ÚOCHB AV ČR

ÚSTAV ORGANICKÉ CHEMIE A BIOCHEMIE
AKADEMIE VĚD ČESKÉ REPUBLIKY
INSTITUTE OF ORGANIC CHEMISTRY AND BIOCHEMISTRY
ACADEMY OF SCIENCES OF THE CZECH REPUBLIC

Institute of Organic Chemistry and Biochemistry

Academy of Sciences of the Czech Republic

VÝZKUMNÉ CENTRUM
UOCHB &
GILEAD SCIENCES

GSRC

GILEAD SCIENCES
& IOCB
RESEARCH CENTRE

Institute of Organic Chemistry and Biochemistry

Academy of Sciences of the Czech Republic

Zdeněk HAVLAS
Director

Iva PICHOVÁ
Deputy Director for Research

Božena PETSCHOVÁ
Deputy Director for Economics

Jiří ŠPIČKA
Deputy Director for the Campus Development

Contents

Introduction

Since 2007 the Institute has changed its legal form, being converted into a Public Research Institution, and also the internal organization changed. The new legal form brought more independence and responsibility. Following the legal requirements we have created a new body, the Board of the Institute. The governing body, the Academy of Sciences of the Czech Republic, named the Supervisory Board, which takes control of the main, mostly economical, decisions of Institute management. The internal hierarchy has been changed into a flat structure model, stressing the role of the scientific individualities, the team leaders. The new team leaders were selected in an international competition, following the Selection Committee recommendation and with the help of the International Advisory Board. There are three categories of the chairs, the Distinguished Professorship (A. Holý and P. Hobza), Senior Research Teams, and we were proud to establish new Junior Teams. Each team is supported by the Institute by providing a startup package, fixed salary resources, equipped laboratory space, and services. The steadily increasing scientific performance of the Institute proves that the changes were in the right direction.

Research at the Institute is broad and interdisciplinary, but can be grouped into six main orientations: medicinal chemistry, biochemistry and molecular biology, organic synthesis and material research, natural product chemistry, spectroscopy and physical organic chemistry, and computational chemistry. The research groups are supported by our service teams; some of whom are also doing research. The Institute gives considerably funding for scientific instruments and offers all equipment needed for an excellent level of research.

The Institute profits from its successes in medicinal chemistry. There are currently 15 drugs produced by various companies from patents held by the Institute. Royalties from patent licensing have filled our budget in the past, but our current royalties from the work of Prof. Holý group, licensed to Gilead Sciences in California, is exceptional. Licensing fees from Gilead Sciences currently represent more than 70% of the Institute's budget. It allows for financing of all the activities of the Institute, and also allows the Institute to save money for building reconstructions and for future use and development.

The Institute is also quite successful in receiving grant support. We are happy that our scientists can find help from our IOCB Grant Office, which was newly established in 2008. The Institute is proud of receiving prestigious ERC advanced grants (for the first time in the Czech Republic), awarded to Prof. Michl and Dr. Schröder.

The Institute invites dozens of excellent scientists and rising stars to present their lectures and to discus scientific topics within the frame of the Invited Lecture Series. As a side effect, the reputation of the Institute is growing.

During the last two years we have been working on a system to commercialize intellectual properties rising from the work at the Institute. The Institute's daughter company, IOCB TTO was recently established with the aim of helping our scientists protect their intellectual property and managing its commercialization, leaving the brains and hands of the scientists free for their scientific work. And inversely, the research aims of the Institute will profit from the efforts of IOCB TTO in future.

The Institute is intensively preparing for the complete remodeling of its campus. This will include construction of a new building devoted to organic synthetic laboratories and reconstruction of two existing buildings. We will start in fall 2009 with remodeling Building C, the GMO laboratories of biochemists. We will also include a new virology laboratory there for testing of our active compounds. Then, we will continue with construction of the new building, designed in a modern style, and later we will complete the reconstruction of our main building, called Building A. After completion, the Institute will be a modern, well equipped research institute. All these activities are paid for with royalties, thanks to the success of Professor A. Holý.

Since 2007 the employees of the Institute have been awarded several distinguished prizes. Professor Antonín Holý was awarded with several awards including an Honorary Professorship from the University of Manchester (UK), the title of "Česká hlava" which is a prize from the Czech Government, a prize from the Czech Literature Fund, an award from the Czech Learned Society, "De Scientia ac Pervestigation Optime Merits", and with Doctor Honoris Causa, awarded by the South Bohemia University. Professor Hobza was invited to present the Charles A. Coulson Lecture at the University of Georgia, Athens. Professor Pavel Hobza was awarded "Česká hlava", a year after Holý. Professor Pavel Jungwirth received the Royal Society of Chemistry Prize, Dr. Helena Kaiserová received a prize from the Minister of Education, and Dr. Jana Roithová received the Otto Wichterle Premium from the Academy of Sciences. This is only to mention a few of the more prestigious awards.

I believe that the future of the Institute looks quite bright. A good economic situation, excellent scientific output, steeply rising performance, inventions converted into innovations, reconstruction and remodeling, all of this fills me with optimism and pride.

In closing, I want to acknowledge the work of the team preparing this book, headed by our Public Relations representative Irena Krumlová, with the excellent help of Michal Hocek, Jakub Hošek, Michal Hoskovec and all teams of the Institute.

Zdeněk Havlas
Director of IOCB AS CR

A Brief History of IOCB...

After World War II, when university activities were renewed, a group of chemistry enthusiasts was formed at the Faculty of Chemicotechnological Engineering at the Czech Technical University under the leadership of Professor František Šorm.
In 1951, the group moved to the building at Flemingovo square, which was constructed between 1923 and 1929. The Central Chemical Institute was formed. An agricultural research in the building was replaced by the „aroma" of chemical experiments... The Institute was formally established on January 1, 1953. Its name was changed to the Institute of Organic Chemistry of the Czechoslovak Academy of Sciences.
The Institute has had many names:

- Institute of Technology of Organic and Explosive Substances
- Institute of Technology of Organic Substances
- Institute of Organic Technology (which still exists at the Institute of Chemical Technology)
- Central Chemical Institute
- Chemical Institute of the Czechoslovak Academy of Sciences (after 1955)
- Institute of Organic Chemistry and Biochemistry of the Czechoslovak Academy of Sciences (1960 – 1992)
- Institute of Organic Chemistry and Biochemistry of the Academy of Sciences of the Czech Republic (1993 – 2006)
- Institute of Organic Chemistry and Biochemistry of the Academy of Sciences of the Czech Republic, v.v.i. (since 2007)

The Institute was authorized to educate graduate students and to award the scientific titles of Candidate of Sciences (CSc., equivalent to PhD) and Doctor of Sciences (DrSc.). The Institute also carried out the first formal theses defenses in the country.
The greatest credit for establishing and developing the Institute belongs to Professor **František Šorm** who became the secretary general of the Academy of Sciences and later its President.

František Šorm (February 28, 1913 – November 18, 1980), was a Czech chemist recognized for synthesis of natural compounds, mainly terpenes and biologically active components found in plants. Šorm, the founder of our Institute, studied at the Faculty of Chemistry of the Czech Technical University (later Institute of Chemical Technology, VŠCHT) completing studies in 1936. During the Second World War, Šorm worked in a chemical laboratory. After the war he returned to the university, and in 1946 was named professor at the VŠCHT. In 1950 Šorm was named professor of organic chemistry at the Charles University in Prague. In 1952 Šorm became the director of the our institute. During 1962 – 69 he served as the second President of the Czechoslovak Academy of Sciences.
In the field of bioorganic chemistry, F. Šorm advanced the knowledge of sesquiterpenoids, medium-ring molecules, and explained the structure of different isoprenoid compounds. He also initiated the study of natural peptides, especially neurohypophyseal hormones and their analogues, some of which were shown to be of major clinical importance. His school of protein chemistry established the primary structure of chymotrypsin and trypsin. While studying the aminoacid sequence in polypeptide chains, Šorm, for the first time, deduced a tentative genetic code. His studies of antimetabolites of nucleic acid constituents as potential cancerostatics or virostatics led to the synthesis and determination of the mechanism of several highly active compounds, for example, 5-azacytidine and 6-azauridine. Finally, he was active in the field of insect juvenile hormones.
F. Šorm was the author or co-author over 1000 of papers and was highly cited. He also co-authored several chemistry textbooks.
The IOCB now awards a medal named after **František Šorm**. A minor planet (3993 Šorm) was named after him in 1988.

Scientific Activities of IOCB

The Institute carries out fundamental research in organic chemistry, biochemistry and related disciplines, focusing in particular on medical and environmental applications. It educates graduate students. It is the seat of the Committee for defence of doctor of science dissertations in organic and bio-organic chemistry.

