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ABSTRACTS

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Krisztina László (ed.)

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Structural and functional analysis of gene expression regulatory proteins in *Staphylococcus aureus*

Ábris Ádám Bendes
e-mail: abris.bendes@gmail.com

Supervisors: Beáta G. Vértessy,
Depsrtment of Applied Biotechnology
and Food Science, BME
e-mail:vertessy@mail.bme.hu

Ibolya Leveles,
Institute of Enzymology,
Biological Research Center, MTA
e-mail: leveles@enzim.hu

Staphylococcus aureus is a facultative anaerobic Gram-positive bacterium, which often appears as a component of the normal skin flora. Around 20% of the population is a long-term carrier of this organism. *S. aureus* can cause a number of diseases ranging from minor skin infections to life-threatening diseases, such as pneumonia, meningitis or Toxic Shock Syndrome (TSS). Genome integrated superantigen-carrying pathogenicity islands (SaPIs) play a major role in spreading virulence genes among populations. The regulation of these pathogenicity islands rely on a specific interaction between a global repressor (Stl) and helper phage related dUTPase. These dUTPases contain a phage specific linker region that presumably interacts with the Stl protein. This interaction induces a conformational change in the Stl, removing the protein from the promoter region thus derepressing the gene.

My work focuses on the functional and structural analysis of the repressor protein Stl SaPIbov1 and the dUTPase from *S. aureus* helper phage Ô11.

Optimization of protein expression (using pETDuet-1 and pET-15b vector systems) and purification (by HisTrap affinity and ionexchange chromatography) of the protein without precipitation proved to be difficult, however, soluble proteins were still obtained and crystallization of both proteins has been successful. We are on the way to solve the structure of the Ô11 dUTPase with the resolution of 2.98Å. The results are recently published in Acta Crystallographica Section F. I measured the thermal stability of the proteins on their own, in complex and in absence or presence of dUPNPP substrate-analogue. CD measurements were performed in order to examine the secondary structures of the proteins. Activity assays, fluorimetry and other experiments were also carried out. Based on literature, I performed a phylogenetic study regarding the diversity and the evolution of the specific linker regions of over 60 *S. aureus* phage dUTPases.

Further measurements may provide a better insight in this specific phage induced regulation system, which might bring us closer to understand and control the virulence of the *S. aureus* bacterium.

Synthesis and evaluation of novel fluorescent nucleoside-polyphosphate sensors

Márton Bojtár bojtarmarci@gmail.com
Supervisor: István Bitter
Department of Organic Chemistry
and Technology, BME
e-mail: ibitter@mail.bme.hu
Consultants: János Balázs Czirok
Department of Organic Chemistry
and Technology, BME
e-mail: czirokjanosbalazs@yahoo.com
Péter Baranyai,
Chemical Research Center of
Hungarian Academy of Sciences
e-mail:pbaranyai@mail.bme.hu

In the past decade great attention has been paid to fluorescent sensing systems capable of the selective molecular recognition of nucleoside polyphosphates (nucleotides). Of all the ribonucleotides, adenosine-5'-triphosphate (ATP) is vital since the binding of ATP by proteins is one of the most prominent molec-

Krisztina László
Faculty of Chemical Enginering, Budapest University of Technology and Economics, H–1521 Budapest,, Hungary

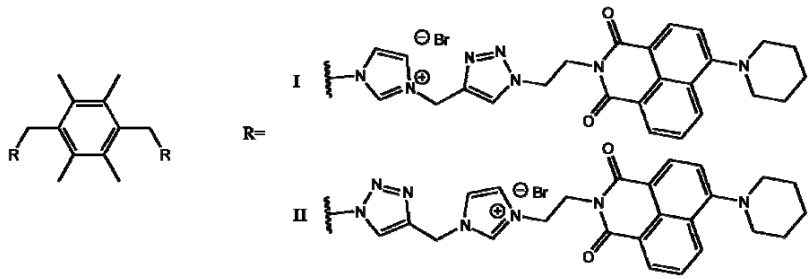

Fig. 1. Scheme 1: structure of receptors I and II

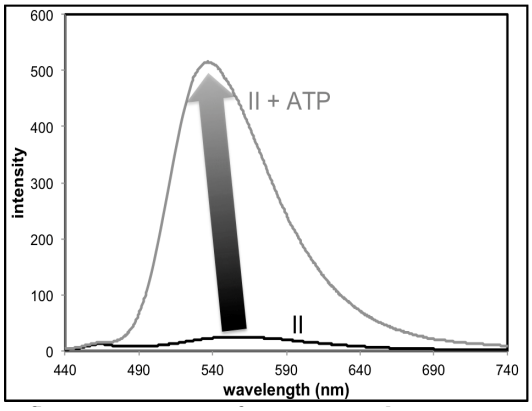

Fig. 2. fluorescence spectra of receptor II and receptor II with ATP

ular recognition events in the nature. Recently, considerable efforts have been devoted to developing fluorescent chemosensors for ATP and guanosine-5'-triphosphate (GTP) working in aqueous solution under physiological pH conditions. The common structural feature of these sensing systems is a cationic receptor site containing $N-$heterocyclic moieties either as part of a cyclophane or linked with a spacer to form podands. Based on literature analogy [1] we aimed at designing and synthesizing novel representatives of the latter type, dipodal receptors **I**, **II** with 4-aminonaphthalimide fluorophore for the selective recognition of nucleoside polyphosphates (Scheme 1).

