_{10}H_7$

As indirect evidence of reaction comes up the developed second method by us for obtaining the same compounds. 4-bromo – 2 – butenenitrile is first obtained by this method, which subsequently reacts with sodium salts of the sulphinic acids:

$$BrCH_2-CH=CH-CN + ArSO_2Na \xrightarrow{CH_3COOH} ArSO_2CH_2-CH=CH-CN + NaBr$$

At both methods, the reactions are carried in aqueous-alcohol medium at molar ratio of the initial reagents. The obtained compounds structure is established by means of spectral methods.

Study of the Reactivity of 5-Substituted Orotic Acids

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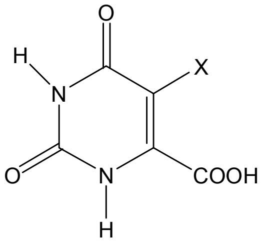
The importance of orotic acid in pyrimidine nucleotide synthesis has been well established [1]. Derivatives of orotic acid substituted at 5-position such as chloro, bromo, fluoro [2,3] have been shown to exhibit orotic acid antimetabolite activity. Only a few potent inhibitor of orotate phosphoribosyltransferase are known such as 5-azaorotate, 5-fluoroorotate and barbituric acid [4]. Investigation of structure-activity relationship of orotic acid analogs is a significant contribution to the better understanding of their biological activity.
Eight 5-substituted orotic acids of the following formula have been synthesized:



where X is: -H (1); $-CH_3$ (2); $-CH_2CH_3$ (3); $-CH_2CH_2CH_3$ (4); -Cl (5); -Br (6); $-NO_2$ (7); $-NH_2$ (8).
Existence of different tautomeric forms of orotic acids derivatives in connection with the presence of the ortho substituent on different manner affect of their reactivity. The rate constants for the esterification of investigated acids with diazodiphenylmethane (DDM) in dimethylformamide were determined at 30 °C using the well known spectrophotometric method [5,6]. Kinetic data for investigated acids have been correlated using linear free energy relationship in the form:

$$\log k2 = \alpha\sigma_I + \beta\sigma_R + \psi v_X + h$$

Partition of the inductive, resonance and steric effect of the substituents have been evaluated from the quantitative values of the coefficients from above equation.

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Helical Chirality of 1-Phenacyl-1,10-Phenanthrolinium Bromides

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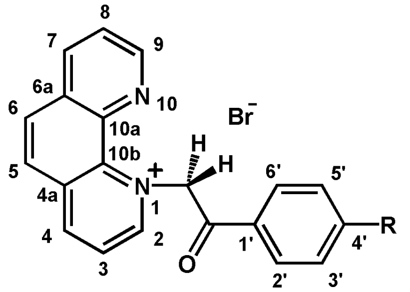
Introduction

Derivatives of 1,10-phenanthroline ('phen') enjoy a diversity of roles and applications in the biological, chemical and solid-state fields. These include e.g. their intercalation in macromolecules, their action as potential herbicides and carcinostatics, and their incorporation in supramolecular photochemical devices. As structure is intimately related to function, possible deviations from the expected planar structure of the 'phen' moiety in its derivatives are of interest in the above context. We have obtained evidence for non-coplanarity of the tricyclic residue in a series of 1-phenacyl-1,10-phenanthrolinium bromides (Fig.1) from ^{1}H-NMR spectra recorded in DMSO-d_6. A crystallographic study of the representative compound **1c** confirmed this helical distortion in the solid state and provided insight into its origin.



1a-d: R: a = H; b = F; c = Cl; d = Br

Fig.1 Structures of the title compounds

^{1}H-NMR study of the title compounds

The spectra of **1a-d** were recorded in DMSO-d_6 on a Varian Gemini 300 BB instrument with TMS as internal standard. An unusually broad signal for the methylene protons at δ = 7.20-7.30 ppm was interpreted as indicating non-coplanarity of the pyridine and pyridinium rings in the series of cations of the title salts.

X-ray crystallographic analysis of the representative compound 1c

The X-ray analysis was based on 3803 independent reflections measured on a Nonius Kappa CCD diffractometer at 203K and yielded R = 0.042, wR2 = 0.126. Significant helical distortion in the cation, reflected in a dihedral angle of 6.8(2)° between the pyridine and pyridinium rings, was observed. This was attributed to accommodation by the tricyclic unit of an intramolecular hydrogen bond C(methylene)-H···N10 with C···N 2.743(5)Å.

Conclusion

Structural modification of 1,10-phenanthroline can induce helical distortion, which in the case of the representative compound **1c** has been accurately measured. Such distortions affect the extent of π-electron delocalisation in conjugated systems of this type, which in turn can affect their solid-state photochemical and related properties. This result therefore merits consideration in the design of materials or molecular devices based on 1,10-phenanthroline and related molecules.

Preparation of Some Starting Materials for the Palladium Mediated Hetero Domino Synthesis of the Steroidal Skeleton

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The intramolecular Diels-Alder cycloaddition of appropriately substituted *o*-xylylenes is an elegant method to obtain complex natural polycyclic systems such as steroids. The limits of the method depend on the availability of the requested benzocyclobutene. In our approach to the synthesis of the steroidal skeleton, we envisaged to obtain the appropriate benzocyclobutene in a two step palladium mediated reaction. The first step consists in a palladium catalyzed cyclisation of a new allenic allylacetate, resulting in the formation of a “living” five membered ring π-allyl-palladium complex, which is trapped by benzocyclobutenyldimethylmalonate in the second step, in a Tsuji-Trost type reaction. For the synthesis of the requested allenic allylacetate we tried several synthetic routes and finally chose, as the most attractive one, the alkylation of the sodium enolate of 4,4-dimethoxycarbonyl-2-buten-1-al with 4-bromo-1,2-butadiene. As in any alkylation of ambident enolates, the central problem of this reaction is the selectivity in the desired C-alkylated product. The reaction was first checked using methyl iodide as an alkylating agent. Several new compounds were synthesized and characterized during these attempts.

Stereochemistry of Heterocyclization of β-Oxonitriles with α- and β-Mercaptoesters: X-Ray Structure Proof

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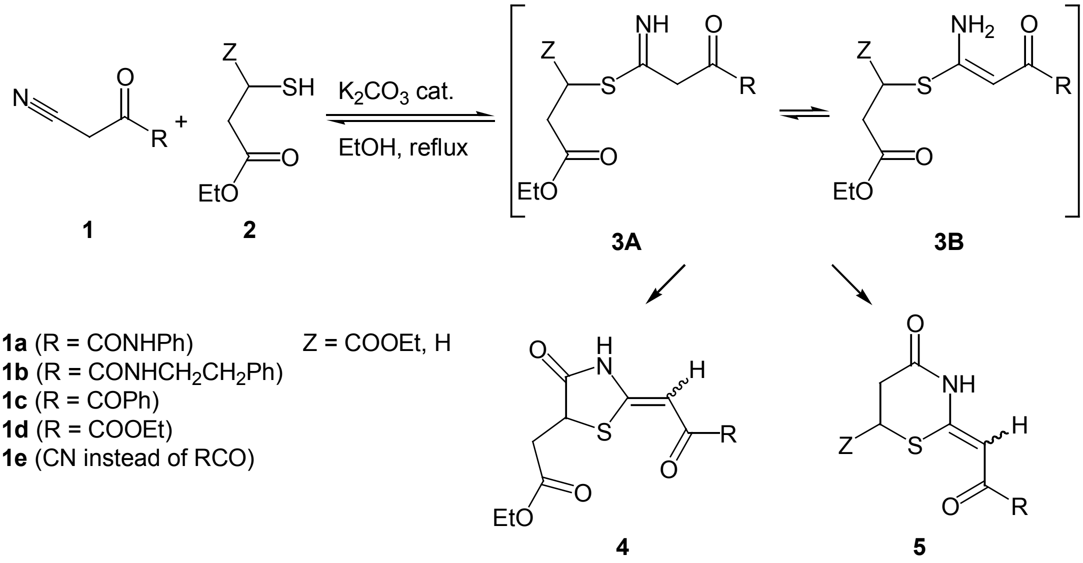
The base-catalyzed reaction of activated nitriles **1** with diethyl mercaptosuccinate **2** (Z = COOEt) proceeds regioselectively to give only 4-oxothiazolidine derivatives **4** in good yields (60 - 80%), though both 4-oxothiazolidine and 4-oxo-1,3-thiazinane derivatives **4** and **5** can be also formed from the intermediates **3** (Scheme).



1a (R = CONHPh) Z = COOEt, H
1b (R = $CONHCH_2CH_2Ph$)
1c (R = COPh)
1d (R = COOEt)
1e (CN instead of RCO)

Scheme

An attempt to obtain six-membered 1,3-thiazinane from the nitrile **1b** and ethyl 3-mercaptopropionate **2** (Z = H) failed and only products resulting from the decomposition of the ester and the nitrile have been isolated. However, the nitrile **1d**, possessing less voluminous substituent R, reacted with ethyl 3-mercaptopropionate to give the six-membered, predominantly *E*-configured 4-oxo-1,3-thiazinane derivative **5d** in a low yield. The structure of this compound has been proved by X-ray analysis which revealed that the molecules themselves are surprisingly planar. A contributing reason for this is the existence of an intramolecular NH···O hydrogen bond [1].

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Thermal Isomerization of Polarized 4-Oxothiazolidines. Dynamic Nuclear Magnetic Resonance Study

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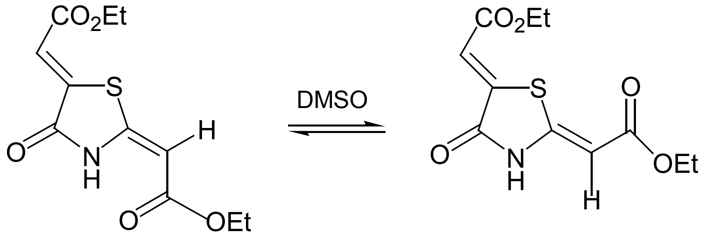
Since the concept of push-pull alkenes was reviewed by Sandström in 1983 [1], the physicochemical properties and chemical reactivity of numerous functionalized compounds of that type have been extensively studied. 4-Oxothiazolidines **1**, with two exocyclic double bonds attached to thiazolidine ring, exemplify typical push-pull compounds which can exist in different configurational forms.



(2*E*,5*Z*)-**1** (2*Z*,5*Z*)-**1**

Scheme

Table. *Selected ^{1}H NMR chemical shifts (σ in ppm) for configurational isomers of 4-oxothiazolidine **1***

Entry	Compound	Solvent	H-2'	H-5'	NH
1	(2*Z*,5*Z*)-**1**	DMSO-d_6	5.69	6.59	
2	(2*E*,5*Z*)-**1**	DMSO-d_6	5.63	6.68	
3	(2*Z*,5*Z*)-**1**	$CDCl_3$	5.83	6.80	10.54
4	(2*E*,5*Z*)-**1**	$CDCl_3$	5.35	6.88	10.82

^{1}H NMR Spectroscopy enables an easy characterization of the (2*E*,5*Z*)-**1** and (2*Z*,5*Z*)-**1** isomers (Table), and whole series of related push-pull 4-oxothiazolidine derivatives as well, due to the fact that they may be thermally isomerized at rates which are within the NMR time scale. An analysis of the isomeric equilibria and determination of the C=C torsional barrier, may provide a more complete understanding of the dynamic stereochemistry of these compounds. In light of these results we wish to report here (i) the kinetics of the configurational isomerization of the stereodefined (2*E*,5*Z*)-**1** in DMSO-d_6 and (ii) determination of the energy barriers separating the configurational isomers of 4-oxothiazolidine derivatives **1** by variable temperature ^{1}H NMR technique.

References:

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X-Ray and Conformational Study of New Modified B-Nor-5,10-Secosteroidal Ketones Containing a Nine-Membered Ring

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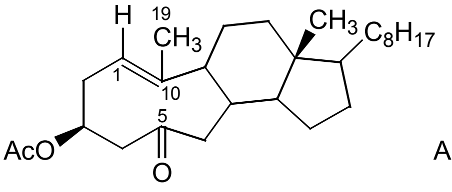
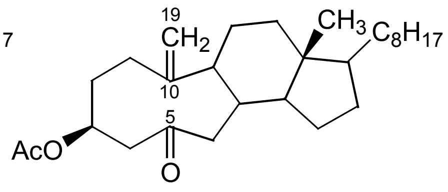
Our previous study [1] has shown that the oxidative fragmentation of 5-hydroxy-B-norcholestan-3β-yl acetates proceed by fragmentation of their C(5)-C(10) bond to give as the primary products a new type of modified steroids containing a nine-membered ring instead of the fused A,B-nor rings, *i.e.* the (*Z*)- and (*E*)-5-oxo-B-nor-5,10-secocholest-1(10)-en-3β-yl acetates (**1** and **2**) and 5-oxo-B-nor-5,10-secocholest-10(19)-en-3β-yl acetate (**3**). Our further investigations have shown that the unsaturated B-nor-5,10-secoketones **1**-**3** behave differently towards reagents which can participate in reactions involving bond formation across the nine-membered ring [2]. This was explained by different stereochemical characteristics of these cyclononenone systems.



1 (*Z*)
2 (*E*)



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In an attempt to gain more insight concerning conformational features of the nine-membered rings in the present work X-ray crystal analysis and detailed ^{1}H- and ^{13}C-NMR spectral analysis were performed on B-nor-secoketones **1**-**3**. Solid state conformations of a nine-membered ring in both compounds contain the 19-Me and 5-oxo groups "β-oriented".The NMR parameters for the characterization of the possible conformations of compounds **1**-**3** were: a) the chemical shifts of the olefinic proton H-C(1); b) the dihedral angles and the coupling constants between H-C(1) and $H_2C(2)$ as well as $H_2C(4)$ and H-C(3); c) the ^{13}C-NMR shifts for C(19) of **1** and **2** and for C(11) of **3**. The ^{1}H- and ^{13}C-NMR spectra showed that the unsaturated nine-membered ring in compound **2** in solution exists in only one conformation, which is similar to the solid state conformation, while the (*Z*)-isomer **1** in solution exists in two conformational forms with different orientation carbonyl group, the predominant (85%) (19-Me(β), 5-oxo(α)), and a minor (15%) identical to the conformation in the crystalline state. The NMR analysis suggests that the nine-membered ring in **3** has one conformation (19-CH_2(β), 5-oxo(β)) in solution.

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UV Study of the Solvent Effect of N-Substituted Stearamides in Protic and Aprotic Solvents

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Due to the special characteristic, the amides of fatty acids found large application in different chemical industry as pharmacy, textile, metallurgy, the industry of surfactants, of plastic mass and etc.

The aim of this work was to synthesize a number of N-substituted amides of stearic acid [1] and to study the solvent effect of amides in some protic and aprotic solvents by UV spectroscopy.

The effect of solvent polarity and hydrogen bonding on the absorption spectra were interpreted by the linear solvatation energy [LSER] concept developed by Kamlet and Taft [2] using a general solvatochromic equation:

$$\nu_{max} = \nu_0 + s\pi^* + a\alpha + b\beta$$

where π^* is the index of the solvent dipolarity/polarizability, which is a measure of the ability of a solvent to stabilize a charge or a dipole by its own dielectric effects; α coefficient represents the solvent hydrogen bond donor (HBD) acidity and β coefficient is a measure of the solvent hydrogen bond acceptor (HBA) basicity; *s*, *a* and b are solvatochromic coefficients.

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Antioxidant Activity of Some Aromatic Herbs from Montenegro

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Introduction

Biodiesel is an alternative transport fuel, produced from domestic and renewable resources. It is simple to use, biodegradable, non-toxic and essentially free of sulphur and aromatic compounds. In Europe, biodiesel is mainly produced from the rapeseed and sunflower oils through transesterification process with methanol, in which fatty acid methyl esters - FAME (the chemical name for biodiesel) and glycerol (a valuable by-product) are obtained.

However, due to their chemical structure, FAME are very labile, easily undergo autoxidation and age more quickly than fossil diesel fuels. In effort to retard and prevent oxidation of the unsaturated fatty acids to corrosive volatile acids various antioxidants are employed.

The aim of the work was to investigate the oxidative stability of FAME treated with some aromatic herbs from Montenegro containing antioxidants.

Materials and Methods

The following aromatic herbs were collected in May 2001: rosemary (Rosmarinus officinalis L.), cultivated leaves; sage (Salvia officinalis L.), wild herba; basil (Ocimum basilicum L.), cultivated leaves; thyme (Thymus vulgaris L.), wild herba; oregano (Origanum vulgare L.), wild herba; marjoram (Origanum majorana L.), wild herba.

The harvested herbs were air-dried at room temperature for 3 days, packed in double walled paper bags and stored 10-15 days at 15°C before use. The rancimat method (Metrohm Rancimat 743) was applied to detect antioxidant activity. 2 g of ground herbs dissolved in 10 g of FAME were heated at 383K in 20 lh^{-1} of continuous air stream. The conductivities were monitored continuously until a sudden rise signifies the end of the induction period.

Results and Discussion

The results of rancimat experiments for oxidative stability of fatty acid methyl esters in presence of investigated aromatic herbs are shown in Table 1.

Table 1. Induction times in rancimat experiments for investigated herbs

	Rosemary	**Sage**	**Basil**	**Thyme**	**Oregano**	**Marjoram**	**Control sample**
SME	5.16	15.26	2.12	5.62	4.10	3.51	2.17
RME	16.43	29.76	8.84	11.59	12.00	14.41	8.93

SME - sunflower oil methyl ester; RME - rapeseed oil methyl ester

The protection factors (PF) were calculated by dividing the induction times of investigated samples by the induction time of control sample. As conclusion all examined herbs, except basil, are very interesting in preventing autoxidation of FAME (biodiesel). Wild sage, growing in Montenegro, shows significant antioxidant activity that will be considered in further investigation.

Reactivity of 2-[(Carboxymethyl)sulfanyl]-4-oxo-4-arylbutanoic Acids with Diazodiphenylmethane. A LFER Study

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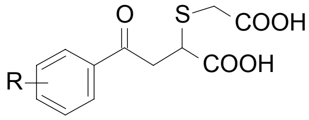
The 2-[(carboxymethyl)sulfanyl]-4-oxo-4-arylbutanoic acids (Chart 1) exert antibacterial[1] and antiproliferative activity[2]. Compounds were synthesized in Michael-type addition of the thioglycolic acid to series of (E)-4-aryl-4-oxo-2-butenoic acids. (E)-4-Aryl-4-oxo-2-butenoic acids were prepared by Friedel-Crafts acilation using maleic anhydride.



R = H- (1); 4-Me- (2); 4-Et- (3); 4-i-Pr- (4); 4-n-Bu- (5); 4-tert-Bu- (6); 3,4-di-Me- (7); 2,5-di-Me- (8); 4-F- (9); 4-Cl- (10); 4-Br- (11)
(Chart 1)

The rate constants for 11 2-[(carboxymethyl)sulfanyl]-4-oxo-4-aryl-butanoic acids in their reaction with diazodiphenylmethane (DDM) were determined in ethanol at 30 °C by the UV spectroscopic method[3]. Diazodiphenylmethane reacts with carboxylic acids as follows:

$$\mathrm{RCOOH + Ph_2C{=}N_2 \rightarrow RC(O)CHPh_2 + N_2}$$

The intention was to study the effects of the substituents on the phenyl nuclei to the carboxylic groups reaction center. The obtained rate constants were analyzed with Hammett, Taft, Yukawa-Tsuno and Swain-Lupton equation. Hammett, Taft and Yukawa-Tsuno approach give good results when hole series of compounds were separated on two groups (alkyl-substituted and halo-substituted compounds). The best results for all 11 compounds were assessed using Swain-Lupton equation:

$$\log k_2 = a \ \mathrm{x} \ \mathbf{F} + b \ \mathrm{x} \ \mathbf{R} + \log k_0$$

Where **F** is field and **R** is resonance Swain-Lupton coefficients (modified by Hansch et.al.[4]) and k_0 are calculated value for unsubstituted acid. Using $\boldsymbol{\sigma_I}$-values[5] in place of **F** we were obtained good correlation too. The finest equations were obtained for 10 alkyl- and halo-, p- and m,p -substituted compounds (Equation 1 and 2, Table 1). Including 2,5-di-Me- substituted compound (8) in correlations the slightly inferior equation were assessed (Equation 3 and 4, Table).

Eq.	F	σ_I	R	logk_0	r	n	sd	F	Compounds Nº
1	0.049	/	-0.306	-0.564	0.9907	10	0.0060	156	1,2,3,4,5,6,7, 9,10,11
2	/	0.041	-0.308	-0.563	0.9904	10	0.0061	152	
3	0.026	/	-0.333	-0.567	0.9826	11	0.0089	98	1,2,3,4,5,6,7, 8,9,10,11
4	/	0.025	-0.332	-0.566	0.9845	11	0.0084	110	

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Reactivity of Pyridinecarboxylic Acid N-Oxides with Diazodiphenylmethane in Various Aprotic Solvents

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Rate constants for the reaction of diazodiphenylmethane (DDM) with 2-, 3- and 4-pirydinecarboxylic acid N-oxides were determined in various aprotic solvents at 30°C using the appropriate UV-spectroscopic method.

The reactivities and the solvent effects are interpreted in terms of the relative influence of the solvent parameters on the reaction rate constants (*k*) of the examined acids. The obtained results are correlated using the total solvatochromic equation, of the form:

$\log k = \log k_0 + s\pi^* + a\alpha + b\beta$,

where π^* is the measure of solvent polarity, β represents the scale of solvent hydrogen bond acceptor basicities and α represents the scale of solvent hydrogen bond donor acidities.

The multiple linear correlation of log k with above aprotic solvent parameters was successful. The correlation equation developed by stepwise regression for all acids showed that the best approach lies in correlation of kinetic data with all above mentioned parameters. The results obtained in the present work for investigated pyridinecarboxylic acid N-oxides was used for discussing the influence of aprotic solvent parameters, and also for comparison with previously determined data for the same acids in various alcohols. [1,2,3]

The opposite signs of the electrophilic and nucleophilic parameters, except for 2-pyridinecarboxilic acid N-oxide are in agreement with the well-known reaction mechanism. Different results for 2-substituted acid are explained by existing strong intramolecular hydrogen bonds.

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Emission Spectra of Some Substituted Phenoxathiin Sulphones and of Some Inclusion Complexes with Cyclodextrins

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Fluorescence natural lifetime and fluorescence quantum yield of some substituted phenoxathiin sulphones have been calculated from absorption and fluorescence emission measurements. For 3-brom-methyl-phenoxathiin sulphone, a solvatochromic study has been performed and the dipole moment change in the excited state has been evaluated. For the same compound, the inclusion complexes with cyclodextrins were studied and the association constants were estimated.

Inclusion of Fullerenol in Water [$C_{60}(OH)_{24}@H_2On$]

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In this paper the simple method of synthesis with water-soluble derivative of fullerenol $C_{60}(OH)_{24}$ starting from $C_{60}Br_{24}$, as well as the newly developed method of separation using the combined cationic/anionic ion-exchange resin is described. Derivative $C_{60}Br_{24}$ was obtained by catalytic synthesis from elementary bromine with $FeBr_3$ as a catalyst. Substitution of bromine atoms in water-alkaline medium yielded fullerenol $C_{60}(OH)_{24}$. Fullerenol $C_{60}(OH)_{24}$: FTIR 3427, 1627, 1419, 1080 cm^{-1}; ^{13}C NMR (D_2O): alkaline reaction mixture δ=77.7 ppm (singlet) δ=140 ppm (multiplete) and pure fullerenol δ=169.47 ppm (singlet) and δ=160-110 ppm (multiplet); MALDI (matrix 2,5-dihydroxybezoic acid) (*m/z*): 721 ($C_{60}H^+$), 802 ($C_{60}(OH)_5{}^+$), 840 ($C_{60}(OH)_7{}^+$), 1091 ($C_{60}(OH)_{22}{}^+$); (matrix α-cyano-4-hydroxycinnamic acid) (*m/z*): 720 ($C_{60}{}^+$), 721 ($C_{60}H^+$), 722 ($C_{60}H_2{}^+$), 737 ($C_{60}(OH)^+$), 852 ($C_{60}(OH)_8{}^+$), 989 ($C_{60}(OH)_{16}{}^+$), 1021 ($C_{60}(OH)_{18}{}^+$), 1043 ($C_{60}(OH)_{19}{}^+$), and minor pik 1057 ($C_{60}(OH)_{20}{}^+$), 1111 ($C_{60}(OH)_{23}{}^+$). DTG, DTA, TG: in temperature of 120–395 ^{0}C, corresponding to the loss of mass of 35.7 % (23.7 OH grops) and at the temperature of od 430 ^{0}C loss of mass was 64.3 %. (temperature of sublimation of C_{60}). The difference in chemical shifts between singlet peaks of alkaline fullerenol mixture (δ=77.7 ppm) and pure fullerenol (δ=169.47 ppm) is probably the consequence of formation of the spherical network of hydrogen bonds between OH groups in fullerenol and water molecules, in which the inclusion compound of fullerenol in water [$C_{60}(OH)_{24}@H_2On$] is obtained. Singlet peak indicates the equivalent screening of all carbon atoms in [$C_{60}(OH)_{24}@H_2On$]. In case of alkaline reaction mixture no hydrogen bond network is obtained because of hydration of excess Na^+, OH^-, and Br^- ions, so the fullerenol molecule has a characteristic singlet peak at δ=77.7 ppm, assigned as C-OH.

Tandem Process Leading to Novel Aza-Spiro Ring Systems

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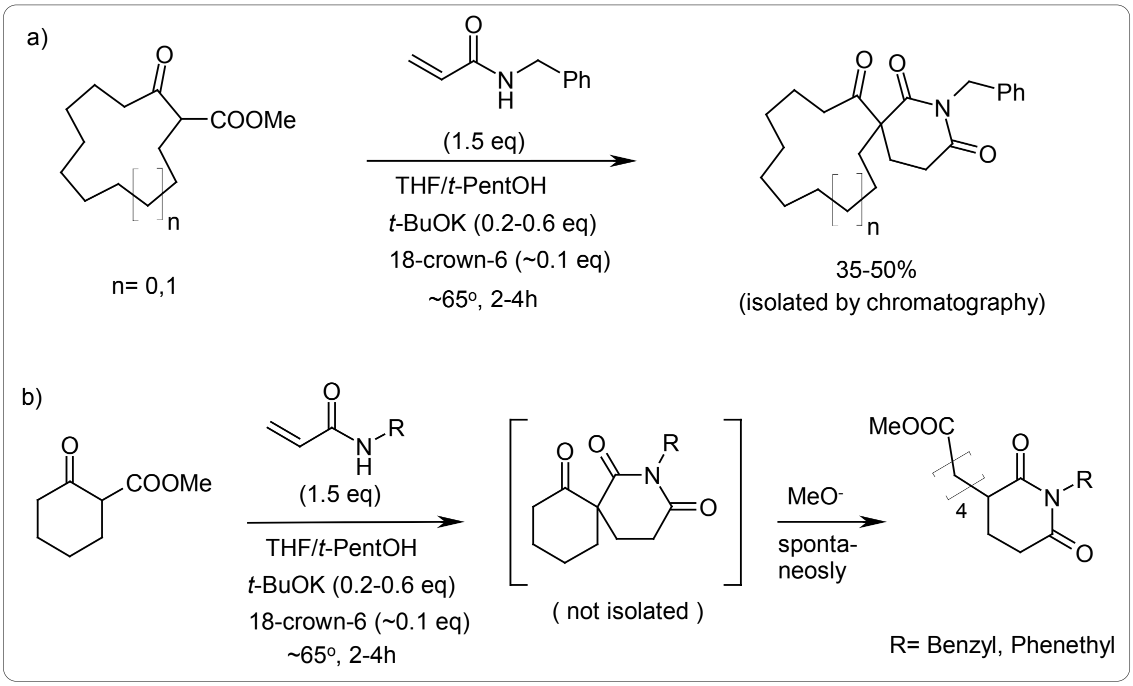
We report a tandem process involving a cyclic β-keto ester (methyl 2-oxo-cyclododecanecarboxylate or methyl 2-oxo-cycloundecanecarboxylate) and *N*-benzyl acrylamide affording substituted glutarimides in novel spiro-ring systems. Mechanistically, the initial step represents 1,4-addition of β–keto ester enolate to the Michael-type acceptor, followed by the glutarimide ring closure, Scheme 1a. In our previous report, we described a very similar domino process, involving methyl 2-oxo-cyclohexanecarboxylate and *N*-alkyl acrylamide, leading exclusively to 3-substituted glutarimides under the same reaction conditions, Scheme 1b.[1] Apparently, the intermediate aza-spiro ring in the later instance is strained enough as to undergo spontaneous cyclohexanone ring fission via ketone cleavage route. The assigned structures were in full agreement with the instrumental data (MS, ^{13}C NMR, ^{1}H NMR, IR).
According to the preliminary optimization results, only *t*-BuOK/18-crown-6 system gave satisfactory yields, while the other examined bases (LiH, NaH, DBU) combined with quaternary ammonium salts were far less effective.
In a view of the fact that *N*-substituted glutarimides are readily reduced to the corresponding piperidines, the present procedure may provide access to various novel aza-spiro ring systems of a potential synthetic and pharmacological significance. Further research is expected to highlight scope and limitations of the process both in terms of the reactant structures and the reaction conditions .

Scheme 1



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Towards the Synthesis of 7-Deoxypaclitaxel C,D-*seco*-derivatives

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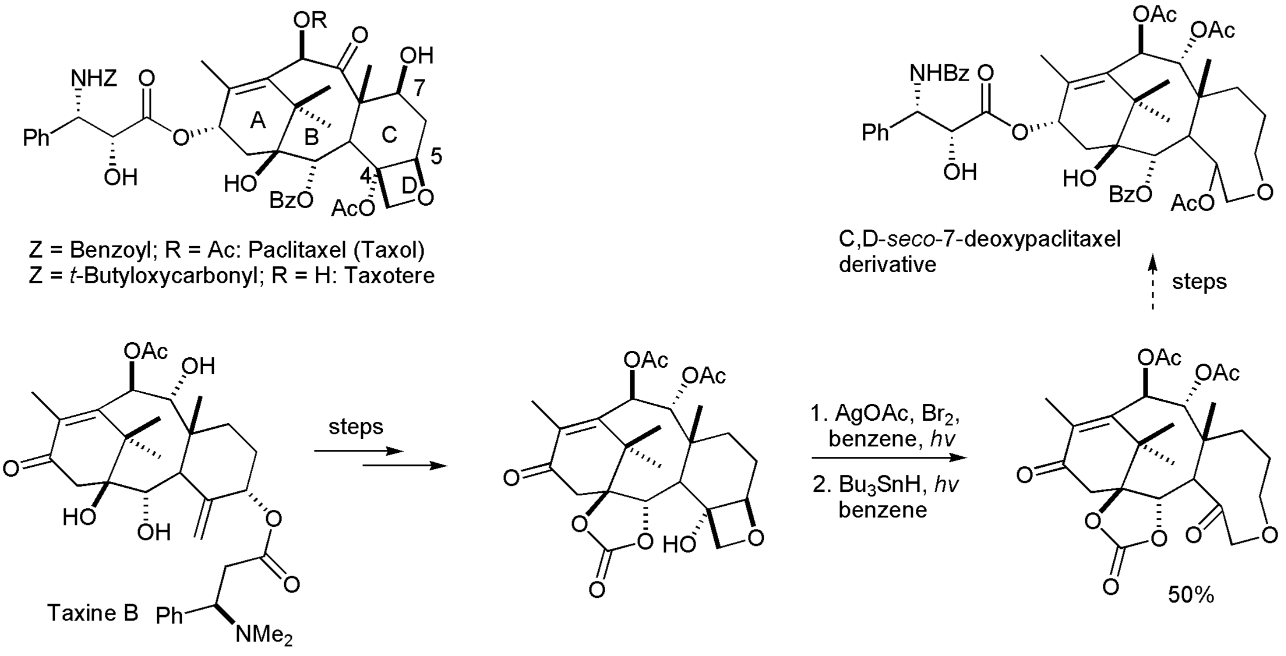
Taxol® (Paclitaxel) – a diterpene isolated from the bark of the Pacific yew (*Taxus brevifolia*) – is currently one of the most efficient clinical anticancer agents. Structure activity relationship (SAR) studies have shown that the oxetane ring is an essential structural element for the antimitotic activity of taxoids.

In order to estimate the effect of conformational constraint imposed by the oxetane ring to the cytotoxicity of taxoids, we endeavored to synthesize C,D-*seco*-paxlitaxel derivatives and evaluate their biological activity. The starting material for this semisynthesis is Taxine B – a pseudoalcaloid readily isolated from the renewable needles of the European yew (*Taxus baccata*). The pivotal step in the synthesis is the fragmentation of the C4-C5 bond, which is achieved by a hypobromite reaction.



Thin-Layer Chromatography of Mixed Tetraoxanes

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Our long-term research has focussed on investigation of retention behaviour of biologically active substances in different planar chromatographic systems [1]. In continuation of these studies, in this work the thin-layer chromatograhic behaviour of recently synthesized mixed steroidal 1,2,4,5-tetraoxanes [2] was examined. The investigated compounds were chromatographed under both normal- (NP) and reversed-phase (RP) conditions. For this purpose unmodified silica gel, polyacrilonitrile sorbent, as well as RP-18 silica were used as sorbents. Normal-phase chromatographic separations were performed using binary mobile phases - ethyl-acetate - toluene and ethyl-acetate - petroleum ether. Binary systems comprising mixtures of methanol, acetone or dioxane (as organic modifiers) and water were used as mobile phases for reversed-phase separation.

On the basis of the results obtained, the effect of the mobile phase composition on retention parameters has been considered.

Also, the retention behaviour of the investigated tetraoxanes was followed by calculating the R_M values. These values were plotted against the vol% of the organic component of the mobile phase in RP-systems i.e. vol% of the more polar organic component of the mobile phase in NP-systems. From results obtained by reversed-phase chromatography, the corresponding hydrophobicity parameters were determined.

The selectivity and the retention mechnisms of employed chromatographic separations were discussed.

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Effect of Acetic Acid Content of the Solvent on the Condensation Rate of Fischer's Base Aldehyde with Anilines

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Condensation of 1,3,3-trimethyl-2-methylenindolin-ω-aldehyde, known as Fischer's base aldehyde (FBA), with anilines in acidic medium is a convenient way for the synthesis of hemicyanine dyes with commercial importance [1,2]. The present work aims to study the effect of acetic acid concentration on the rate of hemicyanine dye synthesis. The kinetics of the condensation of both *para* and *meta* substituted anilines with FBA was investigated spectrophotometrically, in different acetic acid - water mixtures as the reaction medium. It was found that the reaction is reversible. The forward reaction follows a second-order kinetics at constant acidity, first-order with respect both to the aldehyde and the aniline. The rate of the condensation decreased with the increase of the acetic acid concentration (at high concentrations of AcOH) due to the decrease of non-protonated aniline concentration. For example, the observed rate constant of the forward reaction between FBA and 4-aminobenzonitrile diminishes from 11.2 10^{-3}L mol^{-1} s^{-1} to 7.45 10^{-3} L mol^{-1} s^{-1} and to 4.64 10^{-3} s^{-1} mol^{-1}as the content of the acetic acid increases from 30 % to 45 % and 60 %, respectively (see Figure 1). These solvent compositions are close to those used in the synthesis of the dyes.

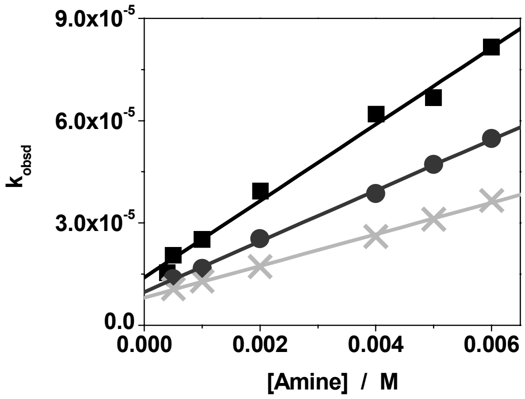

Figure 1. Observed rate constants for different 4-aminobenzonitrile concentrations in the condensation with FBA in 30 % (■), 45 % (●), or 60 % (✕) acetic acid solution at [FBA] = 5.00 10^{-5} M, 30 ºC.

However, at lower acid concentrations (from 0.052 M to 0.364 M), in water-methanol mixture, the rate of the condensation was found to increase with increasing acid concentration. This suggests an acid catalyzed process. The effect of substituents on the aniline ring upon the reaction rate was studied using Hammett plots in order to establish a structure-reactivity relationship and to identify the rate-determining step of the condensation process. Based on the observations, a reaction mechanism is suggested.

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Investigation of Siloxane Activities Toward Basic Equilibration Catalysts

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The well-known siloxane equilibration process consists basically of the continual breaking and reforming of siloxane bonds, caused by the catalytical action of a number of ionic substances, both acidic as well as basic. By sufficiently long reaction times, this catalyzed process leads to the formation of a dynamic equilibrium state, characterized with the corresponding equilibrium reaction mixture composition, named the equilibrate. The over-all rate of the described process depends on the ease of interaction between the applied catalyst and the siloxane bonds of the particular siloxane compounds involved in equilibrations, and will be defined as the siloxane activity.

The applied procedure for the determination of the relative siloxane activities is grounded on the following facts. As already stated above, siloxane equilibrates can not change their compositions by themselves: but, the addition of any other siloxane compound will cause composition changes, which will end with the formation of a new equilibrium state, i.e. new equilibrate. These changes are related to the changes of the length and shape of siloxane molecules present in the mixture, i.e. to the changes of the molecular weight. It seemed therefore to be reasonable and correct enough, to assume that the viscosities and their rate of change in such systems – because being a measure of molecular weights – should give the desired informations about the relative activities of the added siloxanes.

Performing the equilibrations as usual, and measuring the viscosities (as inherent viscosities) as a function of reaction time, it was shown that activities of siloxane compounds can be determined.

The results obtained herein are related to the mutual activities of hexamethylcyclotrisiloxane, D_3, octamethylcyclotetrasiloxane, D_4, tetravinyltetramethylcyclotetra-siloxane D_4^{vinyl}, hexamethyldisiloxane, MM, and of a linear all-methyl oligosiloxane of number average molecular weight of approximately 800, $MD_{8.5}M$, toward tetramethylammonium hydroxide, TMAH, basic equilibration catalyst. The results showed that there was the following decreasing order of activities: $D_3 > MD_{8.5}M > D_4 > D_4^{vinyl} > MM$.

Esterification of Natural Petroleum Acids

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Esters of petroleum acid are compounds that have a wide range of industrial applications, namely for production of colors and polishes, leather, cosmetics, pharmaceutical industry and in many other fields. So far, numerous syntheses of esters of petroleum acids have been done, mainly with the use of acidic catalysts (1, 2), however these reactions are very slow and with low yield.
Our research focused on obtaining a modified protocol for esterification as well as transesterification of natural petroleum acids, to enable us to synthesize esters that had very low yields with classical methods. P-toluenesulphonic acid was used as a catalyst, along with co-catalyst use of microwaves (180-360W). First, we studied esterification of petroleum acids isolated from commercial oil fraction (b.p. 190-400^0 C) of "Velebit" oil of Vojvodina with methanol, ethanol, n-butanol, t-butylalcohol and benzylalcohol. Next, we studied transesterification of methylnaphtenates with t-butylalcohol and benzylalcohol. These were small scale reactions with 100mg of acid (or ester) and 1.5 ml of appropriate alcohol, and the variable parameters were reaction time (10-40 min) and microwave power (180-360 W). Reaction flow and yield were determined using liquid chromatography and IR-spectrophotometry. The best yield of 90.34% was reached in transesterification of methylnaphtenates with t-butylalcohol.

Acknowledgement.
This study was supported by the Ministry for Science, Technology and Development of the Republic of Serbia (Project ”Synthesis of Potential Cytotoxic Agents, Antihormones, Enzyme Inhibitors and Growth Stimulators”, No 1896)

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New Organo-Substituted Phosphazenes. Precursors for Covalent and Non-Covalent Materials

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Different side groups grafted on the cyclic phosphazene polymeric backbone generate materials with different features. Their characteristics may vary from those of elastomers to glasses, from water-soluble to hydrophobic polymers, from bioinert to bioactive materials, and from electrical insulators to conductors. Properties like solubility, hydrophobicity, hydrophilicity, crystallinity, electrical conductivity, glass transition temperature and optical characteristics can be controlled by the nature of the side group.

In recent years, there has been considerable interest in designing organic-inorganic hybrid materials with novel characteristics and enhanced properties. Promising results have been obtained by using cyclo- and poly(organophosphazenes) in the sol-gel process with oxides, such as SiO_2, TiO_2, and ZrO_2.

Also, three-dimensional structures self-assembled through hydrogen bonding have been obtained by using the combination of cyclotriphosphazenes and small organic compounds with bifunctional groups. These results suggest that the cyclotriphosphazene derivative is a useful building block to create polymeric and three-dimensional supermolecules.

Our efforts are focused on the design and preparation of organo-substituted phosphazenes as precursors for hybrid materials as follows:

- a siloxane monomer starting from hexachlorocyclotriphosphazene, $N_3P_3Cl_6$ and 3-(triethoxysilyl)-propylamine, $H_2N\text{-}(CH_2)_3\text{-}Si(OC_2H_5)_3$ for sol-gel processing materials
- a squarate-substituted phosphazene for polymeric supramolecular self-assemblies.

The compounds have been characterized by infrared and NMR spectroscopy, X-ray diffraction method, as well as thermal differential analysis.

Synthesis and Application of Azoic Direct Dyes Based on Non-Mutagenic 4, 4'-Diaminobenzanilide

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Covering the whole color palette the benzidine dyes represented for a long time an important range of practically used dyes. Taking into account the carcinogenic character of benzidine and its derivatives, intensive efforts are made to replace them.

The structural similarity between 4, 4'-diaminobenzanilide and benzidine recommend the former as a valuable replacement for the latter. Previous results revealed encouraging possibilities to improve the tinctorial properties by diversifying the range of coupling components from the salicylic series.

This paper presents the synthesis, and characterization of a series of symmetric and asymmetric direct dyes, containing 4, 4'-diaminobenzanilide as middle component, which cover a color range from yellow to green.

The coupling components (R) used in the synthesis were: N-benzoyl-salicylamide, acid γ (in alkaline, and acid medium); respectively monoazo dyes: *p*-nitroaniline → acid H, and 1-naphtylamino-7- sulphonic acid → 1- naphtylamino-6- sulphonic acid.

The stepwise coupling ability of the 4, 4'-diaminobenzanilide derivative allowed for the preparation of unsymmetrical dyes.

The products obtained have been characterized by UV-VIS spectroscopy and their purity was determined by thin layer chromatography.

Coloristic and fastness properties were determined too. The obtained direct dyes have good affinity towards different textile supports. The affinity and washing fastness are significantly improved by copper treatment.