The Institute has established a long-term cooperation with the American biopharmaceutical company, Gilead Sciences, which deals with research, development, and distribution of novel pharmaceuticals. The institute and the company established a joint research center on July 13, 2006.

Research Areas

Medicinal Chemistry – Provides excellent long-term results, the importance of which exceeds the boundaries of both the IOCB and the Academy of Sciences. Research focuses on the development of pharmaceuticals against leukemia and other cancers, as well as viral diseases such as AIDS and hepatitis.

Biochemistry and Molecular Biology – Deals in particular with the study of the structure and activity of enzymes (proteases), protein components of viruses and other pathogens (HIV, yeasts), and structure and activity of peptides and their analogs.

Organic Synthesis – Deals with general principles of preparation of substances, synthesis of functional molecules with properties suitable for the preparation of nano-materials and materials for molecular electronics and self-assembly.

Chemistry of Natural Products – Deals with the study of plant materials, searches for substances used for communication of insects, determines pheromones and other semiochemicals with subsequent utilization for pest control. Peptides with antibacterial activity are also studied.

Physical Chemistry – Performs organic and bioorganic structure determination by physical methods and studies the relationship between structure and physical properties.

Computational Chemistry – Uses quantum chemistry and molecular simulation to forecast the structure, reactivity, and properties of organic and bioorganic molecules.

Gilead Sciences & IOCB Research Centre

Gilead Sciences, Inc. is providing an annual donation of $1.1 million, for an initial period of five years, to the Institute of Organic Chemistry and Biochemistry (IOCB) for the establishment of the Gilead Sciences & IOCB Research Centre (GSRC). The establishment of the GSRC recognizes the Gilead continued partnership with IOCB and allows for expanded research efforts.
The donation is being used to establish and support the GSRC, which consists of selected research groups led by the scientists at IOCB. Gilead and IOCB have also established the Gilead Distinguished Chair in Medicinal Chemistry. Prof. Antonín Holý of the IOCB is the first to hold the position of Distinguished Chair and will continue to lead research efforts in nucleoside and nucleotide drug discovery. The donation allows IOCB to fund the prestigious Gilead Fellowship in Medicinal Chemistry for post-doctoral visitors and the Gilead Stipend for PhD students.
Gilead and IOCB have also entered into a separate arrangement through which Gilead will provide patent services to the IOCB.

Gilead's commitment to patients suffering from life-threatening diseases is one shared with colleagues at the IOCB, whom have enjoyed a longstanding relationship with Gilead. In 1991 and 1992, Gilead entered into license agreements with IOCB and the Rega Institute in Leuven, Belgium that cover a number of nucleotide analogue compounds, including cidofovir, tenofovir and adefovir. Since that time, three of these compounds have been successfully developed and are improving the quality of life for patients around the globe: Vistide for the treatment of CMV retinitis in patients with AIDS, Viread for the treatment of HIV and Hepsera for the treatment of chronic hepatitis B.

The research groups participating in GSRC

Synthesis and Medicinal Chemistry
A. Holý
M. Hocek

Biochemistry and Molecular Biology
I. Votruba
I. Pichová
J. Konvalinka

Molecular Modeling and Drug Design
L. Rulíšek
Z. Havlas

Centre for New Antivirals and Antineoplastics

Supported by the Ministry of Education, Czech Republic

This Centre was formed in order to facilitate research in the field of new antiviral and antineoplastic agents. The team of participating laboratories has been assembled to have complementary expertise and contains experts from various fields with proven track records and already established collaborations. This complex project addressing various issues of design, synthesis and testing of antiviral and cytostatic compounds and overcoming drug resistance requires a critical mass, both in terms of supplies and in terms of experienced research personnel that can only be achieved in a truly integrated research centre, supported by extensive international collaboration. The team of participating laboratories has been assembled to have complementary expertise and contains experts from various fields with a proven track record and already established collaborations. We therefore expect that the interactions of this group will not only provide an added value, but be truly synergistic.

The research in the field of new antiviral and cytostatic compounds has become one of the most competitive areas in recent years. Several recent spectacular successes of Czech medicinal chemistry provide solid background for further research activities in the field. However, without an integrated approach combining selected experts from core fields (medicinal chemistry, organic synthesis, biochemistry, molecular and cellular biology, molecular virology and oncology), individual groups will have little chance to stay competitive in larger international context.

During the course of the research, collaboration between individual groups of the proposed Centre will increase, thereby enhancing competitiveness. Through frequent communication, regular meetings, and active exchange of students and other research personnel, we intend to create a stimulating and supportive atmosphere, where information and ideas can flow freely. Such interaction increases productivity of laboratories not only through obvious synergy from shared information and reagents, but also in an indirect and subtle way by experiencing research cultures and practices of scientific groups from different laboratories from the Czech Republic.

Subjects participating in the Centre activities

- Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
- Charles University in Prague, Faculty of Science
- Charles University in Prague, Faculty of Pharmacy in Hradec Králové
- Institute of Experimental Medicine, Academy of Sciences of the Czech Republic

The research groups participating in the Research Centre

- Chemistry of nucleotide analogs (A. Holý)
- Metabolism of antimetabolites of nucleic acid components (I. Votruba)
- Organic Syntheses for Biomedicinal Applications (M. Hocek)
- Modified nucleosides (H. Hřebabecký)
- Biochemistry of Viral Proteins (I. Pichová)
- Transition Metal-Catalyzed Transformations (M. Kotora)
- Proteases of Human Pathogens (J. Konvalinka)
- DNA Tumor Viruses (J. Forstová)
- Natural Products and Drug Delivery (M. Pour)
- Drugs in Immunity (Z. Zídek)

Centre for Biomolecules and Complex Molecular Systems

Supported by the Ministry of Education, Czech Republic

The focus of the Centre is to further develop basic theoretical and experimental research of the energy and charge transfer in biomolecules and in complex molecular systems. The main aim is to create premier scientific and training will by coordinating and integrating its five subjects with other groups from EU, US, and other countries.

1. Institute of Organic Chemistry and Biochemistry

A team from the IOCB AS CR is the dominant and coordinating part of the Centre. Its scientific activities include theroretical, computational, and experimental study of the energy, electron, proton, and another ions transfer in biomolecules and complex molecular systems.

- Molecular Modelling, P. Hobza, see webpages of its individual members
- Organic Chemistry, I. Starý
- Proteases of Human Pathogens, J. Konvalinka
- Organic Syntheses for Biomedicinal Applications, M. Hocek

2. Institute of Chemical Technology

A team from ICT will investigate the interactions between molecules, atoms, and ions by the means of methods of statistical thermodynamics, statistical physics, and molecular modelling. The experimental part will cover the area of the drug design and synthesis, and it will study the charge transfer in DNA.

- Statistical Thermodynamics, A. Malijevský
- Molecular Recognition in Analytical Chemistry, V. Král

3. University of Pardubice

The experimental group from the University of Pardubice will study the properties and catalytical activity of metal ions in molecular sieves.

- Surface Effects and Heterogenous Catalysis, R. Bulánek

4. Palacký University in Olomouc

The subject of the theoretical research of the froup from Palackeho University in Olomouc is the study of the protein structure and dynamics, and of the nezyme reactions.

- Molecular Dynamics of Proteins, M. Otyepka

5. Institute of Physics

Laboratory at the Institute of Physics will study the dynamics of the charge transport by the means of ultrafast time-resolved terahertz spectroscopy.

- Terahertz Spectroscopy and Nonlinear Optics, P. Kužel

Distinguished Chairs

Antonín Holý

Gilead Distinguished Professor in Medicinal Chemistry & IOCB Distinguished Chair
e-mail: holy@uochb.cas.cz
www.uochb.cz/holy

Antimetabolites of Nucleic Acid Components

Nucleic Acid Chemistry is a traditional and continuously developing field of our Institute. The Department formed in the 60's around a group of scientists who studied the chemistry of nucleobases, nucleosides and oligonucleotides, and made principal contributions to the development of this field. Outstanding achievements of the past encompass original studies on 6-azapyrimidines and 5-azapyrimidines and their nucleosides which resulted in the discovery of potent antimetabolites (6-azauridine, 2'-deoxy-5-azacytidine), fundamental investigation on the mechanisms of nucleosidation reactions, sugar-modified nucleosides and transformation of nucleoside molecules. In the oligonucleotide chemistry, methods of chemical and enzymatic oligoribonucleotide synthesis were developed in this laboratory. Research in the Group traditionally combines development of novel biologically active compounds with the investigation of their metabolism and mode of action. It is based upon numerous joint investigations of different subjects in medicine: immunology, virology (studies on retroviruses, DNA viruses), antitumor and antileukemic studies, etc., both inside and outside the country. The tissue culture laboratory run by the Group performs the screening of the cytostatic activity *in vitro*.