Receptors **I** and **II** are regioisomers being different from each other by the order of the heterocyclic subunits in the binding arms. The complex formation of both ligands with adenosine-5'-tri-, di-, and monophosphate (ATP, ADP, AMP), guanosine-5'-monophosphate (GMP) guests was evaluated in aqueous solution at pH 7.5 by fluorescence spectroscopy. Distinct ATP selectivities associated with significant turn-on fluorescence was observed over the other nucleotides tested, but receptor **II** exhibited much higher sensitivity with larger log K_{ass} value than the regioisomeric counterpart **I** (Fig. 2). Reasonable explanation was provided for the complexation and the fluorescence enhancement accompanied by the binding process.

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Qualification of endproduct made of novel type of functional cereal milling fraction, understanding the relationship between function and chemical composition

Blanka Bucsella
bucsellablanka@eit.bme.hu
Supervisor: Sándor Tömösközi
Department of Applied Biotechnology and Food Science, BME
e-mail: tomoskozi@mail.bme.hu
Consultant: Szilvia Szendi
Department of Applied Biotechnology and Food Science, BME
e-mail: szendi@mail.bme.hu

The wheat contains a wide spectrum of exploitable biologically active components. The health-promoting dietary fibre content is accumulated mainly in the bran fraction of wheat grain. The new wheat flour fraction was developed in our project at Gyermely Zrt is rich in aleuronic component and is lacking the hard outer layer of seed. This product could reduce the food safety hazard with possessing beneficial nutrients at the same time. The milling fractions containing bran adjacent parts differ in protein, carbohydrate and fibre composition from traditional flours.

In this study, qualification and technological stability of the novel milling product was investigated focusing on correspondence between flour content, rheological properties and endproduct quality. The novel milling fraction was compared to ordinary starchy endosperm based types of wheat flour. Besides chemical analysis, Rapid Viscoanalyzer (RVA) and micro z-arm instruments were used to examine the dough properties of ordinary and novel type of flour. In order to study the performance of the final product standard, baking tests were carried out.

According to the results of the chemical analysis, the novel type of flour contains higher amount of protein and dietary fibre and lower amount of starch than commercial flours. While the effect of protein content and composition on the functional properties of ordinary wheat flour is well studied, our knowledge on the same properties of the new flour is limited. When dietary fibre abundant flour was characterized on the basis of mixing parameters in a micro z-arm mixer, differences were observed depending on protein, carbohydrate and dietary fibre composi-

tion of the flour. The studied rheological parameters of the novel type flour showed retarded dough development and unusually strong dough structure that extended in time. The presence of dietary fibre in flour affected bread quality in terms of volume, internal structure and texture. This bread contains biologically active components and afford lower energy intake.

Acknowledgement

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Raman Mapping of Pharmaceutical Products of Unknown Content Using Chemometric Analysis of Datasets

Attila Farkas
email: farkas.attila88@gmail.com
Supervisor: György Marosi
Department of Organic Chemistry and Technology, BME
e-mail: gmarosi@mail.bme.hu
Consultant: Balázs Vajna
Department of Organic Chemistry and Technology, BME
e-mail: balazs.vajna@gmail.com

Pharmaceuticals of unknown composition have to be characterized in many cases of the scientific, technological and even forensic practice. Counterfeit and illegal products are increasingly present on the drug markets, which, in many aspects, pose economic, medical and analytical challenges. On the one hand these drugs cause economic damage to the original manufacturer of the drug, while on the other hand, lack of effect or negative effects could result in medical issues. Therefore, it is necessary to continue an intensified fight against these drugs. Furthermore, unexpected components and impurities may also occur in legal and marketed pharmaceutical products during the drug development and manufacturing.

The purpose of our experiments was to determine how to characterize solid pharmaceutical preparations that contain unknown components, using Raman spectrometry-based mapping combined with statistical and mathematical tools. Its advantage is that non-destructive analysis can be performed on the samples. The vast amount of data generated during Raman mapping was evaluated by different chemometric methods to achieve the goal.

At first a completely unknown hypothetical model tablet („T") was analyzed [1]. Such preparations of unknown composition can be any tablets on the "black market". Using multivariate data analysis methods the Raman spectra of the pure components and their spatial distribution could also be detected. Then the methods were also tested on model tablets prepared with different manufacturing techniques. Certain technological steps result in very homogeneous component distribution within the product; therefore, it was also studied under these circumstances, which method(s) can be used best to detect the tablet components and technological properties regardless of the technology (i.e. homogeneity).