New Tetrahydroacridine Derivatives from 9-Amino-7-Methoxy-1,2,3,4 Tetrahydroacridine

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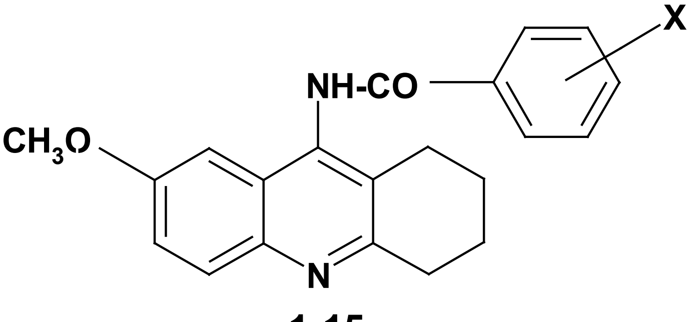
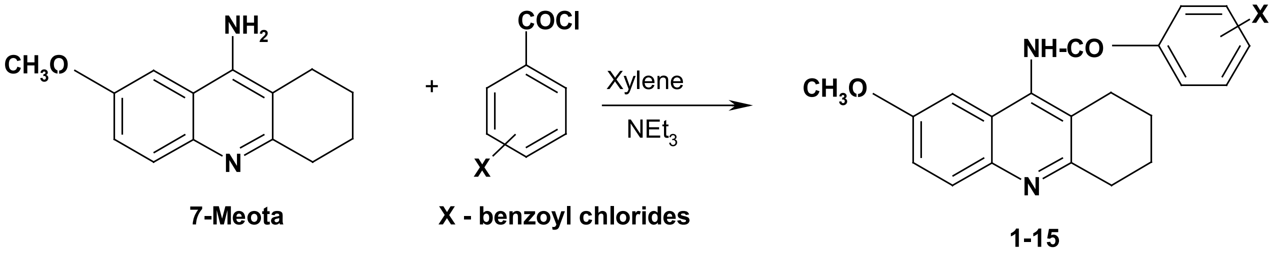
The present work describes the synthesis and spectral characterization of fifteen N-substituted benzamydes having as precursor 9-amino-7-methoxy-tetrahydroacridine (7-Meota). The synthesised compounds are pressumed to have potential activity in inhibation of acetylcholinesterase, which makes possible their application in the treatment of intoxications with organophosphoric poissons.



1-15

where X: Br; CH_3;n-C_4H_9; OH; OCH_3; OC_2H_5;NH_2;NO_2

The synthesis of compounds consists in the condensation of substituted X-benzoyl chlorides with 7-Meota in the presence of triethylamine as acceptor of HCl, in refluxing xylene for 8-10 hours.



The spectral data (IR, 1H-RMN, 13C-RMN, 2D-experiments (HETCOR, COSY H-H) and elemental analysis confirms the structure of the new synthesised compounds.

Synthesis of a Coumatetralyl Salt and the Biological Efficiency of the Preparation

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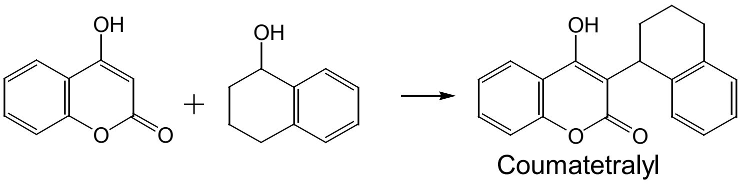
Legal requirements in some areas for the use of rodenticides of the first generation anticoagulants for the control of the rodent population, resulted in the development of the synthesis of coumatetralyl salt.

Due to a relatively low toxicity, legal requirements in some areas are such that only first generation active ingredients can be used in preparations for the control of rodent population. Areas where such requirements are applied are around water courses where there is a possibility that highly toxic chemicals, such are II generation hydroxycoumarin derivatives, can be the cause of contamination.

4-hydroxycoumarin derivative, coumatetralyl, of purity exceeding 98% was synthesized in high yield, Scheme. The existing powder formulation is not practical for further manufacture of ready to use baits. Therefore, a liquid formulation was needed. Due to a low solubility of coumatetralyl in common solvents a method for its salt formation was developed.



Scheme

In order to test the efficacy of the preparation based on coumatetralyl salt a comparative study carried out on laboratory and on field rodents was carried out. The results indicated that the efficacy of ready to use baits based on coumatetralyl salt is increased compared to ready to use baits based on coumatetralyl itself. It is clear that such an effect is due to a higher solubility of the coumatetralyl salt in blood of the rodent. Toxicological experiments that should confirm our statement are in progress.

Chemiluminescence Characterization of Products after the Degradation of Some Fatty Acids

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The fatty acids are the main constituents of the food, and, therefore it is important to know their behavior at the thermooxidative destruction under conditions similar to those intervening at the industrial processing.

The thermoxidative destruction was investigated in the temperature range 50 – 100°C using saturated (stearic and palmitic) and unsaturated (palmitoleic, oleic and linoleic) fatty acids and other nutritive products (fish oil, shark oil) with polyunsaturated acids of omega 3 type.

The investigation presents the evolution in time and the effects of temperature on the structure changes monitored by spectral techniques, FT−IR and chemiluminescence.

The absorbance of the carbonyl (1720 cm^{-1}), aliphatic (725 cm^{-1}) and unsaturated groups (970 cm^{-1}) were used to assess the most important structural changes of fatty acids; the evolution of the typical bands are arguments for the proposed reaction mechanism.

The pro or antioxidant behavior of the species resulting from the destructive process is revealed by chemiluminescence characteristics.

These spectral data have been also used for evaluation of kinetic characteristics of degradation processes.

Cycloaddition Reactions to the 2,5-Di-*t*-butyl-benzoquinone System

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2.5-Di-tert-butyl-hydroquinone **1** is a white product with m.p. 210-212˚C. This substance is obtained from the reaction of hydroquinone with t-butylalchool in concentrated sulfuric acid. By oxidation with potassium bicromate solution and concentrated sulfuric acid, 2.5- di-tert-butyl-hidroquinone **1** is converted into 2.5-di-tert-butiyl-p-benzoquinone **2**, a yelow product with m.p. 152˚C. It is known that **2** by cycloaddition reactions with diazomethane yields two adducts 3 (5.7a-di-tert-butyl-3a,7a-dihydro-3H-indazol-4,7-quinones) and **4** (benzo[1,2-c;4,5-c']dipyrazole-4,8(3aH,4aH)-dione,4a,8a-di-tert-butyl-3a,7,7a,8a-tetrahydro). In our work, we were interested in studying the possibilities of the reactions of bromine with the **3** and **4** pyrazolic adducts. By gas-chromatography coupled with mass-spectrometry (GC-MS) we identified three bromoderivatives. We also studied the reaction of adduct **3** with bromine in basic medium and we recuperated the compound **2**.

Flow-Vacuum Pyrolysis of Some Triazoles

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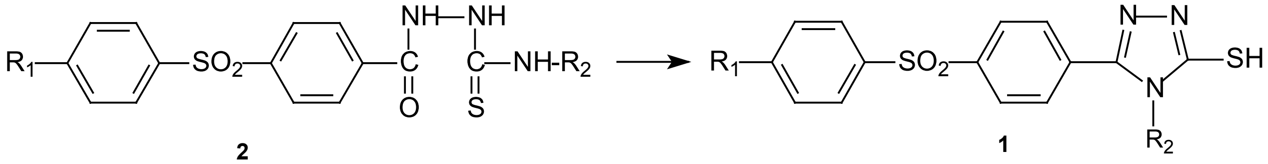
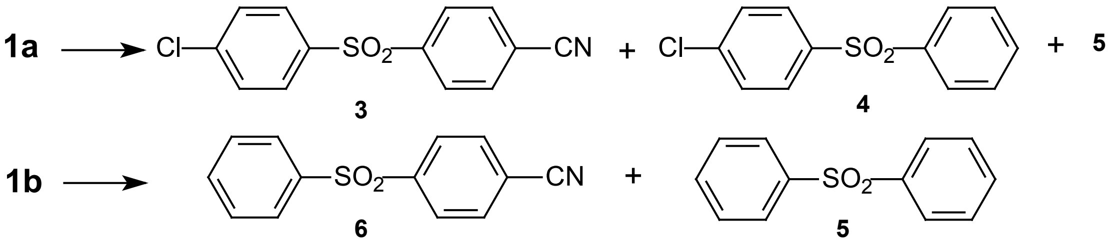
The present work continue our researches on flow-vacuum pyrolyses[1,2]. We describe here the study of thermal behavior of triazoles **1** at different temperatures (between 375 – 750^{0}C), at 1-3 mmHg, in inert atmosphere (4 mL/min argon flow rate) and quartz pyrolysis tube (60 cm length, 1 cm internal diameter, quartz chips filling on 30 cm). The reaction products were studied by GC/MS. The synthesis of **1** was performed by cyclization of thiosemicarbazides **2**[3]:



where: **1a**: R_1 = Cl R_2 = H

1b: R_1 = H R_2 = n-Bu

The pyrolysis reaction mixture contains: 4-chloro-4'-cyano-diphenylsulphone (**3**), 4-chloro-diphenylsulphone (**4**), and diphenylsulphone (**5**) for **1a**, respectively 4-cyano-diphenylsulphone (**6**) and diphenylsulphone (**5**) for **1b**:



The distribution of the reaction products *versus* temperature is presented. A radical mechanism is suggested in order to rationalize the formation of the reaction products:

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A Significantly Improved Procedure for the Preparation of Cyclic β-Keto Esters

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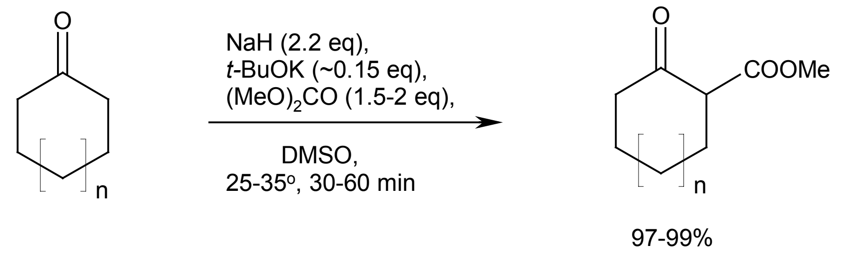
We report an improved method for the preparation of 2-carbomethoxy ketones (β-keto esters), starting from the corresponding cyclic ketones and dimethylcarbonate in DMSO and using NaH/*t*-BuOK mixture as a base. While the reaction itself has been used extensively for decades, it usually requires prolonged heating in hydrocarbon solvents or THF, affording β-keto esters in 70-90% yields, after distillation.[1,2] In the case of thermally labile higher homologs, the unreacted starting ketone and/or impurities must be removed by chromatography. However, according to the present procedure, the reaction is complete in 30-60 min at ~30°, as evidenced by tlc and instrumental methods. After simple aqueous workup, essentially quantitative yields of pure β-keto esters are obtained.

The reaction requires a mixture of NaH (2.2 eq, oil-washed) and *t*-BuOK (0.1-0.2 eq) to proceed smoothly at 25-35°. The presence of *t*-BuOK strongly catalyses the process, as evidenced by rapid H_2 evolution. Addition of 18-crown-6 (0.05-0.12 eq) did not influence the rate significantly. Sodium hydride alone reacts much slower, also requiring higher temperatures (40-50°). On a small scale, (5-10 mmol), both the ketone and dimethylcarbonate (1.5-2 eq) may be added simultaneously, while on larger scale (20-100 mmol), the ketone is added dropwise in order to moderate the H_2 evolution. No side products, nor the starting ketones could be detected by tlc and instrumental methods.

Further examination of the method will reveal the compatibility of various functional groups with the reaction conditions as well as the applicability of carbonates other than dimethylcarbonate.



n= 1, 2, 6, 7

also used: *t*-Bu-cyclohexanone and
7,12-Dioxa-spiro[5.6] dodecan-3-one

(only isolated product,
no contaminats)

References:

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Ring Closing Metathesis/Fragmentation Route to Geometrically Defined Medium Ring Cycloalkenes: the Total Synthesis of (±)-Periplanone C

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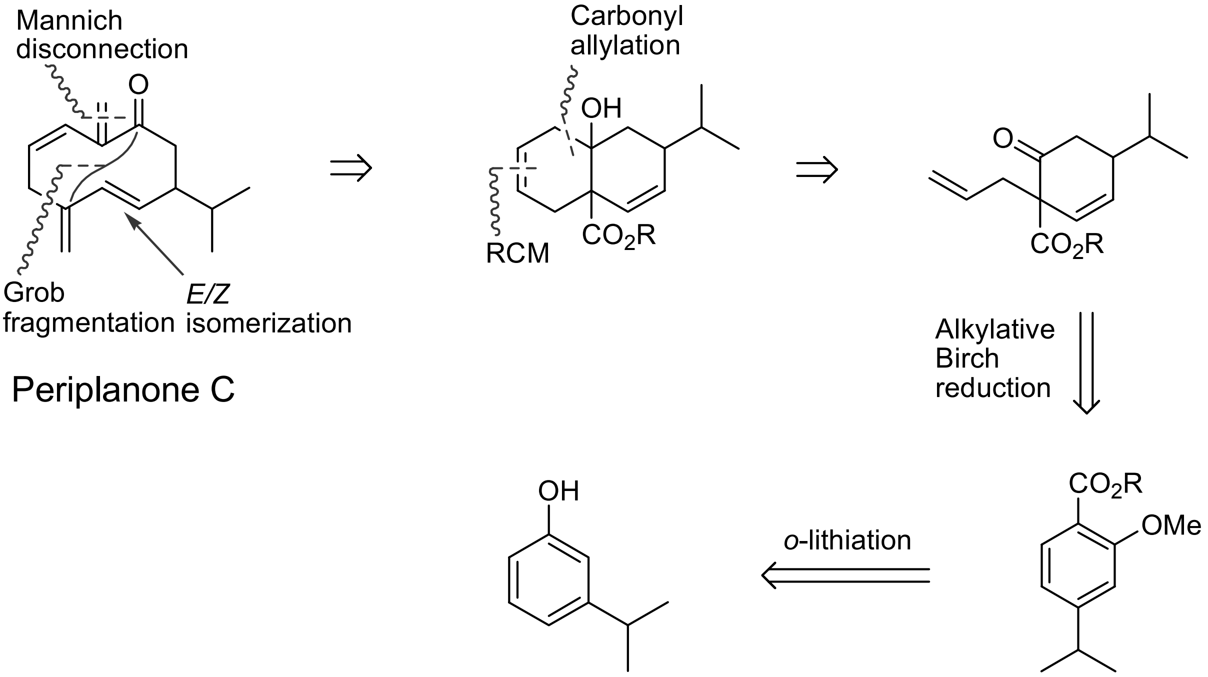
Ring closing metathesis has emerged as one of the most versatile methods for the synthesis of cyclic systems of various ring sizes and has found extensive application in syntheses of complex organic compounds. However, the control of alkene geometry in the medium and large ring cycloalkene products remains an unsolved problem, where the *E/Z* outcome is difficult to predict, or modify.

Our approach to the stereoselective synthesis of medium ring *Z*-cycloalkene relies on the tactical combination of reactions: ring closing metathesis/fragmentation, where the stereochemical constraint associated with small ring closure secures the *Z*-configuration of the alkene bond. The versatility of this method is demonstrated by the total synthesis of Periplanone C – a semiochemical of the American cockroach (*Periplaneta americana*) – which is delineated here in the retrosynthetic format.



Oxidative Transformation of β-D-Glucan from *Saccharomyces cerevisiae*

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1,3-β-D-glucans are widely distributed in microbes, especially in fungi. In recent years many studies suggested that 1,3-β-D-glucans have a variety of biological and immunopharmacologicall activities dependent on the physical state of the glucans, such as solubility in water, molecular mass, degree of branching and conformation[1,2].

β-D-Glucan, one of the major cell wall components of *Saccharomyces cerevisiae,* has been found to enhance immune functions, especially by activating macrophages. However, a major obstacle to the clinical applications of 1,3-β-D-glucan is its low solubility in aqueous media. The purpose of this work is to establish a method to solubilize the 1,3-β-D-glucan from *Saccharomyces cerevisiae.* The present work describes the oxidation of 1,3-β-D-glucan, isolated from the cell-wall of active dry baker's yeast *(Saccharomyces cerevisiae)*, which was commercial product made by Fermentation Industry "Alltech-Fermin", Senta, Serbia and Montenegro. The main structural characteristic of this polysaccharide is a linear chain of (1→3)-linked β-D-glucopyranoses, the part of which is substituted through the positions O-6. The side units or groups are either the single D-glucopyranoses or (1→3)-β-oligoglucosides, linked to the main chain through (1→6)-glucosidic linkages[3]. Oxidative transformation of this polysaccharide was performed by sodium hypochlorite salt of different concentration in aqueous solution. By oxidative degradation, this homopolymer was gradually oxidized to anionic polymers, which decreased the molecular weight at the same time. Solubility of the resulting oxidized polymer were significantly different from the parent glucan, namely significant proportion of the constituents were solubilized during oxidation. The presence of acidic groups in this polymer was evidenced by spectral data.

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Electrosynthesis of New Organic Intermediates

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Using acetylated 2-amino-p-nitrophenyl-1,3-propan diol (*p*-NFS) as starting material and some of its derivatives, it was electrogenerated 2-amino-p-hydroxylaminophenyl 1,3-propan diol and the reactions with different reagents were studied in order to obtain new heterocycles.

Hydroxylamines produced from cathodic reduction of *p*-NFS derivatives present a poor chemical stability in methanol-acetate buffer. Because of a higher stability observed for these reduced species in acetonitrile-water-acetate buffer, subsequent reactions with electrophilic reagents can be performed *in situ* [1]. Surprisingly, the expected hydroxamic acids which could be precursors of benzoxazine diones, were not obtained by adding cyclic anhydrides to a solution of electrogenerated hydroxylamines in acetonitrile-water-acetate buffer and azoxy compounds were the major products. In contrast, benzoxazine diones can be normally prepared in this medium by the addition of phthaloyl dichloride to hydroxylamines resulting from acetylated *p*-nitrobenzylalcohol and triacetylated *p*-NFS. By this way, benzoxazinediones resulting from various *p*-NFS derivatives could be obtained in order to study their biological activities. Moreover, the addition of *p*-toluenesulphonyl chloride to the hydroxylamine electrogenerated from the triacetylated *p*-NFS gives a N-sulphonylated hydroxylamine. This latter can be also obtained by a reversible addition [2] of the nitroso derivative and the *p*-toluenesuphinic acid, so that the reaction of an arylsulphonyl chloride and a phenylhydroxylamine can be an alternative to the preparation of a nitroso compound.

Acknowledgements

The authors are grateful for the financial support provided by the French Government and the AUF projet (Pôle d'excellence régionale 2700 PL 309 Exercice 2003)

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Mechanistic Aspects of 4-Oxothiazolidine-1,2-Dithiole Rearrangement

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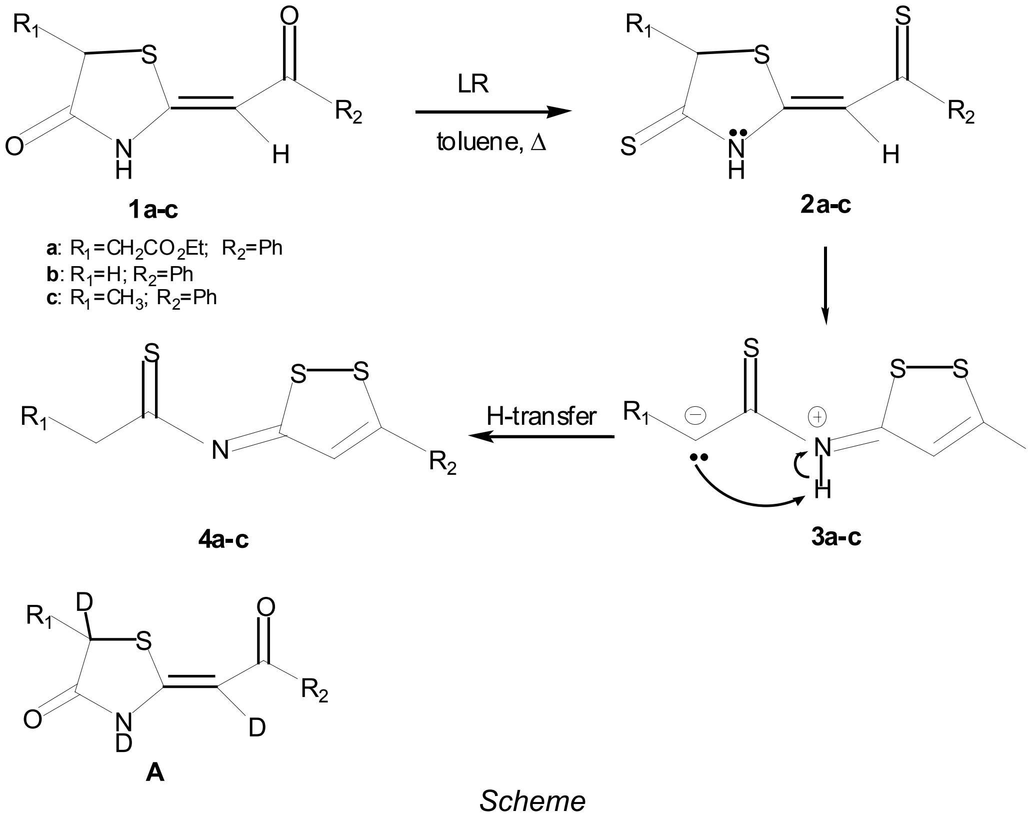
Since the discovery of Lawesson`s reagent [LR: 2,4-bis(p-methoxyphenyl)-1,3-dithiaphosphetane-2,4-disulphide] there has been significant interest for its synthetic application, i.e. the conversion of a wide variety of carbonyls to thiocarbonyl compounds [1].
The mechanistic aspects of the 4-oxothiazolidine-1,2-dithiole rearrangement [2] induced by LR (Scheme) to be discussed include (a) the control over the type of the heterocyclic compounds obtained and (b) the regioselective character of the ring-opening-closing process, which is rationalized in terms of the strongly directing interaction between the nonbonded sulfur atoms (structure 2) prior to the S-S bond formation.



Scheme

The mechanism, which probably involves formation of the thione intermediate **2**, followed by the ring opening-closing process **2**→ **3** and H-transfer, was tested using the partially deuterium-labeled representative (structure **A**) of the series, namely ethyl (*Z*)-(5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (**1a**).

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One-Step Conversion of Ketones to 2-Hydroxy Carbocylic Acids Using Halomethane Reagents

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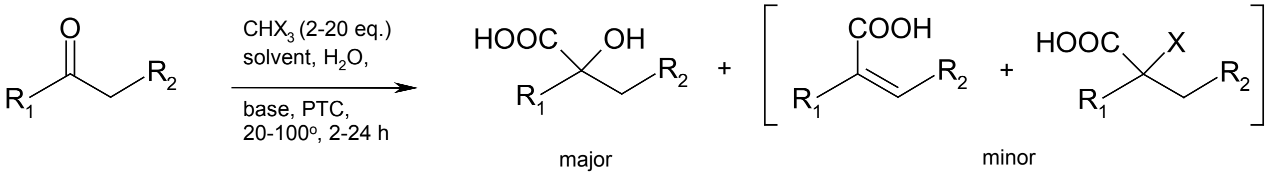
Herein we report a single-step preparation of some aliphatic and aromatic 2-hydroxy carboxylic acids, starting from the corresponding ketones (cycloheptanone, cyclooctanone, acetophenone, propiophenone, dibenzylacetone, 4-ethyl-cyclohexanone) and halomethanes ($CHCl_3$, $CHBr_3$ or CHI_3).[1] The transformation proceeds in various biphasic aqueous/organic mixtures, in the presence of strong bases (NaOH, LiOH, KOH or DBU) and phase-transfer catalysts (TEBA, trioctylmethyl ammonium chloride, 18-crown-6). Tested organic solvents included PhMe, *i*-PrOH, *t*-BuOH, *t*-PentOH, CH_2Cl_2, excess $CHCl_3$ or $CHBr_3$ and DMSO. Depending on the structure of the starting ketones and the reaction parameters (solvents, temperature, base) the hydroxy acids were obtained in variable yields (~45-80%), in some cases contaminated with conjugated acids and/or 2-halo acids, as determined by chromatographic and instrumental methods. Generally, higher temperatures favor better yields of hydroxy-acids. Purification was achieved by crystallization and/or dry-flash chromatography.

The present synthesis of 2-hydroxy acids is a useful alternative to cyanohydrine synthesis, particularly on a large scale, as it is a single-step transformation using much less toxic reagents than HCN.



R_1, R_2 = cycloalkyl, alkyl, aryl; X= Cl, Br

CHX_3 = $CHCl_3$, $CHBr_3$, CHI_3; solvent: i-PrOH, t-BuOH, t-PentOH, $CHCl_3$, $CHBr_3$, CH_2Cl_2, PhMe;

base: LiOH, NaOH, KOH, DBU; PTC: 18-crown-6, TEBA, $Bu_3(Bn)NCl$, $Oct_3(Me)NCl$

Various possible mechanistic pathways were studied using semiempirical MNDO-PM3 model. Solvent influences upon the course of the reaction were simulated using COSMO model.

1. Bromoform as a reagent in the novel synthesis of conjugated acids from ketones, Vesna D. Kiricojević, Jelena B. Đorđević, Željko J. Vitnik and Milovan D. Ivanović, *XLI Annual Meeting of the Serbian Chemical Society*, Beograd, january 23-26th, 2003., Book of Abstracts, page 193

Enantiodivergent Synthesis and Antiproliferative Activity of (+)- and (−)-Muricatacin 7-oxa Analogues

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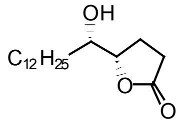
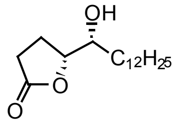
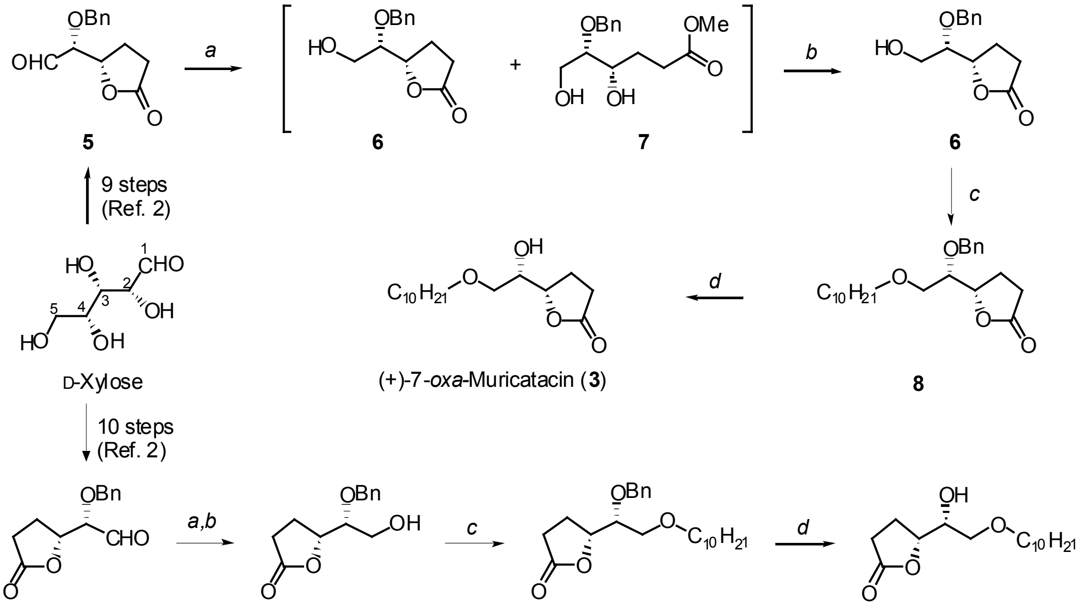
Muricatacin is an acetogenin related γ-lactone that was recently isolated from the plant *Annona muricata*[1]. Interestingly the natural product is a mixture of (+)- and (–)-enantiomers (**1** and **2**). Since both **1** and **2**, as well as certain isosteric analogues, showed cytotoxic activity against some human tumour cell lines, they had attracted considerable attention of synthetic organic chemists. Herein we report on an enantiodivergent synthesis of two novel muricatacin 7-*oxa* analogues **3** and **4**, starting from D-xylose. Reduction of the aldehido-lactone **5**[2] with $NaBH_4$ in methanol gave the corresponding primary alcohol **6** along with an equal amount of the ester **7**. The crude mixture was treated with aqueous trifluoroacetic acid to complete the lactonization of **7** to **6**. Reaction of **6** with 1-bromodecane, in the presence of Ag_2O and AgOTf afforded **8**, which was subjected to catalytic hydrogenolysis over 10% Pd/C to give the target **3**. By using the same reaction sequence, *ent*-**5** was converted to the enantiomer **4**. Antiproliferative activity of **3** and **5** against K562 and MCF7 cell lines was estimated by MTT test.



(+)-Muricatacin (**1**)



(–)-Muricatacin (**2**)



(*a*) $NaBH_4$, MeOH, 0°C, 1.5 h; (*b*) TFA, 0°C→rt, 2 h; (*c*) $C_{10}H_{21}Br$, Et_2O, Ag_2O, AgOTf, reflux, 7.5 h; (*d*) H_2, 10% Pd/C, EtOAc, rt, 19 h.

References:

1. Rieser, M. J.; Kozlowski, J. F.; Wood, K. V.; McLaughlin, J. M. *Tetrahedron Lett.* **1991**, *32*, 1137.
2. Popsavin, V.; Krstić, I.; Popsavin, M. *Tetrahedron Lett.* **2003**, *44*, 8897.

Reactivity of Pyridinecarboxylic Acids with Diazodiphenylmethane in Various Aprotic Solvents

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Rate constants for the reaction of diazodiphenylmethane (DDM) with 2-, 3- and 4-pirydinecarboxylic acids were determined in various aprotic solvents at 30°C using the appropriate UV-spectroscopic method.

The present work is a result our father investigation of the reactivity pyridinecarboxyic acids in various solvents. [1,2]

In order to explain the obtained results through solvent effects, the obtained reaction rate constants (*k*) of the examined acids were correlated using the total solvatochromic equation, of the form:

$$\log k = \log k_0 + s\pi^* + a\alpha + b\beta,$$

where π^* is the measure of the solvent polarity, α represents the scale of the solvent hydrogen bond donor acidities (HBD) and β represents the scale of the solvent hydrogen bond acceptor basicities (HBA). The correlation of the kinetic data were carried out by means of multiple linear regression analysis and the influence of aprotic solvents on the reaction of the examined acids with DDM was discussed. The results presented in this paper for the investigated acids were compared with the kinetic data for piridinecarboxylic acids in various alcohols obtained in the same chemical reaction, under the same experimental conditions.

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1. B. Jovanović, S. Drmanić, and M. Mišić-Vuković, *J. Chem. Res.*, **9**, 1998, 554.
2. S. Drmanić, B. Jovanović and M. Mišić–Vuković J., *Serb. Chem. Soc.,* **65(12)**, 2000, 847.
3. S. Drmanić, B. Jovanović, A.D.Marinković, and M.Mišić-Vuković*, J. Serb. Chem. Soc.*, **68(7)**, 2003, 515.

New Synthesis of γ-Butanolides

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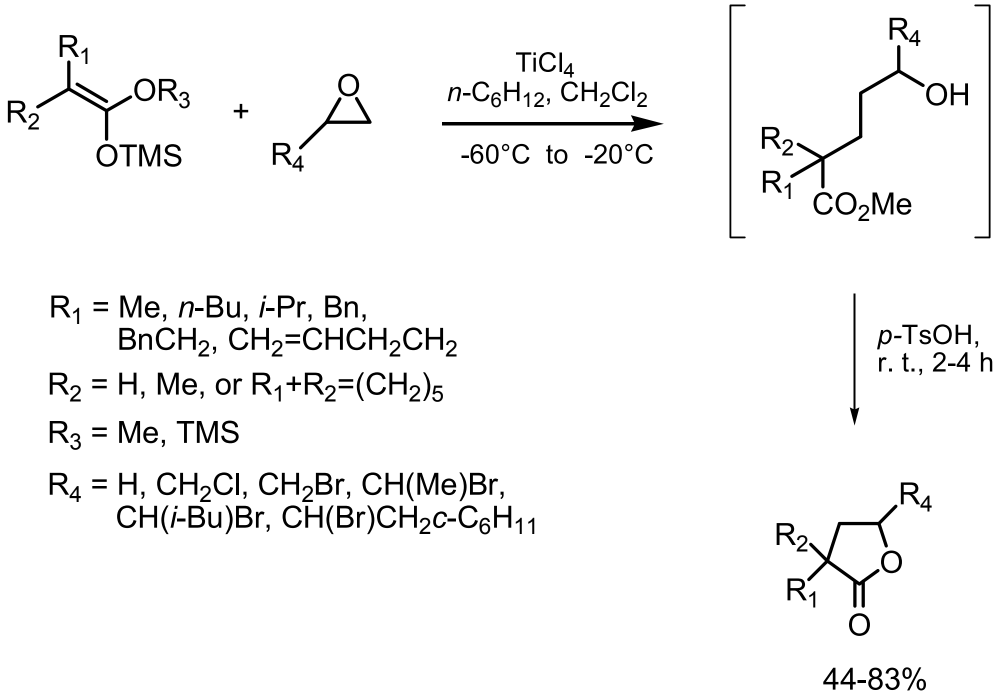
Epoxide ring opening with organometallic reagents is a well known reaction and synthetically highly useful method of carbon-carbon bond formation. Contrary to non-stabilized organometallics, lithium enolates of ketones and esters are unreactive.

We developped a new method for the synthesis of γ-butanolides, which relies on epoxide ring opening with silyl ketene acetals under the conditions of the Mukaiyama reaction. The initial products of the reaction are γ-hydroxy esters, which are subsequently converted into the corresponding lactones. With epihalohydrins the nucleophilic attack occurs regioselectively at the less substituted epoxide end; γ-haloalkyl-γ-butanolides thus obtained are amenable to further synthetic transformations.



R_1 = Me, *n*-Bu, *i*-Pr, Bn, $BnCH_2$, $CH_2{=}CHCH_2CH_2$

R_2 = H, Me, or $R_1+R_2=(CH_2)_5$

R_3 = Me, TMS

R_4 = H, CH_2Cl, CH_2Br, CH(Me)Br, CH(*i*-Bu)Br, $CH(Br)CH_2$*c*-C_6H_{11}

Synthesis of 5-(3- and 4-Substituted Phenylazo)-4,6-dimethyl-3-cyano-2-pyridones *via* 3-(Substituted Phenylazo)-pentene-2,4-diones

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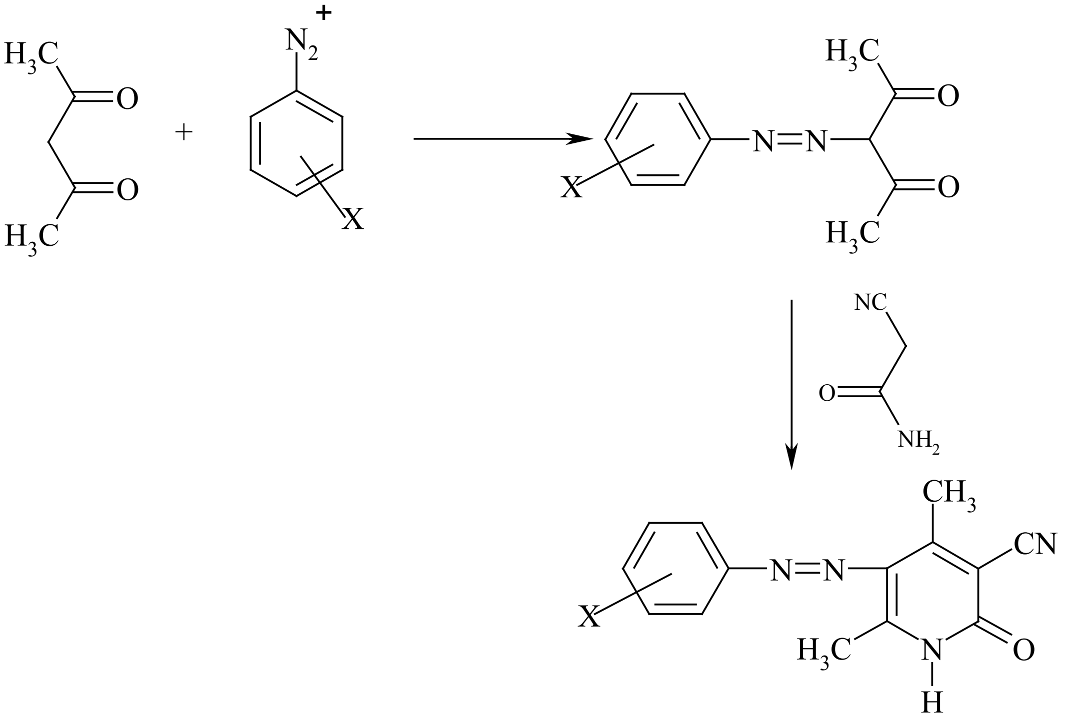
The pyridone azo dyes are usually synthesized by the diazotisation-coupling reaction. The usual way of synthesis of pyridone azo dyes is to first, diazotise substituted aniline and than to couple the product with the pyridone[1]. The other way is to use procedure given in Scheme 1[2]. In this procedure acetylacetone is coupled with diazotised substituted aniline to give an intermediary, which is then cyclized with cyanoacetamide to obtain pyridone azo dye.

Eighten 5-(3- and 4-substituted phenylazo)-4,6-dimethyl-3-cyano-2-pyridones were synthesized using modified procedure given in Scheme 1 (14 new compounds). The azo dyes were obtained in very good yields up to 80%. The obtained new azo dyes were characterized by melting point, UV/vis, ^{1}H NMR and MS data. HPLC analyses were also performed. The colour of these dyes was determined on the basis of reflectance spectra and described in the CIELAB colour space. The influence of structure on the colour of investigated pyridone azo dyes was discussed.



Scheme 1. Synthesis of 5-(3- and 4-substituted phenylazo)-4,6-dimethyl-3-cyano-2-pyridones

References:

1. Chen C, Wang I., *Dyes and Pigments*, **15** (1991) 69.
2. Elgemeie G, El-Zanate, Mansour A., *Bull. Chem. Soc. Jpn.*, **66** (1993) 555.

Electrochemical Bromination of Teroids

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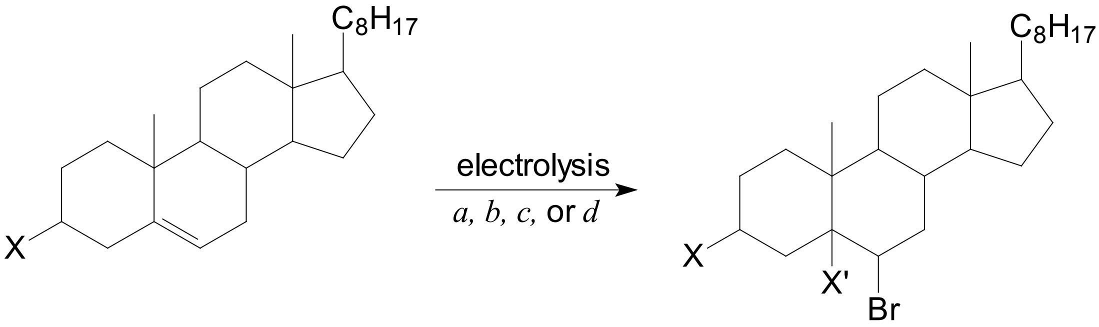
Electrochemical bromination of 5-cholestene (**1**, X = H), cholesterol (**1**, X = OH), cholesteryl acetate (**1**, X = OAc) and 3-chloro-5-cholestene (**1**, X = Cl) (see Scheme) have been achieved by constant current electrolysis (50 mA, 2 F/mol) of the solution of tetraethylammonium bromide and the corresponding substrate in dichloromethane, acetic anhydride, acetonitrile and methanol as the solvents. Electrolysis was performed in a divided electrochemical cell (ceramic membrane), at room temperature, by using a graphite anode and an aluminum cathode.



1 X = H, OH, OAc or Cl **2** (X' = Br)
3 (X' = OMe)

Reaction conditions: a) – dichloromethane, $(C_2H_5)_4NBr$; b) – acetonitrile, $(C_2H_5)_4NBr$; c) – acetanhydride, $(C_2H_5)_4NBr$; d) – methanol, $(C_2H_5)_4NBr$
Scheme

The corresponding 5,6-dibromo derivatives **2** were isolated as the products by column chromatography (SiO_2 / toluene - ethyl acetate 9:1) in moderate to good yields (up to 63%). When methanol was used as the solvent 6-bromo-5-methoxy derivatives **3** are also obtained.

Kinetic Study of the Reaction Between Sodium Chloroacetate and Potassium Ethyl Xantogenate

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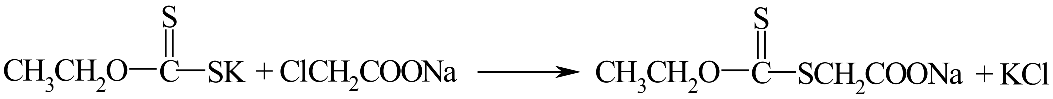
Sodium ethyl xantogene acetate (NaEtXAc) is precursor in the synthesis of thiocarbamates [1-4]. Since such compounds generally have fungicidal properties [5], a detailed study the synthesis of NaEtXAc is a very valuable information for its production.

Synthesis and kinetic study of the following reaction have been performed:



$$CH_3CH_2O-\overset{\overset{\displaystyle S}{\|}}{C}-SK + ClCH_2COONa \longrightarrow CH_3CH_2O-\overset{\overset{\displaystyle S}{\|}}{C}-SCH_2COONa + KCl$$

The reaction kinetic of the synthesis of sodium ethyl xantogene acetate from potassium ethyl xantogenate and sodium chloroacetate in distilled water as reaction medium at t = 25°C, 30°C, 35°C and 40°C, was investigated. Reaction was folloved using the conductrometric method with equimolar initial concentration of the reactants. The rate constants for both reactants and products were calculated from data. On the basis of the reaction constants thermodynamic parameters were calculated and discussed.