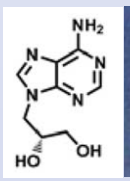
The present research in the Group concerns mainly the design and synthesis of analogues of nucleic acid components including modified nucleobases, nucleosides with modified sugar moiety, nucleotides with modified phosphomonoester linkage (acyclic nucleoside phosphonate analogues, ANP) and isolation of target enzymes, transport and metabolism studies of active compounds.

Current grant support

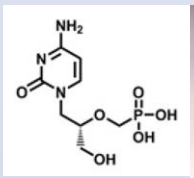
Academy of Sciences (1QS400550501), Ministry of Education, Youth and Sports (1M0508), Institute of Organic Chemistry and Biochemistry AS CR (Z40550506), National Institutes of Health U.S.A. (1UC1AI062540-01) and by Gilead Sciences, Inc.
(Foster City, U.S.A.).

Our approved drugs:

Duviragel™ (antiherpeticum)

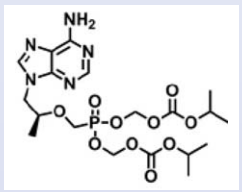


Vistide™ (cidofovir injection)

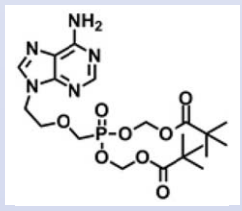


Organic chemistry part:
Antonin Holý, Prof., DSc, dr.h.c.mult./
Head of the Team/Gilead Distinguished Chair
Michal Česnek, PhD / Scientist
Dana Hocková, PhD / Scientist
Hubert Hřebabecký, PhD / Senior Scientist
Marcela Krečmerová, PhD / Scientist
Miroslav Otmar, PhD / Scientist
Karel Pomeisl, PhD / Scientist
Jindřich Fanfrlík, PhD / Postdoc
Ondřej Baszczyński, MSc / PhD Student
Jiří Blažek, MSc / PhD Student
Milan Dejmek, MSc / PhD Student
Petra Břehová, PhD / Postdoc
Radim Nencka, PhD / Postdoc
Martin Hrebíček, MSc / PhD Student
Šárka Chalupová, MSc / PhD Student
Petr Jansa, MSc / PhD Student
Michal Šála, MSc / PhD Student
Jaroslav Günter / Research Assistant
Lucie Čechová / Technicians
Yvetta Černá / Technicians
Julie Křelinová / Technicians
David Mařák / Technicians
Běla Nováková / Technicians
Jaroslava Sklenářová / Technicians
Barbara Česneková / Secretary

Viread™ (tenofovir disoproxil fumarate)



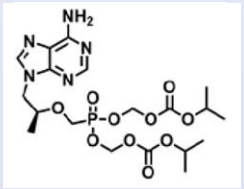
Hepsera™ (adefovir dipivoxil)



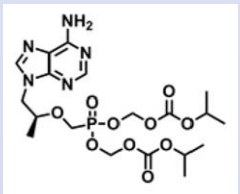
Antimetabolites of Nucleic Acid Components

Biochemistry part:
Ivan Votruba, DSc / Scientist
Viktor Cvilink, PhD / Postdoc
Helena Kaiserová, PhD / Postdoc
Marika Matoušová, PhD / Postdoc
Miroslav Hájek, PhD / Postdoc
Markéta Schinkmanová, PhD / Postdoc
Jana Günterová / Research Assistant
Květoslava Horská / Research Assistant
Romana Krejčová / Research Assistant
Eva Tloušťová / Research Assistant
Marie Marešová / Technicians
Karolína Müllerová / Technicians
Lenka Pohlová / Technicians
Dana Prášková / Technicians
Ludmila Tovčigrečko / Technicians

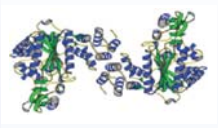
Truvada™ (emtricitabine and tenofovir disoproxil fumarate)



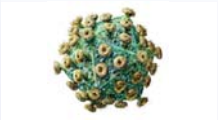
Atripla™ (efavirenz, emtricitabine and tenofovir disoproxil fumarate)



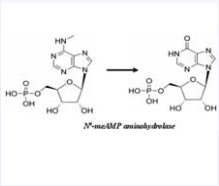
Systematic SAR activity study in this field further implicates the effect of various structural alterations at the purine heterocyclic base of the pharmacophore. For example, N-substitution of the exocyclic amino groups at purine bases exposed enhanced antiviral effects against cytomegaloviruses and herpes zoster viruses.



5-Substituted pyrimidines and related compounds will be synthesized with the aim to find novel thymidine phosphorylase inhibitors as potential anti-angiogenic agents for cancer chemotherapy.



The investigation of antiviral activities is performed in collaboration with the Rega Institute, Katholic University Leuven (Belgium) and with Gilead Sciences (USA). It focuses on identification of novel types of antivirals.



N^6-Methyl-AMP aminohydrolase – It was shown that this so far unknown enzyme catalyzes the hydrolytic deamination of natural substrates N^6-meAMP, N^6,N^6-dimethyl-AMP and N^6-medAMP to IMP and/or dIMP, respectively. This enzyme also efficiently converts N^6-substituted ANPs to the active guanine analogs, potential antineoplastic and antiviral agents.

Selected recent papers and patents

1. De Clercq, E.; Holy, A.: *Nature Reviews Drug Discovery* **2005**, 4(11), 928-940.
2. Krecmerova, M.; Holy, A.; Piskala, A.; Masojidkova, M.; Andrei, G.; Naesens, L.; Neyts, J.; Balzarini, J.; De Clercq, E.; Snoeck, R.: *J. Med. Chem.* **2007**, 50(5), 1069-1077.
3. Lebeau, I.; Andrei, G.; Krecmerova, M.; De Clercq, E.; Holy, A.; Snoeck, R.: *Antimicrobial Agents and Chemotherapy* **2007**, 51(6), 2268-2273.
4. Nencka, R.; Votruba, I.; Hrebabecky, H.; Jansa, P.; Tloustova, E.; Horska, K.; Masojidkova, M.; Holy, A.: *J. Med. Chem.* **2007**, 50(24), 6016-6023.
5. Cesnek, M.; Holy, A.; Masojidkova, M.; Kmonickova, E.; Zidek, Z.: *Bioorg. Med. Chem.* **2008**, 16(2), 965-980.
6. Holy, A.; Otmar, M.; Piskala, A.; Votruba, I.; Kovarik, A.; Fojtova, M.; Bartova, E.: *PCT Int. Appl.* **2008**, WO 2008083634.
7. Holy, A.; Otmar, M.; Piskala, A.: *PCT Int. Appl.* **2008**, WO 2008101448.
8. Schinkmanová, M.; Votruba, I.; Holý, A.: *Biochem. Pharmacol.* **2006**, 71, 1370-1376

Pavel Hobza

IOCB Distinguished Chair, Computational Chemistry
e-mail: pavel.hobza@uochb.cas.cz
www.uochb.cz/hobza

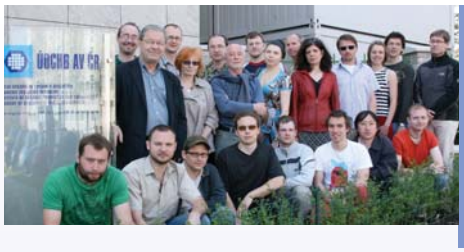
Benchmark Quantum Chemical Calculations on Complexes of Biomolecular Building Blocks

Non-covalent interactions play an important role in the structure determination of biomolecules and consequently their biological function. The double-helical structure of DNA which is prerequisite for its biological function (storage and transfer of genetic information) results from these interactions among DNA bases, sugars, phosphates and surrounding waters. Similarly, the protein folding (the process leading to protein native structure which fulfill the protein function), one of the most important biological process, is to a high degree affected by non-covalent interactions among aminoacid side-chains and aminoacid side-chains and backbone. Theoretical description of non-covalent interactions represents one of the most difficult tasks of the nowadays computational chemistry. Highly accurate methods covering the correlation (dispersion) energy should be applied. Since biological processes occur in a water environment and at room temperature, it is necessary to pass from a static (quantum mechanical) description to a dynamic description realized by molecular dynamic (MD) simulations. Highly accurate description of dynamic processes is obtained by performing the "on-the-fly" *ab initio* MD simulations.

Current research includes theoretical studies of non-covalent interactions in general, hydrogen bonding and improper blue-shifting hydrogen bonding, the role of dispersion energy in biomacromolecules and nanostructures and in protein folding, benchmark calculations on interaction energies and geometries of extended molecular complexes, development and/or modification of computational methods suitable for the prediction of non-covalent interactions in biomolecules, "on-the-fly" ab initio molecular dynamic simulations of bioprocesses, and, recently, docking and drug design. Intensive cooperation with experimental (chemically and biologically oriented) as well as theoretical groups was established.