In some cases the analytes may contain polymorphic contaminants of the active substance or excipients with very similar chemical structure. In these cases the pure spectra are strongly correlated with one another. Such cases were investigated by analyzing mixtures of API polymorphs and glucose polymers. Besides the spectra, the concentration of two components may also be strongly correlated. Such samples were prepared with electrospinning and hot-melt extrusion and were analyzed with Raman mapping to determine the formulation characteristics of stable colloidal dispersions [2].

All above mentioned practical issues were solved by selecting and using the appropriate mathematical methods.

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The synthesis of N-arylethyl arylacetamides and the related isoquinoline derivates under microwave conditions

Tamás Földesi
e-mail:tamasfoldesi2@gmail.com
Supervisors: György Keglevich,
Department of Organic Chemistry and Technology, BME
e-mail:gkeglevich@mail.bme.hu
Mátyás Milen, EGIS Pharmaceuticals
e-mail:milen.matyas@egis.hu
Alajos Grün,
Department of Organic Chemistry and Technology, BME
e-mail:agrun@mail.bme.hu

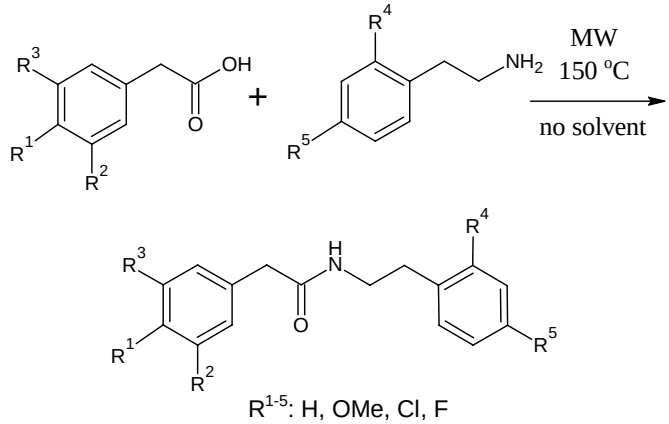
The amide function plays an important role in bioorganic chemistry and is present in numerous natural products, plastics, drugs and pesticides. Therefore, the synthesis of amides is important in organic chemistry. The carboxylic amides may be prepared by the acylation of amines by carboxylic acids directly above 100°C, or in the presence of well-known condensing agents.

Microwave (MW) irradiation is a useful tool to conduct reactions efficiently in short reaction times. Condensation is a typical reaction that may be accomplished well under MW conditions. Not only thermally well-established esterifications and

amidations of carboxylic acids, but otherwise thermally impossible reactions could also be performed under MW irradiation. The use of the MW technique is often accompanied by solventless conditions offering an additional advantage.

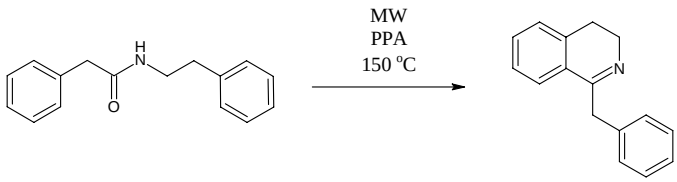
It was a challenge for us to study the condensation of arylacetic acids with and 2-aryl-ethylamines under MW and solventless conditions. The resulting amides are valuable intermediates of the Bischler-Napieralski ring closure reaction. Beside this, these amides may be the starting materials for a variety of alkaloids or their synthetic derivatives.

First we studied if the use of the MW technique offers an advantage in the condensation reaction of phenylacetic acid and 2-phenylethylamine. Equimolar mixtures of the reactants were irradiated at 130˚C, 140˚C and 150˚C to afford the corresponding amides in practically quantitative yields after reaction times of 120 min, 60 min and 22 min, respectively. In the comparative thermal experiment carried out at 150˚C, the reaction time was 100 min. It can be seen that, the amidation became much faster on MW irradiation. Then the optimum temperature of 150˚C was adopted to the condensation of other model compounds. Twenty-six amides were prepared by us that have been characterized by ^{1}H and ^{13}C NMR, as well as HR-MS spectral data.



R^{1-5}: H, OMe, Cl, F

Then we studied the Bischler-Napieralski ring closure reaction under MW conditions. We tried to replace phosphorus oxichloride with the combination of MW irradiation and a more environmentally friendly reagent. Poliphosphoric acid could be used for this purpose and the reaction can be realised without solvents.



Optimization of *in vitro* neurotoxic model system for drug candidate molecules

Gábor Hámornik
e-mail:dzsibrail@gmail.com

Supervisor: Balázs Herberth
EGIS Pharmaceuticals Ltd.
e-mail:herberth.balazs@egis.hu

The neurodegenerative diseases, such as Alzheimer's disease or stroke, are the most common causes of deaths in western countries. Since the reasons of their formation are still unknown, there are not highly effective drug compounds. Therefore, this field is one of the most important targets of drug discovery.