References:

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2. Davies W., McLaren J. A., *J.Chem.Soc.*, (1951) 1434
3. Mylius E., *Chem. Ber.*, 6 (1973) 312
4. Mehring J. S., Sayen R. J., *US Patent* 4,298,624 (1981)
5. Walter W., Bode K. D., *Angew. Chem.*, **79(7)** (1967) 285

Lewis Acid Catalysed Phenylselenoetherification of Some Alkenols

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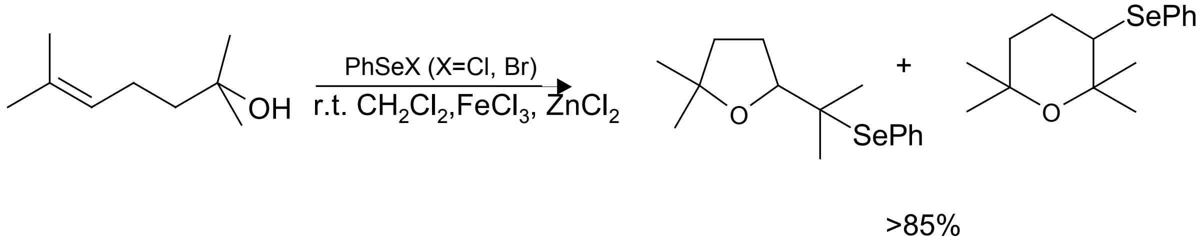
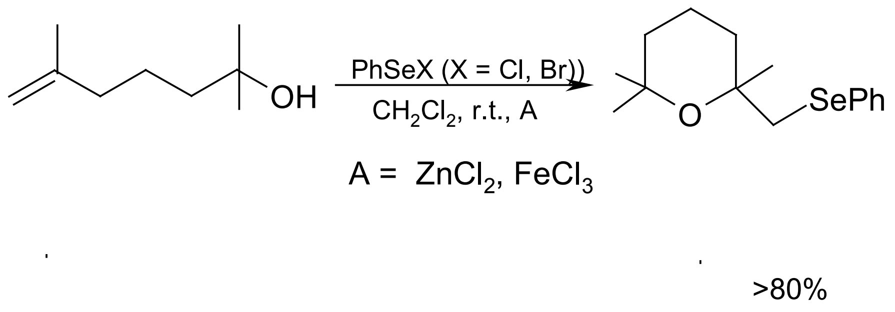
Serbia and Montenegro

During the last years, cyclic ethers units are important synthetic targets in organic and medicinal chemistry due to their widespread occurrence in many complex natural compounds exhibiting important biological activities.

An improved procedure for intramolecular cyclization of some alkenols using PhSeX (X = Cl, Br) has been developed. We found that cyclization can be facilitated in the presence of some Lewis acids as catalysts. In the presence of Lewis acids ($ZnCl_2$ and $FeCl_3$) high yields of cyclic ether products are obtained. Also, the additives influenced dramatic increase in reaction rate. All reactions underwent in a few minutes (without additives reaction time is half an hour to several hours).





References:

1. Konstantinović S., Bugarčić Z., Milosavljević S., Schroth G., Mihailović M. Lj.: *Liebigs. Ann. Chem.* 1992, 261.
2. Mojsilović B., Bugarčić Z.: *Heteroatom Chem*. 2001, **12***,* 475.

New N-Substituted Bis-Barbitoxy-Xylylenes

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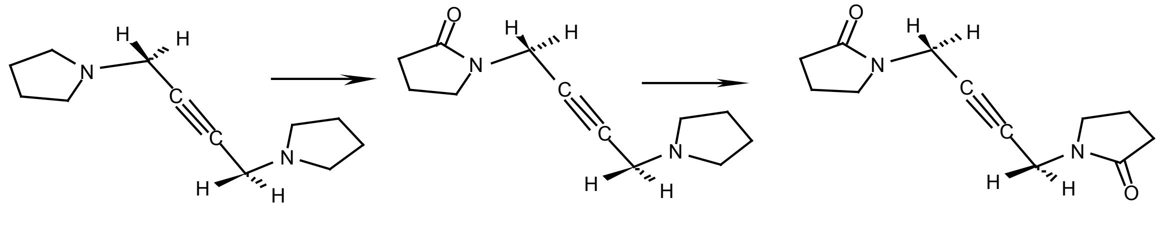
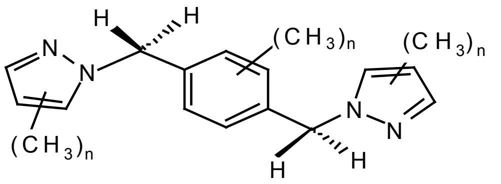
University of Medicine and Pharmacy Carol Davila, Faculty of Pharmacy
Bucharest, Romania

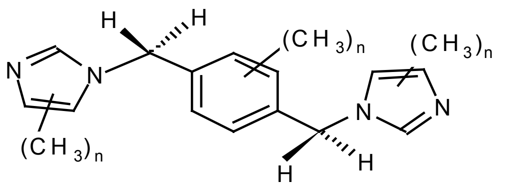
Everett's research[1,2] concerning tremorine has shown that this compound is characterized by an intense analgesic activity, in case of both experimentally induced and pathological pain.



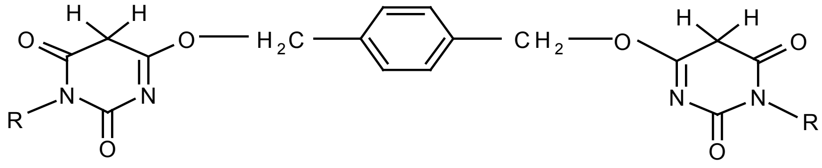
Tremorine *Oxotremorine* *Dioxotremorine*

Afterwards, it was proven that the metabolites of tremorine (oxotremorine and dioxotremorine) present a very intense analgesic activity (more intense than morphine), but with a major disadvantage: they induce a syndrom similar to Parkinson's disease in laboratory animals. It is presumed that the analgesic activity of tremorine is due to the presence of the acetylenic bond with four π electrons which determine a hyperconjugation with non-participant electrons of nitrogen atoms. The aim of ulterior research was the replacement of the acetylenic bond with an aromatic system with six π electrons. Pyrolidine rings were replaced with variously substituted azoles.





The results of pharmacological tests have confirmed the hypothesis and new compounds with less intense analgesic, but with anticonvulsant activity were obtained (they determined an increase of the latency of the anticonvulsant effect with 83,75 – 102,56% in comparison to phenobarbital, in experimentally induced convulsions). Considering the results of previous research[3], we concluded that the anticonvulsant activity is maintained if the azole rings are replaced by barbituric rings having one substituted nitrogen atom.



$R = CH_3, C_2H_5, C_6H_5$

The new compounds were physically and spectrally characterized (UV-VIS, IR, ^{1}H-NMR). The purity of the compounds was verified by HPLC and GC-MS.

References:

1. G. M. Everett, L.E.Blocus – Science, **124**, 70, 1956
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3. T.O.Nicolescu, M.Iovu, F.Nicolescu - α,α'-Bis[N-imidazolo]xylenes with analgesic activity – *2nd International Conference of the Chemical Societies of the South-Eastern European Countries, on Chemical Societies for Sustainable Development*, Vol. I, 314, june, 6-9, 2000, Halkidiki, Greece.

Kinetics of the Reactions of Cycloalkenylcarboxylic and Cycloalkenylacetic Acids with Diazodiphenylmethane in Various Solvents

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The rate constants for the reaction of different cycloalkenylcarboxylic and cycloalkenylacetic acids with diazodiphenylmethane (DDM) were determined in a range of fifteen various solvents at 30°C using the appropriate UV-spectroscopic method. In order to explain the kinetic results through solvent effects, the second order rate constant of the examined acids were correlated using the total solvatochromic equation, of the form:

$$\log k = \log k_0 + s\pi^* + a\alpha + b\beta,$$

where π^* is the measure of solvent polarity,, β represents the scale of solvent hydrogen bond acceptor basicities and α represents the scale of solvent hydrogen bond donor acidities.

The correlation of the kinetic data were carried out by means of multiple linear regression analysis. Using this correlation, the effects of the hydroxylic solvents can be clearly shown by separating them into those influencing the ground and the transition state. The opposite signs of the electrophilic and the nucleophilic parameters are in agreement with the well known mechanism of the reaction of carboxylic acids with DDM. Also, the agreement between the experimentally determined and calculated kinetic data is a reliable confirmation of the applied model.

Additional evidence of the solvent effect on the structure-reactivity relationship in the reaction of cycloalkenylcarboxylic and cycloalkenylacetic acids with DDM was also obtained by the correlation of Taft polar substituent constants $\sigma*$, for corresponding cycloalkenyl groups, with the ratio of solvatochromic coefficients *s/a* and *s/b*. The existence of these correlations is a strong evidence of the proportionality between the structure characteristics of investigated acids and solvatochromic effects in the reaction of carboxylic acids with DDM in different solvents.

Synthesis, Separation and Characterization of Structural Vinyldithiin Isomers

Vesna Nikolić, Mihajlo Stanković, Ljubiša Nikolić, Dragan Cvetković

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Vinyldithiins (2-vinyl-4H-1,3-dithiin and 3-vinyl-4H-1,2-dithiin) are pharmacologically active compounds. They take part in the inhibition of thrombocyte aggregation, regulation of systolic and diastolic blood pressures, have diuretic properties and vasodilative activity. They are degradation products of pharmacologically active allyl thiosulfinate found in the aqueous extract of garlic (*Allium sativum* L.). They can be synthesized from thioacrolein by condensation reaction, whereby structural isomers are produced, 2-vinyl-4H-1,3-dithiin as the primary product, and 3-vinyl-4H-1,2-dithiin as a by-product.

Vinyldithiins were synthesized from allyl thiosulfinate by mild heating for 90 minutes in a nonpolar solvent medium. Structural vinyldithiin isomers were separated from the reaction mixture by thin layer chromatography on silica gel G 60 using n-hexane, and detected by 50% solution of sulfuric acid. The R_f values obtained for 2-vinyl-4H-1,3-dithiin and 3-vinyl-4H-1,2-dithiin were 0.19 and 0.43, respectively. The reaction mixture was analyzed by liquid chromatography and the structural isomers of vinyldithiin were separated, and the retention times determined: R_t = 25 min and R_t=17.7 min for 2-vinyl-4H-1,3-dithiin and 3-vinyl-4H-1,2-d, respectively, under the following conditions: *Column*: LiChrosorb® RP-18 (5 μm), 4.6 mm x 250 mm; *Flow*: 1.2 cm^3/min; *Temperature*: 20 ^oC; *Pressure*: 277 bar; *Detection*: 205 nm; *Injected volume*: 20 μl; *Mobile phase A*: water-acetonitrile, 62:38, v/v; *Mobile phase B*: water-acetonitrile, 80:20, v/v.

Time t, min	0	10	20	50	60
B, %	0	0	45	45	0

The structural characterization of the separated vinyldithiin structural isomers was determined by use of UV, FT-IR and MS spectroscopy.

This paper forms part of MNT 2.11.0029. B project, financed by the Ministry of Science, Technology and Development of the Republic of Serbia.

The Synthesis and Decomposition of Benzonorbornane Annelated Methyl (Cyclopropylcarbinyl)-N-Nitrosourethane

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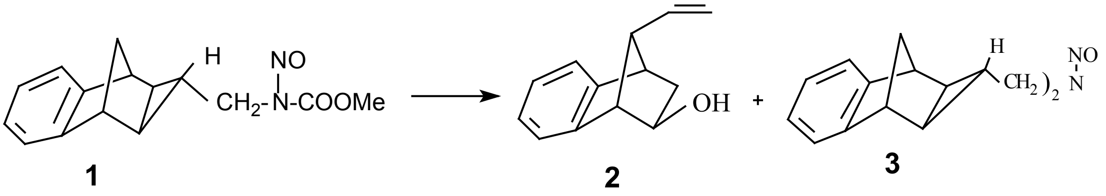
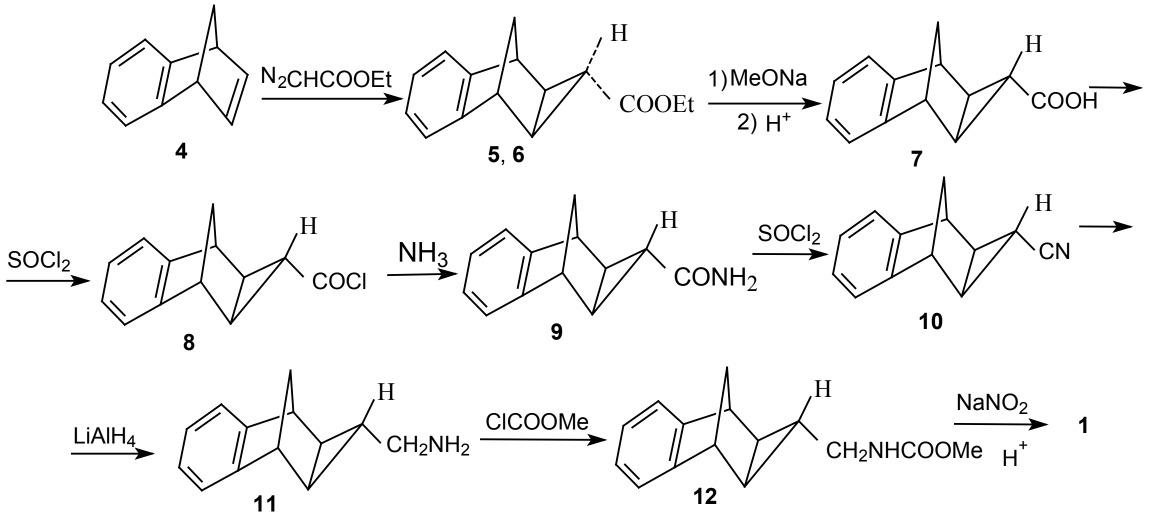
The decomposition of methyl(1aβ, 2α,7α,7aβ-tetrahydro-2,7-methano-cyclopropylcarbinyl[b]naphthalene)-N-nitrosourethane(**1**) with several base has been studied. In all the case obtained two compounds: alcohol (**2**) and N-nitosoamine(**3**).



Methyl N-nitrosourethane **1** was prepared by the nitrosation of the urethane **12** with dinitrogen tetroxide. The nitrosourethane was purified by recrrystalisation from ethanol and showed no detectable impurities by NMR. The urethane **12** was obtained starting from benzonorbornadiene **4** by following succession of reactions:



The structure of new compounds were fully confirmed by the spectral data(^{1}H -, ^{13}C -NMR, IR) and elemental analysis. A reaction mechanism is suggested.

Cycloadditions of t-Butylcyanoketene to Dienes

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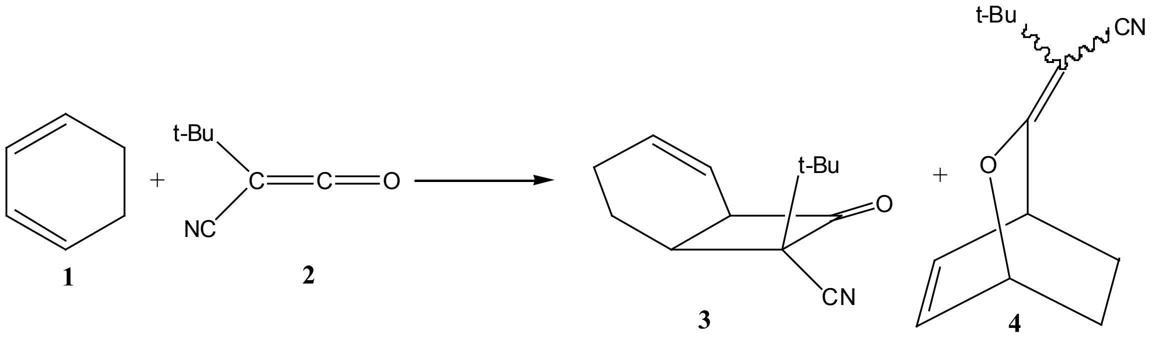
Cycloadditions of t-butylcyanoketene (TBCK) to 1,3-cyclohexadiene and cyclopentadiene are discussed.

In the reaction with 1,3-cyclohexadiene two products (a cyclobutanone **3** and an ether **4**) are formed:



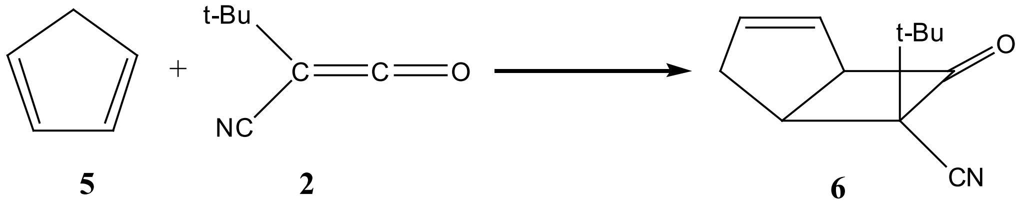
The composition of the reaction mixture depends on the temperature.

At –10°-0°C the cyclobutanone is the only product, while in benzene at reflux the ether is the main product.

By distillation of **3** the transformation **3**-**4** occured. The explanation of this fact may be either a cycloreversion followed by a new concerted reaction, or an oxo-Cope transposition.

The structures of products **3** and **4** are proposed on the basis of IR and ^{1}H-and ^{13}C-NMR spectra.

The reaction of the same ketene with 1,3-cyclopentadiene is also discussed:



In this case the reaction is regio and stereospecific as a result of a concerted cycloaddition.

The Design and Synthesis of a Steroidal Peptidomimetic

Vladimir D. Pavlović, Mira S. Bjelaković*, Natalija M. Krstić*, Svetislav V. Gojković*,
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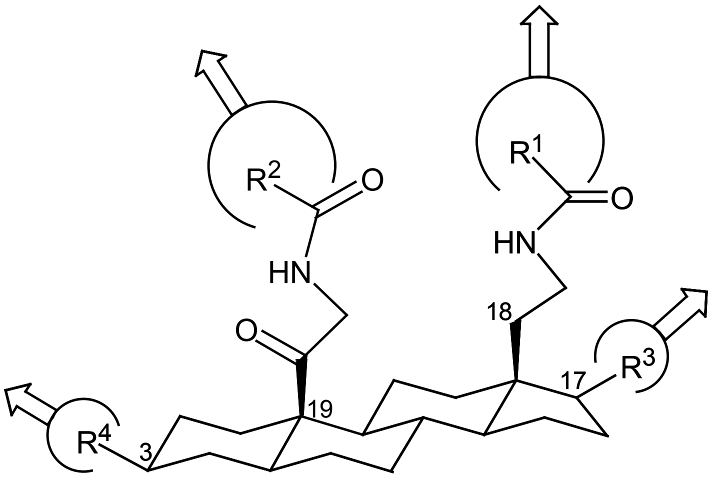
In the last ten to twenty years, we have witnessed an impressive progress in biological sciences to which, however, chemical concepts have also made a substantial contribution. Peptidomimetics have emerged as an active field at the interface of bioorganic, organic, and medicinal chemistry. This interest derives from the expectation that such molecules will have both better biostability and oral bioavailability than their peptide counterparts. The steroid nucleus was of interest for several reasons: (1) many steroids are drugs with excellent oral bioavailability; (2) the rigid steroid nucleus should reduce the tendency for hydrophobic collapse of appended peptide chains; and (3) a large body of steroid literature permits regio- and stereoselective introduction of functionality.

In his original **TASP** (**T**emplate **A**ssembled **S**ynthetic **P**roteins) concept, M. Mutter proposed to mimic parts of the surface of biologically interesting proteins by fixing smaller peptides, which are believed to be responsible for the binding to relevant receptors to semi-rigid templates [1].

We decided to apply the TASP concept to the rigid framework of steroids as templates. The project was called **STAP** (**S**teroid **T**emplate **A**ssociated **P**eptides). One of among possibility to generate STAP-molecules, which promises versatile applications, is systematically reproduced on the following figure.



In this case, one could fix different side-chains, or even better different peptidic sequences to the two angular methyl groups – C(18) and C(19). With an appropriate substitution in position C(3) and/or C(17) additional peptidic chains could be introduced or, the lipophility or solubility of the molecules could be modified. In addition, one could introduce four peptidic residues, which could be, of course, connected or cyclized in a desired fashion.

In the present work we describe the design and synthesis of one novel steroidal peptidomimetic using 18-cyano pregnenolone acetate as a starting material.

References:

1. (a) M. Mutter (1988) Peptides Chemistry and Biology, Proc. 10th Amer. Peptide Symp. (G. R. Marshal, Ed.), Escom Leyden, p. 349;
   (b) I. Ernest, S. Vuilleumier, H. Fritz, M. Mutter, Tetrahedron Letters, 31, 4015 (1990).

Solvent Effect on the Electronic Absorption Spectra of Some Newly Synthesized Azo-Dyes

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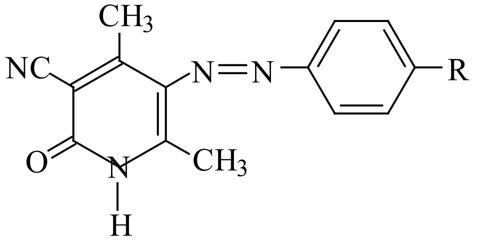
The effect of protic and aprotic solvents on electronic obsorbrion spectra of some newly synthesized azo dyes, presented in Table 1

Table 1. Structre of investegated compounds



Compound	substituent R	Compound	substituent R
1	**m - OCH_3**	**6**	**m - NO_2**
2	**m - Cl**	**7**	**p - NO_2**
3	**p - Cl**	**8**	**H**
4	**m - C_2H_5**	**9**	**m - CN**
5	**p - $COCH_3$**	**10**	**p - CN**

was examined. Positions of absorbtion maxiuma in various solvents are in correlation with dielectric constant of the solvent. In the same solvent good correlation between the wavelenght of absorbtion maxima and Hammett's substituent constant was obtained. In order to explain the resusults, the absorbtion frequencies of the electronic transitions of the compounds were correlated using a total solvatochromic equation of the form: $\nu_{max} = \nu_o + s\pi^* + a\,\alpha + b\beta$, where π^* the measure of solvent polarity. β represents the scale of solvent hydrogen bond acceptor basicities and α represents the scale of solvent hydrogen bond donor acidities. Correlation of spectroscopic data was carried out by means of multiple linear ragression analysis.

Synthesis of 3-(4-Methyl-benzoyl)-5-arylidene-thiazolidine-2,4-dione Derivatives

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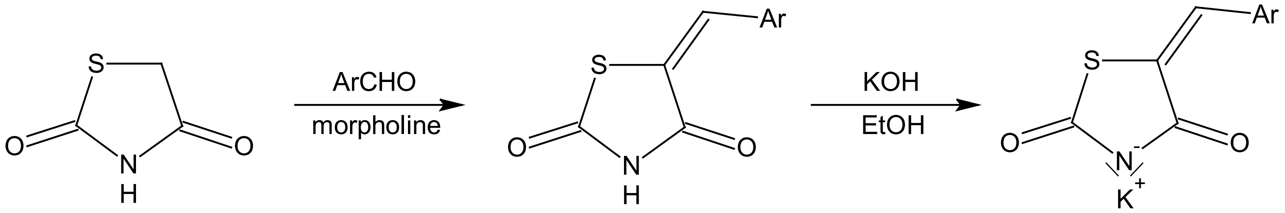
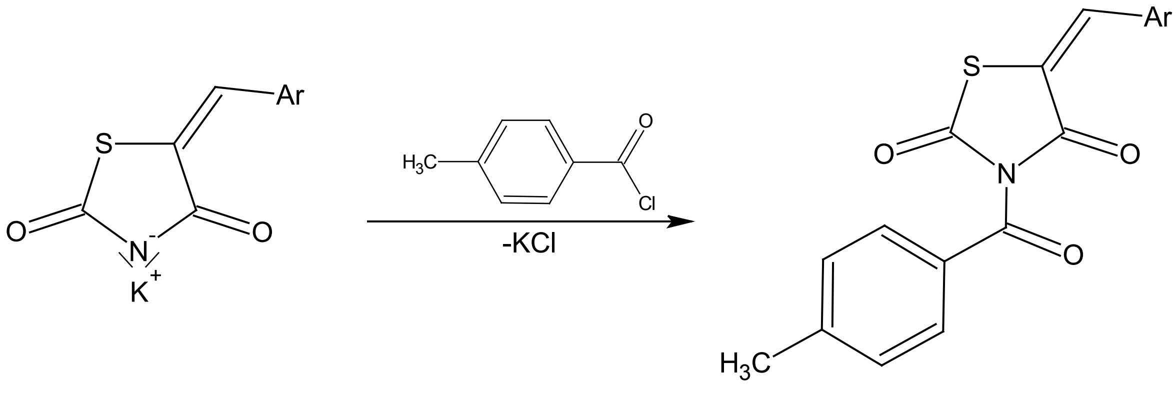
Substituted 5-arylidene-thiazolidine-2,4-diones have a broad spectrum of biological activities.
3-(4-Methyl-benzoyl)- group can be found as substructure in heterocyclylbenzenes which can be used as herbicides and defoliants.
By the base catalyzed condensation reaction between thiazolidine-2,4-dione and aromatic aldehydes were obtained 5-arylidene derivatives and then transformed in their potassium salt.



By the reaction with 4-Methylbenzoyl chloride were synthesized 3-(4-Methyl-benzoyl)-5-arylidene-thiazolidine-2,4-diones.



The biological activity of the novel 3-(4-Methyl-benzoyl)-5-arylidene-thiazolidine-2,4-diones will be tested.

Synthesis and Biological Activity of Novel Tiazofurin Analogue with a 3'-Amino Isosteric Group

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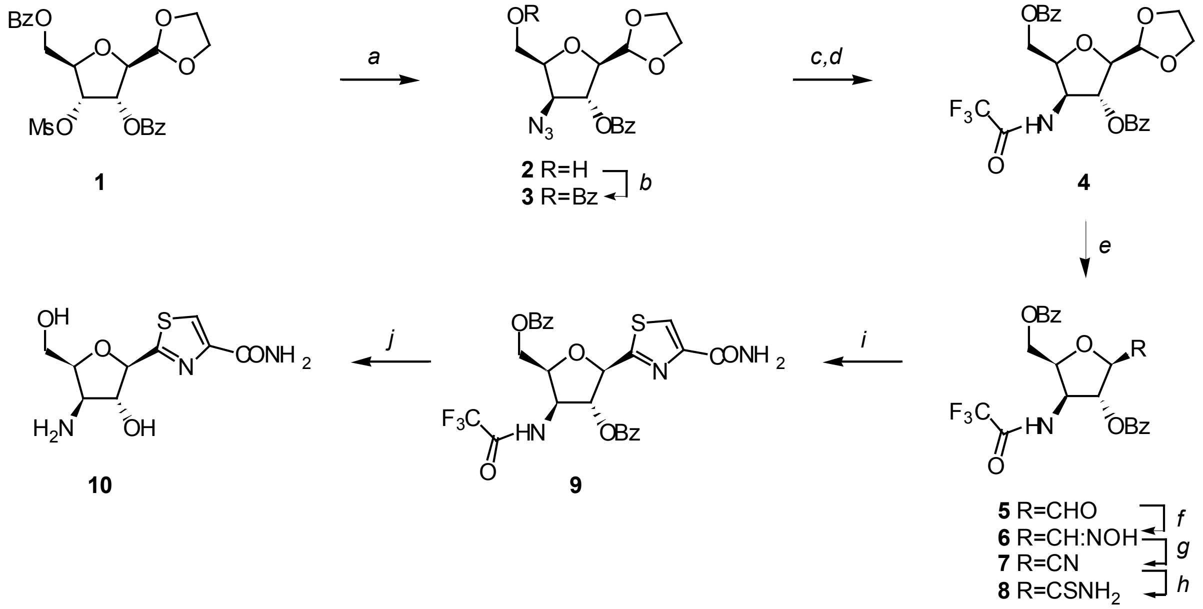
A multistep synthesis of novel tiazofurin analogue **10** was developed starting from the mesylate **1**, which was readily available from D-glucose[1]. Compound **1** smoothly reacted with sodium azide in dimethyl sulfoxide to afford the desired 4-azido derivative **3** accompanied with a small amount of the 5-*O*-debenzoylated product **2**. Benzoylation of the crude reaction mixture afforded **3,** which was further converted to the 4-trifluoroacetamido derivate **4** by two functional group manipulations. Hydrolysis of **4** with a mixture of CF_3CO_2H-HCl-H_2O gave the unstable aldehyde **5**, which was converted to the nitrile **7** by a multistep sequence presented in the reaction scheme. Treatment of **7** with hydrogen sulphide in pyridine gave the corresponding thioamide **8**. Reaction of **8** with ethyl bromopyruvate gave the protected *C*-nucleoside **9**. Removal of the protecting groups in **9** occurred simultaneously with ammonolysis of its ethyl ester function to afford the free *C*-nucleoside **10**. Antiproliferative activity of **10** against K562 and MCF7 cell lines was examined with respect to tiazofurin as a reference compound.



(a) NaN_3, DMSO, 120°C; (b) BzCl, Py, rt; (c) H_2/Pd-C, EtOH, rt; (d) $(CF_3CO)_2O$, Py/CH_2Cl_2, 0°C→rt; (e) TFA-HCl-H_2O, 4°C; (f) NH_2OHxHCl, AcONa, EtOH, CH_2Cl_2, rt; (g) MsCl, Py, rt; (h) H_2S, Py, rt; (i) $BrCH_2COCO_2Et$, EtOH, ↑↓; (j) NH_3, MeOH, rt.

References:

1. Popsavin, M.; Torović, Lj.; Spaić, S.; Stankov, S.; Kapor, A.; Tomić, Z.; Popsavin, V. *Tetrahedron*, 2002, ***58***, 569.

A Comparative Study of the Efficiency of Cu(II) Containing Catalysts on the Kinetics of 2-Aminophenol Oxidation

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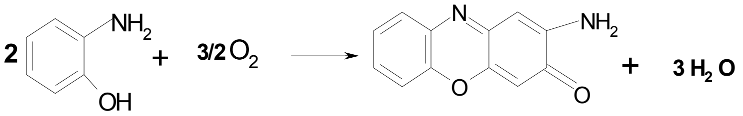
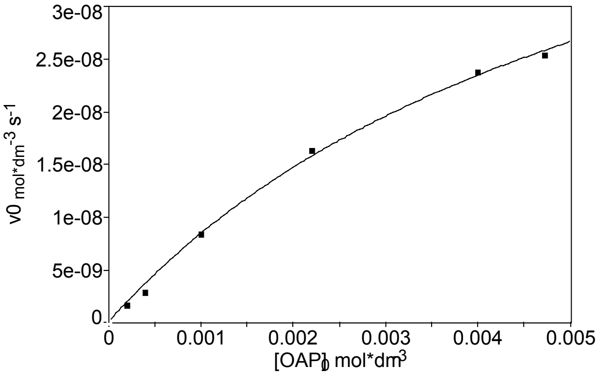
Biological treatment of wastewaters using common or biocatalysts is often the most economical path for removing organic pollutants such as phenols. Recently, new methods for purification and isolation of cheaper and efficient enzymes were developed [Karam, J., Nicell, J. A., *J. Chem. Biotechnol.* **69**, 1997, p.141-150]. Tyrosinases are biocatalysts widely spread in plants, even in sub-aquatic environment and can be also used in natural conditions, without further transformations. The oxidation of 2-aminophenol (OAP) to 2-amino-3H-phenoxazin-3-one (APX) under natural conditions (neutral pH, ambient temperature) proved to be a very slow process (the half time being about 23 days) [Oancea, D, Puiu, M., *Central Eur. J. Chem*, **3**, 2003, p. 233-241]. This reaction occurs at reasonable rates in the presence of tyrosinase, (E.C.1.14.18.1) or other copper containing catalysts [Prati, L., Rossi, I. M., *J. Mol. Cat.*, **75**, 1992, p. 347-355]. A comparative study on the efficiency of mushroom tyrosinase and several Cu (II) compounds on the oxidation with air of 2-aminophenol was performed. The literature data concerning the oxidation of aminophenols and aromatic amines in the presence of tyrosinase from microbial sources (*Neurospora crassa*, *Streptomyces lividans)* indicate a Michaelis - Menten kinetics [Toussaint, O., Lerch, K., *Biochemistry* **26**, 1987, p. 8567-8571, Ogawa, H., Nagamura, Y., Ishiguro, I., *Hoppe-Seyler's Z. Physiol. Chem.*, **364**, 1983a, p. 1059-1066]. The overall process occurs according to the following stoichiometric equation:



OAP **APX**

The kinetics of 2-aminophenol oxidation catalysed by both mushroom tyrosinase and copper compounds in aqueous medium, was studied using a spectrophotometric method. The reaction was followed in a semi-batch reactor in air-saturated solution. The kinetics in the initial conditions for the enzymatic reaction is of Michaelis-Menten type, similar to earlier literature data for microbial tyrosinase.



Michaelis-Menten plot in initial conditions

The analysis of the kinetic progress curves indicated a slower reaction, which proved to be due to a non-competitive inhibition of the reaction products. The kinetic parameters for both initial and extended conversions were evaluated and reported. The reaction rates of the same process catalysed by Cu (II) compounds in neutral and basic media were also evaluated and compared to the enzymatic ones. The kinetics in the initial stage in neutral media indicates an enhanced activity of the biocatalyst.

New 2-Substituted 2,3-Dihydro-[1,3]Thiazines and Precursors thereof: Synthesis and Structure Characterization

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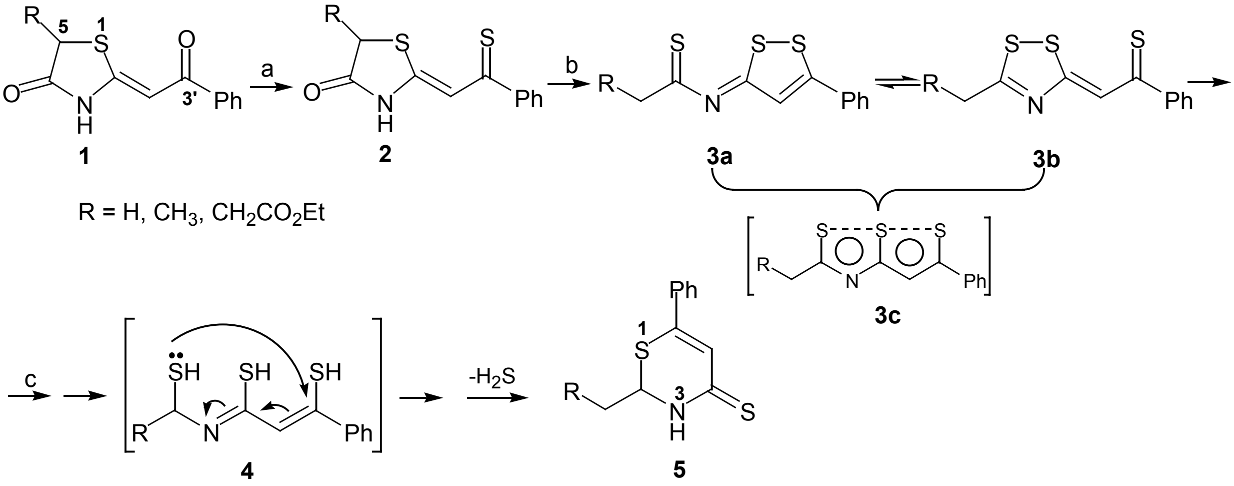
In recent communication [1] we have shown that Lawesson's reagent (LR) can be successfully applied for an efficient *in situ* synthesis of functionalized 1,2-dithioles **3a** (Scheme) by a ring opening-closing process of 5-substituted or unsubstituted 2-alkylidene-4-oxothiazolidines **1.**



Scheme *Reagents and conditions*: a) LR, toluene, 90-95 ^{0}C, 10 min; b) LR, 90-95 ^{0}C, 4.5 h; c) $NaBH_4$, EtOH, r.t., 24 h; LR (Lawesson's reagent): 2,4-bis(4-methoxyphenyl)-1,2,3,4-dithiadiphosphetane 2,4-disulfide

The present work based on the conversion of the model compounds **1** into the thione derivatives **2** by using 1 equivalent of LR, supports our previous presumption that the regioselective process **1 ✸ 3** is initiated by the O,S-exchange reaction at the C(3') atom.

In addition, a new ring-transformation of compounds **3**, based on the presence of disulfide function, will be addressed. Thus, a one-pot reductive ring-opening reaction of 1,2-dithioles - presumably better represented as having the trithiapentalene bicyclic structure **3c** - to **4,** followed by the cyclization and H_2S extrusion, led to 2-substituted 2,3-dihydro-[1,3]thiazines **5** in moderate yields.

References:

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A New Synthesis of Substituted Dioxolanes Used as Precursors for Anti-AIDS Drugs

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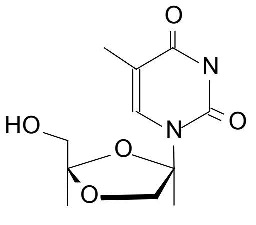
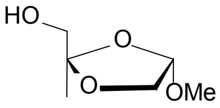
The present work aims to develop a new route for synthesis of (±)-3'-oxa-3'-deoxitimidine, **1** (*Dioxolan T*, known as an active anti-AIDS drug[1,2]) starting from relatively non – expensive new materials.

Since the final product **1**, is obtained by a SN_2 reaction of 2–hydroxymethyl-4-methoxy-1, 3-dioxolane, **2**, the acces to *trans* – **2**, represents the key step of the envisaged synthesis.



1



2

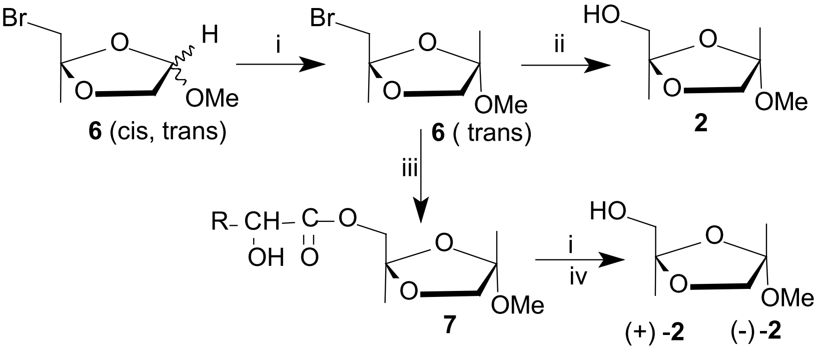
AcO -CH_2-CH=O **3**

HO-CH_2-$CH(OMe)_2$ **4**

Br-CH_2-CH=O **5**

In the first attempt a condensation of glycolaldehyde on one side protected to hydroxy-group (the acetate **3**) and on the other side protected to carbonyl-group (the acetal, **4**) was performed. Although the condensation product (*cis, trans*-**2**) was obtained in a convenient yield, this method is not conceivable due to the unacceptable yields in the synthesis, by various methods, acetate **3**.

Taking into account the above conclusion the strategy was directed to synthesis of 2-bromomethyl-4-methoxy-1, 3-dioxolane, **6**, by condensation of acetal **4** with easily accessible bromoacetaldehyde, **5**.



i: tlc; ii: NaOH, 70h; iii: potassium S (-)-lactate, MeCN/$CHCl_3$, BuN^+Cl^-, 18h; iv: H_2O, HO^-.
Scheme 1

The condensation product **6** (67% *trans,* 33% *cis*) is separable by t.l.c (silicagel; petroleum ether: diethylether 80:20) thus affording desired product **2** in overall yield of 30-35%. For the intermediate **6** arises also the access to enantiomerically pure (+)-**2** and (-)-**2** by phase-transfer synthesis of diastereomeric mixture **7**, separable by t.l.c. (Scheme 1).

References:

1. B. Belleau, C .A. Evans, H. A. Tse, H. Jin, D. M. Dixit, *Tetrahedron Lett.,* 1992, **33**, 6949.
2. R. F. Rondo, N. Nguyen-Ba, *Drug Discovery Today,* 2000, **5**, 465.

Enantioselective Solid Phase Synthesis

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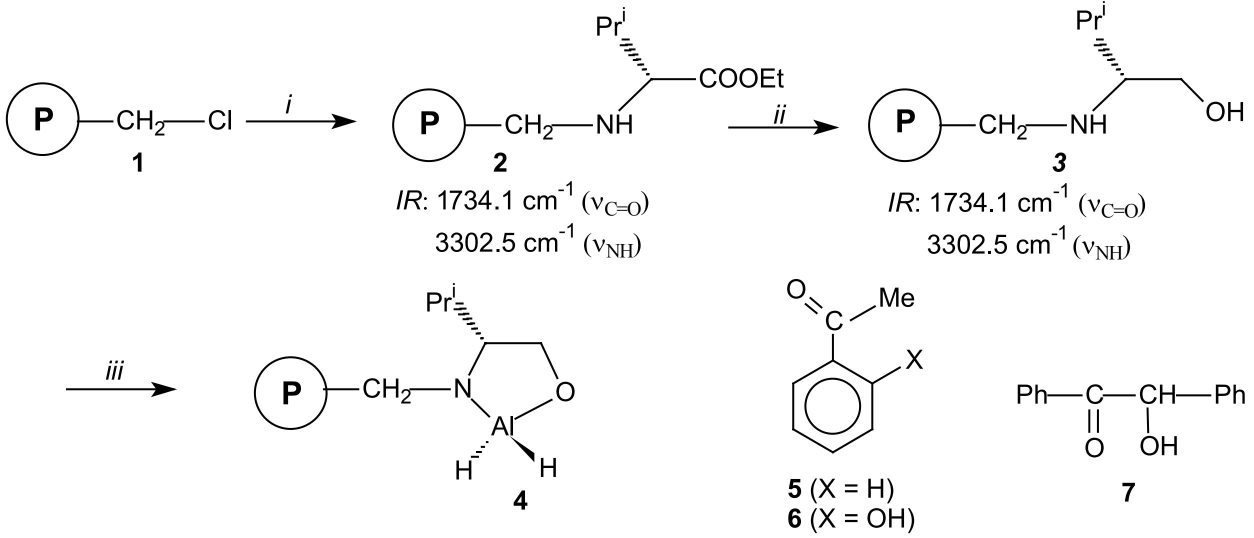
We report here our attempts to perform enantioselective reduction of prochiral ketones using solid-phase technique. In this respect an optically active reagent **4** was obtained following a previously described method[1]. This consists in condensation of lithium-aluminium-hydride on a polymeric support using as linker optically pure L-valinol (*Scheme 1*).



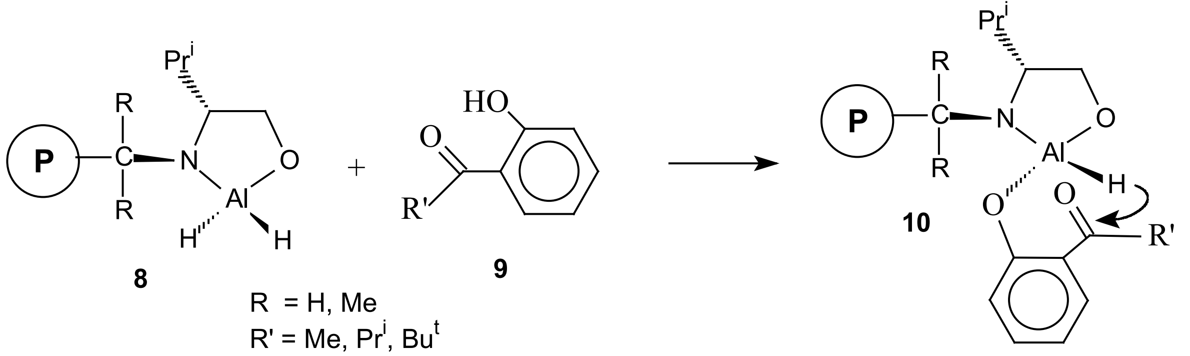
IR: 1734.1 cm^{-1} ($\nu_{C=O}$)
3302.5 cm^{-1} (ν_{NH})

IR: 1734.1 cm^{-1} ($\nu_{C=O}$)
3302.5 cm^{-1} (ν_{NH})

i: **1** (2 mmol-CH_2Cl), L(+) $H_2N\text{-}CH(Pr^i)CO_2Et$ (3mmol), $NaHCO_3$ (6mmol), THF (30mL), 65°, 24h; *ii*: **2** (0.9mmol), $LiAlH_4$ (2.7mmol), THF (30mL), 20°C, 48h, under Ar; *iii*: **3** (0.8mmol), $LiAlH_4$ (0.8mmol), THF(10mL), 0°, 2h.