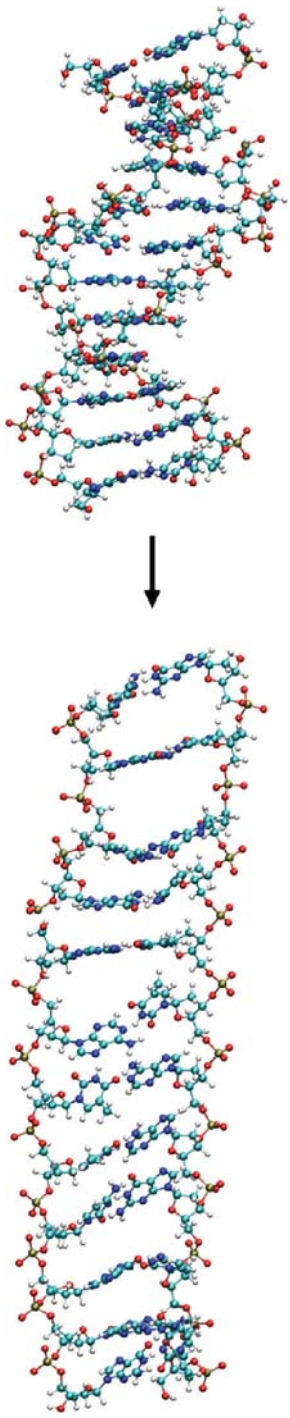
Current grant support

Academy of Sciences (Z40550506), Ministry of Education, Youth and Sports (LC512, Prof. Hobza is the pricipal investigator), Academy of Sciences (Praemium Academiae awarded to Prof. Hobza in 2007).



Hobza Pavel, Prof., DSc, FRSC / Head of the Team
Bludský Ota, PhD
Kabeláč Martin, PhD
Lankaš Filip, PhD
Lischka Hans, Prof.
Nachtigall Petr, Assoc. Prof.
Nachtigallová Dana, PhD
Špirko Vladimír, PhD, DSc
Šponer Jiří, Prof., DSc
Vondrášek Jiří, PhD
Bronowska Agnieszka, PhD / Postdoc
Martin Korth, PhD / Postdoc
Pitoňák Michal, PhD / Postdoc
Ran Jiong, PhD / Postdoc
Řezáč Jan, PhD / Postdoc
Berka Karel, MSc / PhD Student
Kysilka Jiří, MSc / PhD Student
Přenosil Ondřej, MSc / PhD Student
Rubeš Miroslav, MSc / PhD Student
Zelený Tomáš, MSc / PhD Student
Brettlová Pavlína, Bc / Student
Gráfová Lucie, Bc / Student
Kolář Michal, Bc / Student
Pecina Adam, Bc / Student
Pluháčková Kristýna, Bc / Student
Sedlák Róbert, Bc / Student
Vymětal Jiří, Bc / Student
Fačkovec Boris / Student
Hostaš Jiří / Student
Držata Tomáš / Student
Černá Helena / Research Assistant
Polách Jiří / Technician

Molecular Dynamics (MD) Simulations and "On-the-fly" MD Simulations on Biomacromolecules; Drug Design



Structure of DNA if the dispersion energy is covered (above) and if this energy is not considered (below)

Selected recent papers

1. Pitonak, M.; Neogrady, P.; Cerny, J.; Grimme, S.; Hobza, P. "Scaled MP3 Non-Covalent Interaction Energies Agree Closely with Accurate CCSD(T) Benchmark Data" *ChemPhysChem.* **2009**;10(1):282-289.
2. Cerny, J.; Kabelac, M.; Hobza, P. "Double-Helical -> Ladder Structural Transition in the B-DNA is Induced by a Loss of Dispersion Energy" *Journal of the American Chemical Society.* **2008**;130(47):16055-16059.
3. Valdes, H.; Spiwok, V.; Rezac, J.; Reha, D.; Abo-Roziq, A.G.; de Vries, M.S.; Hobza, P. "Potential-energy and free-energy surfaces of glycyl-phenylalanyl-alanine (GFA) tripeptide: Experiment and theory" *Chemistry-a European Journal.* **2008**;14(16):4886-4898.
4. Vondrasek, J.; Kubar, T.; Jenney, F.E. Adams, M.W.W.; Kozisek, M.; Cerny, J.; Sklenar, V.; Hobza, P. "Dispersion interactions govern the strong thermal stability of a protein" *Chemistry-a European Journal.* **2007**;13(32):9022-9027.
5. de Vries, M.S.; Hobza, P. "Gas-phase spectroscopy of biomolecular building blocks" *Annual Review of Physical Chemistry.* **2007**;58:585-612.
6. Jurecka, P.; Sponer, J.; Cerny, J.; Hobza, P. "Benchmark database of accurate (MP2 and CCSD(T) complete basis set limit) interaction energies of small model complexes, DNA base pairs, and amino acid pairs" *Physical Chemistry Chemical Physics.* **2006**;8(17):1985-1993.
7. Vondrasek, J.; Bendova, L.; Klusak, V.; Hobza, P. "Unexpectedly strong energy stabilization inside the hydrophobic core of small protein rubredoxin mediated by aromatic residues: Correlated ab initio quantum chemical calculations" *Journal of the American Chemical Society.* **2005**; 127(8): 2615-2619.
8. Jurecka, P.; Hobza, P. "True stabilization energies for the optimal planar hydrogen-bonded and stacked structures of guanine center dot center dot center dot cytosine, adenine center dot center dot center dot thymine, and their 9-and 1-methyl derivatives: Complete basis set calculations at the MP2 and CCSD(T) levels and comparison with experiment" *Journal of the American Chemical Society.* **2003**;125(50):15608-15613.
9. Hobza, P.; Havlas, Z. "Blue-shifting hydrogen bonds" *Chemical Reviews.* **2000**;100(11):4253-4264.
10. Muller-Dethlefs, K.; Hobza P. "Noncovalent interactions: A challenge for experiment and theory" *Chemical Reviews.* **2000**;100(1):143-167.

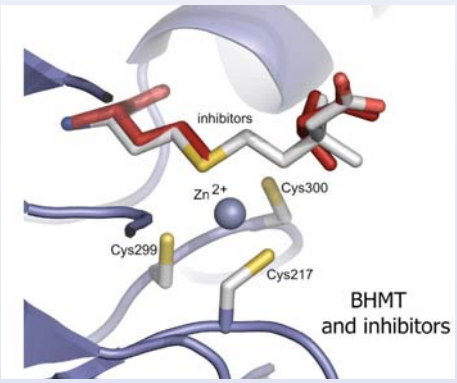
Research Teams

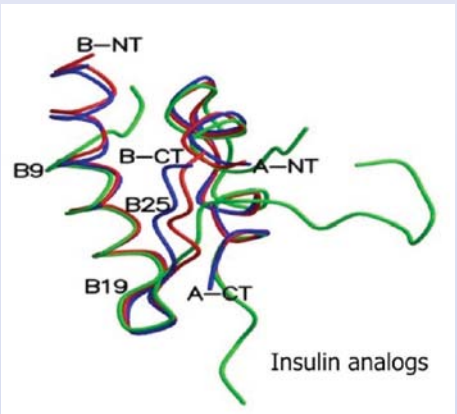
Jiří Jiráček

Senior research team in Biochemistry and Molecular Biology
e-mail: jiracek@uochb.cas.cz
www.uochb.cz/jiracek

Biological Chemistry for the Study of Living Systems

Jiří Jiráček, PhD / Head of the Team
Lenka Maletínská, PhD / Scientist
Irena Selicharová, PhD / Scientist
Blanka Železná, PhD / Scientist
Michaela Collinsová, PhD / Postdoc
Jan Pícha, PhD / Postdoc
Václav Vaněk, PhD / Postdoc
Lenka Žáková, PhD / Postdoc
Emília Antolíková, MSc / PhD Student
Jana Maixnerová, MSc / PhD Student
Resha Matyšková, MSc / PhD Student
Jana Mládková, Bc / Student
Jitka Viková / Technician
Hedvika Vysušilová / Technician





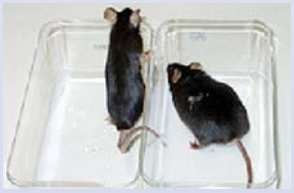
The research of our group is of a strongly multidisciplinary character and its core activities are designed to rationally employ the tools of advanced organic synthesis in modern biochemical, biological and pharmacological strategies for the study of living systems and for the development of biologically active compounds. Our group has several different research projects: (i) Design, synthesis and biological characterization of **inhibitors for betaine-homocysteine S-methyltransferase (BHMT)**, an important mammalian enzyme involved in the synthesis of methionine from homocysteine in liver and kidney. (ii) Synthesis and biological characterization of new **insulin analogs**, which may help in better understanding of the interaction of insulin with its receptor and in the treatment of diabetes. (iii) We use **2D-electrophoresis** for the identification of protein markers in various cell lines (normal, cancer, inhibitor-treated etc.). (iv) Our research is also focused on peptides such as CART (cocaine and amphetamine regulated transcript) peptide or ghrelin involved in the **regulation of food intake** and processes related to obesity. This project aims at elucidating the regulatory pathways and relationship of peptides involved in feeding related processes, both *in vivo* and *in vitro*.