The patomechanism of these above diseases are often known in details. Many stress processes take place in the background of these disorders such as protein aggregation, stress hormones, inflammatory processes, oxidative stress, energy deficiency, signal factors disturbance and glutamate neurotransmitter induced excitotoxicity. In my experiments I dealt with the last four which take part in most of diseases' patomechanism.

In trying to discover effective drugs, there are many model systems available to imitate the occurrences taking place in the central nervous system and to screen drug candidate molecules. I have applied my investigations *in vitro* primary neuronal cultures in the EGIS Molecular Pharmacological Laboratory, which are available for investigation of the process taking place in the brain therefore we can examine directly the neurotoxical occurrences.

I used and optimised detection techniques, such as MTT (4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) general viability assay, fluorescent membrane potential (FMP) assay for measuring neuronactivity and the experiments based on immuncitochemical dyes.

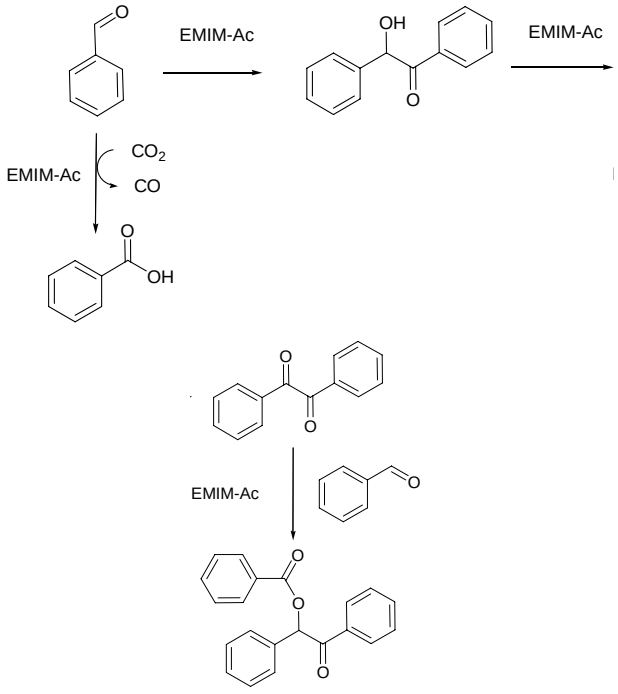
In my research I had success in modelling the above mentioned processes. The oxidative stress was induced using hydrogen peroxide (H_2O_2), the excitotoxicity using glutamate treatment. In addition the energy and signal factor deficiency were modelled by deprivation of different components of the cultures' medium. Furthermore I identified the optimal concentration ranges where the neuroprotective drugs can stop or turn back the cell dying processes. I determined the advantages of the detection techniques and integrated them in my model. The MTT assay was applied for large numerous neuronspecific viability screening tests, the FMP technique for detection of disturbance of neuronal activity which occur mild toxicity stage and the immuncitochemical investigation for identifying the cell composition of the cultures and for following the morphological changes of the toxicity. Finally there was a complex investigation protocol of screening neuroprotective candidate molecules set up which involved the planting of the cells through the control tests to the large numbered drug screen. Therefore the model is sufficient for the requirements of the drug discovery such as specifism of neurotoxicity, high throughput and reproducibility.

I plan in the future to develop the model further to expand the toxicity types (amyloids, stress hormones, inflammatory). In addition I would like to distinguish the cell death types induced by the stresses and also identify the molecular targets of the neuroprotective found compounds.

An organocatalytic ionic liquid – carbon dioxid reduction?

Zsolt Kelemen
e-mail:kelcsi@mailbox.hu
Supervisor: Oldamur Hollócki
Materials Structure and Modeling Research Group of the Hungarian Academy of Sciences
e-mail:holloczki@gmail.com
Consultants: József Nagy
Department of Organic Chemistry and Technology, BME
e-mail:jozsefnagy@mail.bme.hu
László Nyulászi
Department of Analytical and Inorganic Chemistry BME
e-mail: nyulaszi@mail.bme.hu
Tibor Pasinszki
Institute of Chemistry,
Eötvös Loránd University
e-mail:pasinszki@chem.elte.hu

Recently, we have shown that with basic anions (such as acetate) imidazolium salts can be deprotonated in the gaseous phase, thus, a carbene and the corresponding acid can formed. The aim of the present work is to see if the carbene concentration within 1-ethyl-3-methylimidazolium-acetate (EMIM-Ac) ionic liquid is high enough to act as a catalyst e.g. in the benzoin condensation, potentially uniting the field of organocatalysis and ionic liquids.



Scheme 1.

Thus, benzaldehyde was stirred in EMIM-Ac under argon at 60 **?**C for six hours, and benzoin could be isolated in good yields (67%) after workup. However, under air or carbon dioxide atmosphere other reactions have also been observed (**Scheme 1.**), yielding the same oxidized products in both cases. The formation of the products benzoic acid, benzil, and 2-oxo-1,2-diphenylethyl benzoate can be rationalized according to the mechanism depicted in **Scheme 1**. This mechanism also involves a hydroacylation step, which could be reproduced by the reaction of benzil and benzaldehyde catalyzed also by EMIM-Ac. Since in the process carbon dioxide has been suggested as oxidant, beyond the synthetic applicability of these reactions, their importance in environmental chemistry should also be emphasized.