Scheme 1

In order to established mechanistic details of the asymmetric induction , the reduction od hydroxyketones **6** and **7** was compared with the standard acetophenone, **5**. 2-Hydroxyacetophenone, **6**, showed an increased enantioselectivity as compared to acetophenone providing the importance of chemical bonding of the substrate to the reducing reagent *via* the OH group.



R = H, Me
R' = Me, Pr^i, Bu^t

Scheme 2

The transmission of chiral information from the L-valinol structure to the reduction center involves the configurations of nitrogen and aluminium atoms as well as the conformation around the $C_{C=O}$-C_{Ar} bond. Consequently we have studied the enantioselectivity for the reduction of the compounds **9** as a function of the nature of key substituents R and R' (*Scheme 2*).

References:

1. B.Altava, M.I.Burguete, E.Garcia-Verdugo, S.V.Luis, O.Pozo, R.V.Salvator, *Eur. J.Org. Chem.*, **1999**, 2263.

DABCO, A Reagent for the Deprotection of Benzylic Trimethylsilyl Etherus Under Microwave Irradiation in a Solventless System

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A trialkylsilyl group is one of the most common and widely used protecting groups.[1] This kind of protection was originally introduced to increase the volatility and stability of hydroxy groups and nowadays is applied in total and multi-step syntheses in organic chemistry.[2] As a matter of fact the silyl ether group is the gold
standard for protection of hydroxy groups.[3] Although several methods have been reported for the deprotection of silyl ethers,[4] the development of mild, efficient, eco-friendly and selective deprotections of trimethylsilyl ethers continues to be a significant aspect of organic chemical transformation.

DABCO / Pd(0) has been used for the highly efficient deprotection of peptides.[5] It has also been widely used as a catalyst for the Baylis-Hillman reaction.[6] DABCO has also been reported as a catalyst for the acceleration of benzoylation reactions.[7] DABCO has been applied for the synthesis of a zeolite as a structure directing agent[8] and can catalyze the self and cross-condensation of α-acetylenic ketones.[9] It has also been used to catalyze the coupling of α-keto-esters with acrylonitrile[10] and for the dimerization of α, β- unsaturated ketones and nitriles.[11]

In this communication,we wish to introduce DABCO as a novel and efficient reagent for deprotection of trimethylsilyl ethers under microwave irradiation in solventless system.

References:

1. a) Green, T. W.; Wuts, P. G. M; *Protective Groups in Organic Synthesis* ; John Wiley, New York, 1991; 2nd Ed;
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2. Corey, E. J.; Ching, X. M.; *The Logic of Chemical Synthesis*; John Wiley & Sons, New York, 1989.
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4. a) Habibi, M. H.; Tangestaninejad, Sh.; Mohammadpoor Baltork, I. B.; Mirkhani, V.; Yadollahi, B. *Tetrahedron Lett.*, **42**, 6771 (2001**)** and references cited therein,
   b) Klaas, M. R.; Kunz, M.; Warwel, S. *J. Mol. Catal. B: Enzym.*, **7**, 283 (1997);
   c) Brook, M., A.; Balduzzi, S.; Muhamed, M.; Gottardo, Ch. *Tetrahedron*, **55** , 10027(1999).
5. Zorn, Ch.; Gnad, F.; Salmen, S, Herpin, T.; Reiser, O. *Tetrahedron Lett*., **42**, 7079(2001).
6. a) de Souza, R. O. M. A.; Vas Concellos, M. L. A. A.; *Catal. Commun.*, **5**, 21(2003);
   b) Krishna, P. R.; Manjuvani, A.; Kannan, V.; Sharma, G. V. M.; *Tetrahedron Lett*., in press(2003);
   c) Kumar, A.; Pawar, S. S. *Journal of Mol. Catal.*, in press (2003);
   d) Krishna, P. R.; Sekhar, E. R.; Kannan, V. *Tetrahedron Lett.*, **44**, 4973(2003);
   e) Kumar, A.; Pawar, S. S. *Tetrahedron*, **59**, 5019(2003).
7. a) Shieh, W. Ch.; Lazanov, M.; Loo, M.; Repi, O.; Blacklock, T. J. *Tetrahedron Lett.*, **441**, 4563(2003)
   b) Shieh, W. Ch.; Lozanov, M.; Repi, O. *Tetrahedron Lett.*, **44**, 6943(2003).
8. Takevahi, T.; Beck, L. W.; Davis, M. E. *Microporous Mesoporous Mater.*, **33**, 197(1999).
9. Ramachandran, R. V.; Rudd, M. T.; Reddy, M. V. R. *Tetrahedron Lett.*, **40***,* 3819(1999).
10. Basavaich, D.; Bharathi, T. K.; Gowrissinari, V. V. L. *Tetrahedron Lett*., **28**, 4351(1987).
11. Ibid, **28**, 5703.

Push-Pull (*Z*)-5-Substituted 2-Alkylidene-4-Oxothiazolidines: Precursors for the Synthesis of Condensed 2-Alkylidenethiazolidines

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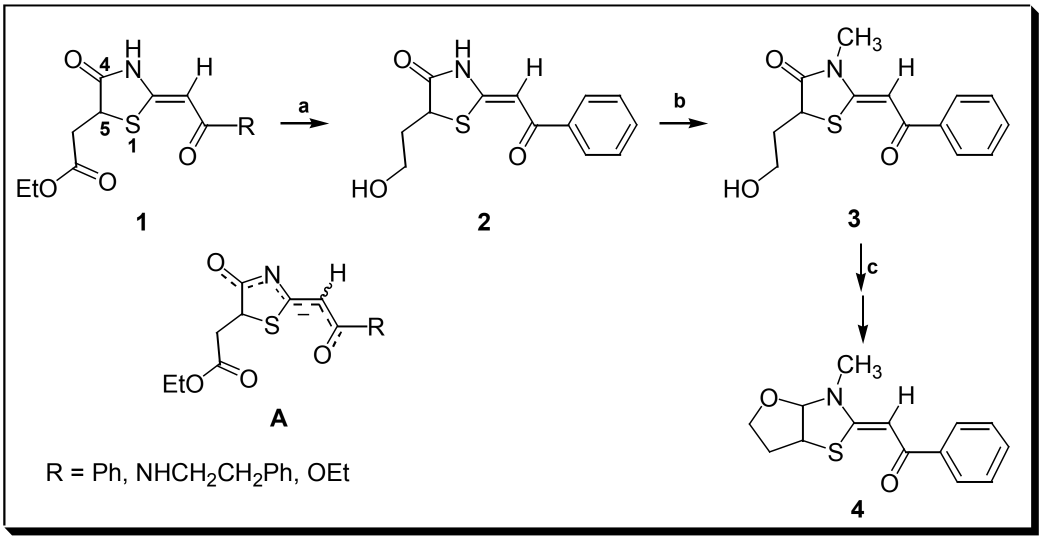
Our specific interest has been directed toward the systematic investigation of the reactivity of push-pull 4-oxothiazolidines **1** possessing the prochiral exocyclic C=C bond and an ester functionality at the C(5) atom. It has been shown that the regioselective reduction of the ester group by a tenfold molar excess of $NaBH_4$ is determined by the formation of the highly stabilized anion **A** *via* abstraction of the acidic lactam hydrogen [1]. This requirement is exceedingly demanding in the case of all substrates **1**. In contrast to this, we have shown in the present study that *N*-methyl protected thiazolidines **3** may serve as a starting material for more complex bicyclic structure of type **4**.



Scheme *Reagents and conditions*: a) $NaBH_4$, EtOH, reflux, 3 h; b) MeI, K_2CO_3 cat., acetone, reflux, 1 h; c) $NaBH_4$, EtOH, r.t., 4 h

In order to confirm the utility of **1** as precursors for the condensed 2-alkylidenethiazolidines **4** we investigated the reaction under various experimental conditions. We shall present the details of the chemoselective reduction of *N*-methyl derivatives **3**, which, in a one-pot sequence, comprising reduction, followed by cyclization, were transformed into the bicylic thiazolidines **4**. The mechanistic aspects of the transformation **3✹4**, achieved through cyclization involving the 4- and 5- positions of the thiazolidines **1**, will be also discussed.

References:

1. Marković, R., Baranac, M. Stojanović, *Synlett.*, 2004 (accepted for publication).

Physico-Chemical Characterization of Sulphonated 2-Benzothiazolamines-6-Substitutes

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Cristina Viorica Pop*, Nicoleta Grigoriu**, Laslo Tarko***

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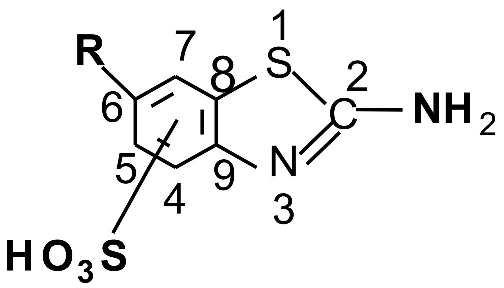
**Politehnica University, Bucharest, Romania*
***The Research Centre of the Ministry of National Defence, Bucharest, Romania*
****The Research Centre for Organic Chemistry C.D. Nenitescu, Bucharest, Romania*

This paper presents the main physical-chemical charecteristics of the 6-substituted 2-benzothiazolamines, with the following formula:



where **R** is: $–CH_3$, $-OCH_3$,-Cl, $-NO_2$

2-benzothiazolamines 6-substituted with $-CH_3$, $-OCH_3$, -Cl, have been sulphonated with oleum of 22-24% SO_3 in specific conditions for every substitute, resulting in 6-substituted 2-benzothiazolamines as sulphonic acids, mixture of 2 isomers (pos. 5,4) for $–CH_3$, -Cl, mixture of 2 isomers (pos. 4,7) for $–COH_3$ and a single product with sulphonyl group in position 4 for $-NO_2$. The obtained products have been rectified by washing with distilled water until pH = 4 - 4,5 and ethyl alcohol 97%, resulting in 8-10 g pure product for every 6-substituted 2-benzothiazolamines , as sulphonic acid isomers for $-CH_3$, $-OCH_3$, -Cl and a single product for $-NO_2$ from 100 g paste product. Resulted mixtures of sulphonated 6-substituted 2-benzothiazolamines, as sulphonic acids have been descibed as follows:

A. By physical-chemical analyses: melting point, distilled water, ethyl alcohol, methyl alcohol solubility, preparative HPLC;
B. Spectral methods: UV , mass, IR and RMN spectra.

Physico-Chemical Characterisation of Benzothiazole Dyestuffs with Sulphonic Groups for Leather and Fur Dyeing

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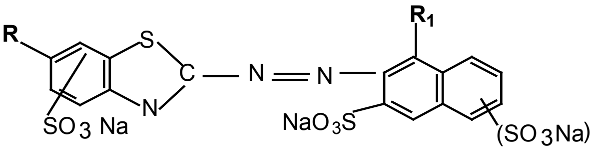
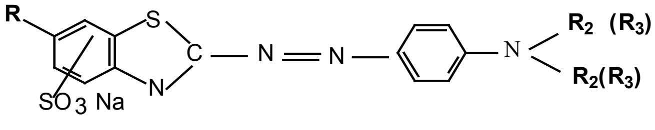
The paper shows a new class of heterocyclical dyestuffs synthetised through diazoting sulphonated intermediary: 6-metil-2-aminobenzothiazol, 6-methoxi-2-aminobenzothiazol, 6-chlor-2-aminobenzothiazol, 6-nitro-2-aminobenzothiazol diasotated which were coupled with the following coupling agents:acetoacetanilide,acid 1- phenil-3-methyl-5-phenylpirasolone-4'-sulphonic, N-phenyl-3-methyl-5-pirasolone,Newille-Winter,Schaffer, Gamma, J, H acid, R Salt, N,N,-Dimethyl anilina N,N,-Diethyl anilina with the general formulas**, (I)** and **(II):**



R = CH_3; OCH_3;Cl; NO_2 ; **R_1** = OH; NH_2

(I)



R_2 =—CH_3; **R_3** =—CH_3 CH_3

(II)

The dyestuffs with sulphonic group obtained from 2-aminobenzothiazol-6 substituted with methyl-, methoxi- and chloro-, and unitary dyes obtained from 6-nitro- were been characterised through the following methods:

A. organoleptic methods: the colour and the appearance of the crystals;
B. physical-chemical analyses :melting point, solubiliy in distilled water, ethylic alcohol, methylic alcohol, thin layer chromatography;
C. spectral methods: UV spectra, MS/MS spectra, IR spectra, NRM spectra.

Conformations in Asymmetrically N-Cyclohexyl-N-Substituted 2-Phenylacetamides

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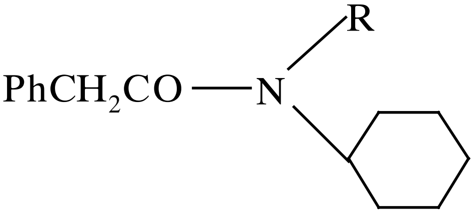
As a part of an extensive study[1-4] on structural characteristics of various N-cyclohexyl-N-substituted 2-phenylacetamides, the FT-IR, ^1H NMR and mass spectra data were obtanied and interpreted. The synthesis of N-cyclohexyl-N-substituted 2-phenylacetamides of general formula



wherein R is n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl were performed according to the common Schotten- Baumann reaction of acylation of amines with phenylacetylchloride. The corresponding secondary N-cyclohexyl-N-substituted amines were obtained by reaction $NaCNBH_4$ with cyclohexanone and corresponding amines.

The ^1H NMR spectra of these asymmetrically N,N-disubstituted amides were studied and peaks were assigned in each cases to two possible conformational isomers, arising from the lack of free rotation about the C(O)-N bond. The relative distribution of cis and trans isomers has been established by means of different coupling constants and the NOE difference technique.

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Alkylation of Benzene with Isobutane

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Alkenes are well-known alkylating agents for aromatics, and the process has been thoroughly investigated and industrially applied. However, alkanes did not raise such an interest, even if they are less expensive and more available. The catalysts for this novel process should be bifunctional, with both acid and dehydrogenating functions. MFI zeolites are well known catalysts, used in many reactions for hydrocarbon conversions. We performed this reaction on Zn/H-ZSM-5 catalysts with different Zn concentrations, using as alkylating agent i-butane.

Several factors were investigated: zinc concentration, temperature, benzene-to-isobutane ratio and presence of air in the mixture.

On the parent zeolite (H-ZSM-5) conversions were low, and alkylated aromatics were in small quantities. As zinc concentration increased, we observed higher conversions and alkylated aromatic amounts. A fraction of the aromatics were obtained directly from butanes through aromatization, the amounts depending on the zinc concentration, and this was checked with reactions only with i-butane as feed.

Temperature had a marked influence on benzene conversion, with values increasing from 5% (at 350°C) to 25% (500°C) - see table. Alkylated aromatic are mainly toluene and xylenes. Only traces of higher aromatics were observed, so we concluded that the process does not consist of a direct, simple alkylation. It is clear that there is a succession of reactions, beginning with the isomerization and cracking of i-butane, and the products of this first step act as alkylating agents.

Temp. (°C)	Liquid fraction (%)						C_B (%)	% Alkylated hydroc.
	Oligomers	Benzene	Toluene	Ethyl-benzene	Xylenes	C_{9+}		
350	7.7	85.9	0.4	1.2	1.8	3.0	5.0	6.4
400	7.1	83.3	2.1	4.0	1.8	4.5	7.8	9.4
450	4.0	67.5	11.5	6.9	6.6	3.5	24.5	28.5
500	-	68.6	14.3	3.2	7.0	6.9	26.0	31.4

Increasing benzene-to-isobutane ratios lead to a decreased selectivity to alkylated hydrocarbons. Adding air to the feed was intended to transform the reaction into an oxidative dehydrogenation, but it only acted as a diluting agent, with lower values for the conversion and selectivity to alkylated aromatics.

Synthesis and Properties of Some 1,3,5-Trisubstituted Isocyanurates as Universal Bonding Agents in Composite Materials

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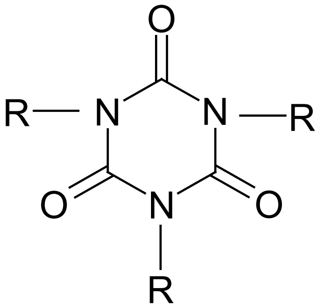
A series of 1,3,5-trisubstituted isocyanurates of the general formula



where R is: CH_2CH_2OH, $CH_2CH_2CH_2OH$, CH_2-CH=CH_2, CH_2CH_2CN and CH_2CH_2COOH were synthesized according to a modified literature procedure. The experimental investigation included modification of the synthetic procedure in terms of starting materials, solvent, temperature, isolation techniques, as well as purification and identification of the products. All of the synthesized isocyanurates were identified by melting points, FTIR, ^1H NMR and UV spectroscopic data.

Isocyanurates are a class of bonding agents which provides an interaction of a filler with a resin to form composite material. In the last ten years 1,3,5- trisubstituted isocyanurates have been found to be suitable bonding agents in polymer chemistry[1]. The functunal group on the isocyanurate must be reactive or compatible with the groups in the resin. 1,3,5-Trisubstituted isocyanurates are also suitable for bonding an explosive substance which is a special filler known as an oxidizer in the resins in order to form a special type of composite known as a composite propellant[2].

In this investigations the results of observation of the interaction between ammonium perchlorate, hydroxyl terminated polybutadiene, carboxyl terminated polybutadiene, polybutadiene acrylonitrile acrylic acid, polypropylene ether, cyclotrimethylenetrinitramine and bonding agents synthesized in this work by means of FTIR spectroscopic method are presented.

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Solvent Effects on the Structure-Activity Relationships of Hydantoin Derivatives

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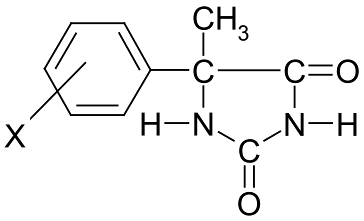
Hydantoins are important anticonvulsant drugs. Also there is a number of other biological activities as antiarrhythmic drugs, bactericides, fungicides and drugs in cancer therapy [1]. The structure-activity relationships of 5-phenyl-5-alkyl hydantoins has been, and continues to be, an ongoing study [2]. The previous results [3] clearly continued the hypothesis that hydrogen bonding was an essential factor on the anticonvulsant action of these compounds.
Our research about the biological activity of hydantoins was focused on the determination of structural and chemical behaviour of these compounds using spectroscopic and physico-chemical methods. In this work absorption spectra of sixteen 5-(3- and 4-substituted phenyl)-5-methyl hydantoins (Scheme 1) were recorded in fifteen solvents in the range 200-400 nm.



(X = H, 4-OH, 4-NH_2, 4-OCH_3, 4-CH_3, 4-Cl, 4-Br, 4-CN, 4-$COCH_3$,
3-NH_2, 3-OCH_3, 3-CH_3, 3-Cl, 3-Br, 3-CN, 3-NO_2)

Scheme 1. Fundamental structure of the hydantoin derivatives studied

The effects of solvent polarity and hydrogen bonding on the absorption spectra are interpreted by means of linear solvation energy relationships using a general equation of the form $\nu = \nu_0 + s\pi^* + b\beta + a\alpha$ where π^*, β and α are the solvatochromic parameters that measure solute dipolarity-polarizability, hydrogen-bond acceptor basicity and hydrogen-bond donor acidity. The correlation equations are combined with the corresponding equation for octanoil-water partition coefficients and electronic and steric parameters of substituents to generate new equations that demonstrate the exact relationships between solute-solvents interactions and structure activity parameters.

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Synthesis of Some 3-(Thiazol-4-yl)-4-hydroxy Coumarines

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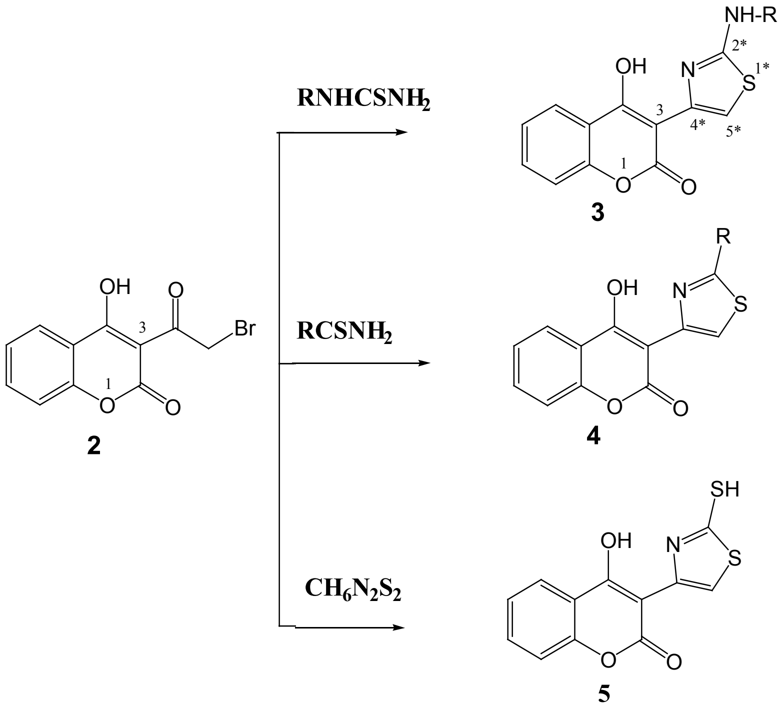
We report an easy and efficient procedure for the synthesis of eight 3-(thiazol-4-yl)-4-hydroxy-chromen-2-one derivatives. 3-Acetyl-4-hydroxy-chromen-2-one (1) was brominated with phenyltrimethylammonium tribromide to afford 3-(2-bromoacetyl)-4-hydroxy-chromen-2-one (2) whose reactions with thiourea, thioacetamide and ammonium ditiocarbamate gave respectively 3-(2-amino-thiazol-4-yl)-4-hydroxy chromen-2-one (3), 4-hydroxy-3-(2-methyl-thiazol-4-yl)-chromen-2-one (4a) and 4-hydroxy-3-(2-mercapto-thiazol-4-yl)-chromen-2-one (5). In a similar manner, compound 3-(2-bromoacetyl)-4-hydroxy-chromen-2-one (2), was treated with four mono-N-substituted thioureas and thiobenzamide to gave the corresponding 3-(thiazol-4-yl)-4-hydroxy-chromen-2-one derivatives



3 R= H
3a CH_3
3b C_6H_5
3c R=$C_6H_4CH_3$
3d R=$C_6H_4OCH_3$

4 R = C_6H_5
4a R = CH_3

N-(2-Fluorophenyl)sydnones and Pyrazoles. Long Range Coupling of F with H and C Atoms from Heterocyclic Rings

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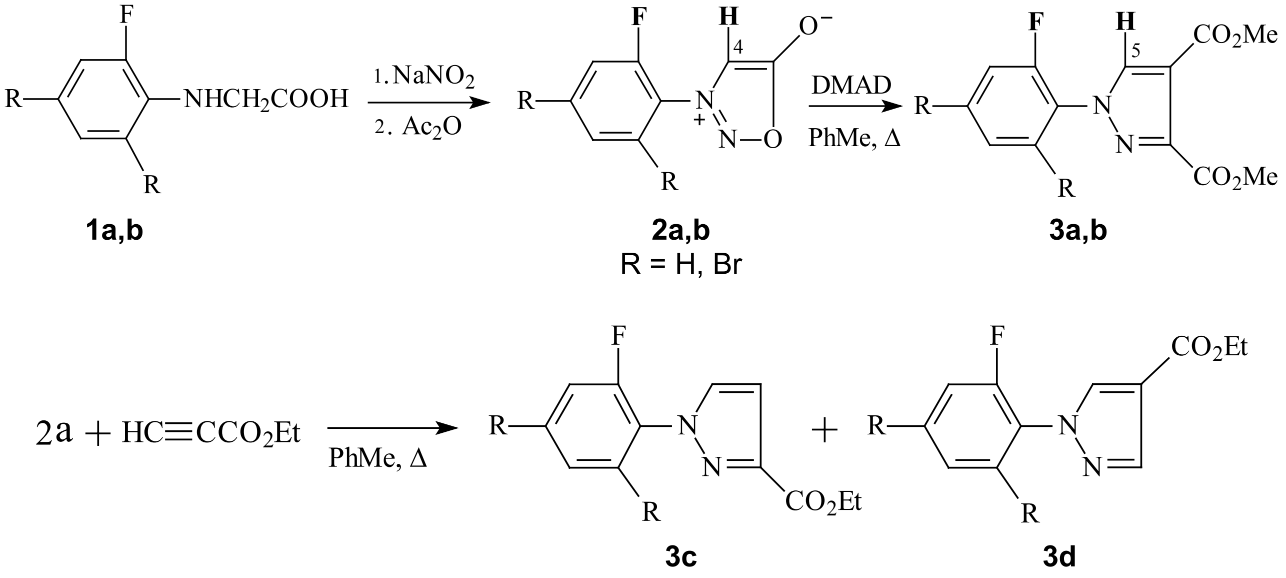
Sydnones **2a,b** were prepared by a standard procedure from N-(2-fluorophenyl)glycines **1a,b** by nitrosation and subsequent cyclization with acetic anhydride.

The 1,3-dipolar cycloaddition reaction between sydnones **2a,b** and dimethyl acetylenedicarboxylate (DMAD) gave the corresponding pyrazoles **3a,b**. The reaction of 3-(2-fluorophenyl)sydnone (**2a**) with ethyl propiolate gave a mixture of regioisomers **3c** and **3d** in 3:1 ratio.

In the ^{1}H-NMR spectra of sydnone **2a** and pyrazoles **3a,d** the H-4 (in sydnone) and H-5 (in pyrazole) appeared as doublets with the coupling constants of 2.5 Hz, due to the long range H,F coupling. In the sydnone **2b** and pyrazole **3b** these hydrogen atoms appeared as sharp singlets. Also, long range C/F coupling was observed in sydnone **2a** and pyrazole **3a** (doublet with J = 6.0 Hz for C-4 in **2a** and J = 9.0 Hz for C-5 in **3a**), whereas the corresponding carbons in sydnone **2b** and pyrazole **3b** appeared as singlets.

The effect of conjugation between benzene and heteroaromatic rings *vs*. steric hindrance on the ground state is discussed.



1a,b **2a,b** **3a,b**

R = H, Br

3c **3d**

Scheme

Composition and Antimicrobial Activity of Essential Oils of Some Medicinal Plants

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Essential oils from the medicinal plants (Salvia officinalis L., Juniperus communis L., Eucalyptus globulus Lab., Mentha piperita L., Matricaria chamomilla L.,) were investigated for composition and antimicrobial activity. Dried and milled plants were hydrodistilled for 2,5 h using a Clevenger-type apparatus. Composition of the essential oils was analyzed by GC-FID. The major components were:

- Salvia officinalis L.- α-thujone (31,06 %), camphor (26,18 %), limonene (7,89 %)
- Juniperus communis L – α-pinene (29,59 %), myrcene (3,35 %), β-pinene (2,96 %)
- Eucalyptus globulus Lab. – limonene (86,63 %), 1,8-cineole (3,98 %)
- Mentha piperita L. – menthol (42,31 %), menthyl-acetate (20,27 %), menthone (7,71 %)
- Matricaria chamomella L.–farnesene (40,50 %),bisabolol oxide A(5,24 %), hamasulene (4,87 %)

The antimicrobial action of the above mentioned essential oils was determined earlier [1] with the following microorganisms: Bacillus subtilus, Escherichia coli, Streptococcus haemoliticus A, Staphylococcus aureus, Pseudomonas aeruginosa, Aspergillus niger, Candida albicans, Sarcina sp., Saccharomyces cerevisiae.

In this paper, antimicrobial activity of essential oils of the above mentioned plants, diluted with 96 % ethanol in rate 1:1 with the same microorganisms using disc-diffusion method [2] was investigated. Comparing the inhibition zones (mm) between concentrated and diluted essential oils it could be concluded that the diluted oils of Mentha piperita L. had the same antimicrobial activity against Bacillus subtilus, Escherichia coli and Streptococcus haemoliticus A as the concentrate oils, but against Staphylococcus aureus, Candida albicans and Sarcina sp. the activity was much reduced. The oil from Juniperus communis L. which had the widest spectrum as well as the greatest effect of antimicrobiall activity, with dilution held up activity only against Candida albicans and Sarcina sp. The diluted oil of Eucalyptus globulus Lab. showed antimicrobial activity against Candida albicans, somewhat more efficient against Escherichia coli and Sarcina sp. but it was less active against the other microorganisms. The essential oils of Salvia officinalis and Matricaria chamomilla in the diluted ethanol solution didn't show significant activity except the oil of Salvia officinalis against Bacillus subtilus and Escherichia coli.

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Synthesis of an Europium Metallodendrimer as a Nuclease Mimic

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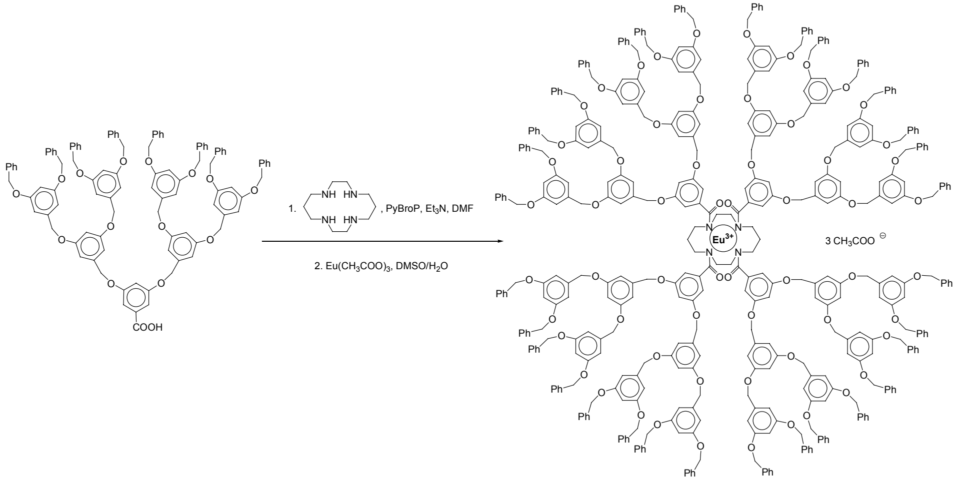
There is a continuous interest in synthesizing macrocyclic complexes of lanthanides because of their potential applications in fundamental and applied sciences[1]. Macrocyclic and macroacyclic complexes of paramagnetic lanthanide metal ions have attracted widespread interest and find extensive biomedical applications as contrast enchancing agents in magnetic resonance imaging, as NMR shift reagents and as catalysts for cleavage of RNA, which is primary target of this research[2].

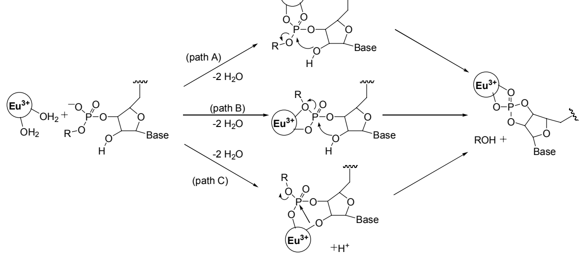
We investigated to join together two parts of research fields of supramolecular chemistry, the polyaza compounds and the dendrimers. The conjunction of the above compounds leads firstly to compounds with interesting molecular architecture and mainly expects applications uses as chemical nucleases for sequence specific cleavage of RNA.

The efficiency of macrocyclic complexes of lanthanide metal ions in blocking gene expression through cleavage of m-RNA requires the maintenance of high intracellular concentration. In an attempt to increase the cellular concentration of the polyaza europium complexes, based on our previous research, that oligonucleotide-dendrimer conjugates have an improved cellular uptake[3], we synthesized lipophilic dendrons building blocks (branches) of Fréchet-type and incorporated them into macrocyclic polyaza compounds (core) to yield a new type of ligand for lanthanide ions based on dendritic architecture (Figure).

The branches of the dendrimer is designed to be lipophilic so that the reagent is membrane permeable and bring the metal-ligand complex close to m-RNA and so to catalyze a transesterification reaction as illustrated in Figure.

The europium (III) complex is a first candidate for cellular uptake experiments and testing for sequence specific cleavage of RNA through phosphodiester hydrolysis.





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Fluorescent Probes for the Study of Enzymes

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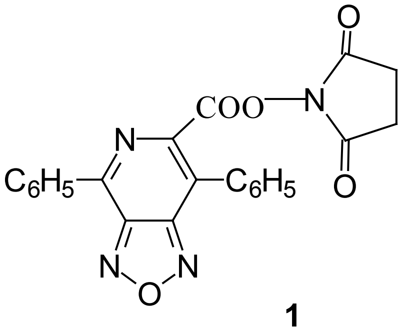
Recently, many fluorescent probes have been developed and used to study the structure and function of enzymes. Some of these probes are substrates for enzymes like proteases or phosphatases.

Starting from fluorescent 4,7-diphenyl-1,2,5-oxadiazolo[3,4-c]pyridine-6-carboxylic acid[1] (DOPC) was synthesized the corresponding succinimidyl ester (DOPC-S-ester, **1**) by two step of reaction.[2]



1

DOPC-S-ester was used as protein fluorescent marker to label bovin serum albumine (BSA) fraction V and casein Hammerstein at amino groups. In order to test labeled casein (DOPC-casein) as protease substrate trypsin IX (porcine pancreas) was chosen.

The fluorescence properties of DOPC-casein as well as those of hydrolysate mixture were measured. The effect of tryptic hydrolysis was an increase in fluorescence intensity of DOPC-casein hydrolysate mixture.

These preliminary results suggest DOPC-casein as a potential fluorogenic substrate for trypsin IX.

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Investigation of the *Bordetella pertussis* metabolism

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Pertussis (whooping cough) can effectively be controlled by immunization with a vaccine consisting of inactivated whole cells of *Bordetella pertussis,* microrganism that cause this disease. In order to increase a yield of *B. pertussis* production, the fermentation broth is usually enriched with various substances that promote cell growth. *B. pertussis* needs such a compounds due to the fact that it does not have functional TCA cycle and glycolysis. Also, the growth medium needs to have C:N ratio similar to *B. pertussis* composition in order to avoid ammonium accumulation because it leads to decrease of growth rate and final cell densities.

In this research, standard Cohen-Wheeler broth was enriched with various compounds (glutamate, succinate, nicotinamide, pyruvate, and lactate) or combination of them, with a purpose of optimizing composition of fermentation broth for cultivation of *B. pertussis*. Addition of Na-glutamate and Na-lactate increased specific growth rate and final cell density. Optimum concentrations of added Na-glutamate and Na-lactate for production were 12 mM and 6 mM, respectively. The simultaneous supplementation of growth medium with optimum concentrations of Na-glutamate and Na-lactate increased final cell densities for 30% compared to Cohen-Wheeler broth. On the other hand, addition of succinate led to decrease of growth rate. Obtained results indicate that supplementation of standard Cohen-Wheeler broth with optimal concentrations of growth factors can significantly improve productivity of pertussis vaccine production.

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Synthesis of Amyl Isobutyrate Catalyzed with Lipase from *Candida rugosa*

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Amyl esters of short-chain fatty acids are important flavor and fragrance compounds widely used in the food, beverage, cosmetic and pharmaceutical industries. The extraction of natural flavor esters is insufficient to fulfill needs of industry and production by fermentation is too expensive for commercial exploration, so certain amount of esters has to be obtained by synthesis. Enzymatic synthesis is very attractive because it can be carried out at moderate temperatures and pressures compared to chemical synthesis (1). Although transformation is usually performed in organic medium, certain amount of water is necessary. The water is needed to retain the enzyme in catalytically active conformation in organic solvent. On the other hand, presence of water in the reaction mixture promotes reverse reaction and therefore, decreases yield of product (2).

The synthesis of amyl isobutyrate using lipase from *Candida rugosa* was investigated in this work. The synthesis was carried out in pure isooctane and isooctane with various concentrations of water (56mM, 167mM, and 278 mM). The highest activity of lipase was determined in system with 56 mM of water in which yield of 85% of amyl isobutyrate was achieved after 48 h. On the other hand, the yield of ester was lowest in a pure isooctane, only 20%. Obtained results indicate that production of amyl isobutyrate, from amyl alcohol and isobutyric acid, can be successfully performed with lipase from *Candida rugosa*. Additionally, it was confirmed that concentration of water is very significant factor in enzymatic production of esters, which has to be optimized in order to achieve maximal yield of product.

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Effects of the Quinone Antitumor Agent Avarone and Its Derivatives on the Glycolitic Enzyme Hexokinase

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It is well known that antitumor sesquiterpene α-methylene lactons and quinone methides, such as helenalin, taxodone, vernolepin, eupacunin and eupatorin acetate inhibit certain glycolytic enzymes, such as hexokinase and phosphofructokinase. A Michael-like reaction with sulfhydryl-containing enzymes was proposed as the mechanism of action of these agents.

Quinones are also known to undergo a Michael-like addition of nucleophiles such as thiols. In previous studies it was shown that antitumor agent avarone covalently modifies β–lactoglobulin by addition of lysine amino groups[1] and bovine serum albumin by addition of cysteine mercapto groups[2].

In this work, inhibition of sulfhydryl containing glycolitic enzyme hexokinase by avarone and its derivatives was studied. Avarone and its derivatives inhibit hexokinase activity efficiently. For instance, avarone inhibits the enzyme activity more than 50% even at 1,6 μM concentration. Covalent modifications were also studied by SDS gel electrophoresis.

The inhibition of hexokinase, and consequentely of glycolitic metabolism is probably not the principal mechanism of action of avarone, but the fact that it reduces the energy available to cells has an additive effect to other modes of action of avarone.

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Synthesis and Charaterization of Aluminum Histidine Complexes

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Aluminium is toxic element which upon entering blood stream or tissues and cells may exibit inhibitory action on enzyme systems (lactate dehydrogenase, catalase, phosphatase, etc) binding to proteins and amino acid oligomers. From blood-stream aluminium is transferred to cells via transferrin -transferrin receptor mechanisam. Active site of enzymes and proteins which bind aluminium mostly involve histidine residues. Hence,to elucidate the mechanisam of aluminium toxicity it is necessary to study its interactions with histidine. Histidine may act as a tridentante ligand ($-COO^-$, $-NH_2$, imidazole pyridinic nitrogen) and primary goal of this work was to establish the mode of coordination of histidine to aluminium .

In the previous work [1]we found that Al and histidine form in solution, the complexes Al His^{2+}, $AlHHis^{3+}$, $Al(HHis)(His)^{2+}$, the later one being dominant between pH 4-6. This complex was synthetized starting from $AlCl_3$ and l-histidine and its composition was confirmed by elemental analysis: Al 6.6 wt %, Cl^- 17.2 wt % so that it could be formulate as $[Al(\ HHis)(His)\ ]Cl_2$ or $[Al(OH)(HHis)_2\ ]Cl_2$. The IR spectrum of the complex is shown in Fig. 1, the IR spectrum of histidine hidrochloride is shown in Fig 2. It is seen that in the region of NH_3^+, $-COO^-$ and -C=N- vibrations (v_{NH_3} = 1498 cm^{-1}, v_{coo^-} = 1629 cm^{-1} and $v_{c=N-}$ = 1512 cm^{-1}) the complex show shift of the bands toward higher energy and decrease in intensity. New intensive bands at 2923 cm^{-1} appear and 1577 cm^{-1} appear.

R_0 diffractogram of the complex (Fig 3.) shows nine intensive reflections which confirm ortorombic structure of the complexes .

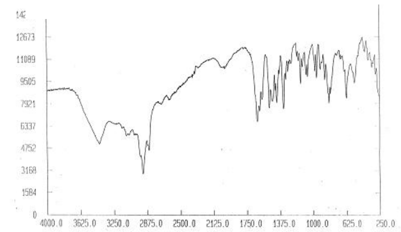

Fig 1. IR spectra of complex Al-Histidine

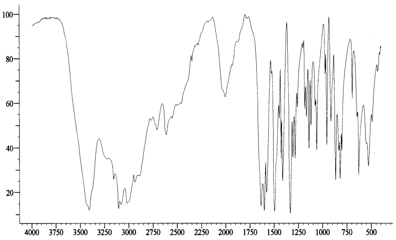

Fig 2. IR spectra of Histidine -hidrochloride

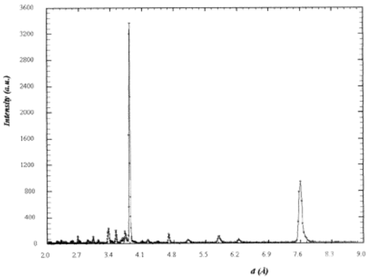

Fig 3. R_0 diffractogram of the complex

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Composition and Antimicrobial Activity of the Essential Oils of Some Aromatic Plants

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In this paper, composition and antimicrobial activity of the essential oils of the following aromatic plants Laurus nobilis L., Carum carvi L., Foeniculum vulgare Mill.,Artemisia dracunculus L. and Humulus lupulus L. were investigated.

The essential oils were isolated from the milled dried plants by a Clevenger type apparatus for 2 h [1]. The chemical composition of the essential oils was determined by GC-FID analyses. The greatest number of compounds (101) is in the oil of Humulus lupulus L. and (99) from Laurus nobilis L., but the essential oil of Carum carvi L. contains fewer components (41). The main compounds were:

- Laurus nobilis L. – 1,8-cineole (41,04 %), camphene (8,84 %), α-pinene (5,15 %)
- Carum carvi L. – carvone (58,71 %), limonene (37,71 %)
- Foeniculum vulgare Mill. - fenchone (29,29 %), anethole(24,22 %)
- Artemisia dracunculus L. – estragole (82,19 %)
- Humulus lupulus L. – myrcene (39,68 %), α-humulene (21,85), β-karyophylen (13,21 %)

The effect of the essential oils of the above mentioned plants on the growth of some major groups of microorganisms (Bacillus subtilis, Escherichia coli, Streptococcus haemoliticus A, Staphylococcus aureus, Pseudomonas aeruginosa, Aspergillus niger, Candida albicans, Sarcina sp., Saccharomyces cerevisiae) was investigated earlier [2] using usual method [3].