Current grant support

Academy of Sciences (Z40550506), Ministry of Education, Youth and Sports (LC06077), Grant Agency of the ASCR (KJB400550702) and Czech Science Foundation (303/09/0744).

Selected recent papers

1. Selicharová, I., Smutná, K., Šanda, M., Ubik, K., Matoušková, E., Buršíková, E., Brožová, M., Vydra, J., Jiráček, J. "Two-dimensional electrophoretic analysis of a new human cell line EM-G3 derived from breast cancer progenitor cells and comparison with normal mammary epithelial cells" *Proteomics* **2007,** *7*, 1549-1559.
2. Žáková, L., Hančlová, I., Kazdová, L., Protivínská, E., Šanda, M., Buděšínský, M., Jiráček, J. (2008) "Insulin analogs with modifications at position B26. Divergence of binding affinity and biological activity" *Biochemistry* **2008**, *47*, 5858-5868.
3. Maletínská, L., Maixnerová, J., Matyšková R., Haugvicová, R., Pirník, Z., Kiss, A., Železná, B. "Synergistic effect of CART (cocaine- and amphetamine-regulated transcript) peptide and cholecystokinin on food intake regulation in lean mice" *BMC Neurosci.* **2008**, *9*, 101.
4. Pícha, J., Buděšínský, M., Šanda, M., Jiráček, J. "Synthesis of norlaucine-derived phosphonopeptides" *Tetrahedron Lett.* **2008**, 49, 4366
5. Liboska, R., Pícha, J., Hančlová, I., Buděšínský, M., Šanda, M., Jiráček, J. "Synthesis of methionine- and norleucine-derived phosphinopeptides" *Tetrahedron Lett.* **2008**, 49, 5629



Lean and obese C57Bl mice

Jan Konvalinka

Senior research team in Biochemistry and Molecular Biology
e-mail: konval@uochb.cas.cz
www.uochb.cz/konvalinka

Proteases of Human Pathogens

In our laboratory we identify and study different enzymes as possible targets for therapeutic intervention. Currently, we work on three different enzymes. The first one, an already well established pharmaceutical target, is ***HIV protease***. We study the structure, function, and inhibition of this enzyme, as well as the development of antiviral resistance in AIDS patients treated by protease inhibitors.
Another target is ***glutamate carboxypeptidase II***, a membrane-bound peptidase expressed in a number of tissues, including the brain and prostate. In the human brain it plays an important role in several pathological processes (stroke, diabetic neuropathy, Alzheimer's disease, *etc.*). Inhibitors of this enzyme might serve as neuroprotectants or potential anticancer drugs.
The newest member in our project portfolio is ***serine racemase*** from human brain. This project includes analysis of the unexpected role of D-amino acid in the central nervous system. In all the projects, we clone, express, and characterize recombinant proteins, develop activity assays, identify novel substrates and inhibitors of the enzymes, and (in collaborations) analyze the 3-D structures of these pharmacologically relevant proteins.

Current grant support

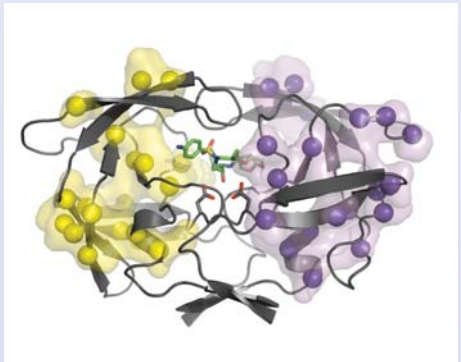
6th framework of the EU (contract No. 037693), 7th framework of the EU (projects HEALTH-2007- 201095 and HEALTH-2007-2.3.2-1), Ministry of Education, Youth and Sports (1M0508, LC512) and Gilead Sciences, Inc. (Foster City, USA)

Selected recent papers

1. Nijhuis, M. *et al*. "A Novel Substrate Based HIV-1 Protease Inhibitor Drug Resistance Mechanism". *PloS Medicine* **2007**, *4*, 152-163
2. Šácha, P. *et al*. "Expression of Glutamate Carboxypeptidase II in Human Brain" *Neuroscience* **2007**, *144,* 1361-1372
3. Hlouchová, K. *et al*. "Biochemical characterisation of human glutamate carboxypeptidase III" *J. Neurochem.* **2007,** *101*, 682-696.
4. Kožíšek, M. *et al*. "Molecular analysis of the HIV-1 resistance development: enzymatic activities, crystal structures, and thermodynamics of nelfinavir-resistant HIV protease mutants" *J. Mol. Biol.* **2007,** *374*, 1005–1016
5. Bařinka, C. *et al.* "Structural Basis of Interactions between Human Glutamate Carboxypeptidase II and Its Substrate Analogs" *J. Mol. Biol*. **2008,** *376*, 1438-1450.
6. Kožíšek, M., Grantz Šašková, K. *et al.* "Ninety Nine is Not Enough: Molecular Characterization of Inhibitor Resistant HIV-1 Protease Mutants with Insertions in the Flap Region" *J. Virol.* **2008,** *82*, 5869-5878
7. Kožíšek, M. *et al.* "Inorganic Polyhedral Metallacarborane Inhibitors of HIV Protease: A New Approach to Overcoming Antiviral Resistance" *J. Med. Chem.* **2008,** *51,* 4839-4843.

Human embryonal kidney cells expressing GCPII (immunohistochemistry using specific monoclonal antibody GCP05 and fluorescein-labelled secondary antibody)

Jan Konvalinka, PhD / Head of the Team
Jan Závada, MSc / Scientist
Dan Andersson, PhD / Postdoc
Taťána Majerová, PhD / Postdoc
Klára Grantz Šašková, MSc / PhD Student
Klára Hlouchová, MSc / PhD Student
Hillary Hoffman, BA / PhD Student
Jana Jirásková, MSc / PhD Student
Milan Kožíšek, MSc / PhD Student
Václav Navrátil, MSc / PhD Student
Pavel Šácha, MSc / PhD Student
Tomáš Knedlík, MSc / PhD Student
Michal Navrátil / PhD Student
Jana Pokorná / Research Assistant
Karolína Šrámková / Research Assistant
Jakub Began / Student
František Sedlák / Student
Jiří Schimmer / Student
Michal Svoboda / Student
Jan Tykvart / Student
Jitka Krčmářová / Technician
Jana Starková / Technician



X-ray structure of highly mutated resistant variant of HIV protease prepared from an AIDS patient. Mutations are depicted by coloured circles (structure determined and artwork prepared by Pavlina Rezacova, IOCB).

Michael Mareš

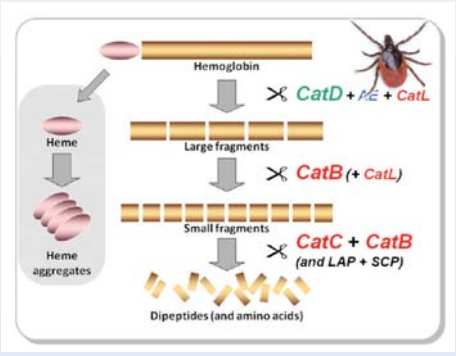
Senior research team in Biochemistry and Molecular Biology

e-mail: mares@uochb.cas.cz

www.uochb.cz/mares

Cathepsin Proteases in Pathology

Michael Mareš, PhD / Head of the Team
Martin Horn, PhD / Postdoc
Lucie Marešová, PhD / Postdoc
Martina Nussbaumerová, PhD / Postdoc
Jana Pytelková, MSc / PhD Student
Adéla Jílková, MSc / PhD Student
Martin Máša, MSc / PhD Student
Milana Štajfová, MSc / PhD Student
Iva Žebrakovská, MSc / PhD Student
Zuzana Kovářová, Bc / Student
Jindřich Srba, Bc / Student
Irena Pražáková / Technician



Cathepsins and hemoglobin digestion in ticks.

X-ray structure of schistosomal cathepsin B with a lead inhibitor.