Applying nanofiltration to reduce hardness of thermal water

András Király
e-mail:kiraly.andras@ch.bme.hu
Supervisor: Csilla Tonko
Department of Chemical and Environmental Process Engineering, BME
e-mail:tonko.csilla@kkft.bme.hu
Edit Cséfalvay
Department of Chemical and Environmental Process Engineering, BME
e-mail:csefalvay@kkft.bme.hu

Geothermal conditions are extremely favourable in Hungary. As a consequence of the lithospheric thinning the geothermal gradient is approximately 45˚C/km. In addition, thermal water is accessible on 70% of the territory of our country, at lowest temperature of 30˚C. In the light of these facts, the geothermal potential is above 60 PJ/year – which, from the point of view of energetics, can be utilized in two different ways: for supplying heat or generating electricity.

The energetic utilization of thermal water is determined by several parameters such as severe limit values for leaking thermal water into surface water, the legal obligation concerning reinjection of thermal water; and furthermore the problems deriving from the chemical composition of thermal water also present serious challenges. The present paper investigates the opportunities of preventing scaling by membrane technologies.

There are several methods in practise to control the scaling of calcium and magnesium ions [1, 2], but in this case the special properties of thermal water force us to keep its high temperature and apply a process avoiding the cooling of thermal water on the one hand, and on the other hand a process avoiding the formation of harmful by-products is required. Recently membrane technologies gain ground step by step. Out of the latter procedures, reverse osmosis (RO) and nanofiltration (NF) are the most suitable for water softening - in this study we investigate the applicability of NF.

The nanofiltration membranes are widely used in the field of watertreatment. There are studies available which deal with general softening and prove the effectiveness of this method. How-

ever, thermal water has special requirements in case of nanofiltration. NF has numerous advantages as opposed to other conventional technologies. On the basis of their separation mechanism, this method promises to be suitable for solving the problem of scaling.

Our measurements were performed on a Thin Film NF DK (GE Osmonics) membrane, thermostated at 50˚C and at a pressure of 35 bar with four different samples (from four Hungarian cities – Eger, Komárom, Mályi and Mezőkövesd) using batch plant (CM-CELFA Membrantechnik AG P-28). Experiments were carried out so far as the permeate yield reached 95%, so the initial water sample was concentrated to 5 (V/V)% of the initial. Besides water flux, the conductivity and the concentration of permeates and retentates were measured and analysed during the experiment by using ionchromatography (Column: Metrosep C3; eluent: 5 mmol/l HNO_3).

The results showed that NF DK could achieve the rejection of Ca^{2+} and Mg^{2+} approximately 90% and 80%, respectively. Besides a relatively high permeate flux ($\sim$252 l/m^2/h) we reached a 92%-rejection of Ca^{2+} and an 88%-rejection of Mg^{2+} in case of the thermal water from Komárom. The system also resulted in the reduction of the monovalent ions of Na^+ and K^+ up to 54% and 43%.

We examined the scaling properties of thermal water after the filtration with the help of a chemical equilibrium modelling software called Visual MINTEQ 3.0 (based on U.S. EPA's MINTEQA2 software). The results of the four samples' permeates proved that we have been successful in preventing scaling.

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The effect of curcumin on the processing stability of Phillips type polyethylene

Balázs Kirschweng

e-mail:shineing@gmail.com

Supervisors: Enikő Földes
Institute of Materials and
Environmental Chem.
Chemical Research Center,
Hungarian Academy of Sciences
e-mail:efoldes@chemres.hu
Dóra Tátraaljai
Laboratory of Plastics and Rubber Technology,
Department of Physical Chemistry
and Material Sciences, BME
e-mail:tatraaljai@mail.bme.hu

Polyethylene is one of the most widely used polymers, applied in many areas. The material is exposed to heat, shear, and a small amount of oxygen during processing. Without adequate stabilization this leads to degradation reactions: chain scission and/or extension, ultimately to the formation of a network, resulting in the deterioration of the mechanical properties. In practice, synthetic antioxidants are used to hinder these reactions, but several questions were raised regarding the effect of the reaction products of phenolic antioxidants on human health, which are still not answered. Therefore the interest is getting focused on the potential use of natural antioxidants. The aim of our work is to select some natural antioxidants, which can efficiently hinder the degradation of polyethylene during processing without any danger of possible health damage when dissolving from the polymer during application, and may even have some positive physiological effects. In this study the effect of curcumin was investigated and compared to that of the most commonly used phenolic antioxidant.