The investigations of antimicrobial activity have continued with ethanol solution of the oils (1:1). The diluted oil of Artemisia dracunculus L. had similar antimicrobial activity as concentrated essential oil except against Bacillus subtilus and Staphylococus aureus when showed smaller antimicrobial activity. There were no significant differences in the antimicrobial activity of concentrated and diluted essential oils obtained from Laurus nobilis except against Candida albicans where dilute oils did not show activity. The diluted oil of Carum carvi L. held up activity against Escherichia coli and Bacillus subtilis, while the diluted oils of Foenicilum vulgare Mill. and Humulus lupulus L. had less significant activity only against Sarcina sp. and Bacillus subtilis respectivly.

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Do Nucleobases and Nucleosides Use Separate Carriers on the Myocardial Cell Membrane?

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Endogenous nucleosides and nucleobases have significant roles in numerous metabolic processes in the cell. Their synthetic analogues are widely used in therapy of viral and malignant diseases. Both endogenous and synthetic nucleosides and nucleobases are hydrophilic and diffuse through the plasma membrane very slowly. Their efficient permeation, and thus their release and salvage, are dependent on special transport proteins present on the cell membrane. The purpose of this study was to investigate the influence of purine and pyrimidine nucleobases on transport characteristics of adequate endogenous nucleosides through sarcolemma of cardiomyocytes. The experiments were conducted on the isolated perfused guinea pig heart, using the rapid paired tracers single circulation technique. The study was performed with ^{3}H-labelled nucleosides (adenosine and thymidine) as representatives of purine and pyrimidine nucleosides and ^{14}C-sucrose as an extracellular space marker.
The maximal cellular uptake (U_{max}) and total cellular uptake (U_{tot}) of adenosine and thymidine were determined. The fact that presence of adenine (200 μM) in perfusion fluid did not inhibit cellular uptake of ^{3}H-adenosine, could lead to conclusion that purine nucleobases use separate carriers on the sarcolemma of cardiomyocytes. However, presence of 200 μM of unlabelled thymine caused significant inhibition of both U_{max} and U_{tot} of ^{3}H-thymidine, which implies that pyrimidine nucleobases and nucleosides use the same sarcolemmal carriers to a certain extent.

Interactions of Amino Acids by Chiral Receptors

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Macrocyclic receptors such as cyclodextrins, crown ethers and others compounds present the ability to act as chiral selectors for chiral recognition of some important biological optical active compounds such as amino acids and peptides [1-3].

Cyclodextrins being chiral compounds, have the ability to discriminate between optical isomers, and much attention has been directed toward understanding this aspect of cyclodextrin molecular recognition. This property confers to the cyclodextrins the possibility to be used in analytical science for enantioseparations. The chiral recognition of amino acids and other biological substrates plays an important role in biological processes.

In this contribution we have studied some aspects of complexation between some aromatic amino acids with β-cyclodextrin in aqueous solutions. The stability constants (log K), the reaction enthalpy (ΔH) and entropy (ΔS) of amino acids (L-phenylalanine, D-phenylalanine and DL-phenylalanine) in aqueous solutions by means of calorimetric titration have been determined. The effects of physicochemical parameters involved in the process of complexation such as the structure of cyclodextrin, the pH, and the structure of amino acid have been studied. Also the factors that govern both the enantiomeric discrimination (D versus L) and the magnitude of chiral discrimination (K_D/K_L) have studied. In this respect, the nature of interactions between the host and guest species involved in present study has been investigated.

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Proteolytic Activity in the Serum of Patients with Malignant Diseases

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Proteolysis occurs in normal tissue but is limited in duration and subject to strict regulation at many levels. A general aspect of malignant neoplasms may be an inbalance of proteolysis, which favors invasion.

Cancer invasion and metastasis is the results of several interdependent processes. Extracellular proteolytic enzymes (eg, serine proteases and metalloproteases) have been implicated in cancer metastasis. The premise behind this theory is that release of proteolytic enzymes from tumors lead to the breakdown of basement membranes and the extracellular matrix, thereby faciliting cancer cell invasion into the surrounding normal tissue.

Proteolytic enzyme activity was compared in the serum of patients with gastric cancer and control group. Activity was determined spectrophotometrically (410 nm) by the rate of hydrolysis of BAPNA (Nα-benzoyl-α-arginine *p*-nitroanilide hydrohloride). In investigation 50 patients were observed, 35 with gastric cancer and 15 as the control group.

Results showed increase expression of enzyme activity on BAPNA substrate for diseases persons than the control group.

Some Aspects of MTD Method Application in the QSAR Study of Several Series of Anti-HIV Compounds (HEPT and URIDINE Derivatives)

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AIDS (acquired immunodeficiency syndrome) and related disorders are etiologically linked to members of the lentivirus subfamily of retroviruses. These lymphocytopathic lentiviruses have been characterized and designated human immunodeficiency virus type 1 (HIV-1) and human immunodeficiency virus type 2 (HIV-2), of which the former has been found to be prevalent in causing the disease[1].

The MTD[2] method is a QSAR approach based on *minimal steric difference*, a measure for steric misfit between two molecules. It allows a guess of the receptor cavity shape.

Here we present a comparative QSAR study of a series of 2`,3`-dideoxypurine nucleoside analogues – as shown in Fig. 1(a), a series of URIDINE compounds, and of a series of thymine derivatives shown in Fig. 1(b), a series of HEPT derivatives[1].

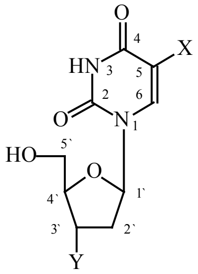

Figure 1a. The general structure of URIDINE Nucleoside Derivatives

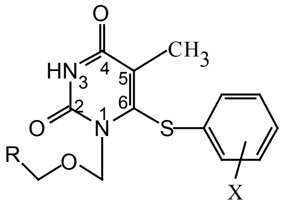

Figure 1b. The Structure of HEPT Derivatives

The uridine derivatives studied in this work bind at the substrate-binding site, and the steric and electronic properties of some substitutes have been found to govern the activity. The correlation equation for the 14 uridine compounds is:

$$\mathbf{A = 9.898 - 0.856\ MTD^{14} \qquad r = 0.849}$$

The obtained correlative results are good for the series of HEPT derivatives (11 compounds):

$$\mathbf{A = 7.77 - 0.63\ MTD^{11} \qquad r = 0.816}$$

However, the number of analyzed compounds is not big enough and their structural variation restricted. The hydrophobic character of those increases the anti-HIV activity by means of growing the degree of enzymatic inhibition of RT, acting upon the allosteric hydrophobic site (situated in the neighborhood of the catalytic site of the enzyme) which imposes steric compulsions, revealed by our QSAR analysis with the MTD method.

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The Interaction of Uranyl Ions with the Anticancer Drug Bleomycin and Native DNA

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Bleomycins is a family of glycopeptides-derived antibiotics isolated from the culture medium of *Streptomyces Verticillus* as their copper chelates Bleomycin[1] A2 (Figure), which differs from other naturally occurring bleomycins only in the cationic C-terminus, is the major component of the anticancer drug Bleoxane®, which is used for the treatment of Hodgkin's lymphoma, Carcinomas of the skin, head, neck, and testicular cancers.[1-3]

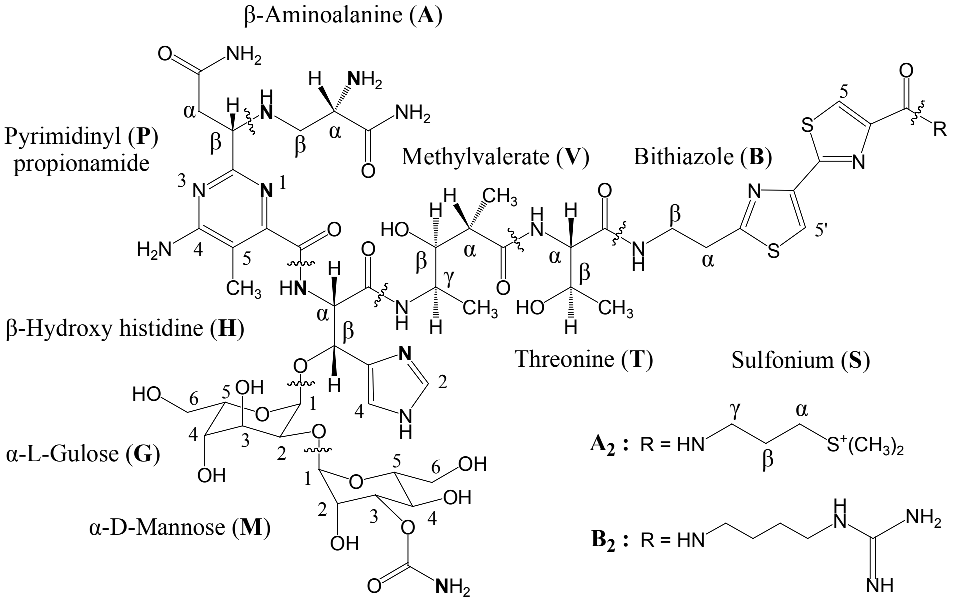

Figure. Structure of the major bleomycins

The uranyl ion has been used as a staining agent in electron microscopy, mainly due to its high affinity for the phosphates of the DNA back-bone. The interaction of the uranyl(VI) ion (UO_2^{2+}) with the bleomycin is studied by absorption, circular dichroism, fluorescence and NMR spectroscopy.
The study of the interaction of bleomycin with UO_2^{2+} under different conditions has been carried out. After ten days at neutral pH and 60 ^{0}C a main product can be observed. The exact structure has not been defined yet. The interaction with calf-thymus DNA is under investigation.
The aim of these experiments is to study the efficiency of the formed complex binding to DNA.

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Spectral Study and Theoretical Modelling of the Interaction of Actinomycin D with Nucleic Acids

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Actinomycin D is an antitumor antibiotic that contains a planar 2-aminophenoxazin-3-one chromophore and two cyclic pentapeptide lactones. The biological effect of this drug is believed to be the consequence of its ability to bind to duplex DNA, which results in the inhibition of RNA polymerase activity.

The aim of the present study was to investigate the interaction of actinomycin D with nucleic acids (double and single-stranded) and the influence of ionic strength on the binding, using UV-VIS absorption spectroscopy.

The results show similar values for the binding constants of actinomycin D to double and single stranded DNA, indicating a similar affinity for nucleic acids.

The study of the binding of actinomycin D to double stranded DNA at different NaCl concentration indicates a slight dependence of the binding constant on the ionic strength, which arises from the increased phosphate spacing that results from intercalation. This dependence on ionic strength allows dissecting the binding free energy into its non-electrostatic and electrostatic contributions. The magnitude of non-electrostatic contribution at the binding free energy is much greater than the electrostatic contribution, in agreement with the fact that actinomycin D is an uncharged intercalator. The non-electrostatic free energy contribution is independent of salt concentration, and reflects the contribution of hydrogen bonding, hydrophobic and van der Waals interactions to the stability of the drug – DNA complex.

In this context, a theoretical modeling of the interaction of actinomycin D with double and single-stranded sequences of DNA was performed. For both actinomycin D – single-stranded DNA and actinomycin D – double-stranded DNA adduct formation, the binding energy calculated as the difference between the energy of optimized complex by molecular mechanic (MM^+ method) and the sum of the energy of separately molecules, having the same geometry like in complex, have a similar value, indicated a similar affinity of the drug for nucleic acids.

In order to identify and analyze potential hydrogen bonding, SHB program especially conceived for the study of the drug-DNA interactions based on Extended Huckel calculation of the Mulliken overlap populations was used [1]. The results show specific hydrogen bonds between the base (adenine and guanine) of DNA and threonine residues of the cyclic pentapeptides.

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New Approaches Regarding the Biological Effects of Phosphorus (V) Heterocyclic Compounds

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p-Tolyldichlorophosphine, involved in a Mannich type reaction[1-2], together with o- aminophenol or 1,2- diaminopropane and acetone, generated two phosphorin-2-oxide ring compounds, containing oxaza or diaza groups, namely: 2-tolyl-3,3-dimethyl-1,4,2-benzoxaza-phosphorine-2-oxide and 2-tolyl-3,3-dimethyl-5-methyl-1,4,2-diaza-phosphorine-2-oxide. The two compounds were fully characterized by MS, IR, UV, ^{1}H-NMR, and gas chromatography.

Taking into consideration that chlorophyll contents in plants were revealed to have connection with nitrogen and phosphorus concentrations at growth early stage, and because the above mentioned compounds can be considered as phosphonic analogous of naturally occuring α-aminoacids, it was expected from them to develop biological activity. That is the reason why the present study was also developed to investigate the effects exhibited by different concentrations of the two phosphorus heterocyclic compounds on chlorophylls a and b contents, as well as on chlorophyll a/b ratio of wheat, after treatment with the above mentioned compounds.

Chlorophylls concentrations were determined by analysis of the UV-visible spectrum of the extracted pigments in 80% acetone. For calculations, the standard extinction equations reported by Lichtenthaler[3] were used.

Comparing the data resulting from the treatments with 2-tolyl-3,3-dimethyl-5-methyl-1,4,2-diaza-phosphorine-2-oxide and 2-tolyl-3,3-dimethyl-1,4,2-benzoxaza-phosphorine-2-oxide, we can conclude that both these substances exhibit biological activity in wheat, especially at 50 ppm concentration, when both chlorophyll a and b concentrations are significantly increased.

It is to be underlined that a very good connection between chlorophyll content response and all the other changes concerning the general development of the monocotyledonous plant, was registered.

At the same concentration, a comparison between the effects obtained with the two compounds revealed that the increases in chlorophyll content is higher when 2-tolyl-3,3-dimethyl-5-methyl-1,4,2-diaza-phosphorine-2-oxide was used.

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Different Docking Protocols Applied to the Theoretical Study of Albumin - Ligand Interaction

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Human Serum Albumin (HSA) is a globular protein, whose abundance and wide range of endogenous and exogenous ligands it can interact with, account for its place as the most important drug transporter protein in blood. In the present work different docking protocols (Genetic Algorithms, Local Search, Simulated Annealing, etc. and their combination) are applied to study the HSA interaction with a series of ligands of pharmaceutical relevance (warfarin, halothane, etc.). The theoretical results are correlated with literature experimental data and the optimization of protocols is made on this basis. The most efficient and accurate protocols are used in the prediction and analysis of the interaction of potential drugs with HSA. The analysis is made in terms of interaction energy and identification of the responsible amino-acidic residues in the interaction. Semi-empirical and DFT studies on the ligands structures are also presented.

Activity of Some Platinum(II/IV) Complexes Against Mouse Fibrosarcoma L929 and Human Astrocytoma U251 Cells

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The new platinum(II) complex, dichloro(*O,O*-dibythyl-ethylenediamine-*N,N*′-di-3-propanoate)platinum(II), [Pt(dbeddp)Cl_2], was synthesized and characterized by elemental analysis, infrared and ^1H and ^{13}C NMR spectroscopy. This complex was obtained in the direct reaction of $K_2[PtCl_4]$ and dbeddp·2HCl in the presence of LiOH.

In order to investigate the capacity of novel Pt complex, as well as tetrachloro(*O,O*-dibuthyl-ethylenediamine-*N,N*′-di-3-propanoate)platinum(IV) and tetrachloro(*O,O*-dipentyl-ethylenediamine-*N,N*′-di-3-propanoate)platinum(IV) [1], [Pt(dbeddp)Cl_4] and [Pt(dveddp)Cl_4], respectively, to reduce tumor cell growth, they were applied to cultures of mouse fibrosarcoma L929 and human astrocytoma U251 cells, and cell viability by crystal violet staining and MTT reduction measured in the cultures after 24 hours of incubation. As detected by both viability tests and with both cell lines, only complexes [Pt(dbeddp)Cl_2], [Pt(dbeddp)Cl_4] and [Pt(dveddp)Cl_4] markedly reduced viability of the tumor cells. Interestingly, complexes [Pt(dbeddp)Cl_4] and [Pt(dveddp)Cl_4] diminished tumor cell numbers to the level achieved with recognized anti-tumor drug cisplatin.

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Ethanolamine Salts of Bromo-Substituted Benzoic Acids, as Potential Bioregulators

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Bioregulators can be defined as either natural or synthetic compounds, which are applied directly to a target plant to alter its life processes or its structure, to improve quality, increase yields, or facilitate harvesting. Applied as a spray to foliage or as a liquid drench to soil around a plant's base, in low concentrations, usually measured in parts per million (ppm) and in some cases parts per billion (ppb), bioregulators produce major growth changes**.** Chemicals that promote straight growth, and stimulate rooting, cambial activity, and also parthenocarpic fruit development, are commonly called auxins.

These chemicals contain in their molecule an aromatic nucleus and at least a carboxylic group or its functional derivatives.

The target was to obtain some water-soluble ammonium salts, which could be more biologically efficient than the acids they resulted from, which are not water-soluble [1-3].

The salt formation is often used as a simple chemical tool for modifying some physicochemical properties of a compound having ionisable functional groups in order to overcome some undesirable feature of it and to improve its biological performance.

These salts being water-soluble are better absorbed by the plant and can penetrate easier the cell membrane.

In this paper, the synthesis, the characteristics of ammonium salts of two bromo-benzoic acids with ethanolamine, and the biological activity of them have been presented. These salts were obtained under reflux using a molar ratio acid: ethanolamine 1:1, and ether, or acetone, as reaction medium. The two synthesized salts are:

I 2-hydroxyethylammonium-3-bromobenzoate

II 2-hydroxyethylammonium-4-bromobenzoate

Elemental analysis of nitrogen and halogene were in agreement with the expected stoichiometry, and FT-IR spectra, for each of the compounds, were consistent with salt formation. UV assay for the determination of corresponding benzoic acid concentration in the salt was also in agreement with the salt formation.

Analyzing the results of the Tsibulskaya-Vassilev general test carried out on twenty variants for monocotyledonous and on the same number of variants for dicotyledonous it was observed that the two compounds have a spectacular stimulating effect, especially for dicotyledonous.

They increased the height of the plant by 7-30% when were tested on monocotyledonous and by 31-36% on dicotyledonous. The length of the main root at dicotyledonous was increased by 15-78%. The best effect of the two salts was on rhisogenesis at dicotyledonous, the number of the adventitious roots increased by 63-122%.

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Detection, Induction and Isolation of an Extracellular Lipolytic Enzyme from the Antibiotic-Producing Strain *Streptomyces hygroscopicus* CH-7

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Lipolytic enzymes are currently attracting enormous attention because of their biotechnological potential, ranging from the use in laundry detergents to stereospecific biocatalysis. Most of the lipases used in industry are microbial enzymes, of both fungal and bacterial origin. Bacteria produce different classes of lipolytic enzymes including carboxylesterases (EC 3.1.1.1), which hydrolyse small ester-containing molecules, true lipases (EC 3.1.1.3), which display maximal activity toward water insoluble long-chain triglycerides, and various types of phospholipases.

Streptomycetes are Gram positive soil bacteria, which exhibit remarkable capability for the synthesis of secondary metabolites and use numerous extracellular hydrolytic enzymes to degrade organic material in their natural habitat. In the culture filtrate of Streptomyces hygroscopicus CH7, the producer of polyketide antibiotics, lipolytic activity was detected. The activity was measured spectophotometrically at 410 nm, using a pNPP (p-nitrophenyl palmitate) as a substrate.

The aim of this study is increasing enzyme yield by fermentation as well as isolation and partial characterization of obtained enzyme. During fermentation the maximum of lipolytic activity is attained at the end of logarithmic growth phase. Induction of lipolytic enzyme activity is tested by addition of olive oil, tributyrin, detergents Tween 80 and Tween 20, as well as lecithin to the medium as sole carbon source or in the combination with glucose. The enzyme is inducible with the possibility to increase its production a few times by adding Tween 80, triacylglicerols as well as phospholipids. The lipase was isolated by precipitation of 70 % ammonium sulfate and hydrophobic chromatography on Phenyl Sepharose CL-4B. The enzyme was purified 14 times and effects of pH and temperature on the activity were obtained.

Additional Spectroscopic Evidence for a Saccharin Molecule Embedded in Ionic Cesium Saccharinate

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The FT IR spectra of protiated and partially deuterated analogues of two nowel cesium saccharinates, $Cs(C_7H_4NO_3S)(C_7H_5NO_3S)\cdot H_2O$ (**1**) and $Cs(C_7H_4NO_3S)\cdot 0.5H_2O$ (**2**) are studied. The presence of ν(NH) absorption (Figure), along with the ν(CO) and $\nu(SO_2)$ frequency values in the spectrum of **1**, represent inevitable evidence that this compound is an adduct of molecular saccharin. Previous spectra-structural and structural correlations in metal saccharinates are employed in conjunction with IR spectral data to make structural inferences about the compound.The appearance of low-frequency ν(NH) absorption continuum in the spectrum of **1** suggests certain degree of dynamical disorder of the proton within the assymetric $[N{-}H\cdots N]^-$ hydrogen bonds of saccharinato ion-molecule couples. In addition, one (C_s) or two (C_{2v}) crystallographic types of non-hydrogen bonded water molecules are situated in its lattice. Structural criteria for estimation of the proton position within the adduct dimmers, based solely on various descriptors of the degree of saccharinato sulfocarboximide ring distortion, are proposed. It is shown that in addition to the diversity of bonding modes expressed by its deprotonated form, saccharin can also be incorporated in solid-state structures as a molecule, even in a typically ionic salt.

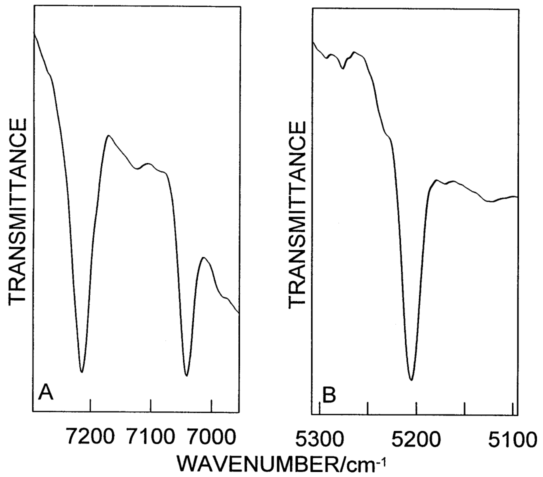

Figure. The 2ν(OH) (A) and 2ν(NH) (B) overtone regions in the spectrum of $Cs(C_7H_4NO_3S)(C_7H_5NO_3S)\cdot H_2O$.

Expression of Genes Involved in mRNA Splicing in Response to Anticancer Drugs

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Pharmacogenomics is a term used to describe the study of how your genes affect your response to drugs. In this study we have examined the expression of three genes involved in pre mRNA splicing, among which SR-A1 gene, which was recently identified by our associates [1] and it was previously found to be overexpressed in aggressive ovarian cancers. The other genes were SC35 and SRp20. β-actin gene was used as a control gene. The expression of the genes was examined in two human leukemia cell lines, K562 and U937 in response to the addition of the anticancer drug bleomycin (Bleocin®) and the complex In(III)-Bleomycin. Before the addition of the compounds, their cytotoxic effect in the cell lines used was examined with two in vitro cytotoxicity assays. The concentration of the compounds used and the incubation time were chosen based on their cytotoxic effect (alive cells > 50%). Total RNA was extracted from the cell lines and it was reverse-transcribed. The genes were amplified using the Polymerase Chain Reaction (PCR) and their expression was examined using agarose gel electrophoresis.

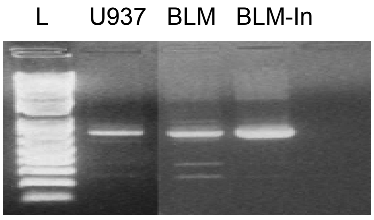

Fig 1. Expression of SC35 in U937 cells

In both human cell lines, human chronic myeloid leukemia (K562) and human histiocytic lymphoma (U937) the expression of SRp20 gene was the same after treatment with Bleomycin and In(III)-Bleomycin. In U937 cells the expression of SR-A1 gene was the same as compared to the untreated cells. The expression of SC35 gene differed as regards the compound used. After treatment with Bleomycin, the gene was expressed more that in the untreated cells, but after the addition of the complex In(III)-Bleomycin the gene was overexpressed (Fig 1). Studies have shown that the overexpression of SC35 gene, compared with the untreated cells, is a result of an increase in apoptosis (programmed cell death) of the leukemia cells [2]. In K562 cell line the new SR-A1 gene had different expression in response to Bleomycin and In(III)-Bleomycin. The treatment with complex with In(III) lowered the expression of the gene, which is not caused by Bleomycin alone (Fig 2). As regards SC35 gene, its expression was less when treated with Bleomycin and it was even less when treated with In(III)-Bleomycin.

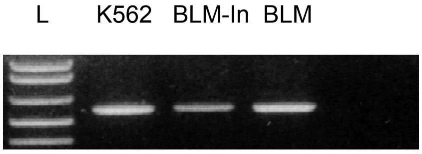

Fig 2. Expression of SR-A1 in K562 cells

The results indicate that the expression of the genes tested was different if cells were treated with Bleomycin alone or in complex with In(III). Bleomycin alone caused some alterations in the expression of the genes, which is most probably due to induction of apoptosis.

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Antiangiogenic Properties of Isoflavones

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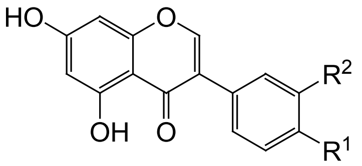
Isoflavonoids are a group of diphenolic hormone-like compounds that are of great interest, particularly because of their association with Western diseases like coronary heart disease, but also of their anti-carcinogenic potency.

Antiangiogenic strategies are emerging as an important tool for the treatment of cancer and inflammatory diseases[1,2].

In the present investigation we synthesized and tested the antiangiogenic properties of the natural isoflavones 5,7,4’-trihydroxy-isoflavone (genistein) **1** and 5,7,3’,4’-tetrahydroxy-isoflavone (orobol) **2**, as well as the non natural isoflavones 5,7-dihydroxy-4’-fluoro-isoflavone **3** and 5,7-dihydroxy-3’,4’-difluoro-isoflavone **4**.



1: R^1=OH, R^2=H

2: R^1=OH, R^2=OH

3: R^1=F, R^2=H

4: R^1=F, R^2=F

The above compounds were tested for their effect on angiogenesis in the chicken chorioallantoic membrane (CAM) assay, as well as for their capacity to inhibit VEGF-induced endothelial cell proliferation and expression of the Ets 1 transcription factor, known to be implicated in the regulation of new blood vessel formation[3-5]. We found that all isoflavones inhibited angiogenesis, albeit with different potencies. Furthermore, the chemical structure of the different isoflavones suggests a structure-activity relationship.

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Inhibition of Na,K-ATPase Activity by Digoxin after Photochemical Treatment

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Digoxin belongs to the group of digitalis glycosides, the most frequently used drugs to improve cardiac contractility in the treatment of congestive heart failure. The main pharmacological effect of the cardiac glycosides is Na^+/K^+-ATPase inhibition. These drugs, usually isolated from medical plants, can be exposed to the visible and UV irradiation. Since light can cause photochemical decomposition of drugs, the measurement of digoxin induced inhibition of Na,K-ATPase activity was considerd to be a good test for the determination of the degree of degradation after the photochemical treatment. Using the ATPase assay the therapeutic efficiency of digoxin exposed to the UV irradiation compared to the untreated drug can be evaluated.

Aqueous solution containing $1x10^{-3}M$ digoxin was irradiated for 2.5, 5.0, 7.5, 10.0, 20.0, 40.0 minutes by Xe-lamp. The digoxin concentration in the solution after the irradiation was determined by HPLC and by measurement of Na,K-ATP-ase activity. In this later case, the concentration dependent inhibition curve representing Na,K-ATPase activity vs. digoxin concentration was constructed, which served as the calibration graph for determination of digoxin concentration in irradiated sample. Na,K-ATP-ase activity was determined in a standard incubation medium (200 µl), containing 50 mM Tris – HCl (pH 7.4), 100 mM NaCl, 20 mM KCl, 5 mM ATP and protein (2 mg/ml) in the presence of 2 µl of the irradiated digoxin solution. In all experiments the enzymatic activity in the presence of digoxin was calculated as the percentage of the control value of the standard incubation mixture.

The results obtained by standard analysis (HPLC) and enzymatic activity measurements were in aggreement within ±10%. It is obvious that the prolonged irradiation time induced the decreasing of digoxin concentration, which was reduced by 100% after 40 minutes of irradiation and exhibited a first order kinetics. However, no degradation products were detected by HPLC.

Prevention and Recovery of the Hg^{2+}-induced Inhibition of Porcine Cerebral Cortex Na^+/K^+-ATPase by Gluthathione

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Inhibition of porcine cerebral cortex Na^+/K^+-ATPase activity by $HgCl_2$, in the absence and presence of –SH containing ligand, gluthathione (GSH), was studied. Furthermore, the purpose of this work was to examine the ability of this ligand to prevent and recover the $HgCl_2$-induced inhibition. In the absence of GSH, dose-response inhibitory effect of $HgCl_2$ on Na^+/K^+-ATPase activity was obtained. The half-maximum inhibition (IC_{50}) of Hg^{2+}, as calculated from the experimental curve (enzyme activity versus $HgCl_2$ concentration) was achieved at 7.0×10^{-7} M $HgCl_2$.

The presence of gluthathione in the reaction mixture, at a concentration of 10 mM, prevents enzyme inhibition, at $HgCl_2$ concentrations below 10 mM. In the presence of Hg^{2+} at concentration higher than 10mM, the inhibition curve drops sharply and the IC_{50} value of $HgCl_2$ is almost five orders of magnitude higher than IC_{50} value in the absence of investigated ligand.

Effect of gluthathione (within the range 10^{-6} -10^{-2}) on the recovery of inhibited Na^+/K^+-ATPase activity was investigated in the presence of 5.0×10^{-5} M $HgCl_2$, since at this concentration $HgCl_2$ induced complete inhibition of Na^+/K^+-ATPase. Moreover, the recovery of the Hg^{2+} induced inhibition was not achieved, even when GSH present in concentrations above 0.01M.

Effect of Bile Acid Salts on the Biochemical Parameters of Kidney and Liver Function

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The application of bile acids and their salts in pharmacotherapy is gaining more and more importance. Their action is manifested as the improvement of pharmacodynamic and pharmacokinetic properties of drugs, although the pharmacological effects of bile acids are also important. In our earlier investigations we found that sodium $3\alpha,7\alpha$-dihydroxy-12-oxo-5β-cholanate (sodium salt of 12-monoketocholic acid) is an effective enhancer of insulin nasal absorption in rats [1]. The same substance applied nasally and subcutaneosly lowered the blood glucose level in rats [2]. However, little is known about the effect of bile acids on functioning of the kidneys and liver. The aim of this work was a comparison of the influence of 12-monoketocholate on the liver and kidney functions with that of ursodeoxycholate and deoxycholate, which have already been clinically tested.

The investigation was carried out on white Wistar male rats, treated intravenously either with saline solution (1 mL/kg), or with sodium salts of 12-monoketocholic acid, ursodeoxycholic acid or deoxycholic acid in a dose of 4 mg/kg. The treatment lasted 7 days and 24 hours later the animals were anaesthetised with urethane, 0.75 g/kg, i.p. and after ligature of their urethral channel, the urine was collected during three hours for biochemical analyses. After that the animals were sacrificed by cardiopunction, and blood was used for determination of hematological parametres and the serum, obtained after centrifugation, was used to determine biochemical parametres. Also, kidney and liver samples were taken for determining the liver and kidney glutathione and proteins concentrations.

Bile acids did not cause significant changes either in the investigated serum biochemical parameters or hematological parameters. The urine parameters showed no significant changes compared to control. Treatment with bile acid salts had no influence on the content of reduced glutathione in the rat liver and kidneys, the exception being treatment with 12-monoketocholic acid, which caused an increase in the liver by 25% in comparison with control. The obtained results indicate that treatment with bile acid salts showed no toxicity, at least when the investigated parameters are concerned.

Acknowledgment.

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Polyphenols as Anti-Invasive Drugs

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Growth and invasion are tumor activities that are responsible for the fatal outcome of untreated cancer patients. Invasion, however, is a more resistant problem than growth, and anti-invasive agents are sadly lacking in clinical practice. Progress in this field can be expected from a better knowledge of the molecular mechanisms of invasion, from the development of relevant invasion models *in vitro* and from the synthesis or isolation of new compounds as candidates for anti-invasive drugs. The search for anti-invasive treatments led us to synthesize and screen novel compounds for their effect in an assay for invasion *in vitro*. The assay consisted of organotypic confronting cultures of invasive human MCF-7/6 mammary carcinoma cells with embryonic chick heart fragments. Number of novel polyphenolic compounds were synthesized chemically and Characterized with UV, IR, NMR and Mass spectroscopy. These compounds were tested for their anti-invasive activities in Human MCF-7/6 cells at various concentrations. These polyphenols were compared with some other anti-invasive Chalcones. Our data indicated that these chemically synthesized polyphenols were highly active as compared to Chalcones. Further our study showed that these polyphenols are having good anti-invasive properties without being cytotoxic for the cells.

The Investigation of the Conditions for the Determination of N-Acetyl-β-D-glucosaminidase Isoenzymes in Neutrophilis

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Recognition of the leukemic cell type is crucial for the diagnosis, management and prognosis of different types of the disease. In the leukemias not only cell type but stage of differentiation must be assessed. Classification of the leukemic cell has generally rested on its morophological, histochemical and imunological characteristics. Such studies may be complemented by the recognition of certain biochemical markers. The studies on the lysosomal hydrolases in blood leukocytes showed that the activities and properties of various lysosomal hydrolases from different leukocyte types are not the same. The changes of N-acetyl-β-D-glucosaminidase (E.C.3.2.1.30, NAG) activity in different types of leukemia suggest that NAG may be a useful biochemical marker for the differentiation of subtypes of acute lymphocytic and myelo(mono)genous leukemias. It is not known whether the enzymatic abnormality is derived from abnormal hematopoiesis in leukemia or wheter the alterations reflect an intrinsic variability in disturbance of the control mechanisms of these enzymes and in altered cellular metabolism The analysis of isoenzimic profiles of NAG partially clarify the significance of lysosomal enzymes in malignant cells. Therefore, the aim of this paper is the investigation of conditions for separation and determination of NAG isoenzyme activities in neutrophils.

Ion-exchange chromatography on DEAE cellulose was applied to separate the isoenzyme forms of NAG from neutrophils of healthy persons. Neutrophils were separated from peripheral blood cells using three steps. Most of the red blood cells were removed by sedimentation with 6% dextran. Leukocytes and lymphocytes rested suspended in solution. Remaining red blood cells and platelets were removed by hypotonic lysis. Mononuclear cells were separated from neutrophils using Ficoll-Hypaque sedimentation. The neutrophils sink to the bottom of the Ficoll, mononuclear cells remain at the Ficoll/isolate interface. Total NAG activity and protein concentration were measured in sonicated cell extracts. The cell extract was applied to DEAE cellulose column (1 x 13 cm) previously equilibrated with 0.01 mol/l phosphate buffer of pH 7.0. The NAG activity in the fractions was determined by 2-methoxy-4-(2'-nitrovinyl)-phenyl-N-acetyl-β-D-glucosoaminide as the substrate (calibration curve: $y=0.854x + 0.00499$, $r=0.999$).

Analysis of the elution profiles of NAG showed that good separation of the major A and B isoenzyme forms of urinary NAG using this method was achieved. The B form was eluted with 0.01 mol/l phosphate buffer of pH 7.0, while a linear concentration gradient (0-0.3 mol/l) of sodium chloride in the same buffer was used for the A form. The fractions of the dominant A form activity in the total activity of healthy persons were from 49 to 57%. The fractions of the B form activity were from 7 to 15%. Beside the major A and B isoenzymes of NAG, the A_2 form was also isolated. It was eluted with 0.4 mol/l of sodium chloride in a phosphate buffer of pH 7.0. Its percent fractions in total NAG activity of healthy person were from 35 to 45%. It was concluded that the applied method is appropriate for the separation and determination of NAG isoenzymes in neutrophils.

Separation of Placental Cell Membrane IGF-binding Receptors Using Lectin Affinity Chromatography

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Receptors that specifically bind insulin-like growth factors (IGFs) –I and –II and insulin receptor are N-glycosylated. Reviewing the literature the speculations concerning the potential existence of glycoisoforms of IGF-I receptor were found, but no results explicitly demonstrated that.

In this work IGF-binding receptors (IGF 1R, IGF-II/Man-6-P receptor and insulin receptor) were isolated from human placental cell membranes after their solubilization. Immobilised wheat germ agglutinin (WGA) was used to separate these receptors from the other proteins that bind IGFs in solubilizates (affinity chromatography).

The specific elution of IGF-binding receptors bound to WGA-agarose column by discontinual gradient of N-acetyl-D-glucosamine (GlcNAc) solution pH 7.5 revealed the existence of at least three peaks of the IGF-binding activity. Furthermore, application of 0.5 M GlcNAc solution pH 3.0 eluted another type of molecules which tightly bound IGF-peptides (and insulin). The chromatographic profile of the IGF-binding receptors indicated that there are several populations of receptors in placental cell membranes in respect to their oligosaccharide moieties. Insulin receptors bound to WGA-agarose were also shown to elute in multiple peaks when subjected to discontinual gradient of sugar solution.

These results strongly suggest the existence of more than one population of IGF-binding receptors on placental cell membranes, ie. glycoisoforms of the receptors. These glycoforms are not expected to have different ligand-binding properties but the potential physiological significance of their existence may lie in their different targeting to various membrane compartments. This fact may further influence different cell signalling pathways.

Evolution of Sulfide Biogeoceoenosis: Long-Term Studies

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Sulfide biogeocoenosis are specific by their characteristical features both in relation to the basic energetic substrate and the source of electrons (sulfides of iron and other metals) and to present microorganisms, and they are usually with low content of organic substance. Specific microorganisms of these habitats are chemolithotrophic thionic bacteria. Interactions the substrate-thionic bacteria cause changes of the habitat feature and composition resulting in alteration of the microbiological pattern [1].

Waste dump (liquid and solid surface samples) of sulfide copper deposit in Bor (East Serbia) is the biogeocoenosis which has been studied since 1975 [1-3]. The latest results are from November 2003 [4]. Periodically we have monitored mineralogical-petrographic composition (RDA), basic physical, physical-chemical and chemical parameters, sulfur and iron speciation, as well as the number of total thionic bacteria, *Acidithiobacillus ferrooxidans,* total denitrifiers and some chemoorganoheterotrophs.

The results obtained prove that the biochemical and chemical activity of thionic bacteria [oxidation of sulfides and iron(II), generating of iron(III)-ions and sulfuric acid], alter the solid substrate: the content of sulfides is decreased, primary minerals are transformed into secondary ones. Out of iron compounds, the amorphous base-iron(III) sulfates are dominant. In the last years, occurrences of calcium sulfate minerals are pronounced. Low pH values (2-4), high mineralization and redox potential, high concentration of iron(III), sulfates and copper are characteristics of waters on this locality, but their concentrations are being decreased or stagnate in the last years, which is the result of an evident trend in reduction of the number of thionic bacteria as the key “biological agent” of the surface loose aerobic layer and the solid substrate and waters in evolution of sulfide biogeocoenosis.

These natural processes endanger the environment (surface and ground waters) and due to the irretrievable loss of useful metals (copper) they are the economic loss, but if they are directed, intensified and controlled (bacterial leaching) then a cheap metal is obtained from waste and non-balance raw materials (low grade ores) and this biogeotechnological procedure compared to the classical pyromettalurgy represent the proper “green technology”.

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Antimicrobial Activity of Some Plant Extracts Used in Folk Medicine

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This study examines the antimicrobial activity of acetone, ethanol, methylene chloride, ethyl acetate and water extracts of four plant species. The dried extracts of the whole plant of*Tusilago farfara L (Compositae), Arctium lappa (Compositae), Analgallis arvensis (Primulaceae*) and *Euphrasia officinalis* (*Scrophulariaceae)* were tested in vitro against 10 bacterial species and 10 fungal strains by the agar diffusion method. The results of the screening are listed in Table 1.
Ethanolic extracts of*Tusilago farfara L* and *Euphrasia officinalis* have the greatest antibacterial efficiency (39%), followed by values of *Arctium lappa* for about 21%.
Moreover, it was determined that ethanol and water extracts of four plant species have antifungal effects against *Trichoderma* and *Aspergillus* species *(57%).*

Table 1. Antimicrobial activity of plant extracts

Plant		*Tusilago farfara*		*Arctium lappa*		*Analgallis arvensis*		*Euphrasia officinalis*	
EXTRACT MICROORGANISM		EtOH	H_2O	EtOH	H_2O	EtOH	H_2O	EtOH	H_2O
1	Pseudomonas fluorescens	27	19	17	0	0	0	39	23
2	Pseudomonas glycinea	21	23	17	0	0	0	37	27
3	Pseudomonas phaseolicola	17	17	17	0	0	0	29	27
4	Bacillus mycoides	19	17	0	0	0	0	37	23
5	Bacillus subtilis	19	23	17	0	0	0	27	25
6	Erwinia carotovora	17	17	0	0	0	0	27	23
7	Agrobacterium tumefaciens	25	17	21	0	0	0	29	27
8	Klebsiella pneumonia	17	17	17	0	0	0	29	29
9	Azotobacter chrococcum	19	19	21	0	0	0	29	31
10	Enterobacter cloacae	17	19	0	0	0	0	27	33
11	Trichoderma viride	34	34	31	24	37	34	43	43
12	Trichoderma harzianum	57	57	35	43	39	37	50	41
13	Doratomyces stemonitis	0	0	0	0	0	0	62	32
14	Aureobasidium pullulans	0	0	0	0	0	0	0	0
15	Alternaria alternata	0	0	0	0	0	0	0	0
16	Aspergillus niger	0	0	0	0	0	0	0	0
17	Aspergillus glaucus	50	56	0	0	52	47	62	26
18	Penicillium verrucosum	0	22	36	61	25	19	63	38
19	Penicillium cyclopium	37	33	32	55	31	29	47	28
20	Mucor mucedo	27	27	26	22	27	35	46	28

a. Values are inhibition zone in mm and an average of triplicate
b. Concenration of extracts are 15mg/disc for bacteria and 50 mg/disc for fungi species
c. Tetracycline and nistatine as standards (100 mm)

Synthesis and Antimicrobial Activity of Some 4-(Phenylazo) Phenoxy Acetic Acids

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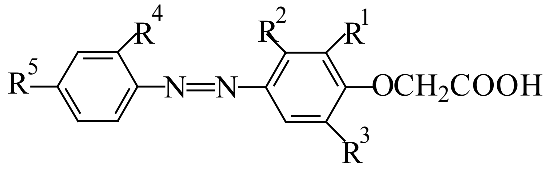
Using a method described in previous paper [1] we obtained fiftheen new 4-(phenylazo) phenoxy acetic acids having general formula.



where $R^1 = Cl, CH_3$, Br, allyl; $R^2 = Cl, CH_3$; $R^3 = Cl, CH_3$;
$R^4 = CH_3$; $R^5 = Cl, CH_3, CN$;

These azomonoethers were prepared by condensation of chloroacetic acid with salt of some 4-(phenylazo) phenols.