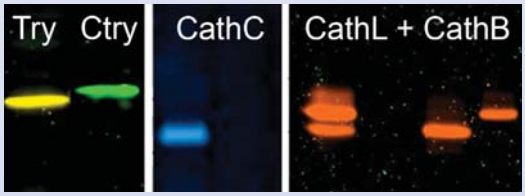
Cathepsins are critical for the metabolism and performance of important human parasites. Our research focuses on the molecular mechanisms of cathepsin-mediated processes using biochemical and proteomics approaches. (A) In **blood-feeding parasites**, cathepsins function as digestive proteases that degrade hemoglobin, a key nutrient from the host blood. Thus, cathepsins represent a pharmacological target for suppression of parasite metabolism. We investigate two blood-feeding parasites: (i) *Schistosoma* helminths are the causal agent of **schistosomiasis**, which afflicts more than 250 million people. Our research concentrates on drug design of schistosomal cathepsin inhibitors. (ii) *Ixodes* ticks are the vectors of **encephalitis and Lyme borreliosis**; we characterize hemoglobinolytic cathepsins applicable in the development of molecular anti-tick vaccines. (B) Allergens produced by dust and storage mites are a major contributor to the rising incidence of allergic diseases such as bronchial asthma or atopic dermatitis. We identify mite-derived cathepsins as novel allergens and investigate their inhibition as a potential strategy for regulation of **allergic hypersensitivity**.

Current grant support

Academy of Sciences (Z40550506), Grant Agency of the ASCR (IAA400550705, IAA400550617, KJB400550516), Grant Agency of the CR (206/06/0865), and by the Sandler Foundation (USA).

Selected recent papers

1. Pytelková, J.; Hubert, J.; Lepšík, M.; Šobotník, J.; Šindelka, R.; Křížková, I.; Horn, M.; Mareš, M. "Digestive α-amylases of the flour moth Ephestia kuehniella – adaptation to alkaline environment and plant inhibitors" *FEBS J.* **2008**, accepted
2. Sojka, D.; Franta, Z.; Horn, M.; Hajdušek, O.; Caffrey, C.R.; Mareš, M.; Kopáček, P. "Profiling of proteolytic enzymes in the gut of the tick Ixodes ricinus reveals an evolutionarily conserved network of aspartic and cysteine peptidases" Parasit. Vectors **2008**, 1, 7.
3. Hubert, J.; Hýblová, J.; Münzbergová, Z.; Pekár, S.; Kudlíková, I.; Dolečková-Marešová, L.; Stejskal, V.; Mareš M. "Combined effect of antifeedant α-amylase inhibitor and predator Cheyletus malaccensis in controlling the stored mite pest Acarus siro" Physiol. Entomol. **2007**, 32, 41-49.



Imaging of mite cathepsins with synthetic active-site probes.

Iva Pichová

Senior research team in Biochemistry and Molecular Biology
e-mail: iva.pichova@uochb.cas.cz
www.uochb.cz/pichova

Microbial Proteins

Research in this laboratory is mainly focused on the role of proteins involved in different steps of the life cycle of retroviruses and on the molecular pathogenesis of yeast species of the yeast genus *Candida.*

Our long-term goal in **retrovirus** research is to contribute to the knowledge of the mechanisms of retroviral assembly, maturation, and integration. Current projects are centered on understanding how the structure motifs of viral proteins contribute to the architecture of the viral particles. HIV, Mason-Pfizer monkey virus (M-PMV) and Mouse mammary tumor virus (MMTV) are employed as models for these studies. We use molecular genetics, biochemical, and structural approaches to define functions of viral proteins and to identify cellular components involved in these processes.

In ***Candida*** research, our laboratory is interested in understanding the role of secreted aspartic proteases (Saps) of *Candida albicans*, *parapsilosis,* and *tropicalis* in a variety of cellular processes ranging from metabolism to host-pathogen interactions. We intend to identify and characterize factors influencing the SAP gene regulation, intracellular trafficking, protein structure, and enzymologic properties of Saps by using molecular, microbial, and biochemical methods.

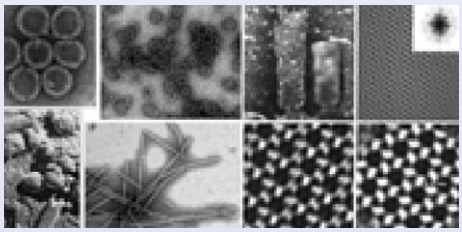
Current grant support

ESF and Czech Science Foundation (SCO/06/E001,), Ministry of Education, Youth and Sports (1M0508, LC531), EU STREP scrInSilico, and Gilead Sciences, Inc. (Foster City, USA).

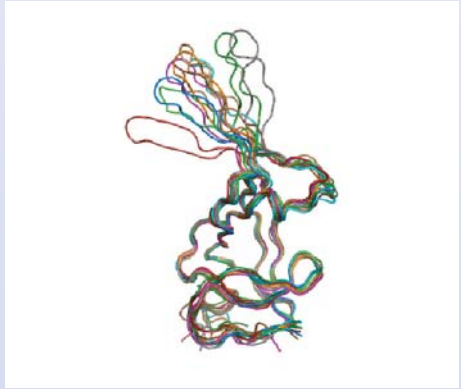
Selected recent papers

1. Zábranská, H., Tůma, R., Kluh, I., Svatoš, A., Ruml, T, Hrabal, R, Pichová, I. **2007**. The Role of the S-S Bridge in Retroviral Protease Function and Virion Maturation. *J. Mol. Biol.* 365, 1493 – 1504.
2. Wildová, M., Hadravová, R., Štokrová, J., Křížová, I., Ruml, T., Hunter, E., Pichová, I., Rumlová, M. (corresponding authors) 2008. The effect of point mutations within the N-terminal domain of Mason-Pfizer monkey virus capsid protein on virus core assembly and infectivity. **2008**. *Virology*. 380, 157 – 163.
3. Vlach, J., Lipov, J., Rumlová, M., Veverka, V., Lang, J., Srb, P., Pichová, I., Hunter, E., Hrabal, R., and Ruml, T. **2008**. D-retrovirus morphogenetic switch driven by the targeting signal accessibility to Tctex-1 of dynein. *PNAS* 105, 10565-10570.
4. Hrušková-Heidingsfeldová O. **2008**. Secreted proteins of Candida albicans. *Front Biosci.* 13, 7227-7242.
5. Matoušková, P., Luxová, A., Matoušková, J., Jiroš, P., Svatoš, A., Valterová, I., and Pichová, I. **2008**. A delta9 desaturase from Bombus lucorum males: Investigation of the biosynthetic pathway of marking pheromones. *Chembiochem* 9, 2534-152541.

Iva Pichová, PhD / Head of the Team
Olga Hrušková, PhD / Scientist
Michaela Rumlová, PhD / Scientist
Petra Matoušková, MSc / PhD Student
Marcela Wildová, MSc / PhD Student
Zuzana Vinterová, MSc / PhD Student
Václava Bauerová, MSc / PhD Student
Karolína Bohmová, MSc / PhD Student
Dagmar Grundová / Technician
Darina Horňáková, MSc / PhD Student
Michal Doležal, MSc / PhD Student
Jiří Dostál, PhD / Postdoc
Romana Cubínková / Technician
Aleš Zábranský, PhD / Scientist
Helena Zábranská, PhD / Scientist
Jan Snášel, PhD / Postdoc
Ivana Křížová / Research Assistant
Romana Hadravová / Research Assistant
Elena Dolejší / Technician
Mária Čechová / Research Assistant



In vitro assembly of M-PMV truncated Gag



NMR structure of M-PMV protease monomer

Zdeněk Havlas

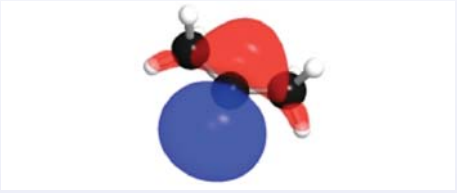
Senior research team in Computational chemistry

e-mail: havlas@uochb.cas.cz

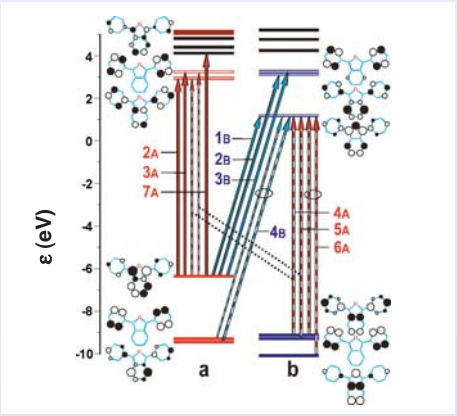
www.uochb.cz/havlas

Theoretical Chemistry

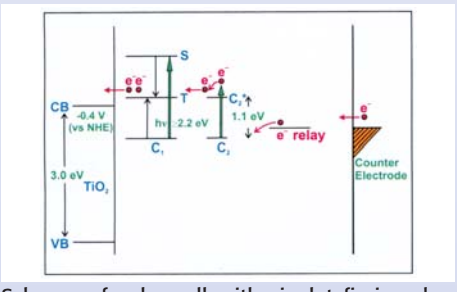
Zdeněk Havlas, DSc / Head of the Team
Mojmír Kývala, PhD / Scientist
Jakub Chalupský, MSc / PhD Student



σ-orbital of the CH_3-X-CH_3 biradical, for which the zero-field splitting was calculated.