Tipelin FS 471 grade Phillips type additive-free polyethylene powder was provided by TVK, Hungary. The polymer was stabilized with 1000 ppm curcumin, and with a mixture of 1000 ppm curcumin + 2000 ppm P-EPQ. The neat polymer and samples processed with synthetic antioxidants (Irganox 1010 and Sandostab P-EPQ) used in the industry were studied for references. The polymer and the additives were homogenized in a high speed mixer, and extruded six times using a single screw extruder. Samples were taken after each extrusion step. The polymer was characterized by different methods: infrared spectroscopy; color, rheological (melt flow index, dynamic viscosity, creep compliance), and residual oxidative stability measurements, mechanical tests, as well as by optical microscopy.

The results show that curcumin is a more efficient processing stabilizer of polyethylene either alone or in combination with a secondary antioxidant than the hindered phenol used for reference. The drawback of curcumin is its coloring effect. The orange color of the polymer limits the area of its application.

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Luminescence study of Au(I) complexes of a new xantphos-type ligand

Éva Kunsági-Máté

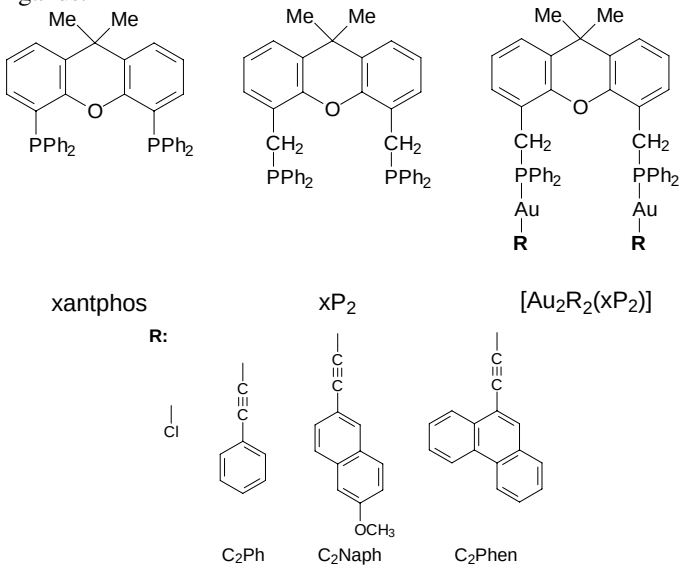
e-mail: kunsagievi@gmail.com

Supervisors: Miklós Kubinyi
Department of Physical Chemistry and
Material Science, BME
e-mail:kubinyi@mail.bme.h)
Péter Baranyai
Chemical Research Centre,
Hungarian Academy of Sciences
e-mail:barap@chemres.hu

The synthesis and study of organic gold compounds has become an important research field in the past few years, because their application offers many new possibilities on several scien-

tific fields (medical science: anti – rheumatoid arthritis and anti – tumour agents; materials science: luminescence materials). [1, 2]

The xantphos ligand is known from the literature. Its homologue, the 4,5-bis(diphenylphosphinomethyl)-9,9-dimethylxanthene (xP_2) is a new compound which has been synthetized in the framework of BME / CRC cooperation. Our goal was to compare the Au(I) complexes of the two types of ligands by luminescence studies. The complexes contained Cl and aromatic ethynyl (Ph, Naph, Phen) derivatives as other ligands.



The complexes were studied in solid and solution phase (solvent: CH_2Cl_2). The spectra were recorded using stationary and time resolved luminescence spectroscopy methods (TCSPC – time correlated single photon counting, measurement of phosphorescence decay). Beside fluorescence, we also observed phosphorescence in case of each complex in solid state at room temperature. In addition, the complexes with aromatic acetylene derivative ligands were phosphorescent also in solution.

The $[Au_2Cl_2(xantphos)]$ complex shows a bright orange luminescence with short lifetime [3, 4] in solid state, which is caused presumably by the presence of aurophilic interaction. By X-ray diffraction measurements, in the xP_2 analogue's chloro-complex the gold – gold distances are relatively large, in accord of which its luminescence spectra don't show any characteristic feature related to gold-gold interactions. The crystal structures of the Au(I) complexes with aromatic ethynyl type ligands have not been determined yet, their luminescence properties, however, suggest the presence of gold-gold interactions.

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Delocalization and dispersion errors of density functionals

Pál Dániel Mezei

e-mail:mezeipal@ch.bme.hu

Supervisor: Gábor István Csonka

Department of Inorganic and Analytical Chemistry

e-mail:csonkagi@gmail.com

Kohn-Sham density functional theory (DFT) [1] is currently one of the most commonly-used methods of electronic structure calculation in condensed matter physics and quantum chemistry. These methods introduce a quite efficient treatment of the electron correlation compared to the wave-function based configuration interaction methods. The remaining problem is that the exact form of the exchange-correlation functional is not known. Thus reasonably accurate approximate functionals have to be constructed. The performance of these approximate functionals must be tested by appropriate test databases. One such database is the general main group thermochemistry, kinetics, and noncovalent interactions (GMTKN30) [2] composed of 30 smaller subsets. In this paper we focus on the Diels-Alder reactions (DARC) subset.