The new synthesized compounds were characterized by elemental analysis (C, H, N,), determination of melting points and molecular weights by mass spectrometry and UV-Vis, IR, NMR, SM spectra. The spectral analysis helped us to establish the structure of these compounds. IR and UV spectra showed characteristic bands due to the ether function, azo and carboxyl group. The absorption bands at isomeric acids are very close. The ^{1}H-NMR spectra showed a singlet integrating for one proton of carboxyl group, un singlet integrating for two protons of methylene group and a multiplet for the aromatic protons.

All these new compounds were screened for their antibacterial activity against Staphilococcus aureus, Streptococcus pyogenes, Escherichia Coli, Pseudomonas aeruginosa, Proteus vulgaris and for their antifungal activity against Candida albicans by disk diffusion method.

The results of the screening indicate the title compounds carrying methyle substituents possess better activity against all the organisms tested.

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New Biological Active Complexes of Some *d* and *f* Metals Based on N,N'-Dimethylbiguanide

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N,N'-dimethylbiguanide (metformine), is a powerful anti-hyperglycaemic agent, used for the treatment of diabetic patients with non-insulin dependent diabetes mellitus. The major effect of N,N'-dimethylbiguanide is to either potentiate or mimic the insulin action. This N-substituted biguanide derivative is a bidentate ligand which has a versatile chelating capacity.

Taking into acount the biological role of some *d* metal ions, we study the synthesis and the characterization of some new Cu(II), Cr(III), Fe(III), Ni(II), Mn(II), Co(II), La(III), Ce(III), complexes with N,N'-dimethylbiguanide.

The complex compounds synthesized are highly coloured powders and have been characterized by elemental analysis, molar electrical conductivity, FT-IR, electronic and EPR spectra.

The antimicrobial activity of the investigated ligands and complexes were done by

microdiscs paper diffusion and microdilution methods, against eleven gram-positive and gram-negative bacteria strains and two fungi species. Phenol was used as a positive control.

The results show that all compounds present antimicrobial activity against most of the tested species. The complexes with Cu(II), Mn(II), Ce(II) and La(II) show the increased antibacterial and antifungal activity with an inhibition diameter beetwen 10-20 mm, than the other complexes analysed, which present an inhibition diameter beetwen 0,1-10 mm.

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Barley Lipid-Transfer Protein Thermal Unfolding Followed by Differential Scanning Calorimetry

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Nonspecific lipid transfer proteins (nsLTPs) belong to multigenic plant protein family. They have a possibility of binding different types of monoaciyated and diacylated lipid molecules including fatty acids, fatty acyl-Co A, lyso-phosphatidilcholine. Ns LTPs are small proteins, with molecular masses of about 9 kDa, and have basic pI (8.8-10). *In vivo* LTPs are synthesized with N-terminal signal peptide, they follow a secretory pathway, and they locate in extracellular layers, cell walls or cutins and in vacuolar structures (1). Although many data are available on nsLTPs their real phyisiological function is still unclear. Structural, biochemical and physiological information has confirmed that the key role of ns LTPs is in plant resistence to biotic and abiotic stress (2).

The aim of this work was to study thermal stability of isolated barley LTP; obtain thermodymamical parameters of protein unfolding (T_d - temperature of denaturation, ΔH^{cal} - calorimetric enthalpy ΔH^{VH} - van't Hoff enthalpy) and to eventually propose LTPs possible role in plant temperature resistance.

We have isolated and characterized LTP from domestic brewer's barley grain. Molecular mass of LTP and pI was determined by means of SDS-PAGE and IEF-PAGE, respectively. Thermal unfolding of protein was followed by differential scanning calorimetry (DSC) method. We investigated thermal stability of purified LTP, and LTP fractions obtained after each purification step. All DSC scans were carried out on MicroCal MC-2 Scanning Calorimeter, MicroCal Inc. Northampton, MA, and USA. All protein solutions were degassed ~1 min with gentle stirring under vacuum before loaded into the calorimeter cell. Scans were performed in the temperature range from 20°C to 100°C, protein concentration was 1.8 mg/ml. Scan rate was 90°C/h. Origin software was used for DSC data analysis (non two-state curve fitting model, for estimating thermodynamical parameters of protein unfolding: Td, ΔH^{cal}, ΔH^{VH}). Total amount of protein (mg/ml) was determinated gravimetrically.

From obtained DSC curve of pure protein it can be seen that process of thermal unfolding of LTP protein is complex: there are two endothermal transitions (T_{d1}=38°C and T_{d2}=90°C) and between them one exothermal transition (T_3=52°C). It can be proposed that LTP protein has two domains with different thermal stability, which need not to be structural domains (3). We suggest that obtained exothermal transition represents process of ligand dissociation from protein molecule caused by thermal unfolding. We obtained thermodinamical parameters of LTP protein unfolding: Td1=38°C ΔH^{cal1}=16.53 cal/mol ΔH^{VH1} =73.69 cal/mol and Td2=90°C ΔH^{cal2}=45.66 cal/mol ΔH^{VH2}=35.5 cal/mol respectively.

From our data it can be proposed that LTP can have role in plant temperature resistence, considering high thermal stability (second thermal transition at 90 °C) and so that can be one of its physiological functions.

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Synthesis and Luminescent Properties of Biotinylated Acridium Amides. New Detection Reagents for Immunoassay Applications

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Chemiluminescence immunoassays based on non-radioactive cyclic hydrazides [1], dioxetanes [2] or oxalic acid derivatives [3] have been known for many years. Although the technique offers improvements in terms of reagent stability over the use of radioisotopes, it also presents certain disadvantages. Thus, oxalic acid derivatives have poor solubility in water, while immunoassay is performed in aqueous solution. Also, the chemiluminescent reactions of cyclic hydrazides proceed only in the presence of a catalyst. In contrast, chemiluminescence of acridinium derivatives (esters or amides) does not need an additional catalyst. It can be simply triggered by alkaline hydrogen peroxide and a much lower chemiluminescenct background can be achieved. The first acridinium ester, which has a succinimidyl moiety as the reactive group for coupling to biomolecules, was reported in 1983 [4]. Since, a number of derivatives have been synthesized to achieve greater stability and higher chemiluminescence. However, synthetic routes to such compounds are complex because antibody-binding functional groups are introduced on the labile phenyl ester group.

The aim of this work was to prepare novel chemiluminescent biotinylated acridinium amides and to determine their chemiluminescence efficiency. As far as we know, with the exception of isoluminol derivatives[5] little is known about biotinylated conjugates. Biotin is covalently bound to the chemiluminescent acridinium moiety through 1,2-diaminoethylene as spacer molecule. The major advantage of biotinylated acridinium amides over biotinylated isoluminols is the improved reproducibility of their chemiluminescent measurements, probably due to the absence of added catalyst. Moreover, as these compounds show strong fluorescence intensity in aqueous solutions, this property has been utilized in fluorogenic immunoassays. Preliminary results showed that this reagents enabled measurement of solid phase-immobilized biotinylated mouse IgG with a detection limit of ca. 1 ng/assay.

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Biologically Active Complex Compounds with Phenothiazine Derivatives as Ligands

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Phenothiazine derivatives are well-known for their biomedical action and their neuroleptic and antitumoral activities are based probably on the formation of some complex compounds with active *d*- metals in biological systems.

This paper presents the results of separation and characterization of some complex compounds of Cu(II) with phenothiazine substituted derivatives 2-[(10-methyl-10H-phenothiazin-3-yl methylene)-amino]-benzenethiol (L^1) and 3-phenothiazin-10-yl-propionic acid (2-hydroxy-indol-3-ylidene)-hydrazide (L^2).

The complexes were tested for their biological activity.

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Influence of Treatment Time and PEG 6000 Concentration on Dextransucrase Precipitation

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Dextransucrase catalyzes the production of dextran, a glucan of high molecular weight. Dextransucrase from *Leuconostoc mesenteroides* B-512 F, bacterial strain wich is most commonly used for producting dextran industrially, sinthesizes dextran with about 95% α-1,6 bonds. In this report we have studied the influence of treatment time and polyethylene glycol (PEG 6000) concentration on dextransucrase precipitation.

Dextransucrase was obtained in crude form by cultivating *Leuconostoc mesenteroides* B-512 F with the pH maintained in the range 6.6 to 6.7. The supernatant after cell removal, pH adjustment to 5.2 and adding merthiolate in an amount of 0.005% was used as the enzyme solution.

After the removal of precipitable form of dextransucrase by centrifuging, the enzyme solution was mixed with 50% aqueous solution of PEG 6000, and after being left for 20 minutes to precipitate and centrifuged, the supernatant was removed by decantation and the precipitate was resuspended in a buffer. The supernatant obtained after precipitation and the extracts were tested for dextransucrase activity and protein content, and the activity of dextransucrase was determined in the residual precipitate after the extraction.

Dextransucrase activity in solution was determined by increasing amount of reducing sugars. The contents of reducing sugars were determined by a modified ferricyanide method with fructose, and protein content according to Bradford with the use of BSA as a standard.

The results obtained indicate that equilibrium was reached shortly after the precipitation. In all the cases studied there was a positive activities balance in the precipitation process (109% to 123%). It was found that the greatest part of dextransucrase precipitated between 7% and 13% PEG. The increase of PEG content above 18% did not contribute to increasing of the precipitated activity. Most of the precipitated activity passed to the solution at first extraction with buffer. Most of the protein was precipitated between 2% and 10% PEG. Further increase of PEG content caused much slower increase of the precipitated protein quantity.

Based on the results obtained, the optimum procedure for dextransucrase purification could consist in two steps: precipitation with 8% PEG in order to remove most of the ballast proteins, and precipitation with 16% PEG in order to achieve precipitation of the greatest part of precipitable dextransucrase.

Stability of Chlorophyll Complexes with Heavy Metals: UV/VIS and FT/IR Studies

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Introduction

The chlorophyll (Chl) has a major function in photosynthesis. In chemical terms, Chl is a chlorin, porphyrin derivate (cyclic tetrapyrrol with isocyclic cyclopentanone ring, fused to pyrrole ring at C13^1-C13^2), where central metal magnesium ion (Mg^{2+}) is coordinated with four symmetric pyrrole rings (Fig.1). Several toxic heavy metals, zinc (Zn), cadmium (Cd), mercury (Hg), lead (Pb), nickel (Ni) and copper (Cu), are easily absorbed by plants. Once absorbed, they penetrate to plant tissues (including leaves) and in higher concentrations they may inhibit photosynthesis by replacing the labile bonded central Mg^{2+} ion and forming chlorophyll-heavy metal complexes (Chl-HMS). The Chl-HMS complexes lose photosynthetic function, and this, as a final consequence, may lead to plants fatal end. That is why is so important to measure difference between the Chl-HMS complexes and unsubstituted chlorophylls; for this purpose in this work UV/VIS and FT/IR spectroscopies have been employed. The HMS-Chl complexes are prepared *in vitro* by using several heavy metals with different affinities toward central Mg^{2+} position in Chl molecule. However they have affinity toward other position, too: between C-13^3 keto (C=O) group and the enolic form of C-13^{1}keto group they can make peripheral chelat complexes). The chosen heavy metals (Cu, Zn and Pb) are well known pollutants.

UV/VIS and FT/IR spectra

Chlorophylls have two major absorption regions: in the "red" (Q band) and in the "blue" (Soret or *B* band) ranges of VIS region. Stability of the Chl-HMS complexes were checked out by VIS spectroscopy by recording the spectra (a) with constant HMS concentration but after different time periods following the complexes formation (t_C), (b) with different, increasing HMS concentrations, for the same t_C value . The changes were detected both in the "blue" (B-band) and "red" (Q-band) ranges. In the "red", a "blue" (hypsochromic) (Q)-band shift has been observed for Cu and Zn-Chl complexes - relative to t_C time - and the "red" (batochromic) shift for the Pb-Chl complexes (Fig.2). The FT/IR spectrum of unsubstituted Chl shows expected band at 1699 cm^{-1} assigned to the free 13^{1}C=O group and band at 1737 cm^{-1} assigned to the ester 17^3,13^{3}C=O groups. In the FT/IR spectrum of Cu-Chl the 1699 cm^{-1} band has disappeared, but the latter one is shifted to 1729,95 cm^{-1} (Fig.3). An interaction between Chl molecule and Cu^{2+} ion to form peripheral chelat metal-Chl complex has been suggested (band at 1119 cm^{-1} in FT/IR spectrum of Cu-Chl complex is assigned to the 13^{1}C-O enolic group).

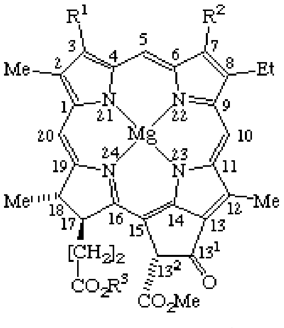

Fig.1. Molecule Chl-Structure

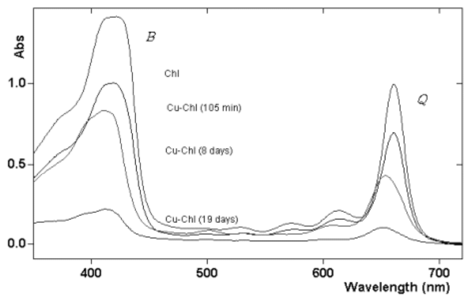

Fig.2. UV/VIS spectra of Chl

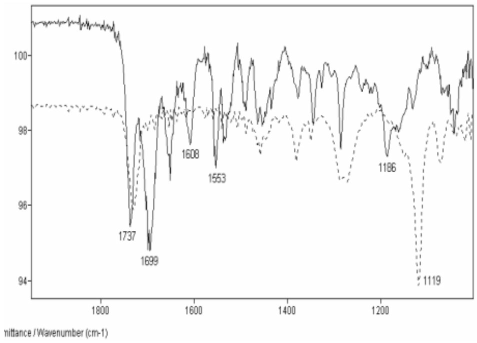

Fig.3. FT/IR spectra of Chl (—) and Cu-Chl (····)

Antibacterial Activity of Complexes with 2-Aminobenzimidazole Derivatives

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Physico-chemical characteristics

Chlorides of copper(II) and nickel(II) react with 1-benzyl-2-aminobenzimidazole (L^1) or 1-(4-methylbenzyl)-2-aminobenzimidazole (L^2) to give complexes of the type $[ML_2Cl_2]\cdot nH_2O$ (M=Cu or Ni; $L=L^1$ or L^2; n=0.5 or 1). The complexes were synthesized and characterized by elemental analysis of the metal, molar conductivity, magnetic susceptibility measurements and IR spectra. The molar conductances of the copper(II) complexes in DMF solutions indicate that the complexes behave as non-electrolytes. The values of molar conductivity in the case of nickel(II) complexes indicate that one of the coordinated chloride anions has been replaced by DMF molecule. The room temperature effective magnetic moments and IR data of the complexes suggest that all Cu(II) and Ni(II) complexes have a tetrahedral configuration, which is realized by participation of the pyridine nitrogen of two organic ligand molecules, and two chloride anions.

Antimicrobial activity

The antimicrobial activity of the benzimidazoles and their complexes were evaluated against *Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus sp.* and *Saccharomyces cerevisiae.* The results of antimicrobial investigations indicate that most effective compound is 1-(4-methylbenzyl)-2-aminobenzimidazole. In the case of *Saccharomyces cerevisiae* the ligand 1-benzyl-2-aminobenzimidazole and its complexes are not active. Of the complexes, the most active compounds are those containing nickel(II). On comparing the biological activity of the ligand and its complexes, it was found that complexes are more effective against the bacteria.

Effect of Laurel (*Laurus nobilis* L.) and Bastard Balm (*Melittis melissophyllum* L.) Ether Essential and Fullerene on the Production of OH Radicals

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Laurel (*Laurus nobilis* L.) is well-known as a remedy, spice, as well as a holy tree from the ancient times and the earliest notes. Today it is used as a secondary medicament. Laurel leaves oil is used as carminative, excito-aromatic, nervine and in perfume production. Oil is usually used in the mixture with other medicaments. The laurel plant contains several classes of secondary plant products. The fruit consists of 30% fat and 1% ether oil, sugars, starch, and basorine, while the leaf contains bitter substances and tannin. Essential oil mostly contains cineol and alpha-pinen.

Bastard balm (*Melittis melissophyllum* L.) leaves contain essential oil (0.02-0.3%), which consists of monoterpene aldehydes, alcohols, ketones and esters (geranial, neral, citronelal, geraniol, nerol, citronelol, linalool, etc). Essential oil exhibit spasmolitic action.

In this study we investigated the effect of laurel leaves and berries ether oil on production oh hydroxil radicals. Beside that, we were examining sinergistic effect of these ether oils and carbon tetrachloride and derivative of fulerene.

The crude n-hexane extract of laurel leaves and berries and bastard balm was obtained by the Soxhlet extraction of powdered plants material with n-hexane. 10% (v/v)solutions of extracts in 50% ethanol were prepared. The effects of these ether oil on production of hydroxil radicals radicals was determined by monitoring the chemical degradation of deoxyribose. Reaction is initiated by hydroxyl radicals obtained in Fenton's reaction, which yields products that react with thyobarbituric acid (TBA test). Obtained products, among which malonyl-dialdehyde is the most important, are determined by spectrophotometric metod according to Buege-Aust.

Pure preparations of derivative of fulerene and carbon tetrachloride were usedi in different amounts.

Laurel leaves and berries ether oil, as well as bastard balm ether oil, increased both the production of OH radicals, but this increase was lower as mass concentration of ether oils increased. Combination of laurel leaves and carbon tetrachloride decreased production of OH radicals in comparasion of carbon tetrachloride used alone, but the production of OH radicals was still significantly higher in comparasion to control group (statistically speaking).

Fulerene derivative used alone increased the production of OH radicals. Combination with these ether oil and fulerene increased the production of OH radicals even more.

Effects of Cholic Acid on the Transport of Lidocain Between Two Phases

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CMC

The aim of this work was to determine the influence of critical micellar concentration (CMC) of sodium cholate on transport of lidocain from water solution into the organic layer (dibutylether). Decrease of lidocain concetration in the aqua layer was determined at 264 nm, using UV/Vis spectroscopy. Successive measurings were performed in different time periods.

Bile acids

Bile acids are amphiphilic molecules. In aqueous solutions and with a critical micellar concentration, free molecules aggregate, forming micelles. If present in CMC, bile acids increase the permeability of lipophillic membrane (modify bordering surface). Presence of bile acid in aqueous solution of lidocain produces Onsager-effect (electrophoresis), also. In these two ways, the transport of lidocain from the aqueous to the organic layer is enhanced.

Results

0.1 % lidocain solution is used as blind-probe for measuring the transport kinetics of lidocain into the organic layer. In an identical aqueous solution of lidocain Na cholate was added, in CMC (7.5 mmol/dm^3), and a decrease of lidocain concentration in aqueous layer was monitored. It′s concentration was proportional to the solution absorbance at 264 nm, considering that Na-cholate does not exhibit absorption at that range. Measurements were performed at following time intervals: 1, 5, 10, 15, 30, 45, 60, 90, 120 and 150 min.

The D values (fast extraction coefficient) were determined from graph [c(%) / t(min)] plotted from the obtained results. The following values were obtained: D = -0.0537 for lidocain transport in absence of sodium cholate, and D = -0.0907 in presence of sodium cholate in CMC. After 150 min K values (distribution coefficient) reaching 0.3529 and 0.7015 were obtained for solutions of lidocain, and lidocain + sodium cholate, respectively.

Conclusion

The obtained D-values indicated that the transport of lidocain was prompted – D-values doubled in the presence of bile acid. This effect cans infulence the time of action of a drug. Results obtained for the K value showed an increased amount of lidocain penetrating the organic layer, increasing activity of the transported compound.

These results suggested possibility of applying cholic acid to improve the activity of pharmacologically active substances. Further investigation on pharmacological parameters of these compounds is still in progress.

Natural Aluminosilicates in Pig Nutrition: Biochemical Evaluation

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The use of adsorbents (zeolites, bentonites and other aluminosilicates) is a broadly applied measure used by the livestock industry to improve nutrition and protect animals from harmful effects of toxic substances. *In vivo* evaluation of adsorbent supplementation is related to its efficacy and possibilities of impaired nutrient utilization. ATN ("antitoksična smeša kao dodatak stočnoj hrani visoke hranjive vrednosti") is a combination of hydrated sodium calcium aluminosilicate, activated carbon, and natural sources of vitamins, microelements, essential amino acids, and fatty acids. The objectives of this study were to assess possible toxicity of ATN and to demonstrate positive effects of ATN supplemented pig diet on pig performance. Body weights, hematological and serum biochemical analyses were performed and the results point out mostly undisturbed mineral status and preserved homeostasis of the investigated biochemical parameters in the ATN supplemented group when compared with control group and referent values.

New Beta 3-Adrenoceptor Agonists for Antidiabetic Drugs

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In the early 1980s a new class of beta-adrenergic receptor, named beta-3, has been identified; compounds with agonist properties on such receptor were found to have remarkable anti-obesity and antidiabetic properties in rodents.

The poster presents the chiral synthesis of certain compounds belonging to the substituted ethanamines class, starting with 4-hydroxybenzoldehyde and 3-chlorobenzaldehyde; the main reaction parameters are presented, as well as the purification methods used for obtaining the pure enanthiomeres.

The obtained compounds represent new beta-3-adrenergic agonists to be used in the synthesis of antidiabetic and antiobesity drugs.

Isolation of Pharamacologically Active Thymic Fractions and Investigation of Biological Activity by Using the *in vivo* Hemolytic Plaques Method

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It is known that the thymus gland plays an important role in certain immunological disorders. Investigation of the function and properties of this gland shows that the thymus contains pharmacological components with immunological properties. Therefore we investigated the possibility of using thymus extracts as an immunomodulating pharmaceutical drug.

The goal of this study was to determine biologically active components of thymus extract.

Extract of calf thymus was prepared and fractioned into lipid and nonlipid components.

The lipid component was fractioned by column chromatography(1) (Silica gel 60, Merck) into neutral lipids, phospholipids and glycolipids. Each lipid component was characterized by thin layer chromatography and gas–mass chromatography, using FID detector. The fraction which contained biologically active peptides was isolated from the nonlipid component of thymus extract, using Folch method (2).

After evaporation and lyophilization of this material, peptides content was determined by Biuret method (3). Isolated peptides were characterized by IR and NMR. Analyses of IR and NMR spectra indicated the presence of characteristic bands and peaks for peptides.

Biological activity of isolated fractions was determined by *in vivo* hemolytic plaques method (4-6). Biological investigations were performed on Wistar rats aged 13-18 months, with involuted thymus. The peptide fraction of nonlipid thymus extract component showed significant increase of hemolytic plaques. The phospholipid fraction also showed increase of hemolytic plaques. Glycolipid and neutral lipid fractions did not express significant immunological response.

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Biosynthesis and Biological Potentials of Some Ingredients for the Pharmaceutical Industry

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It is known that natural nucleosides and nucleotides play a main role in processes of biosyntheses and in the molecular mechanisams of genetic information protection. Different kinds of nucleoside analogues today represent major and numerous antiviral and anticancer agents, as well as immunomodulators or regulators of gene expression.

The goal of this study was to examine *Thermotrix thiopara* and *Bacillus stearothermophylus* specific cultivation conditions, which provide an effective biotechnological production of different enzymes necessary for new nucleoside and nucleotide analogue biosyntheses (phosphatase, purine and pyrimidine phosphorylase, adenylate cyclase), as well as antioxidative enzymes, superoxide dismutase and catalase (SOD i CAT)[1-3]. Under defined optimal conditions of “batch“ fermentation (specific nutrition broth, temperatures, pH, aeration, mixing, choosen precursors and inductors of target enzyme production), important biologycal materials enriched with thermostable and highly active target enzymes were obtained. The obtained cell-free extracts were tested in a number of enzymatic reactions and possibilties of efficient bioconversion of different natural nucleosides and nucleotides to new nucleoside analogues (different types of triazole nucleosides, purine and pyrimidine analogues) were found. The procedures applied for the isolation of these compounds from a reaction mixture after the completion of enzymatic reaction (fractional protein precipitation, chromatographic purification on selected types of ion-exchange columns, crystallization in eluates, gel chromatography on Sephadex), provide for the resulting high-purity products, which could be important as potential antiviral and anticancer agents. The key conditions for growth and proliferation of tested bacterial strains were defined, including highly active adenylate cyclase, and low activity of interfering enzymes, which ensures the use of obtained cell-free extracts in the enzymatic synthesis of cyclic nucleotide cAMP, as the basic compound in the synthesis of new potential anticancer agents.

Our experimental results have confirmed possibilities of the effective use of the tested thermophilic bacterial strains in biological preparations, enriched with thermostable and highly active antioxidative enzymes, superoxide dismutase and catalase that play a key role in the protection of body cells against the influence of the extremely reactive free radicals. The chemical structures and specific activity of obtained purified enzymes was determinated. These enzyme preparations have important use in modern “antioxidant” therapy for many diseases associated with an “oxidative stress”.

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Influence of Metal Ions and Protein Denaturants on α-Amylase Activity

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α-Amylase (1,4-α-D-glucan glucanohydrolase, EC 3.2.1.1) hydrolyses starch, glycogen and related polysaccharides by randomly cleaving internal α-1,4-glucosidic linkages. It is widely distributed in various bacteria, fungi, plants, and animals and has a major role in the utilization of polysaccharides. α-Amylase is an important industrial enzyme /1/. As well as being used as an additive in detergents, it can be used for such things as the removal of starch sizing from textiles, the liquefaction of starch, and the proper formation of dextrin in baking /2/. This paper has presented the results of investigations on the influence of metal ions and protein denaturants on α-amylase activity.

Bacillus sp. 57_4 producing amylase enzyme was isolated from different samples of soil. A standard inoculum medium was used for the production of amylase by *Bacillus* sp. 57_4 (g/l): soluble starch 10.0, peptone 5.00, yeast extract 5.00, K_2HPO_4 1.00, $MgSO_4 \cdot 7H_2O$ 0.20, pH=7.0. The submerged cultivation was performed with 50 ml of the liquid media in the 250-ml Erlenmeyer flasks on the reciprocal shaker at 200 rpm at 37°C for 96h. α-Amylase activity was assayed by measuring the reducing sugar released during the reaction, using starch as the substrate, according to the modified ferricyanide method /3/. The unit of the amylase activity (U) represents a quantity of enzyme producing the amount of reducing groups equivalent to 1 μmol of glucose per minute at 37°C. The influence of $FeCl_2$, $CuCl_2$, $CaCl_2$, NaCl, EDTA, SDS, urea and guanidine hydrochloride on α-amylase activity were investigated.

The metal ions, except Ca^{2+} and Na^+, inhibited the enzyme activity. The inhibition by Cu^{2+} and Fe^{2+} was prominent - the enzyme activities decreased to about 4% and 20% of the control, respectively. The enzyme was very sensitive to EDTA inhibition, but stimulation of activity by Ca^{2+} was not registrated. Increasing of amylase activity by chloride anion were observed. Protein denaturants, such as SDS and guanidine-HCl, decreased the activity of the enzyme. In contrast, urea had no significant influence on the enzyme activity, even at 6M.

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New Complexes of d and f Metals with Acridine. Synthesis and Biological Activity Studies

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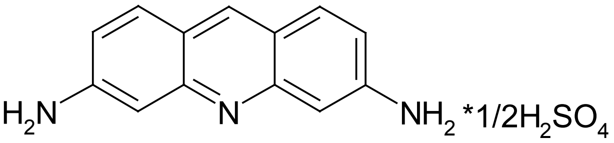
This paper presents the synthesis, the physical, chemical and biological characterization of Cu(II) and Gd(III) with 3,6-diaminoacridine (proflavine) - **1**.



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The new complex compounds resulted where isolated as brown powders and characterized by elemental chemical analysis, molar electric conductivity data, infrared and electronic spectra.

The biological activity was tested in solid medium on different bacterial strains by minimum inhibitory diameter determination of the microbial culture. The results show an increase antibacterial activity of the Gd(III) complex compare to ligand and metalic salt.

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Synthesis and Anti-Aromatase Activity of Some New Steroidal D-Lactones

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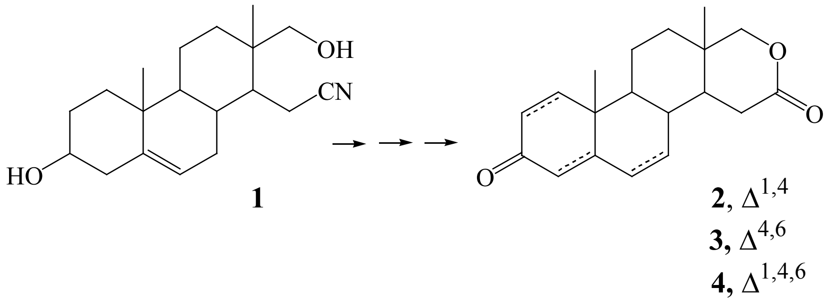
Aromatize is a cytochrome P450 enzyme that catalyzes conversion of androgens into estrogens in the last step of estrogen biosynthesis. Compounds that inhibit aromatize have potential applications in the treatment of advanced estrogen-dependent tumors such as breast cancer, endometrial cancer, prostatic hyperplasia, and prostate cancer.

With the aim of studying anti-aromatize activity of some D-modified steroid compounds we synthesized several new D-homo derivatives of 5-androstene. Starting from 3β,17-dihydroxy-16-cyano-16,17-seco-5-androstene[1] (**1**) and having in mind the fact that extra units of unsaturation in the A and/or B rings of 4-androstendione and its derivatives[2], lead to a change in the anti-aromatize activity, we synthesized D-homo lactones with the 4-ene-3-keto function and its 1,4-diene (**2**), 4,6-diene (**3**) and 1,4,6-triene (**4**) analogs .



Anti-aromatize assay showed that compound **4** possesses a relatively high anti-aromatize activity (IC_{50} 0.277 μM). Inhibition potency was 2 times lower in comparison to the activity of aminoglutethimide (IC_{50} 0.14 μM).

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Protein Adducts and Heavy Metals

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Heavy metals (lead, cadmium, mercury and arsenic) are widely found in our environment. Animals are exposed to these metals from numerous sources, including contaminated air, water, soil and food. Recent studies indicate that transition metals act as catalysts in the oxidative reactions of biological macromolecules therefore the toxicities associated with these metals might be due to oxidative tissue damage. These metals depleted cells' production of reactive oxygen species (ROS). Enhanced generation of ROS can overwhelm cells' intrinsic antioxidant defenses, and result in a condition known as "oxidative stress". Cells under oxidative stress display various dysfunctions due to lesions caused by ROS to lipids, proteins and DNA. Consequently, it is suggested that metal-induced oxidative stress in cells can be partially responsible for the toxic effects of heavy metals.

The aim of this paper of ours has been to show and prove the presence of protein modification of albumin as a consequence of oxidant action of ROS, as well as the existence of a possible hepatocytes impairment. The presence of protein modification of albumine in blood serum has been proven by double immunodiffusion test, and by SDS-PAGE after affinity chromatography. Lipid peroxydation was determined by TBA spectrophotometricaly. These experiments have been done on sheep of “Ile de France” breed (n=20).

The results of the above experiments have indicated to the presence of protein modification of albumin in blood serum. Serum-albumin fragmentation has been proven by presence of proteins of relative molecule mass of 40 000-26 000 Da. In all the samples examined an increased lipid peroxidation ($p<0,001$) compared to the control group values. Based on the above mentioned results a conclusion can be drawn that the ROS bring about hepatocytes' impairment, whereas the presence albumin fragments as well as increased lipid peroxidation may serve as clinical parameters in impairment monitoring heavy metals.

Strategies for Lipase-Catalyzed Synthesis of Lipophilic Derivatives of Natural Antioxidants

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Natural plant antioxidants such as flavonoids and phenolic acids have multiple biological activities including anti-carcinogenic, anti-inflammatory, anti-bacterial and anti-viral activity. These compounds are particularly interesting as natural antioxidants and used as food integrients, in cosmetics and in various other commodities. However, the relative hydrophilic nature of these antioxidants reduces their effectiveness in stabilizing lipophilic systems (oils, fats). Chemical preparation of lipophilic derivatives of such natural antioxidants often will not meet EC food regulations and therefore chemical modification of such compounds is not applicable in the food industry. Thus, enzyme-catalyzed reactions under mild reaction conditions are a good alternative.

In this work we describe four different approaches for the biocatalytic synthesis of lipophilic derivatives of flavonoid glucosides catalyzed by *Candida antarctica* lipase B: a) the direct esterification or transesterification with various acyl donors in non aqueous organic solvents, b) the direct esterification with fatty acids in microheterogeneous ternary water-organic mixtures (surfactant-less microemulsions) c) the acylation in solvent-free systems and d) the acylation of flavonoids after their adsorption onto a solid support of silica gel. The conversion rates as well as the yield of the reaction depend on the system used. In all cases the synthesis of flavonoid esters is regioselective.

Protein and Enzyme Profiles of Certain *Bacillius* Probiotic Strains

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Probiotics are naturally occurring friendly bacteria that are an integral part of the digestive system. They can stimulate the immune system, stave off bacteria and viruses and help with food and nutrient assimilation.

Biochemical characteristic of probiotic strains *Bacillus* G1 (isolated from probiotic preparation), *Bacillus cereus* var. bactisubtyl and *Bacillus subtilis* PY79, was compared.

In accordance with SDS PAGE, protein profiles of *Bacillus* G1 and *Bacillus cereus* var. bactisubtyl are very similar, whereas, the number and ordering of proteins bands of *Bacillus subtilis* PY79 is different.

Our results showed that all investigated strains produce amylase, urease, catalase, superoxide dismutase and peroxidase. *Bacillus subtilis* PY79 has highest catalase and superoxide dismutase activity. *Bacillus cereus* var. bactisubtyl urease activity is lower than for the other two strains. A considerable difference in lecitinase activity was detected between three strains. As opposed to *Bacillus subtilis* PY79, *Bacillus cereus* var. bactisubtyl *and Bacillus* G1 have lecitinase activity.

According to our results, all tested strains have proteolytic activity on gelatin and casein. Zymogram on gelatin, as substrate, indicates that proteolytic enzyme profile is the same for *Bacillus cereus* var. bactisubtyl and *Bacillus* G179. *Bacillus subtilis* PY79 has more bands with proteolytic activity, with wider Mr range.

It can be conclude that *Bacillus* G1 is more resemble to *Bacillus cereus* var. bactisubtyl, than to *Bacillus subtilis* PY79.

Hydrogen Bonding as a Stabilizing Factor of the Dopamine D2 Receptor – Ligand Complex

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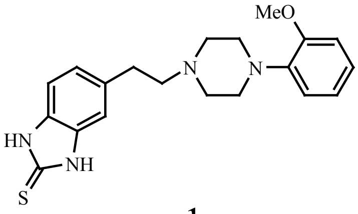
The aim of our investigations is discovery of more selective and more potent dopaminergic ligands[1]. Compound **1** was the starting template for further examination. In order to examine influence of bridge length on binding affinity, ligand with propylene bridge **2** and ligand with oxoetylene bridge **3** between arylpiperazine and benzimidazole-thione part of the molecule were synthesized. Binding assays showed that both of them have increased affinity toward D2 receptors.

Docking analyses, Energy and ESP calculations were performed to gain insight into the differences in the ligand affinity.

We observed possibility of new hydrogen bond formation as a viable explanation of increased affinity of ligands **2** and **3**. Ligand **2** can form additional hydrogen bond with His 189, while in case of ligand **3,** besides the His 189 hydrogen bond, atypical C-H•••O hydrogen bond can be formed between ligand O atom and Phe 185.



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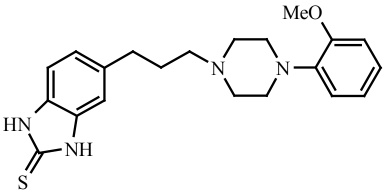

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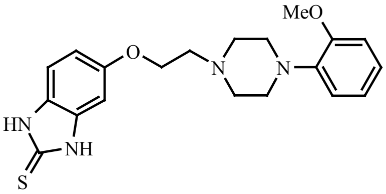

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New Key Intermediates for the Synthesis of Isoprostanes

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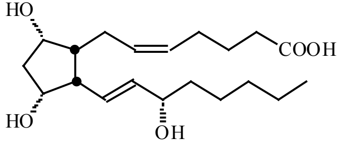
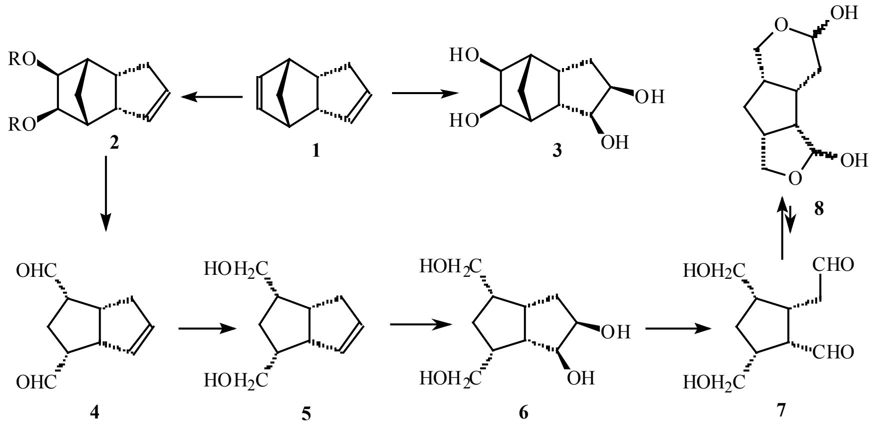
The isoprostanes[1-3] are a new family of compounds[2], similar in structure to prostaglandins, having a *cis*-corelation of the side chains linked to the cyclopentane ring. These are produced in vivo in humans by free radical-mediated oxidation of membrane-bound arachidonic acid, independent of the cyclooxygenase enzymes. Though levels of F_2-isoprostanes in the normal human biological fluids exceed levels of prostaglandins, their role is stil not clear understood. Many total synthesis were realized for obtainig adequate quantities from these isoprostanes for biological studies, but until now no analogue were synthesized.

Starting from *endo*-dicyclopentadiene we realized the synthesis of a new *stable key intermediate* **8** having the functional groups for linking both side chains of the isoprostanes in the requested *cis*-corelation.

Endo-dicyclopentadiene was *cis*-hydroxilated with permanganate to the dihydroxylated compound **2a**, characterized also as the diacylated derivatives **2b** and **2c**, than the diol was oxidatively ($NaIO_4$) transformed in dialdehyde **4**, reduced with $NaBH_4$ to the stable cristalyzed compound **5**. After hydroxylation of the double bond, of the resulting tetrol **6** was transformed to the dialdehyde **7**. The resulting *cis*-aldehyde groups, on the same side of the cyclopentanic ring, with the hydoxymethyl groups on the same side, gave the *stable*, *crystalyzed cyclic dilactol* **8.** This new key intermediate have the reqested aldehydic groups for introducing both side chain through the known regio- and stereoselective Wittig and Horner-Emmons olefinations.



F_2-Isoprostanes



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Tetraoxane Antimalarials Based on a Deoxycholic Acid Carrier

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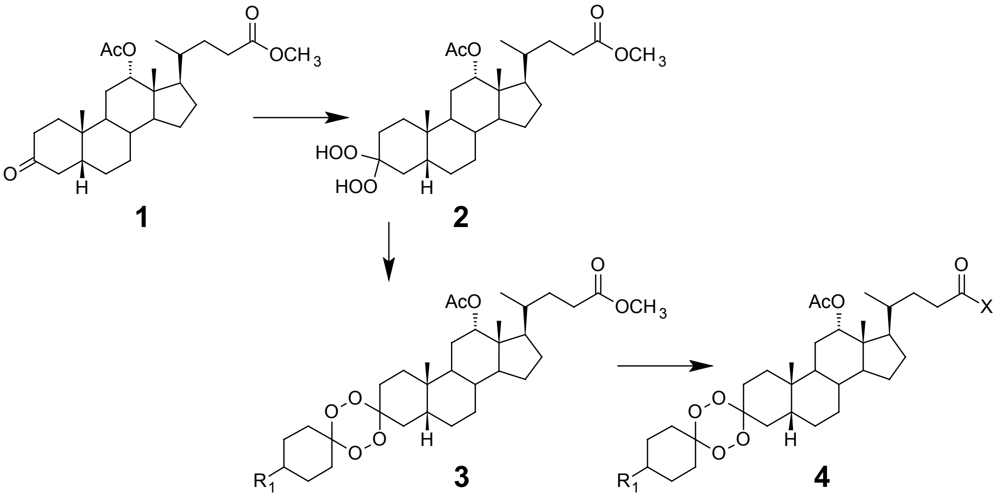
Malaria is a major health problem in many southern countries, and is caused by multiplication of the protozoan parasite *Plasmodium falciparum* in erythrocytes. Present resurgence of malaria, development of resistance to standard antimalarial drug chloroquine (CQ), and lack of proper treatment, affect 300-500 million people annually causing over 1.5 million deaths. In a continuation of our investigation of steroidal tetraoxanes we synthesized new mixed tetraoxanes based on desoxycholic acid derivatives. They were synthesized according to procedure described before[1] (Scheme 1).



Scheme 1

Our compounds have been screened as potential antimalarials, and their promising activity against *P. falciparum* chloroquine-resistant and susceptible strains, as well as against mefloquine-resistant strains, will be discussed. In addition, the pronounced antiproliferative activity of our compounds against a diverse panel of human cancer cell lines will be presented. Finally, we will compare the respective activities to that of cytotoxicity against healthy cells.

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Synthesis and Cytotoxic Activity of Novel a Tiazofurin Analogue with a 2'-Dodecanoylamido Isosteric Function

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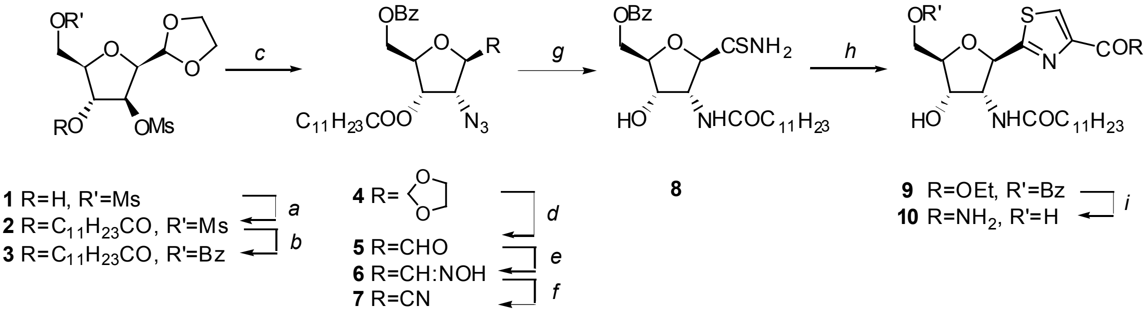
A multistep synthesis of novel tiazofurin analogue **10** has been achieved starting from D-glucose. Reaction of **1**[1] with dodecanoyl chloride in pyridine gave **2**, which was further converted to the nitrile **7** by a multistep sequence outlined in the reaction scheme. Treatment of **7** with hydrogen sulphide in the presence of DMAP resulted in an interesting one-pot transformation. The sequence involved a successive conversion of the nitrile group to the thioamide function, a reduction of the azido group to the corresponding amino function, followed by an intramolecular *O*→*N* acyl transfer to furnish the 3-dodecanoylamido derivative **8**, a key intermediate for the preparation of target **10**. Cycloconden-sation of **8** with ethyl bromopyruvate gave the corresponding thiazole **9**, which was subsequently treated with saturated ammonia in methanol to afford the deprotected *C*-nucleoside **10**. The newly synthesized tiazofurin analogue **10** was preliminary tested for its cytotoxic activity against the K562 and MCF7 malignant cell lines.