$S_0 \rightarrow S_x$ electronic excitations in 1,3-diphenylisobenzofuran, a model for study of the singlet fission mechanism. Orbital scheme and excitations were calculated at the CC2/TZVPP level.



Scheme of solar cell with singlet fission dye. Ideally, from each photon two electrons are produced.

The research team deals with quantum-chemical investigation of selected properties of mainly organic molecules as well as with the development of methods for their calculation. First, we are interested in spin-dependent relativistic effects like spin-orbit coupling, spin-spin coupling or parity-violation coupling. These are responsible for various phenomena comprising zero-field splitting, radiative and radiationless spin-forbidden transitions or tiny differences between electronic-state energies of enantiomers. The focus is on predicting photophysical and photochemical properties of synthetically or biologically relevant molecules. Next, the team is involved in the project concerning the improvement of the efficiency of the titanium dioxide based solar cells. We study the possibility of a singlet fission mechanism in excited organic dyes. After conversion of the first excited singlet state of a dye into a pair of triplets, the dye can, in principle, inject two electrons into the crystalline titanium dioxide thus enhancing the efficiency of the solar cell by a factor of two. Last but not least, we are also engaged in predicting the pKa values of nucleotides in their aqueous solutions. We use the method COSMO-RS, the combination of the quantum chemical dielectric continuum solvation model COSMO with a statistical thermodynamics treatment for realistic solvation simulations.

Current grant support

Academy of Sciences (Z40550506), Ministry of Education, Youth, and Sports (ME09114, LC512) and by Gilead Sciences, Inc. (Foster City, U.S.A.)

Selected recent papers

1. Srnec M., Chalupský J., Fojta M., Zendlová L., Havran L., Hocek M., Kývala M., Rulíšek L.: Effect of spin-orbit coupling on reduction potentials of octahedral ruthenium(II/III) and osmium(II/III) complexes. *J. Am. Chem. Soc.* **2008,** *130*, 10947-10954.
2. Kožíšek M., Svatoš A., Buděšínský M., Muck A., Bauer M.C., Kotrba P., Ruml T., Havlas Z., Linse S., Rulíšek L.: Molecular design of specific metal-binding peptide sequences from protein fragments: Theory and experiment. *Chem. Eur. J.* **2008,** *14,* 7836-7846.
3. Babiak P., Němcová A., Rulíšek L., Beier P.: On the miscibility of ethers and perfluorocarbons an experimental and theoretical study. *J. Fluor. Chem.* **2008,** *129*, 397-401.
4. King B.T., Körbe S., Schreiber P.J., Clayton J., Němcová A., Havlas Z., Vyakaranam K., Fete M.G., Zharov I., Ceremuga J., Michl J.: The sixteen $CB_{11}H_nMe_{12-n}$ anions with fivefold substitution symmetry: Anodic oxidation and electronic structure. *J. Am. Chem. Soc* **2007,** *129*, 12960-12980.
5. Havlas Z., Kývala M., Michl J.: Spin-orbit coupling in biradicals. 5. Zero-field splitting in triplet dimethylnitrenium, dimethylphosphenium and dimethylarsenium cations. *Mol. Phys.* **2005,** *103*, 407-411.

Pavel Jungwirth

Senior research team in Computational Chemistry
e-mail: pavel.jungwirth@uochb.cas.cz
www.uochb.cz/jungwirth

Molecular Simulations of Proteins, Peptides, Membranes, and Self-assembled Monolayers in Aqueous Solutions

With molecular resolution, we model structure and chemical dynamics of finite pieces of matter (clusters, nanodroplets, systems with extended surfaces, solvated biomolecules, membranes, etc.). Our aim to unravel fundamental aspects of ion solvation in anisotropic and inhomogeneous environments. The systems under investigation range from the surfaces of aqueous droplets to solution/protein interfaces. Using molecular dynamics simulations and quantum chemical methods we are attempting to establish the mechanisms which drive ions to these interfaces and to one another. These specific ion effects have been observed since the late 1800s and termed lyotropic (Hofmeister) series, but only now is it becoming feasible to investigate the molecular forces involved with atomic detail. Applications of our reserach range from protein precipitation/denaturation and controlling enzymatic activity to establishing properties of phospholipid bilayers. Our related research activities concern modeling aqueous interfaces relevant for atmospheric chemistry and physics, and electron solvation, pertinent to radiation chemistry and DNA damage.

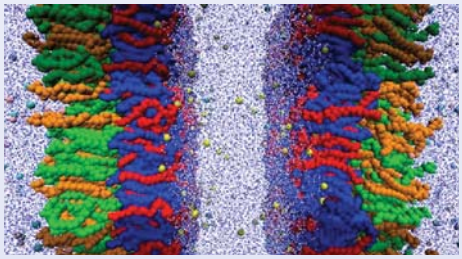
Current grant support

Czech Science Foundation (203/08/0114), Ministry of Education, Youth, and Sports (LC 512), and the FP-7 program Euromembranes.

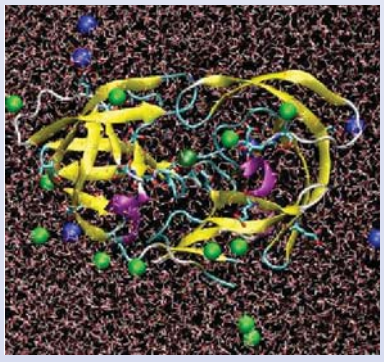
Selected recent papers

1. Ions at aqueous interfaces. Faraday Discussions, **2009**, 141, 9.
2. Lund, M.; Vrbka, L.; Jungwirth, P.: Specific Ion Binding to Non-Polar Surface Patches of Proteins. *Journal of the American Chemical Society*, **2008**, 130, 11582.
3. Lund, M.; Jungwirth, P.; Woodward, C. E.: Ion Specific Protein Assembly and Hydrophobic Surface Forces. *Physical Reviews Letters*, **2008**, 100, 258105.
4. Buch, V.; Milet, A.; Vacha, R.; Jungwirth, P.; Devlin, J. P.: Water surface is acidic. *Proceedings of the National Academy of Sciences*, **2007**, 104, 7342.
5. Vrbka, L.; Vondrasek, J.; Jagoda-Cwiklik, B.; Vacha, R.; Jungwirth, P.: Quantification and rationalization of the higher affinity of sodium over potassium to protein surface. *Proceedings of the National Academy of Sciences*, **2006**, 103, 15440.

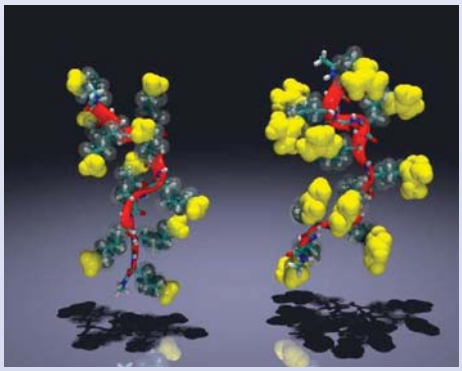
Pavel Jungwirth, Assoc. Prof., DSc / Head of the Team
Martina Roeselová, PhD / Scientist
Eric Wernersson, PhD / Postdoc
Milan Szori, PhD / Postdoc
Robert Vácha, MSc / PhD Student
Jan Heyda, MSc / PhD Student
Ondřej Maršálek, MSc / PhD Student
Michal Petrov, MSc / PhD Student
Eva Pluhařová / Student
Jiří Polách, MSc / System Manager
Helena Černá, MSc / Secretary



Molecular model of a cellular membrane



HIV protease in a salt solution



Structures of polylysine and polyarginine in water

Lubomír Rulíšek

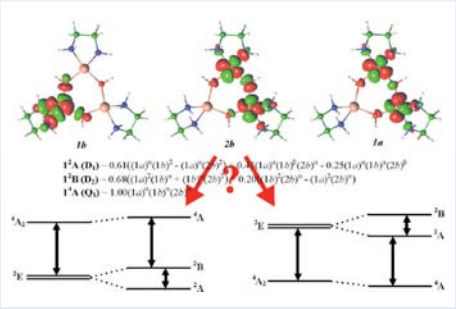
Junior Research Team in Computational Chemistry

E-mail: rulisek@uochb.cas.cz

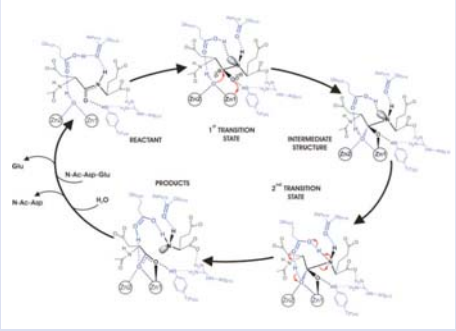
www.uochb.cz/rulisek

Theoretical Bioinorganic Chemistry

Lubomír Rulíšek, PhD / Head of the Team
Martin Lepšík, PhD / Postdoc
Martin Srnec, MSc / PhD Student
Vojtěch Klusák, MSc / PhD Student
Ivana Beššeová, MSc / PhD Student
Ondrej Gutten, Bc / Student
Václav Navrátil, Bc / Student



Multi-reference calculations correlated with the spectroscopic data for the two key reaction intermediates in the reduction of O_2 to H_2O by the multicopper oxidases.