We analyzed the DFT errors of reaction energies in the DARC subset, and found that some of the reactions produce systematically the same errors compared to the estimated coupled cluster CCSD(T)/complete-basis reference reaction energies taken from the literature. We thus showed that the DARC subset can be simplified. We also analyzed the basis set errors, and found an augmented triple-zeta basis set, denoted aug-cc-pVTZ(-f,-Hd), that approximates the basis-set limit DFT reaction energies within 1 kcal/mol error. This basis set is suitable for DFT benchmark calculations and it can replace the very expensive quadruple-zeta basis sets used in the earlier benchmarks. We show that increasing the weight of exact exchange component [3] in the global hybrid functionals, e.g., in the Perdew-Burke-Ernzerhof (PBE) hybrid, linearly changes the reaction energies and compensates the endothermic DFT reaction errors. However, the global mixing of exact exchange with DFT exchange adds a constant exothermic correction to DARC reactions, so it might increase the accuracy of the too-endothermic DFT reaction energies but it does not much increase the precision of the calculations. The PBE functional supplemented with double-damped dD10 dispersion correction improves not only the accuracy but also the precision of the results. These calculations are twice as fast as the corresponding global hybrid calculations. These improved results show that among the origins of the DFT errors are intramolecular dispersion interaction errors present in the various components of the DARC test set.

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Synthesis and reactions of optically active P-heterocycles

Dávidné Nagy

e-mail:keltatenger@gmail.com

Supervisor: György Keglevich
Department of Organic Chemistry
and Technology, BME
gkeglevich@mail.bme.hu

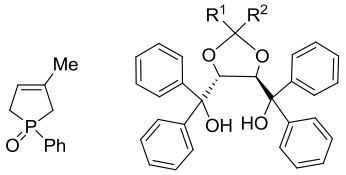
Consultants: Bagi Péter
Department of Organic Chemistry
and Technology, BME
pbagi@mail.bme.hu
Fogassy Elemér
Department of Organic Chemistry
and Technology, BME
efogassy@mail.bme.hu

Optically active P-derivatives are widely used in synthetic organic chemistry. Compounds containing P-asymmetric center cannot be found in the natural pool of chirality, so the primary source of enantiopure P-heterocycles is resolution and asymmetric synthesis.

Our research group found a convenient and efficient method for the resolution of 1-substituted-3-methyl-3-phospholene 1-oxides (**1**) using TADDOL-derivatives (**2**) or Ca^{2+}salts of (*R*,*R*)-dibenzoyl-tartaric acid (**3a**) and (*R*,*R*)-di-*p*-toluoyl-tartaric acid (**3b**). [1,2]

Based on the earlier results of our research a group resolution method was to developed for 1-propoxy-3-methyl-3-phospholene 1-oxide which was not available in optically active form.

We were the first who synthetised optically active dichlorocarbene adduct (**4**), 3- and 5- methyl-1-phenyl-4-chloro-1,2-dihidrophosphinine 1-oxide (**5**) and 1-phenyl-4-chloro-5-methyl-1,2,3,6-tetrahidrophosphinine 1-oxide (**6**). It was investigated whether the optically active six-membered P-heterocycles (**4-6**) should be prepared by resolution or by transformation of the corresponding optically active derivatives.



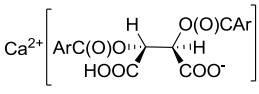
1

Y: aryl, alkyl,alkoxy

2

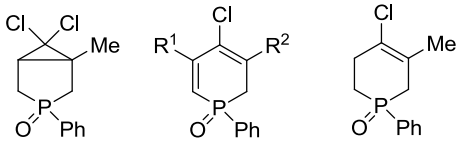
R^1, R^2 = Me, Me

R^1, R^2 =



3

Ar: Ph (**a**), 4-MePh (**b**)



4 **5** **6**

R^1	Me, H	(A)
R^2	H, Me	(B)

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Synthesis and study of enzyme-responsive amino acid-based hydrogels

Barnabás Szilágyi

e-mail: szilagyiba88@gmail.com

Supervisor: András Szilágyi
Department of Physical Chemistry
and Materials Science, BME
e-mail:aszilagyi@mail.bme.hu

Consultants: Árpád Némethy
Department of Physical Chemistry
and Materials Science, BME
e-mail:anemethy@mail.bme.hu
Anna Magyar
Research Group of Peptide
Chemistry, ELTE-MTA
e-mail:magyar@elte.hu

Effectiveness of therapeutic drugs can be improved significantly by controlled drug delivery, where changes of the internal parameters of the human body induce the liberation of the drug at a given time and place. Apart from the responsive abilities of the drug delivery system – most important parameters being pH, temperature and the presence of certain enzymes –, biocompatibility and biodegradability are indispensable properties when it comes to its medical application. Thus, an amino acid-based polymer gel as controlled drug delivery systems is a promising possibility [1].