(*a*) $C_{11}H_{23}COCl$, Py, +4°C, 22 h; (*b*) KOBz, DMF, 100°C, 8 h; (*c*) NaN_3, DMSO, 110°C, 70 h;
(*d*) TFA-HCl-H_2O, +4°C, 8 days; (*e*) $NH_2OH \times HCl$, AcONa, EtOH, CH_2Cl_2, rt, 4 h;
(*f*) MsCl, Py, −15°C→rt, 2.5 h; (*g*) H_2S, DMAP, EtOH, rt, 8 h;
(*h*) $BrCH_2COCO_2Et$, EtOH, ↑↓, 50 min; (*i*) NH_3, MeOH, rt, 6 days.

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Antiradical Activity of Different *Equisetum arvense* L. Extractors

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Equisetum arvense L. (Horsetail, Shave-grass, Bottle-brush, Paddock-pipes, Dutch Rushes, Pewterwort) is a herb that is used for urinary and prostatic disease, managing enuresis, managing irritable symptoms of the urinary system, repair lung tissue after pulmonary tuberculosis and other disease, metabolic or hormonal oedema, haemorrhage, wounds, rheumatism, chilblains. This herb is a potent heart and nerve sedative and also it has even found its way into folk medicine treatments for cancer.

The horsetail (*Eqiusetum arvense* L.) plant material was successively extracted and the obtained methanol, petroleum ether, chloroform, ethyl acetate, n-butanol and water extracts were assayed for their antioxidant properties. The antiradical efficacies of the extracts were evaluated on their ability to scavenge relatively stable 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals using ESR spetroscopy.

The highest DPPH free radical scavenging activity, SA, (41.14% - 100%) was obtained in the presence of different concentrations (0.070-0.1 mg/ml) of n-butanol extract. The methanol, ethyl acetate and water extracts also showed a significant SA when they were applied in a higher range of concentrations (0.1-0.25mg/ml). But the petroleum ether and chloroform extracts didn't shown any SA.

Also, it was evident that antiradical activity of horsetail extracts correlated with total phenolic content determined using Folin-Ciocalteu reagent. These activity are attributed to their hydrogen donating ability and scavenging effect of active constituents in these investigated extracts.

In conclusion, the results presented here show that *Equisetum arvense* L. could be considered as a natural antioxidant source.

A Newly Synthesized Bis-Azo Dye as a Spectrophotometric Reagent for Trace Determination of Copper in Foodstuffs, Blood Sera and Body Tissues

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A newly synthesized bis-azo dye, 2,6-bis(1-hydroxy-2-naphthylazo)pyridine has been found to be a very sensitive and highly selective reagent for copper. Beer's law is followed upto 1.6 ppm with an optimum concentration range between 0.25 to 1.0 ppm for copper(II) ions. Sandell's sensitivity of the color reaction was calculated to be 0.0012 $\mu g\ cm^{-2}$ with molar absorptivity of $5.2x10^4$ l. mole^{-1} cm^{-1} at 570 nm. Copper levels have been estimated with the reagent in milk, food-grains, tea-leaves, human blood sera and body tissues and were compared with the copper levels found in those samples using AAS.

Copper is an essential trace element that plays a vital role in various enzyme systems, its deficiency not only reduces activity of copper containing enzymes but also some enzymes those do not contain copper[1] and hence its deficiency can be lethal. Copper is pumped into the secretory pathway to tyrosinase, a copper dependent enzyme involved in the formation of the pigment melanin[2]. Its highest concentration is found in brain and liver[3,4]. The infant's body contains about three times the amount of copper to an adult body[3], which means that their metabolic needs are much greater than the adults. Copper deficiency during pregnancy can cause an inherited disorder that leads to low copper concentrations in infant's brain which severely retards neurological development[1]. In human blood, copper bound to serum albumin is considered to be a transport form of copper(II)[4]. In copper deficiency induced anemia in spite of elevated levels of iron in liver, the rate of hemoglobin synthesis is significantly reduced. The deficiency affects the cardiovascular system and causes extensive damage to heart and arteries[5,6].

This element is widely distributed in our food system. Food and Nutrition Board[7] has proposed an allowance of ~2 mg daily for an adult. The maximum tolerable daily intake for copper is 0.5 mg/kg body weight[8]. In case of acute copper deficiency, copper supplemented food may be recommended. While adequate quantities of copper are essential for normal physiological processes, but excess intake poses threat to human health. Therefore this metal requires special attention in the food selection.

We synthesized a new bis-azo dye, 2,6 bis(1-hydroxy-2-naphthylazo)pyridine using the Anderson and Nickless[9,10] method that showed a good sensitivity and high selectivity for copper(II) ions. Keeping in view the biological importance of copper this method was utilized to determine copper levels in some foodstuffs, blood sera and body tissues.

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Spectroscopic and Calorimetric Characterization of Glycine and Alanine Salts of 12-Tungstophosphoric Acid

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Polyoxometalates (POMs) have been in focus of scientists not only as catalysts, superionic proton conductors, analytical and biochemical reagents and nanomaterials, but more and more because of their antineoplastic, antiviral, antitumoral and anticoagulant bioactivity [1].

Recently we have reported anticoagulant effect of 12-tungstophosphoric acid (WPA) [2], observed its anticancer effect [3] and proved its antiviral activity against the plant viruses, *Tobacco mosaic tobacovirus* and *Cucumber mosaic cucumovirus* [4]. The latest activity could specially have the great economic effect.

While it is obvious that the POMs biochemical activity has been well documented, the primary mechanism for that action has remained elusive. One of the possible pathways is POMs interaction with proteins, responsible both for positive bioactivity as well as of possible toxicity. So, in aim to attain better activity and get more information about the nature of WPA binding with proteins, we synthesized compounds of WPA with amino acids glycine (Gly) and alanine (Ala), as representative model proteins. In this contribution we present the results of FTIR, liquid NMR and calorimetric characterization of the obtained compounds.

Comparing the FTIR spectra of new synthesized compounds with the FTIR spectrum of WPA, some changes that could be explained by forming the hydrogen bonds between amino acids and WPA, could be observed. Changes are registered as splitting and red shifting of some bands in region characteristic for host network of Keggin anions, as well as appearing strong hydrogen bond bands in stretching region at about 3200 and bending region at about 1670-1730 cm^{-1}.

In addition, liquid calorimetric measurements of NH_3 adsorption by the investigated compounds were also performed. The obtained results showed that compounds of WPA with Gly and Ala had no acidity. That means that hydrogens from WPA, which have been documented as active acid centers, are blocked in the synthesized compounds by hydrogen bonds.

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Multicomponent Reactions of Siloxycyclopropanes for the Synthesis of Unnatural Amino Acids and Peptides

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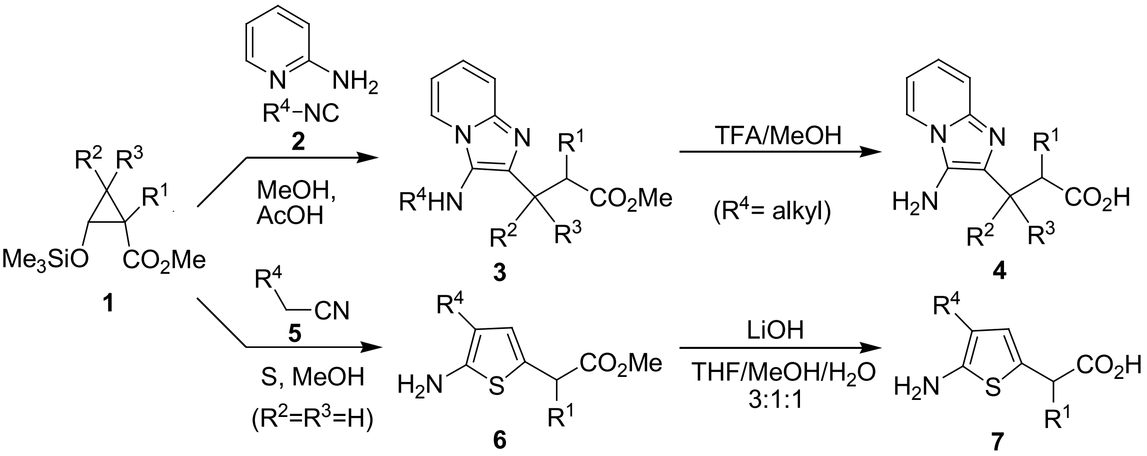
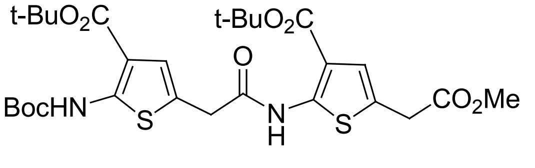
Multicomponent condensations represent a powerful synthetic strategy for rapid and efficient synthesis of small molecules. As a part of our research interest we explore Ugi-type condensations[1] and Gewald reaction[2] as synthetic routes towards unnatural amino acids and compounds with amino acid-like backbone. In all those reactions siloxycyclopropanecarboxylates serve as starting material and as equivalents of carbonyl compounds.

Siloxycyclopropanecarboxylates react with 2-aminopyridine and several isocyanides in a three-component condensation under acidic conditions[3] and yield 3-aminoimidazo[1,2-*a*]pyridines **3** that can be converted into unnatural amino acids **4**.

Gewald reaction includes condensation of masked carbonyl compounds with activated nitriles and sulfur in the presence of amine,[4] yielding substituted thiophenes **6** and consequently unnatural amino acids **7**.



Synthesized unnatural amino acids may serve as building blocks for small peptides such as dipeptides **8** and **9**.



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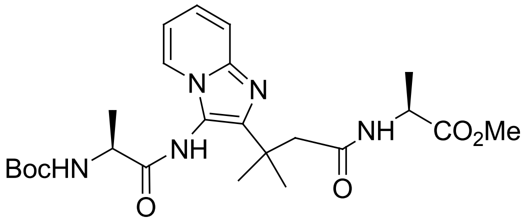

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A QSAR Study of the Acute Toxicity of New, Substituted 2-(1H-Pyrazol-1-yl)- acetanilides with Potential Local Anesthetic and Antiarrhytmic Action

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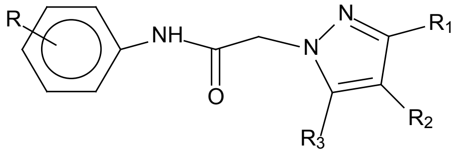
Two group of totally eighteen [I,II] substituted 2-(1H-pyrazol-1-yl)acetanilides (*Chart 1*) were synthesized by N-alkylation of substituted pyazoles with alkyl-substituted 2-iodoacetanilydes. The new compounds have ben carcterized by UV/Vis., ^{1}H NMR, ^{13}C NMR and MS spectra.



Group **1**[I]:
R = 2,6-di-Me-, 2,6-di-Et-; $R_1 = R_3$ = H-, Me-, R_2 = H-, I-, NO_2-

Group **2**[II]:
R = 2-Me-, 3-Me-, 4-Me-; $R_1 = R_3$ = H-, Me-, R_2 = H-, I- NO_2-

Chart 1.

Infiltration and local anesthetic action, antiarrhytmic action and acute toxicity on mice were determinated[1,2]. Lidocaine hydrochloride and quinidine sulfate are used as a control. All tested compounds exert lower toxicity than the controls. Compounds unsubstituted at pyrazolyl ring, from both groups, exert the lowest toxicity. Acute toxicity of each group of compounds was correlated with sum of σ values of substituents at phenyl- and pyrazolyl-rings and calculated ClogP values, by means of multiple regressions analysis. The strong structure-activity relationship of the Hansch type was found. Literature σ-values were used: 1. For phenyl-substituents and R_3-group at pyrazolyl ring, those derived for substituted anilines[3]; 2. For R_1 and R_2 group at pyrazolyl ring, those derived for substituted benzoic acids[4]. Multiple regressions analysis has high correlation coefficients.

Group **1** regression equation:

$$\mathrm{Log}\ (\mathrm{LD}_{50}) = 0.765(\pm 0.122)\ !-1.012(\pm 0.431)\mathrm{x}\ \Sigma_{\mathrm{phenyl}}\,\sigma\ !!-0.012(\pm 0.010)\mathrm{x}\Sigma_{\mathrm{pyrazolyl}}\,\sigma\ !-0.207(\pm 0.041)\mathrm{xClog}P$$

Regression Statistics: $r = 0.938$; $sd = 0.049$; $n = 8$

Group **2** regression equation:

$$\mathrm{Log}\ (\mathrm{LD}_{50}) = 0.661(\pm 0.044)\ !-0.472(\pm 0.123)\mathrm{x}\ _{\mathrm{phenyl}}\,\sigma\ !-\ !0.164\ (\pm 0.056)\mathrm{x}\Sigma_{\mathrm{pyrazolyl}}\,\sigma\ !-\ !0.172(\pm 0.023)\mathrm{xClog}P$$

Regression Statistics: $r = 0.974$; $sd = 0.033$; $n = 10$

Equations described the influence of hydrofobycity of whole molecule, and of electronic effects in phenyl and pyrazolyl rings, on the acute toxicity (LD_{50}) of investigated compounds on the tested animals. Coefficients associated with parameter described the extent of its influence. Extent of the influence of the electronic effects at phenyl-group on the toxicity in first group of compounds versus the second one are unproportionately larger, concerning the number of substituents (two Me- or Et-substituents in group **1**, one Me-substituent in group **2**). Magnitude of electronic effects on the pyrazolyl ring in group **1** vs. group **2** is much smaller. Overall lipofilicity effect on the toxicity in both group of compounds are similar.

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New Substituted 2-(Pyrazol-1-yl)-acetanilides with Potential Analgesic Action

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Introduction

We reported earlier[1,2] the synthesis and characterization of some new substituted 2-(pyrazol-1-yl)-acetanilides that exhibited local anesthetic and anti-arrhythmic activity. The new compounds were synthesized by N-alkyation reaction of pyrazole and of its derivatives with several 2'-iodoacetanilides. They have been spectroscopically characterized and pharmacologically tested.
The aim of the study was to find out whether these new compounds evince analgesic action.

Methods

Pharmacological tests on laboratory mice included those for analgesic activity versus noraminophenazone.

Results

The new compounds exhibited analgesic action

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Characterization of Three Bacillus Probiotic Strains

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Production and application of probiotics plays an important role because of positive effects on human health.

It is known that about 16 bacterial species (*Lactobacillus, Biffidobacterium, Streptococcus and Bacillus* genus) can be used as raw material for probiotic preparations.

Miscellaneous bacterial cultures are usually used, because of their synergistic effect.

The goal of this study is characterization of isolated *Bacillus* G1 strain in comparison with two known probiotic strains *B. subtilis* PY79 and *B. cereus* var. bactisubtyl. The tested strains were revitalised and purified. Morphological, physiological and some of biochemical characteristics, as well as resistance to antibiotics, were examinated.

It can be conclude that *Bacillus* G1 is very simmilar to *B. cereus* var. bactisubtyl according to morphology of vegetative cells and spores, sugar fermentation, phospholypase production and growth with lisosyme. *Bacillus* G1 and *B. subtilis* PY79 can grow at high concentration of sodium chloride, but do not grow in anaerobic condition.

During growth, proliferation and sporulisation of bacteria in the liquid media, growth and sporulation curves of tested strains were monitored.

Our experimental results confirmed that tested strain *Bacillus* G1 has high extracellular protease activity, especially metaloprotease.

Computer Aided Studies of the Binding of Arylpiperazine Ligands with a Potential Binding Site in a Model of the Serotonine $5HT_{1A}$ Receptor

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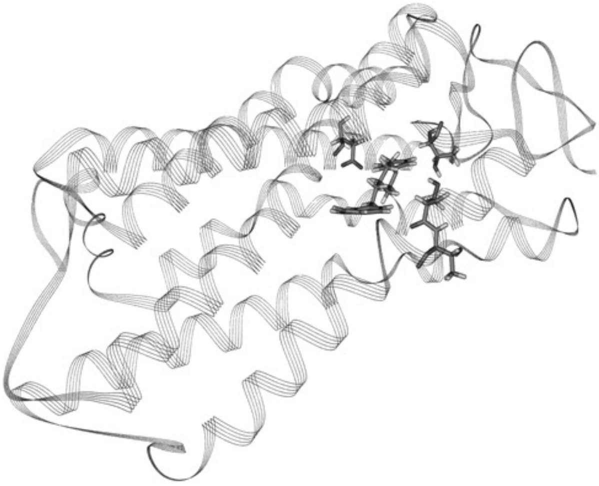
G protein-coupled receptors (GPCRs) form a superfamily of transmembrane proteins with a key role in transduction of signals across the cell membrane. Although they represent a vital information-transfer system in eukaryote biology, their crystal structure has not been determined yet. In order to learn more about mechanism of interactions of GPCRs with ligands we must use computer generated models of GPCR receptor, using crystal structure of bovine rhodopsin as a template.

In this study we investigated the binding properties of serotonine $5HT_{1A}$ receptor and arylpiperazine ligands. Using the data for binding site of $5HT_{1A}$ from previous mutagenesis studies[1] we modified it so that it include all amino acids that could interact with ligand in any way. Unlike previous studies, in this $5HT_{1A}$ receptor model we did not exclude two extracelular loops, because our opinion is that at least one of them could be very significant for positioning the ligand. With this model, using *Docking* module of Insight II[2] program package we simulated the docking of 5-[2-(arylpiperazin-1-yl)ethyl]-1,3-dihydrobenzimidazole-2-thione ligands in this binding site.

Our results confirm that, for ligand to show certain activity in experiment, the formation of the salt bridge between ASP116 and protonated nitrogen in piperazine moiety of the ligand must occur. Further investigation of docked structures showed several more amino acids (for instance SER199 and THR200) in a position that favorizes H-bonding with the dihydrobenzimidazole part of the ligand, which is, besides steric interactions, very significant for the stability of ligand-receptor model and therefore for the increased activity of the ligand.



Structure of complete $5HT_{1A}$ receptor model with docked ligand

References:

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Heat Exchange in a Heat Exchanger Network

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Special attention is paid to energy consumption when designing processes considering its importance in process design. After the synthesis and optimization of a technological scheme of a certain process, it is structurally adjusted to consume a minimal amount of heat. This combinatorial problem is solved by creating a network of heat exchangers.

The regeneration of heat from warm fluids by the addition of cold fluids is the goal of the design of a heat exchanger network and its fitting into a basic process scheme. The optimal combination and distribution of adjoined warm and cold fluids in the process enables the minimal consumption of energetic fluids (water vapour, cooling water, ...) which are a direct cost introduced into the process. The primary references for such investigations are the works of *Linnhoff* [1,2].

As the synthesis and construction of a heat exchanger network, which directly decreases the annual consumption of energetic fluids, represents a difficult optimization problem, two simpler, partial problems were analyzed in this study:

- the minimal consumption of energetic fluids,
- the minimal number of units in the heat exchanger network.

One of these goals may be realized, while both of the goals cannot be achieved simultaneously.

A systematic approach to the synthesis and optimization of a heat exchanger network is described in this study. This approach deals with the optimal combination of warm and cold fluids and the creation of appropriate pairs among them in such a way that the general technological scheme of the process is not modified. This is, therefore, an optimization problem, usually integrated into the problem of optimizing the technological scheme of the process.

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Volumetric Properties of the Binary System Ethanol + Benzene: Experimental Data and Correlation by the Cubic Equation of State

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Densities of the binary system ethanol + benzene and corresponding pure components were measured in temperature range 288.15 – 308.15 K and atmospheric pressure (with an Anton Paar DMA 5000 digital vibrating tube densimeter). From these densities excess molar volumes (V^E) were fitted with the Redlich-Kister equation:

$$V^E = x_i x_j \sum_{p=0}^{k} A_p \left(x_i - x_j\right)^p$$

where the adjustable parameters A_p were obtained by a least-squares method; k is the number of the adjustable parameters determined by means of the F-test.

The V^E data were correlated by the Peng-Robinson-Stryjek-Vera (PRSV) cubic equation of state coupled with the two different types of mixing rule.

Cubic equations of state (CEOS) are frequently used to correlate and predict phase behaviour and thermodynamic properties of a wide variety of binary and multicomponent mixtures in the various process industries. In the past the CEOS approach has been applied successfully to the so called "ideal mixtures" using the van der Waals one fluid (vdW1) mixing rules. To represent complex phase behaviour of highly non-ideal systems containing polar compounds more flexible mixing rules such as the composition dependent and density-dependent were needed.

A new type of mixing rules which combine the free energy models (the excess Gibbs energy G^E or excess free energy A^E) and the CEOS have been successfully applied to very complex systems of diversified nature. In general, there are two approaches for the CEOS/A^E or CEOS/G^E mixing rules. One is based on the infinite-pressure limit, and the other is connected to the zero-pressure limit. Some of these models have been used for correlation and prediction of vapour-liquid (VLE), liquid-liquid (LLE) equilibria and other thermodynamic properties. In this work we used a new class of mixing rules, with van der Waals one-fluid mixing rule and second virial coefficient as constraints, recently developed by Twu and coworkers (TCBT), Fluid Phase Equilibria (158-160 (1999) 271). The TCBT mixing rule has been widely applied for calculation of vapour-liquid equilibria. This approach, based on the PRSV CEOS incorporating the NRTL as G^E equation (CEOS/G^E models), was used here, for fitting of V^E data.

The V^E data of the system ethanol + benzene were correlated in temperature range of 288.15 K to 308.15 K using the vdW1 and TCBT mixing rules. We have tested the ability of these mixing rules to correlate of V^E with a single set of adjusted parameters in temperature range 288.15–308.15 K and correlation of V^E data for each temperature (288.15 K, 298.15 K and 308.15 K), separately.

Zdanovskii Rule Applied for Prediction of the Osmotic Coefficient in Superstaturated Solutions

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Thermodynamic properties of mixed aqueous electrolyte solutions depend on properties of pure electrolyte solutions as components of the mixture. Very often, the ionic strength of the mixed aqueous solution exceeds the ionic strength of the pure electrolyte solution as mixture component. Therefore, it is of crucial importance to predict the thermodynamic properties of the pure electrolyte solutions, as mixture component, at concentrations above their solubility limits.

Zdanovskii empirical rule(1) applied to aqueous threecomponent electrolyte solutions, under isopiestic equilibrium, is based on the experimental fact that linear or approximatelly linear relations exist between the molalities of isopiestic solutions. This rule enables the activity coefficient of a mixture to be estimated, for a specified solvent activity, from data of the pure solutions of each of the individual solutes and vice versa as in case of prediction of properties for supersaturated solutions. For this prediction it is favorable to know more of the isopiestic molalities of the solutions that are diluted with electrolyte for which the prediction is performed in order to obtain better precision by linear extrapolation of isopiestic data.

Zdanovskii rule was, for the first time, applied for the prediction of the osmotic coefficient of supersaturated K_2SO_4(aq) at $T = 298{,}15$ K, by treatment of the isopiestic results of three-component aqueous solutions in which one of the component was K_2SO_4. The results of prediction of the osmotic coefficient of K_2SO_4(aq) was compared to the results of prediction by the Åkerlöf – Thomas(2) rule and by weighted averages proposed by Robinson-Platford Childs(3).

The treatment of large number of isopiestic results for aqueous mixtures of K_2SO_4 with electrolytes of the type 1:2, by Zdanovskii rule, are showing that in supersaturated region, above molality of 0,7 $\mathrm{mol\ kg^{-1}}$, values for the osmotic coefficient are increasing with molality of supersaturated K_2SO_4(aq) while the obtained results of prediction for the systems: H_2O-K_2SO_4-Li_2SO_4 are showing decreasing values of the osmotic coefficient in this concentration region. This results are in accordance with the prediction od osmotic coefficient values of K_2SO_4(aq) by the Åkerlöf – Thomas(2) rule and by weighted averages.

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Mitigation of Flame Initiation and Propagation in Gaseous Fuel-Air Mixtures

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Flammable fuel-air gaseous mixtures have hazardous properties, easily supporting explosions. The consequences of such events can be diminished or even suppressed by means of appropriate additives, able to lower the amount of liberated heat, to decrease the rate of heat release or even to change the reaction mechanism. Widely used additives are inert gases such as nitrogen or argon; diluents such as carbon dioxide or water (vapor) or inhibitors, as halogenated hydrocarbons or metallic carbonyls. The diluents are efficient in quite large amounts (equal to or larger than the oxidant amount) whereas the inhibitors are efficient in low concentrations, barely a few percents. The use of halogen derivatives (halons) as flame retardants or suppressants is, however, strongly limited by their ability to destroy the stratospheric ozone.

In the present paper, the effect of several additives (N_2, Ar, CO_2) on the initiation, quenching and propagation of fuel-air gaseous mixtures was analyzed using measured and calculated data for ethylene- and propylene-air mixtures, over a wide composition range at initial pressures between 20 and 110 kPa. The sought parameters were the quenching distances between flanged electrodes, the minimum ignition energies, the induction periods of ignition (initiation by inductive-capacitive sparks), the peak pressures, the times necessary to reach the peak pressures and the maximum rates of pressure rise (deflagration propagation in closed vessels). These results were completed by values of the expansion coefficients, adiabatic flame temperatures in isobaric and in isochoric combustion, adiabatic explosion pressures calculated according to the assumption that chemical equilibrium is reached in the flame front. Burning velocities were also determined, for the initial stage of explosion propagation in a closed vessel.

The obtained data emphasize important variations of characteristic parameters of flame initiation and propagation, when increasing amounts of diluent (N_2; Ar; CO_2) are added. The dilution effect can be essentially accounted for by heat capacity and thermal conductivity variations, whereas the influence of the halogenated compound (CH_2BrCl) arises from its direct participation to rate-determining process of the initiation or propagation stages.

While fundamental studies concerning the mechanism of flame initiation and propagation offer the possibility to model the complex combustion phenomena, the present data are important for straightforward assessment of the inertization ability of various additives towards gaseous explosions, leading to appropriate safety recommendations.

Three Phase Reciprocating Plate Column Hydrodynamics and Chemical Reaction

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The reciprocating plate column (RPC) has been used as a bioreactor only during the last twenty years. Its basic advantage over a bubble tray column is a greater gas hold-up in the gas-liquid dispersion, greater inter-phase surface and better phases contact, which enables faster mass transfer between the phases. The radial composition uniformity is also very marked in RPC, without bottleneck zones, and without channeled or recycling flow. Good mixing and dispersion of non-miscible phases is achieved with rather little external energy provided by a vibration set. Efficient mixing is achieved thanks to the construction of the mixer, which consists of perforated plates placed at equal distances along the mixer shaft, and their intermittent reverse axial movement in the column.

In the work, a RPC was used with the following characteristics: column internal diameter 2.54 cm, operational height 173 cm, number of plates 65, free plate surface share 51%. Tap water was used as the liquid phase, flowing down (superficial velocity up to 0.9 cm/s), air was used as the gas phase (superficial velocity up to 1.5 cm/s), and polypropylene balls (8.3 mm dia, density 890 kg/m^3, share up to 8.43%) were used as the solid phase.

To determine the axial dispersion in RPC the retention time distribution function was used, determined by excitation (sorbic acid impulse tracer input into the liquid phase), and reaction method (control of the tracer concentration at column output). For single phase (liquid), two-phase (gas-liquid and liquid-solid) and three phase (gas-liquid-solid) systems the correlation equations were used to calculate the axial dispersion coefficients in the column.

The axial dispersion coefficient was used for mathematical modeling of ethanol fermentation in a RPC bioreactor. This bioprocess was carried out using yeast cells *Saccharomyces cereviseae* immobilized in a disk shaped macroporous polymer carrier, 12.7 mm dia and 1.5 mm thick, with 81% porosity. The carrier was synthesized from acrylamide and methyl methacrylate cross-linked with tetramethylol glycoluril. Glucose was used as the substrate.

The ethanol fermentation reaction kinetics analysis in RPC was carried out by mathematical model calculated by computer numeric method. In case the ethanol fermentation was defined by Monod's model, it was proven that the axial dispersion effect had a positive influence on the substrate conversion degree and product yield.

This work was executed within the project "*Green chemistry – base for new materials development, synthesis and engineering processes",* Ev. No. 1456, *financed by the Ministry for Science, Technology and Development of the Republic of Serbia*.

High-Purity Fractional Distillation of Acetone for Use in Microelectronics

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The development of the appropriate conditions and technological scheme for the production of high-purity acetone from a technical grade row material is presented. The thermodynamic aspects of the system acetone-methanol-ethanol-water are discussed, and an adequate method for vapour-liquid equilibria calculations is chosen. The correlative models of WILSON, UNIQUAC and NRTL describe adequately the behavior of the system, while UNIFAC predicts a non-existing azeotrope for the binary acetone-water system and, therefore, it is not an alternative.

The main separation step in the technological scheme proposed, is the purification from volatile components on a teflon distillation column with 32 bubble cap trays and inner diameter of 80 mm. With regard to the restrictions due to the equipment, simulation is used to determine the influence of the important design factors, such as feed and side stream locations, reflux ratio, vapour and liquid flowrates, resulting in an optimized process. The experimental results at this step are presented in comparison with simulation results in order to prove the model adequacy.

Because of the streams configuration, the acetone free of volatile components is distilled further to remove non-volatile soluble impurities. In the final step, submicron particles are removed via microfiltration.

Influence of the Driving Force and the Thermal Effects on the Mass Transfer Efficiency of Packed Distillation Columns

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Experiments are carried out with two packed distillation columns enabling the determination of the mass transfer efficiency expressed as the height of the transfer unit as a function of the composition of appropriately chosen binary systems. Positive, negative, zeotrope, and azeotrope mixtures are tested in the entire composition range.

An extremum-containing dependence of the height of the transfer unit on the composition of the system is observed with all systems studied. The extremum could be regarded as a result of the overall unidirectional (in the case of positive systems) or opposite effect (in the case of negative systems) of the driving force, i.e., the respective gradients of the surface tension, and the thermal effects on the phase boundary.

The results obtained confirm the hypothesis of the simultaneous influence of the gradients of the surface tension and of the thermal effects on the mass transfer coefficients upon distillation in packed columns.

Hydrodynamics of an External-Loop Three-Phase Air-Lift Apparatus

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The paper presents the experimental study regarding the hydrodynamics of an three-phase external-loop air-lift apparatus, for its use in wastewater chemical, physical or biochemical treatment.

It was conceived and realized an experimental installation at laboratory pilot scale up; the main equipment consists of two vertical columns (a riser and a downcomer) connected at the top and the bottom.

Circulation of fluid is induced by the density difference between the riser and downcomer resulting from injecting air in the riser. The gas-liquid-solid system used was air-water-ion exchange resin.

The influence of the following operation parameters was investigated:

- gas flow rate, G_V, [l/h] (gas superficial velocity, w_G, m/s) and mass of wet solid, m_S, [kg] (solid loading, q_S, %), determined by the initial height bed, H_0, [m].

The processing of experimental data has permitted the obtaining of the following relationships (in SI) for:

- the minimum fluidization velocity, $w_{G,mf}$

$$w_{G,mf} = 27.29 \cdot 10^{-5} \left(\frac{8.14 q_S}{72 + 5.29 q_S} \right)^{\frac{1}{0.47 - 0.00814 q_S}} ;$$

- gas holdup in the three-phase fluidized bed, ε_G

$$\varepsilon_G = 1.32 w_G^{0.71} + \frac{0.6}{(19.38 q_S + 263.83) w_G^{0.47 - 0.00814 q_S}} \left(\frac{4.27 q_S^2 + 690 q_S}{10^5 - 650 q_S} - 1.32 w_G^{0.71} \right);$$

- solid holdup in the three-phase fluidized bed, ε_S

$$\varepsilon_S = 0.00392 \frac{q_S}{(19.38 q_S + 263.83) w_G^{0.47 - 0.00814 q_S}}$$

- liquid recirculation velocity in the downcomer, $w_{L,r}$:

$$w_{L,r} = \frac{-7.222 + \sqrt{52.157 + \left(272.244\, w_G^{0.71} - 0.718\, q_S\right)\left[\frac{0.272}{(1 - 1.32\, w_G^{0.71})^2} + 1\right]}}{8.76\left[\frac{0.272}{(1 - 1.32\, w_G^{0.71})^2} + 1\right]}$$

Estimation of the Limiting Oxygen Concentration of Fuel/Air/Inert Mixtures at Elevated Temperatures by Means of Adiabatic Flame Temperatures

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The addition of an inert component to a fuel/air mixture determines the increase of LEL (Lower Explosion Limit) and decrease of UEL (Upper Explosion Limit), until these values finally merge. In the vicinity of this point (the apex of the flammability region), on the upper explosion limit curve, the maximum air concentration is found (the highest air content in the ternary mixture, at which by arbitrary addition of flammable gas an explosion no longer occurs). The corresponding oxygen concentration of the mixture is called the Limiting Oxygen Concentration (LOC). As LEL and UEL, LOC is an important parameter for safety measures against explosions. LOC is usually measured by the same standard methods as LEL and UEL, at progressive dilution of fuel/air mixtures with an inert gas. An alternative method meant to avoid this time- and material-consuming procedure would be of great interest, especially for fuel/air/inert mixtures at elevated initial temperatures, where scarce data are available.

An earlier investigation of a comprehensive set of flammability data at ambient temperature and pressure taken from literature sources [1,2] was made for systems containing nitrogen and carbon dioxide as inert components and their adiabatic flame temperatures were calculated by taking into account the dissociation of gases within the flame. A linear correlation with the form:

$$CAFT^{LOC} = a + b*CAFT^{LEL}$$

was empirically derived for $CAFT^{LEL}$ (Calculated Adiabatic Flame Temperatures of limit fuel/air mixtures at LEL (lower explosion limit)) and $CAFT^{LOC}$ (Calculated Adiabatic Flame Temperatures of limit fuel/air/inert mixtures at the extreme flammability point) [3,4]. The slope and intercept of the correlation depend on the nature of inert gas. The correlation allowed the development of a simple procedure for estimating LOC, when the LEL of fuel/air and the equivalence ratio of the fuel/air/inert mixture at LOC are known.

Similar correlations were found for fuel/air and fuel/air/inert mixtures at temperatures higher than ambient, examining data from recent measurements, reported in [5]. The data refer to mixtures containing nitrogen, carbon dioxide or water (vapour) at 100, 200 and 250˚C. The proposed procedure brings about a useful approach for estimation of LOC, suitable for fuels which are not able to decompose in the absence of an oxidant. The procedure can be used as a preliminary screening method, followed by experimental measurement of LOC.

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Membrane System Used to Separate Citric Acid

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The separations through membrane transport have taken a large applicability lately both in Analytical Chemistry area and also in that of Technological Chemistry.

In this paper there are presented the results obtained for the separation of the citric acid under the action of a potential gradient.

The process was used for the separation of the citric acid from the orange juice in order to establish the operation parameters for an electrodialysis cell. The membrane systems used relied on polyimides varieties.

Taking into consideration the studied process' economic efficiency, expressed in over 40% performance of the citric acid receiving, and the energetic consuming in KW/h, there were obtained the following operation parameters:

1. 1.5 A Intensity,
2. 1.38 A dm^{-2} current density,
3. 4.12 dm^2 specific surface of the membrane,
4. 35 hours electrolysis time,
5. 25 V working voltage,
6. orange juice concentration expressed through the volumetric rate orange / water = 1:1.

Influence of the Backmixing Extent on the Effectiveness of the Extraction Operation

Part One: Extraction of Uranyl Nitrate with Tri-n-Butyl Phosphate

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In this work have been investigated influence of the backmixing extent and concentration of tri-n-butyl phosphate for selected extraction schemes in the next system: water - uranyl nitrate - tri-n-butyl phosphate – diluent (Amsco) on the following values: number of equilibrium stages N_D, theoretical stages N_T and stages number $(N_D - N_T)$ which are the results of the backmixig process in extractors supposing that the concentration of nitric acid is a constant value during extraction. Calculated stages number $(N_D - N_T)$ were used as the measure of influence of backmixing process magnitude and solvent concentration on effectiveness of investigated extraction operation.

Calculation of equilibrium data and construction of equilibrium curves for cited system have been done for wide concentration interval of uranyl nitrate and tri-n-butyl phosphate using mathematics model M.Kopečni – Đ.Petković which is based on expression for equilibrium constant of chemical reactions which have been done during extraction.

For determining of equilibrium stages number – N_D, as theoretical stages number – N_T, procedure of A.Tolić – T.Miyauchi has been used on which program for computer has been made. Computation has been done for selected combinations of proportion of phase flow, inlet and outlet concentrations of uranyl nitrate in water phase and solvent concentration – $c(TBP)$ for various value of backmixing coefficient in water (f) and organic (s) phase.

The obtained results are shown that the stages number $(N_D - N_T)$ considerable increase with growing of the backmixing coefficinet and it is linear relation, so that in general case is valid:

$$(N_D - N_T) = k_{UN} \cdot f$$

where is k_{UN} – linear relation coefficient.

It has been established that increase of tri-n-butyl phosphate concentration brings to exponential decrease of stages number in extractors with that has been done analitical expression of relationship:

$$(N_D - N_T) = f \cdot 31{,}062\, e^{-2.1951 \cdot c(TBP)} \qquad \text{(correlation coefficient: } R = 0{,}997)$$

The obtained correlations give special contribution to quantifycation of backmixing influence in relation of extraction parameters for studied system. Cited assertion are considerable in practice for the choice of extractors or solvent concentrations for the particular extraction operation.

Influence of the Backmixing Extent on the Effectiveness of the Extraction Operation
Part Two: Extraction of Nitric Acid with Tri-n-Butyl Phosphate

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In this work have been investigated the extraction of nitric acid in the system: water - nitric acid - tri-n-butyl phosphate in diluent (Amsco) from the standpoint of the influences of the backmixing extent and concentration of tri-n-butyl phosphate on the following values: number of equilibrium stages N_D, theoretical stages N_T and stages number (N_D -N_T) which are result of backmixig process in extractors for selected extraction schemes. Investigation of these relations enables quantifycation of the system by establishing appropriate correlation relationships which describe the investigated system.

Realization of this work demanded above all, to define equilibrium relationship for nitric acid of the system and reaction mechanism, as like as selection of chemical – technological operation schemes of extraction and backmixing parameters. Calculation of equilibrium data has been done according to mathematics model of J.Čomor – M.Kopečni – Đ.Petković, till N_D, N_T and (N_D - N_T) have been calculated according to procedure of A.Tolić – T.Miyauchi.

Starting from obtained values of stages number (N_D - N_T), as messure influence of backmixing effect, it has been shown, that with increase backmixing effect considerably increase value (N_D - N_T) and it is linear relation. Also, it may be consider that analogous relationship trend has been found at extraction uranyl nitrate by tri-n-butyl phosphate. This increase evident shows to exceptionally backmixing effect.

In expression for calculation of stages number (N_D - N_T) has been included influence of tri-n-butyl phosphate concentration – *c(TBP)* for that follow relationship has been obtained:

$$(N_D - N_T) = f \cdot 18{,}314\, e^{-0{,}7606 \cdot c(TBP)} \qquad \text{(correlation coefficient: } R = 0{,}991\text{)}$$

On the basis of obtained result it may be consider that stages number (N_D - N_T) exponencially decrease by increase of tri-n-butyl phosphate concentration and conversely.

Considerable backmixing influence on requisite stages number of extractor for accomplishing the extraction operation, direct attention to special attention that must give to the choice extractors at which is this undesirable, but inevitable effect is minimale.

Gas-Liquid Mass Transfer in an Air-Lift Apparatus with External Recirculation

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The unit operations and processes intensification has developed various modalities of phase contact and different types of apparatus.

The external loop air-lift aparata represent such an example, can be used in environment protection engineering also in physical, chemical or/and biological treatment processes.

The gaseous phase, air or other gas, can be inert, having the role of liquid phase recirculation in apparatus, or active, reactant (oxidation reactions) or oxygen sources for aerobical biochemical/biological process.

The present paper has like aims the experimental study regarding the gas-liquid mass transfer, the oxygen absorption from gaseous phase (air) in liquid phase (water) in external loop recirculation air-lift apparatus, with their utilization at wastewater treatment.

In this purpose it was conceived and realized an experimental installation at laboratory pilot scale, operated with distilled water-air system and industrial water-air system, following the absorbed oxygen quantity determination and the volumetric mass transfer coefficient function of gaseous phase velocity.

The experiments were realized for an operating time of 120 sec.

Indifferent of utilized systems it is establish that the oxygen saturation concentration it is reached at air velocity of 0.1 m/s.

The gas-liquid volumetric mass transfer coefficient, $k_L\, a\ [s^{-1}]$, has a nonlinear variation increasing with air velocity increasing.

From processing experimental data it was obtained for the calculus of gas-liquid volumetric mass transfer coefficient the following dimensional relation (SI):

$$k_L\, a = 0.18\, w_G^{0.8}$$

The experimental study confirm the possibility of air –lift apparatus utilization like aerobic bioreactor, because the gas-liquid (O_2-H_2O) mass transfer velocity it was be always higher than bio-reaction velocity .

Mathematical Modelling of Supercritical Carbon Dioxide Extraction from Basil Leaves

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New mathematical model developed in order to simulate extraction of the essential oil from basil, member of Lamiaceae family, is presented in this paper. Recent research focused on Lamiaceae family showed that most, if not all, of the essential oil is found on the surface of the leaf in peltate glandular trichomes. Based on these results, a new model was derived in order to simulate the extraction with supercritical carbon dioxide more accurately.

Certain fraction of peltate glands is disrupted during the pre-treatment process and the oil of this fraction is immediately accessible to the supercritical carbon dioxide. Since peltate glands membrane is permeabile for carbon dioxide, the solvent is dissolving in the essential oil inside remaning nondisrupted glands, thereby increasing overall peltate glands volume. Basic hypothesis of the model is that this volume increase leads to membrane disruption for another fraction of peltate glands. This assumption was experimentaly confirmed. Whole leaves of basil, without pre-treatment, were exposed to supercritical carbon dioxide for three hours. After this period pressure was slowely decreased to atmospheric value to avoid quick decompression. SEM of a dozen of basil leaf samples before and after exposure to supercritical carbon dioxide, showed that disruption of peltate gland membranes occurred.