In the first step polysuccinimide (PSI) was obtained by acid-catalyzed thermal polycondensation of L-aspartic acid [2], Succinimide rings make it possible to create a chemical gel by cross-linking polysuccinimide chains. The use of peptides composed of proteinogenic amino acids as cross-linkers is practical for our purposes. By alkaline hydrolysis of peptide-cross-linked PSI – resulting in a polyaspartic acid (PASP) hydrogel - an expectedly non-toxic gel composed solely of amino acids can be obtained. By enclosing a drug in such a gel matrix, its diffusion is blocked until a certain protease enzyme starts cleaving the cross-linker

peptides, resulting in the gel's degradation and the subsequent release of the drug. By choosing the corresponding amino acid sequence of the cross-linker peptide, the gel can be made specific to a protease enzyme. Thus, the location of the drug release can be optimized [3].

A tetrapeptide sequence containing a trypsin-specific cleavage site between the second (Lys) and the third (Phe) amino acid residues was chosen as the cross-linker. In order to perform the cross-linking reaction it is necessary to have free amino functions at both ends of the peptide molecule, which can react with succinimide rings in a nucleophilic ring-opening reaction. These are the αamino group of N-terminal phenylalanine and the εamino group of C-terminal lysine. In order to avoid side reactions during cross-linking, the side chain of the non-terminal lysine and the carboxylic function of C-terminal lysine must be protected. The tetrapeptide was prepared by liquid-phase synthesis using mixed anhydride coupling.

To synthesize the gel, polysuccinimide and tetrapeptide were dissolved in DMSO. Catalysts dibutylamine and phosphoric acid were added to the solution then gelation was carried out at 60˚C. The prepared gel was immersed in pH=8 buffer in order to hydrolyze unreacted succinimide rings to aspartate residues. Finally, the protecting group of the non-terminal lysine of the cross-linker was removed in pH=3 buffer.

In vitro cytotoxicity and cytostaticity assays were carried out on HepG2 (human hepatoma) and HT29 (human colon carcinoma) cell lines. The results of the assays showed that neither polyaspartate, nor the protected, nor the non-protected cross-linker peptide, nor the supernatant obtained by soaking the gel for five days were cytotoxic or cytostatic on the examined cell lines.

A preliminary experiment was carried out to prove the enzymatic degradability of the synthesized gel. A piece of the gel was immersed in trypsin solution and the degradation was observed by naked eye. Polyaspartate gels cross-linked with H-Phe-Lys-OMe and 1,4-diaminobutane were used as control samples. After 5,5 hours the examined gel had dissolved completely, while the control gels remained unaltered. Since the gels differed only in the type of the cross-linker used, it can be declared that the degradation of the examined gel took place due to the enzymatic cleavage of the trypsin-specific cross-linker.

In conclusion, a polymer gel composed solely of amino acid was prepared by cross-linking polysuccinimide with a tetrapeptide, followed by alkaline hydrolysis. According to experiments carried out so far, the synthesized gel is specifically degradable by trypsin and is non-toxic. In light of the results, the gel can be made suitable for controlled drug release.

Acknowledgement

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Upgrading of nitrogen removal by online control of a full-scale activated sludge wastewater treatment plant

Zsombor Vánkos

e-mail: zsomborvankos@gmail.com

Supervisors: Vince Bakos
e-mail:vbakos@mail.bme.hu
Department of Applied Biotechnology and Food Science, BME
Andrea Jobbágy
Department of Applied Biotechnology and Food Science, BME
e-mail:ajobbagy@mail.bme.hu

Consultant: Bence Márialigeti
e-mail:bence.marialigeti@bkszt.hu
BKSZT Ltd.

Through the accession to the European Union Hungary has to be suited for the new regulations regarding the strict limiting values for the treated effluent. Currently, one of the most important tasks is the extension of the treatment capacity for larger quantity of raw wastewater and the upgrading of wastewater treatment plants operating throughout the country. The activated sludge treatment technology is world-wide used, where a heterogeneous microbial community is applied for the biological carbon and nutrient removal. This technology is prevalent in Hungary as well, both for domestic and industrial wastewater treatment.

The aim of this study was the upgrading of the nitrogen removal with the use of nitrate recirculation and by online control and optimization of the aeration system in a full-scale activated sludge wastewater treatment plant. Nitrate recirculation was built up on the experimental biological train of the plant and the continuous analytical follow up of the full-scale experiment was ensured by ammonium and nitrate online sensors. Moreover, supplementary laboratory measurements were carried out from daily composite samples taken from the influent and effluent flows of the experimental train and also from those of the control train (operated simultaneously without nitrate recirculation). In accord to the online measurements, the laboratory results showed that denitrification efficiency can be highly increased by nitrate recirculation, and accordingly, the total nitrogen concentration in the effluent could be markedly reduced depending also on the aeration settings. At the same time, further investigations based on the continuously measured real-time ammonium and nitrate concentrations were implemented. The fine tuning of the current fixed time based aeration regulation, and the optimization of aeration by ammonium and nitrate

concentration control were carried out.

According to the results of this study, both the installation and use of nitrate recirculation and the optimization of aeration control system lead to cost-effective operation and result in markedly lower total nitrogen concentration in the treated effluent.