Mathematical model was applied to simulate extraction data from the literature. Obtained results showed better agreement with eperimental results than models present in literature.

In Situ Electrical Conductivity Investigation of Support-Active Phase Cooperation in Oxide Catalysts Used for Hydrocarbon Oxidation/Combustion

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Supported oxides are widely used in catalysis; the high surface area support allows the dispersion of the active phase (at nano-scale level), increasing markedly the extent of interaction with gaseous reactants and also improves its stability in reaction conditions. It was shown that in many cases the oxide support is also an active participant in catalysis, as it might control the properties of the supported phase, by charge transfer effects. The transferred carriers (from/to the support) are electronic (electrons, holes), ionic (protons, or oxygen ions/vacancies) or of both types . Depending on the extent of these effects, the cooperation between the active phase and the support results in changes of the surface properties of the former, and thus in changes of its adsorption/catalytic behavior. This is particularly important in oxidation, oxidative dehydrogenation and combustion reactions, occurring by Mars-van Krevelen (redox-type) mechanism (involving lattice oxygen of the catalyst as the reactive species), as in this case the electrical properties of the surface dictate oxygen adsorption ability and thus the efficiency of the lattice re-oxidation step.
The paper investigates by ac *in situ* electrical conductivity measurements at 1592 Hz the reciprocal influence between the titania support and some active oxide phases (as vanadia or tin oxide) deposited on it; the dynamics of the catalysts surface in various atmospheres (dry inert or oxygen and in presence of humidity) in conditions which mimic the catalytic process (thus in gas flow, on thermally cycling between 20-400°C) is also studied, pointing to the effects of moisture on oxygen adsorption The possibility to control oxygen adsorption on the deposited oxide by appropriate doping of the support is also discussed.

Simple Kinetic Tests of Complex Catalytic Reactions

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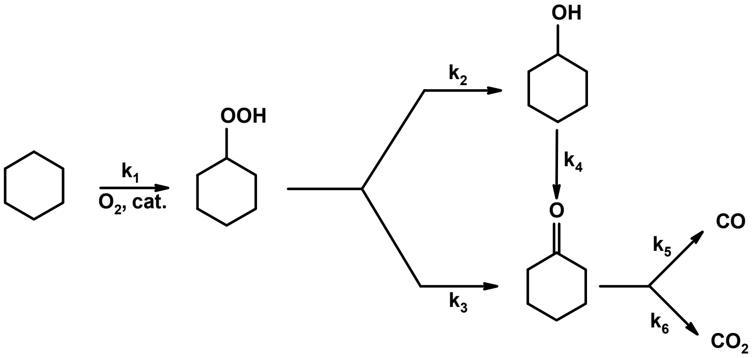
Catalytic reactions usually occur over multiple steps whose kinetics determines the rate of the overall process. An excellent example is air oxidation of cyclohexane (CH) to the mixture of cyclohexanol (CHL) and cyclohexanone (CHN) [1]. The model of the reaction mechanism was proposed [2] with 19 reaction steps, only for the early phase of the reaction (at low conversion levels). For the practical interpretation of the reaction kinetics, a researcher needs the simplified model, containing just enough elements to describe the experimental results. Moreover, the set of the rate constants has to be determined for the particular catalytic system. For the modeling of the reaction kinetics the simplified model (see Fig.) was chosen, because it includes most important system components and has a potential for the proper description of the reaction kinetics [3].

Present study describes procedure applied for the reaction kinetics characterization of the cyclohexane partial oxidation by air, with a poly-4-vinylpyridine resin supported cobalt catalyst. Activity tests were performed in stainless steel, laboratory scale (0.1 dm3), stirred autoclave produced by Autoclave Engineers (170 °C, 2.8 MPa). The concentration changes of the most important products (CH, CHL, CHN, CO, CO_2) where measured by gas chromatography.



A non-linear, least-squares analysis with the simplex optimization method [4] was used to evaluate the optimal values of the rate constants for each kinetic test. In every step of the optimization procedure, the numerical simulation was performed with the Gear algorithm [5] and the simulated concentrations were compared with the experimental ones in both liquid and gas phase. Furthermore, significant computation saving was achieved through decoupling of the kinetic parameters in the dimensionless form of the differential equations. The groups of the rate constants are completely decoupled in this system. Therefore, the dimensionless differential equations where used for the simulation. In the subsequent step, the rate constants where evaluated from the algebraic relations defining the dimensionless parameters. All six apparent rate constants of the working model where determined for the several tested catalysts.

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The Overall Activation Energy of Thermokinetic Oscillations

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Thermokinetic oscillations obtained during the heterogeneous catalytic oxidation of methanol on a Pd-supported catalyst in a dynamic calorimeter were characterized by the overall activation energy. This parameter was determined by using a non-isothermal kinetic model based on the minimum and maximum values of the temperature oscillations.

This method was applied either using bifurcation diagrams with oxygen or methanol as bifurcation parameters or using the dependency of the single oscillations on the concentrations of the reactants. The determined energy activation energy values of the thermokinetic oscillations are within the range for heterogeneous catalytic reactions. These results could be explained by a non-isothermal surface blocking/reactivating scheme based on a Langmuir-Hinshelwood mechanism for the reaction kinetics.

Oxidative Dehydrogenation of Isobutane over a Titanium Pyrophosphate Catalyst

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Recently, the oxidative dehydrogenation of isobutane to isobutene has received considerable attention because of the increasing demand for methyl-tert-butylether. Up to now, several pyrophosphate based catalysts have been claimed to be active and selective for the oxidative dehydrogenation of isobutane [1, 2]. To our knowledge, none of the catalytic properties of titanium pyrophosphate in the oxidative dehydrogenation of isobutane have been yet reported.

The catalytic properties of a crystallized TiP_2O_7 in the oxidative dehydrogenation of isobutane are shown in Table 1. We observe that as the reaction temperature is increased, the isobutane conversion increased. The selectivity for isobutene drops rapidly (from 52.5 to 23.1%) when the reaction temperature is increased from 410 to 490°C, and decreases very slowly between 490 and 550°C (from 23.1 to 21.9%). The selectivity for CO passes through a maximum around 450°C and reach a plateau for reaction temperatures higher than 490°C. It is interesting to note that CO_2 appears in the reaction products at 490°C, and decrease with increasing temperature to the benefit of cracking products formation.

Table 1. Catalytic properties of TiP_2O_7 in the oxidative dehydrogenation of isobutane. Reaction conditions: isobutane/oxygen ratio = 2, W/F = 0.8 .10^{-2} g.min.cm^{-3}.

Temperature (°C)	Conversion (%)	Product selectivity (%)					Rate of isobutane transformation (10^5 mol s^{-1} m^{-2})
		$i\text{-}C_4H_8$	C_3H_6	CH_4	CO_2	CO	
410	3.1	52.5	-	-	-	47.4	0.73
450	6.0	47.6	-	-	-	52.3	1.42
490	13.2	23.1	11.2	-	37.2	28.4	3.12
530	18.1	22.8	13.8	-	34.4	28.9	4.28
550	21.0	21.9	15.4	1.7	31.3	29.6	4.97

From the Arrhenius plot, two temperature ranges can be considered, with obviously a change of activation energy from 80 kJ/mol below 490°C, to 38 kJ/mol above 490°C. This change may be associated with the changes observed in the product distribution above 490°C. We note that a similar change of apparent activation energy, was observed during oxidative dehydrogenation of *n*-butane, on the same catalyst, but at 450°C [3]. In this case, the activation energies were 129 kJ/mol and 38 kJ/mol at low and high temperature, respectively. It is also interesting to note that the values of apparent activation energies at high temperatures are identical for two reactions. On the basis of these results and by analogy with the mechanism proposed for the reaction of n-butane on the same catalyst [4], a mechanism for the oxidative dehydrogenation of isobutane was proposed.

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Process Improvement by a Three-Phase Catalysis Reaction in Active Pharmaceutical Ingredient (API) Production

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The chemical process for propranolol hydrochloride production,an active pharmaceutical ingredient (API), consists of synthesis of two intermediates and the main product. The synthesis of the first intermediate, *1-(1-naphthoxy)-2,3-epoxypropane*, is a process of selective alkylation of α-naphthol with epichlorohydrin using quaternary ammonium salt as phase-transfer catalyst / 1 /.

The paper presents the effect of applying three-phase catalysis reaction to improve the process of API synthesis by increasing the purity of the first intermediate under conditions of synthesis of lower concentration by- products resulting from the parallel and from successive reactions .

Mass transfer phenomena and chemical kinetics were investigated, and the extraction mechanism of Phase-Transfer Catalysis (PTC) confirmed / 2 /.

The paper contains the kinetics of synthesis of the main product and of by - products as a function of concentration and size of particles of phase-transfer catalyst within the range of reaction temepratures and stirring intensity.

Investigation results show the level of significance of the concentration and particle size of phase-transfer catalyst on increasing the regioselectivity for the first intermediate and on improving the process performance using PTC for API production.

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Overall Kinetics of the Isothermal Catalytic Ignition of Fuel-Air Mixtures

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The catalytic ignition of gaseous fuel-air mixtures, having many applications and implications in a variety of combustion problems, as well as in risk assessment and safety promotion in flammable environments, is a complex process arising from several coupled components. The most important are: the chemical reactions on the catalyst surface, the mass and heat transfer between gas and solid surface and the early stages of the gas phase reactions. In spite of the increasing interest on this subject, induced by the new contemporary safety requirements, the catalytic ignition is still an incompletely understood critical phenomenon. When an isothermally heated platinum wire or filament is used as ignition source, the overall kinetics can be conveniently analyzed by means of several measurable ignition properties. Usually these are: the critical ignition temperature at different initial pressures and compositions, the surface and gas phase ignition delays and the critical heat flux necessary to ensure the gas phase ignition, dependent on temperature, initial pressure and composition. The use of a fine wire with small heat capacity and large temperature sensitivity of electrical resistivity allows a fast heating and accurate temperature regulation. A specially designed electrical circuit used to produce a quasi-rectangular jump of the ignition source temperature and to maintain it constant, irrespective of the heat losses and heat generated by the chemical reaction, is presented and its performances are discussed. A dc power supply provides the isothermal heating of the wire connected in series with a standard resistor and used as an arm of a Wheatstone bridge. The bridge unbalance represents the feedback signal used to adjust the applied voltage necessary to ensure an isothermal heating. To minimize the transient period between the initial and working temperature, a supplementary energy is also provided, by discharging across the wire a condenser, previously charged at a suitable voltage. The stationary and transient voltages measured across the standard resistor used in connection with a resistance-temperature calibration curve allow the analysis of the overall ignition process. The obtained thermograms, recorded for air and for fuel-air mixture at the same pressure and temperature, provide the required ignition parameters[1]. Although the detailed kinetics is now available for the catalytic ignition of some simple fuel-air mixtures, the overall kinetics in the steady state still remains a valuable instrument for the analysis of less known or more complex systems. The overall kinetic parameters (reaction order and activation energy) for different fuel-air mixtures, as well as their trend for the ignition, result either from a power rate law or from a Langmuir-Hinshellwood model. Different hydrocarbon-air mixtures (propane, pentane, ethylene, propylene, benzene) with various compositions and initial pressures at different ignition source temperatures were examined. The overall kinetic parameters for the surface reaction ignition are different from those characterizing the gas phase ignition. Some of these parameters are in good agreement with other values reported in literature, obtained with different experimental techniques. One of the most controversial aspects of the catalytic ignition is connected with the inhibition induced by the catalyst on the ignition of the gas phase reaction, explained either by the depletion of the deficient reactant within the gas near the catalyst, accompanied by the formation of an inert layer, or by the catalytic removal of radicals formed in the gas phase. Within restricted ranges of experimental conditions, we found either normal (Arrhenius) temperature dependence of the ignition properties, or inhibitory (anti Arrhenius) effects, a behavior predicted by a realistic theoretical model reported in literature for the isothermal catalytic ignition of an one step overall combustion reaction [2].

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Calculation of Some Mathematical Model Parameters for the *in situ* Epoxidation of Fatty Acid Triglycerides

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Epoxidation is a reaction of forming an oxirane ring, by oxidation of olefinic or aromatic double bond. Unsaturated fatty acids triglycerides can be successfully epoxidized producing plasticizers for PVC from renewable vegetable oils such as soybean oil. As hydrogen peroxide is not soluble in oil, organic peracid is usually used as an oxidation reagent. *In situ* prepared peracid is obtained in reaction mixture from corresponding acid and hydrogen peroxide in the presence of an acid catalyst, usually sulfuric acid or ion exchange resin. That reaction system is multiphase. If sulfuric acid is used, forming of peracid occurs in the water phase (diluted hydrogen peroxide is used), and epoxidation takes place in oil phase. If ion exchange resin is used, the third phase – solid phase is introduced into the system.

Reaction of peracid forming is slow (slower than reaction of epoxidation), and epoxidation is very exothermic. Because of that, hydrogen peroxide is usually added gradually at lower temperatures and then epoxidation is allowed to be proceeding at moderate temperatures during several hours. In this case, mass and heat transfer can be serious limitations for process performance. Also, byproducts can be formed, as an oxirane cleavage consequence, which is possible in acid medium. The degree of side reactions depends on several factors, such as type and quantity of the catalyst, reactants ratio and presence of the solvent. To obtain economically optimal conditions for epoxidation in order to get the product with required characteristics, reliable kinetic model of this complex multiphase system with parallel and consecutive reactions is more then necessary. Mechanism and kinetics of triglycerides and unsaturated fatty acid esters epoxidation has been studied for many years, but more rigorous kinetic models were published in the past few years. Nevertheless, in literature still can not be found complete, theoretically valid kinetic model for *in situ* epoxidation in the presence of the ion exchange resin as the catalyst.

The aim of this paper is to point to further actions in creating more rigorous kinetic model [1] and to consider possibilities for calculation of some kinetic i.e. mathematical model parameters: chemical equilibrium constant for reaction of peracetic acid formation in a solution and phase partition coefficient for acetic acid for oil and water phase.

Comparing calculated and experimentally determined equilibrium composition, it has been concluded that in this paper derived chemical equilibrium constant's dependency on temperature for peracetic acid formation reaction in a solution may be used for kinetic modeling instead the experimental value. It is also established that UNIFAC LLE model can be used for activity coefficient's determination of components in a water phase.

Comparison of the experimental and calculated values of the phase partition coefficient for acetic acid resulted in a conclusion that any of the existing modifications of UNIFAC model can not be used for calculation of that value, because all of them are giving incorrect values for acetic acid activity coefficient in the oil phase.

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The Mechanism of Ferromagnetic Coupling in Cu(II)-Gd(III) Complexes

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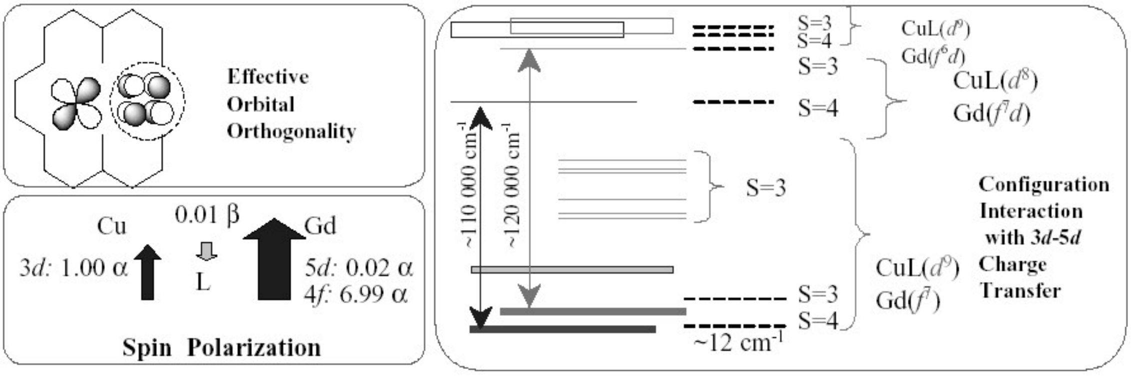
This study offers the first series of the state-of-the-art quantum chemical calculations (CASSCF, CASPT2, MS-CASPT2) and analytical models for the well-known problem of quasi-general ferromagnetic coupling in copper–gadolinium complexes. A system chosen from the chemical report of Costes *et al.* was taken as prototype. At the CASSCF level, calculated results for the experimental structure reproduced the magnetic coupling constant well ($J_{calc} = +7.67$ cm^{-1} *vs.* $J_{exp} = +7.0$ cm^{-1}). For more insight, the study molecule was further idealized by geometry optimization to C_{2v} symmetry. Systematic *ab initio* computation experiments were designed and performed. Owing to specific problems related to the non-*aufbau* ground configuration of the [CuL–Gd] complexes, the calculations were conducted in a nonstandard manner.



We found that the qualitative mechanism of Kahn, assigned to the electron jump from 3*d* of Cu(II) to 5*d* shell of Gd(III), can be presented effectively as the cause of the phenomenon, if CASPT2 MOs are taken as magnetic orbitals. However, the effect is also aided by other configuration interaction channels, like the $f^7 \rightarrow f^6d$ excitations involving the 4*f* and 5*d* shells of Gd(III). We showed that the ferromagnetic coupling is also matched and magnified by spin polarization effects over the ligand, in line with the early assumption of Gatteschi. To be distinguished from the initial hypothesis of Gatteschi, which assumed the role of 6*s* AO of Gd(III), we found that one 5*d*-type AO is actually involved in the polarization scheme. In fact, the Gatteschi and Kahn mechanisms are not mutually contradictory, but are even interconvertible with appropriate changes of the magnetic orbitals. Within C_{2v} symmetry of complexes, the ferromagnetic coupling can be qualitatively regarded as the preponderant influence of interaction channels exhibiting orbital orthogonality (four 3*d*-4*f* contacts) over the nonorthogonal ones (two 3*d*-4*f* contacts). The effective preponderance from ferromagnetic pathways is supported by CASPT2 results. One may explain the generality of Cu(II)–Gd(III) ferromagnetic coupling as being correlated with the large occurrence of approximate pseudo-C_{2v} geometry of complexes. The observed orbital regularity is lost in lower symmetries. Thus, the antiferromagnetic exceptions occur when the molecular asymmetry is advanced (e.g., owing to strong chemical nonequivalence of the donor atoms).

Acknowledgements
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Structure and Reactivity of Carbanion Monosubstituted Pyrimidinium Ylides

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Carbanion-monosubstituted pyrimidinium ylides are interesting intermediates for the organic synthesis. These compounds can react as nucleophilic reagents on the level of ylidic carbon atom to afford new dipolar structures as well as 1,3-dipoles to afford azapyrimidines, otherwise difficult to obtain.

No structure of carbanion-monosubstituted cycloimmonium ylides has been resolved using X-ray diffraction, because these ylides have a fable stability, giving in time dimmers by a [3+3] cycloaddition reaction or other inactivation products.

In this work, a structural study on the reactivity of carbanion-monosubstituted pyrimidinium ylides has been developed, using semiempirical calculations, based on the idea that the totality of the physical and chemical properties of a compound is recorded in its structure. The focus of this theoretical study was on identifying the physico-chemical parameters susceptible to explain the difference between homologous molecules on the level of the electronic structure and the geometry. The method was used to understand why some ylides adopt a near planar structure while others are non-planar. Also the present study propose a methodology for synthesis of new planar carbanion-monosubstituted pyrimidinium ylides as may be required by the organic chemist. Besides, using the frontier moleculat orbital theory, we estimated the reactivity of the virtual reaction centers by their absolute values of atomic orbital coefficients corresponding to the HOMO-LUMO orbitals of some carbanion-monosubstituted pyrimidinium ylides.

It has been demonstrated that the AM1 and PM3 methods give accurate data (geometry, charges) when compared with the experimental data. That is why only the AM1 method has been used in the study of the electronic and structural properties of the carbanion-monosubstituted pyrimidinium ylides.

A correlation between geometrical data on the one hand and the steric and electrostatic data on the other hand was necessary to identify the physical and chemical properties linked to the planarity or the non-planarity of the ylidic systems.

The stability of whole ylide depends essentially on the capacity of the substituent to attract the excess of charge carried by the ylidic carbon atom. The more the substituent of the carbanion is negatively charged the more the considered pyrimidinium ylide has a tendency to adopt a non-planar structure. However, the theoretical calculations suggest us that the angle between the planes P1 of the pyrimidine nucleus and P2 of the carbanion depends more on the steric effects that on the electrostatic effects. The more the substituent of the carbanion is sterically cumbersome the more the pyrimidinium ylide has tendency to adopt a non-planar structure.

It suggest that the synthesis of planar pyrimidinium ylides can be made by putting as substituent on the carbanion, strongly electron withdrawing groups which are not too cumbersome.

The theoretical results were confronted with experimental results to elucidate some fundamental feature of these compounds.

Experimental and Theoretical Study of Some Potentially TICT Forming Compounds

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Experimental and theoretical results on different classes of heterocyclic compounds that can form TICT (twisted intramolecular charge transfer) states are reported and discussed. The investigated compounds contain two moieties with different donor – acceptor character joined by a single bond, that ensures an enhanced mobility. The donor fragments are either pyrollyl or sulfur containing moieties and the acceptors, coumarin, acetylbenzene or izoxazole derivatives. Several experimental criteria for the identification of the TICT states, such as the dependence of the emission band on the excitation wavelength, the increase of the bandwidth with the solvent polarity, etc were employed. Semiempirical and ab intio calculations in vacuo or considering the solvation processes for both the ground (S_0) and excited states (S_1) were performed in order to support the experimental data. The theoretical data indicate the localisation of the frontier orbitals on the two different fragments of the molecule (homo on the donor and lumo on the acceptor). The potential energy surface calculated along the dihedral between the donor and acceptor shows that the orthogonal conformer corresponds to a minimum in the excited state. The energy difference between the S_0, T_1 and S_1 states at the orthogonal conformation is extremely low, indicating a large probability of both the internal conversion and intersistem crossing nonradiative processes. The shape of the PES depends on the polarity of the solvent, the orthogonal conformation being strongly stabilized in polar solvents. There is also a large charge transfer from D to A in the excited state, which increses in polar solvents. All these criteria point to the possibility of TICT states formation for the studied compounds.

Theoretical Investigation of the Electronic Spectrum of HCCS

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In spite of its importance from an astrophysical/chemical point of view the HCCS radical has been subject to a relatively small number of experimental and theoretical studies. The spectrum of HCCS was first detected by absorption spectroscopy in the region between 377 and 417 nm during the flash photolysis of thiophen[1]. The HCCS radical in its ground and first excited electronic state represents one of a few examples of appearance of the Renner-Teller effect in tetra-atomic molecules having been observed until now.

Potential energy surfaces for the X $^2\Pi$ and A $^2\Pi$ electronic states of HCCS are calculated by means of an extensive MRDCI approach[2,3]. The vibronic and spin-orbit structure of the electronic spectrum involving these two species are computed. These calculations are carried out by means of a new variational approach based on the use of normal bending coordinates. The present study questions various interpretations of the A $^2\Pi$ - X $^2\Pi$ spectrum carried out thus far.

On the basis of the results of our *ab initio* calculations all prominent features in the spectrum are interpreted. However, in spite of this apparent agreement between theory and experiment, there are some serious problems, which require special consideration. The most interesting question is whether the radical is linear, as calculated in our study, or slightly bent, as could be concluded on the basis of the fine discrepancies between the original *ab initio* results and the spectra recorded.

In contrast to the X $^2\Pi$ state, which potential surface has proven to be relatively stable with respect to the change of technical parameters in the computational procedure, the A $^2\Pi$ state is characterized with very flat H-C-C bending potential curves at small distortions from linearity, and belongs to the systems for which accurate *ab initio* calculation of structure parameters is particularly difficult.

Nevertheless, we find it justified exploring the consequences of possible quasilinearity of the A$^2\Pi$ state of HCCS on the interpretation of A $^2\Pi$ - X $^2\Pi$ spectra of HCCS and DCCS. In this way series of apparent discrepancies between theoretical and experimental results can be overcome.

Although the present theoretical results do not offer an unambiguous explanation of all features observed, they point out to the possible solution. This was confirmed in resent experimental paper entitled “Is the HCCS radical linear in the excited state?” The authors[4] explained the spectrum with the assumption of a quasilinear excited state geometry.

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Long Term Intensity Responses in Pulsed Modulated Argon d.c. arc Plasma

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The spectral emission intensity responses of the plasma to the power modulation are induced by the changes of the electron and gas temperatures and processes of transport of heat, radiation and heavy particles[1]. Each of these processes has their own temporal development. Study of delayed responses, on a millisecond time scale, can give insight into processes involved with particle diffusion[2].

To observe these responses the arc current is alternated between 9 and 3 A. Power modulation was realized by an electronic switch based on fast MOS-FET transistors connected in parallel with the arc column. The modulation period lasted up to 300 ms with low current interval up to 40 ms. The photomultiplier current was amplified and fed into a digital storage oscilloscope. A PC computer synchronized the oscilloscope and power modulation circuit.

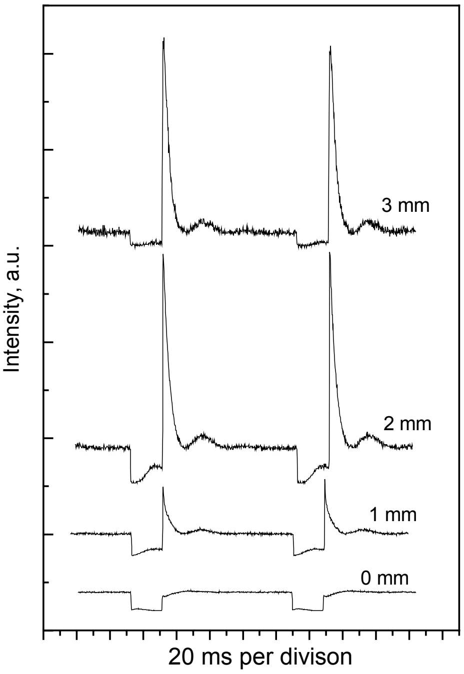

Figure 1. Temporal evolution of the Ar I 696.54 nm line intensity at various distances from the arc axis

The current modulation produces a puzzling variety of responses depending on the kind of light emitting species as well as the spatial position of the observed plasma volume. In this work we have studied the behaviour of a non easily ionised elements (Ar, H and Be) in order to avoid significant influences of a ambipolar diffusion and recombination. We also investigated the intensity response of a continuum radiation, at 430 nm, to resolve electron transport contributions from heavy particles diffusion.

Typical example of the obtained results is shown in Figure 1. As it can be seen from the picture the temporally evolution of intensity strongly depends of the radial displacement from the arc axis. This fact is especially observable at the intensity increase after the current jump. The duration of a low current phase has noticeable influence, as well.

The spatially and temporally resolved studies of plasma species emission provide new information about processes responsible for analyte excitation in d.c. arc plasma.

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Direct Dynamics Study for Atmospheric Reactions

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Transition-state theory[1] is fully explained as a unique and efficient tool for a complete investigation of reaction rates for chemical systems proceeding towards products through a dividing surface separating them from reactants. Dynamical attributes are mainly provided from electronic structure calculations without the intermediacy of fitting a potential energy function. Incorporation of tunneling effect contribution is obtained through a series of different methods, directly depended on the type and accurate description of the reaction's minimum energy path. Certain atmospheric reactions are next presented, fully examined in a similar manner, and compared to available experimental results.

Ab initio calculations have been performed for both the hydrogen-abstraction and halogen-abstraction reactions of mono-halogenated methanes (Cl, Br) by the hydroxyl radical.[2,3] Geometry optimizations and vibrational frequencies calculations were performed for reactants, intermediate complexes, transition states, and products at the PMP2(full)/cc-pVTZ level of theory, with all electrons included in the correlation energy calculation. Canonical transition-state theory with Wigner's tunneling correction has been applied to predict the rate constants as a function of temperature (200–2000 K). For both reacting systems, calculation of rate constants is in good agreement with available experimental results and suggests a quick and feasible methodology for a proper theoretical investigation of reaction kinetics for hydrogen abstractions by hydroxyl radicals from partially halogenated organic compounds. There is no interest for rate constants calculations for the halogen-abstraction reactions, since they are greatly endothermic and proceed through a non-transition state formation minimum energy path.

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Computational Investigation of Stereoselectivity in Intramolecular Diels-Alder Reactions of 2,4-Pentadienyl Butadienamides in the "Remote Stereocontrol Group" Approach

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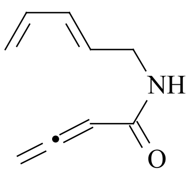
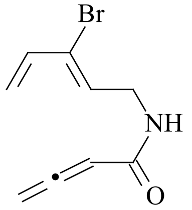
The reaction paths of possible intramolecular pericyclic reactions (**1** – **1.1.** [1,5]-sigmatropic shift and **1.2** Intramolecular [4+2] cycloaddition, **2** - Alder-ene reaction, **3** - Intramolecular [4+2] cycloaddition) of buta-2,3-dienoic penta-2,4-dienylamide (**1**) were modeled as asynchronous concerted processes at semi-empirical theoretical level. The precursor (**1**) and expected products were connected via transition structures (TS) using IRC procedure. Localized TS were fully optimized at different computational levels – AM1, MP2/6-31G(d) and DFT B3LYP/6-31G(d). The reaction path **3** focused our attention. Endo/exo and π-diastereofacial stereoselectivity of amide-tethered Intramolecular Diels-Alder Reaction (IMDA) were investigated into "Remote stereocontrol group" approach.

Boltzmann population of the relative energy of the localized TS predicts as preferable endo cycloadduct computed at MP2/6-31G(d) level. On the contrary AM1, RHF/6-31G(d), B3LYP/6-31G(d) exo cycloadduct is preferred.



(**1**)



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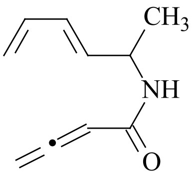

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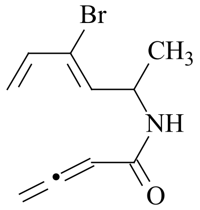

(**4**)

Used theoretical methods predict different distribution between stereoisomers of the precursors (**2**), (**3**) and (**4**). Possible reasons for the contradictory results are discussed.

Chlorine Abstraction Reactions from 2,4-Dichlorophenoxyacetic Acid. Quantum Theoretical Modelling

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The relative energies for the two possible chlorine abstraction dissociation pathways from 2,4-dichlorophenoxyacetic acid were calculated at HF, MP2, and two density-functional-theory-based (DFT) methodologies. Within the DFT approaches, two combinations of exchange and correlation functionals were employed - the B3-LYP, and the PBE1-PBE. For all calculations, the 6-31++G(*d*,*p*) basis set was used for orbital expansion in solving the HF or the Kohn-Sham SCF equations. Fully relaxed scans of the intersections through the full molecular PES corresponding to the two possible chlorine abstraction reaction coordinates were also performed at HF and the two DFT levels of theory. Bader's approach was employed to analyze the molecular electronic density scalar field and the corresponding density gradient vector field of the studied molecular system. Also, a second-order perturbation theory analysis of the Fock matrix (or its Kohn-Sham analog) within the NBO basis for 2,4-dichlorophenoxyacetic acid was performed in order to judge on the possible intramolecular charge transfer interactions. All of the theoretical results were used in the course of a more exact explanation of the degradation properties of 2,4-dichlorophenoxyacetic acid.

Characterization and Classification of Lanthanides by Multivariate Analysis Methods

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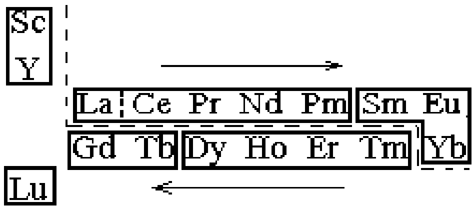
A chemometric study has been conducted on a data set consisting of the 18 characteristics, mainly physical properties of the 14 lanthanides and lanthanum, including also Sc and Y. Classical methods of multivariate analysis, namely Principal Component Analysis (PCA) and Cluster Analysis (CA) were applied. The results obtained by using the “Statistica” software package are presented and discussed concerning the correlations between the properties, and those between the elements themselves. The discussion and findings are based on the tables of correlation, the eigenvectors and eigenvalues of PCA, the 2D- and 3D-representations of the loadings of variables and scores of the elements corresponding to the first principal components, including also the dendrograms obtained by using CA. Loadings scatterplots appeared very useful as a display tool for examining the relationships between properties, looking for trends, grouping or outliers. In the same way, the scatterplots of scores emphasized the difference between La and the lanthanides on the one side and Sc and Y on the other and support setting Lu as their homologue, rather than La. On the basis of these findings, a “periodic system” of the lanthanides is suggested, that agrees well with chemical intuition.



The ”periodic system“ of lanthanides

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Study of Analyte Emission in d.c. Plasma with Aerosol Supply by Abrupt Decrease of the Arc Current

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Temporal and spatial changes in emission intensities following the abrupt modulation of power for an d.c. arc contain fundamental information that is not available in a continuously operating plasma. The charm of this method lies in a fact that it gives information about stationary state of plasma by disturbing it. The decrease of input current produces instantaneous drop of the electron temperature (in a μs time scale) that should result in reduction of spectral line intensity. The spectral line intensity can enhance as consequences of a sudden enlarge of analyte concentration in the observed plasma region, despite the temperature decreases. This enhancement can act on a microsecond time scale although much slower processes provoke it (e.g. recombination)[1].

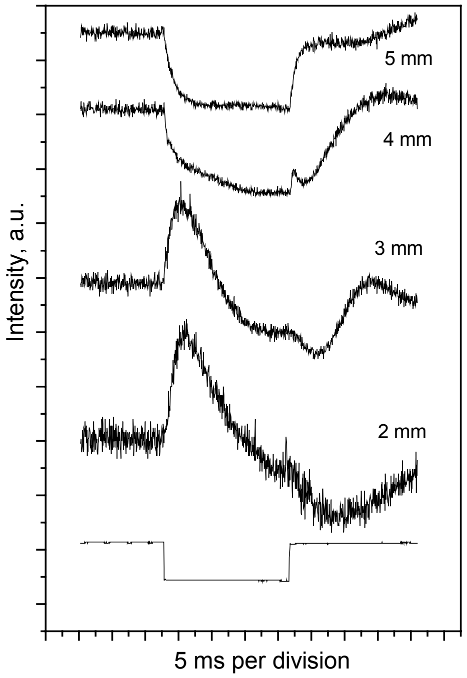

Figure 1. Intensity responces of the Ca I 422.67 nm spectral line at various displacement

The arc device used in this work together with full description of the experimental setup and time resolved measurements is described in details elsewhere[2]. The plasma was projected on a entrance slit of a monochromator on such a way to provide spatially resolved spectral information. Various elements with different ionization energies and atomic weights were nebulized into the plasma as water aerosol.

Figure 1 illustrates a characteristic intensity response of an easily ionized element at different displacement from the arc axis. As it may be seen, at distances closer to the arc axis, the intensity increase with current drop. At longer displacements from the arc axis the intensity jump first decreases and than disappears. Instead of intensity increase the current drop is followed by intensity decrease. The absence of an intensity jump is typical for the elements with high ionization energies at all displacements. This behavior is dominantly determined by ionization energy, which implies that this phenomenon is caused by recombination, and ambipolar diffusion that is characteristic for this kind of plasma[3].

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Experimental and Theoretical Study of the Inclusion Complexes of Some 2,5-Diaryloxazoles with Cyclodextrins

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The host-guest complexes of some 2,5-diaryloxazoles with cyclodextrins were investigated by means of steady-state fluorescence mesurements. The experimental data outline the formation of both 1:1, 1:2 and 2:2 complexes.The association constants were estimated by non-linear regression analysis .The effect on the inclusion process of both the diaryloxazole substituent and the dimensions of the cyclodextrins cavity is discussed. Theoretical study of the complexes is made using semi-empirical (AM1) and molecular mechanics (MM) calculations methods. The electrostatic and van der Waals contributions to the energy was estimated and a disscussion is made on this basis.

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Fatty Acids of Some Serbian Breeding Tobaccos

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There are more than sixty species of the genus *Nicotiana L.* but only *N. tabaccum* ("tobacco") and *N. rustica* ("makhorka") are cultivated commercially as smoking materials. The subject of present investigation were three Serbian breeding tobaccos type *Prilep, Yaka* and *Otlja,* known for their characteristic strong aroma and pleasant sweet smoking taste. There are studies about chemical composition and antimicrobial activity of the essential oil and CO_2 extracts of *Otlja*, *Yaka* and *Prilep,* but to our knowledge nothing is known about the content and composition of fatty acids of these tobaccos, although fatty acids contribute significantly to the flavor and aroma of cigarette smoke.

Isolation and esterification of free and total fatty acids were performed according to known previously published procedures.The methyl esters of fatty acids were analyzed on Agilent 6850 Gas Chromatograph, equipped with HP-1 Methyl Siloxane (30.0 x 320 μm x 0.25 μm) capillary column and FID detector. The identification was carried out by coinjection of authentic compounds and by comparison of their retention times. The total and free fatty acids composition in dried leaves of *Otlja*, *Yaka* and *Prilep* are presented in the Table.

Table. Distribution and abundance of tobaccos' fatty acids (%)

	Otlja		Yaka		Prilep	
Fatty acids	*total*	*free*	*total*	*free*	*total*	*free*
$C_{14:0}$	1.7	0.1	2.1	0.5	2.2	0.5
$C_{15:0}$	4.6	0.2	4.3	0.9	1.3	-
$C_{16:0}$	34.2	5	43.9	16	47.1	17
$C_{17:0}$	1.3	0.2	2.3	0.7	2.1	0.6
$C_{18:3}$ + $C_{18:2}$	36	4.6	27.7	9.0	24.8	8.2
$C_{18:1}$	10.2	1.4	5.1	1.2	5.7	1.3
$C_{18:0}$	9	1.4	11.2	3.9	12.1	4
$C_{20:0}$	3	0.3	3.3	1.2	4.8	1.9
yield ($w_{acids}/w_{dried\ leaves}$)	2.8	1.8	2.4	1.0	2.7	0.9
U/S (unsaterated/saturated)	0.9	0.8	0.5	0.4	0.4	0.4

The presented above leads to a conclusion that there are differences between oriental and semioriental tobaccos in regard to the content of free fatty acids and their U/S values (free and total).

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Volatile Compounds of the Essential Oil of *Calamintha nepeta* (L.) Savi ssp. *nepeta*

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Calamintha nepeta (L.) Savi ssp*. nepeta* belongs to the family Lamiaceae. *Calamintha* species has been subject of intensive studies on over the last few decades, particulary the oil of *C. nepeta,* mainly due to a great diversity in a chemical composition, microbial and fungicidal activities (1).

The aerial parts of flowering plant were collected in August 2000. on the location of mountain Vratarnica, Knjazevac, South Serbia (2). An oil of *Calamintha nepeta* (L.) Savi ssp. *nepeta* obtained by hydrodistillation (3) was analyzed by GC and GC/MS, 11 constituents were identified (96.3%). The main constituents in the oil were pulegone (75.5%). Piperitenone oxide (6.0%), menthone (5.3%) and menthol (4.3%) are significatively present.

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Oxidation Kinetics in High Temperature Water of Some Alloys Used In CANDU Reactor

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The heat transport circuits of nuclear power plant have different water chemistry, corrosion products sources, temperatures and flow rates and these parameters can promote the growth and deposition of oxides with different composition on the surface of the nuclear steam generator tubes.

In conjunction with other compounds produced by in-situ corrosion these deposits originate the so-called, corrosion fouling" phenomenon. One of the consequences of this process is a progressive degradation of the heat transfer capability of the steam generator tubing.

The purpose of this paper was to establish the corrosion kinetics of Incoloy 800, 304L stainles steel, and 516 carbon steel, alloys which are exposed in secondary circuit of nuclear steam generator.

The experiments have been made by static autoclavization at T= 260^0C and p= 5,1 MPa in aqueous solutions with total volatile amine (AVT) and pH=9,7.

The corosion kinetics of these alloys were evaluated by gravimetric analysis and were established specific regression ecuations. The characterization of oxides films have been made by metalographic microscopy and electrochemical methods (potentiodynamic polarization and electrochemical impedance spectroscopy measurements).

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Considerations on the Susceptibility to Crevice Corrosion of Some Titanium Alloys in the Presence of Chloride Ion

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Previous corrosion studies carried out on a wide range of metallic materials shown that titanium alloys are some of the most promising candidates as container materials for the long-term disposal of high-level nuclear waste (HLW) in rock salt formations.

In the case of titanium waste containers, the crevices could potentially occur between the containers walls and the surrounding buffer material used to pack the disposal borehole, in the welded zone container/shielding lid, under a biofilm, etc.

The susceptibility to crevice corrosion of titanium alloys – Ti gr. 2 and gr.12 – in chloride solutions was studied by using some electrochemical methods (corrosion potential – time, potentiodynamic) at 90°C and the static autoclavization of creviced samples at 150°C in chloride solution containing concentrations of 5.85 wt % NaCl (1M), 11.7wt % NaCl (2M), respectively.

In addition, the corrosion rates of titanium alloys were determined gravimetrically and electrochemically for two torque moments (3 NxM and 5 NxM, respectively) to two concentrations of NaCl (1M and 2 M, respectively) and the superficial oxide films were analysed by metallography.

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Corrosion Processes Specific to a CANDU Steam Generator and Mitigation Methods

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The operation and maintenance of steam generator is one of the most crucial and complex elements in the success of pressurized water reactor operations. For many nuclear utilities steam generator remain the leading cause of plant outage hours, high maintenance costs and reduced generating capacity. As a result, more and more utilities are faced with reality that steam generators will not endure the life of the plant, and will require either expensive repairs or complete replacement. Therefore, the effective management of steam generators requires more than solving the problems as they arise; it requires anticipation of issues so that effective planning can be performed in advance. A steam generator strategy must specify a balance between the objectives of reducing short and long term capital and operation and maintenance budgets with the risk of unscheduled or extended outage and reduced plant availability factor.

In the purpose to extend steam generator life most of the remedial measures taken must to address operational effects on steam generator degradation.

Maintenance activities intended to extend steam generator life and reduce the potential for costly forced shutdowns must to be implemented at the Nuclear Power Plants. A comprehensive inspection program is able to detect problems at an early stage so that necessary actions can be implemented.

The Steam Generator tubing degradation caused by corrosion and other age-related mechanisms continues to be a significant safety and cost concern for many Steam Generators. Understanding Steam Generator ageing mechanisms is the key to effective management of Steam Generator ageing and consists of knowledge of Steam Generator materials and materials properties, stressors and operating conditions, likely degradation sites and wear mechanisms.

The paper presents the principal types of corrosion which can occur in CANDU Steam Generator. There are also presented the operation conditions, the specifications referring to the water chemistry and the construction materials of Steam Generator, the factors which have a great influence on the corrosion behaviour during the whole exploitation period of this equipment.

Also the paper presents the most important methods which have like principal objective the mitigation of the degradation processes specific for the CANDU Steam Generator.