The GCPII reaction cycle obtained by combining QM/MM calculations with experimental data.

Metalloproteins are one of the essential elements in biocatalysis. Combining experimental and theoretical efforts may eventually lead to understanding their structure and function fully. In the Theoretical Bioinorganic Chemistry group, we explore, develop and use the combined quantum mechanics/molecular mechanics (QM/MM) calculations with the quantum core described by standard DFT methods or even by multireference methods to unravel the reaction mechanisms of metalloproteins, namely metallopeptidases, multi-copper oxidases, superoxide dismutases, and desaturases. Our computational data are always correlated with the experimental (mostly spectroscopic) data and thus we obtain an insight into the catalytic action of these interesting systems. This accumulated experience is also used in the area of biomaterial design, such as novel metal-binding peptide sequences.

Current grant support

Academy of Sciences (Z40550506), Ministry of Education, Youth, and Sports (LC512), Grant Agency of the ASCR (IAA400040802) and by Gilead Sciences, Inc. (Foster City, U.S.A.).

Selected recent papers

1. Srnec, M.; Chalupský, J.; Fojta, M.; Zendlová, L.; Havran, L.; Hocek, M.; Kývala, M.; Rulíšek, L.: Effect of Spin-Orbit Coupling on Reduction Potentials of Octahedral Ruthenium (II/III) and Osmium (II/III) Complexes. *J. Am. Chem. Soc.* **2008**, *130*, 10947-10954.
2. Kožíšek, M.; Svatoš, A.; Buděšínský, M.; Muck, A.; Bauer, M. C.; Kotrba, P.; Ruml, T.; Havlas, Z.; Linse, S.; Rulíšek, L.: Molecular Design of Specific Metal-Binding Peptide Sequences from Protein Fragments. Theory and Experiment. *Chem. Eur. J.* **2008**, *14*, 7836-7846.
3. Valdés, H.; Klusák, V.; Pitoňák, M.; Exner, O.; Starý, I.; Hobza, P.; Rulíšek, L.: Evaluation of the Intramolecular Basis Set Superposition Error in the Calculations of Larger Molecules: [n]Helicenes and Phe-Gly-Phe Tripeptide. *J. Comput. Chem.* **2008**, *29*, 861-870.
4. Malkov, A. V.; Ramírez-López, P.; Biedermannová, L.; Rulíšek, L.; Dufková, L.; Kotora, M.; Zhu, F.; Kočovský, P.: On the Mechanism of Asymmetric Allylation of Aldehydes with Trichloroallylsilanes Catalyzed by Quinox, a Chiral Isoquinoline N-Oxide. *J. Am. Chem. Soc.* **2008**, *130*, 5341-5348.
5. Klusák, V.; Bařinka, C.; Plechanovová, A.; Mlčochová, P.; Konvalinka, J.; Rulíšek, L.; Lubkowski, J.: Reaction Mechanism of Glutamate Carboxypeptidase II Revealed by Mutagenesis, X-ray Crystallography and Computational Methods. *Biochemistry* **2009**, *48*, 4126-4138.

Ullrich Jahn

Senior Research Team in Natural Products Chemistry
e-mail: jahn@uochb.cas.cz
www.uochb.cz/jahn

Organic Synthesis, Total Synthesis

Total synthesis of relevant natural products is indispensable for the investigation of their formation, the understanding of their biological function and the design of analogs that may have a favorable therapeutic potential. To access such compounds as efficiently as possible, we develop tandem reactions based on oxidative electron transfer that is basically the bridge between different intermediate types and their reactivity patterns. This requires that fundamental questions concerning the mechanism and scope of such processes must be answered. Our oxidative domino processes allow the flexible use of multiple intermediate types in the individual sequence steps. This is inspired by Nature where complex natural products are often assembled by reaction cascades with an unprecedented efficiency. In this respect, we are especially interested in the chemistry and biochemistry of autoxidatively formed lipid metabolites, of alkaloids, lignans and terpenes. The biological properties of the synthesized natural products are evaluated, and synthetic analogs of them are derived and this requires the development of another new methodology again.

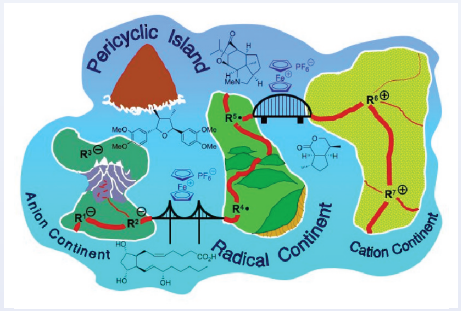
Current grant support

Czech Science Foundation (203/09/1936), Academy of Sciences (Z40550506)

Selected recent papers

1. U. Jahn, E. Dinca „Total Synthesis of 15-F_{2t}-Isoprostane Using a New Oxidative Cyclization of Distonic Radical Anions as the Keystep„ *Chem. Eur. J.* **2009**, *15*, 58-62.
2. U. Jahn, T. Durand, J.-M. Galano „Beyond Prostaglandins Chemistry and Biology of Cyclic Oxygenated Metabolites from Polyunsaturated Fatty Acids Formed by Free-Radical Pathways" *Angew. Chem. Int. Ed.* **2008**, *47*, 5894-5955.
3. U. Jahn, D. Rudakov „Tetrahydrofuran Lignans via Tandem Oxidative Anionic-Radical Processes or Reductive Radical Cyclizations" *Org. Lett.* **2006**, *8*, 4481-4484.

Ullrich Jahn, PhD / Head of the Team
Leigh Ford, PhD / Postdoc
Yvonne Kavanagh, PhD / Postdoc
Bertrand Puget, PhD / Postdoc
František Kafka, MSc / PhD Student
Tanja Lau, MSc / PhD Student
Petr Šebesta, MSc / PhD Student
Pratap Jagtap, MSc / Research Assistant
Alexandre Pichavant, MSc / Research Assistant



Václav Čeřovský

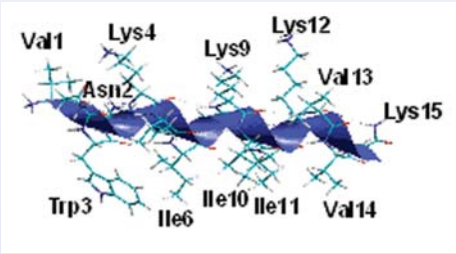
Senior research team in Natural Products Chemistry

e-mail: cerovsky@uochb.cas.cz

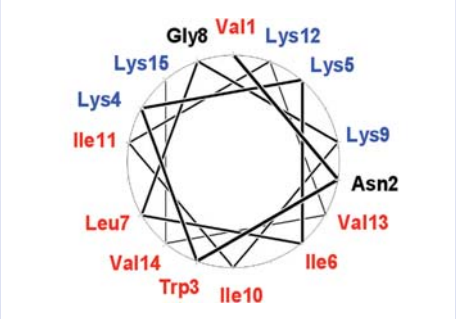
www.uochb.cz/cerovsky

Novel Antimicrobial Peptides Isolated from Insects

Václav Čeřovský, PhD / Head of the Team
Jiřina Slaninová, PhD / Scientist
Jan Hlaváček, PhD / Scientist
Vladimír Fučík, PhD / Scientist
Lenka Monincová, MSc / PhD student
Petr Niederhafner, MSc / PhD student
Rudolf Ježek, MSc
Lenka Borovičková, MSc
Hana Hulačová / Technician
Jitka Čermáková / Technician
Malgorzata Plačkova / Technician



α-helical structure of lasioglossin III, the antimicrobial peptide which we isolated from the venom of the wild bee *Lasioglossum laticeps* (lateral view).



In a helical wheel projection lasioglossin III shows a hydrophobic sector with hydrophobic amino acids residues (red) on one side of the α-helix and hydrophilic sector (black and blue) dominated by five cationic Lys residues (blue) on the opposite side. α-helical antimicrobial peptides adopt such a secondary structure within the bacterial cell membrane which is important for their antimicrobial action.

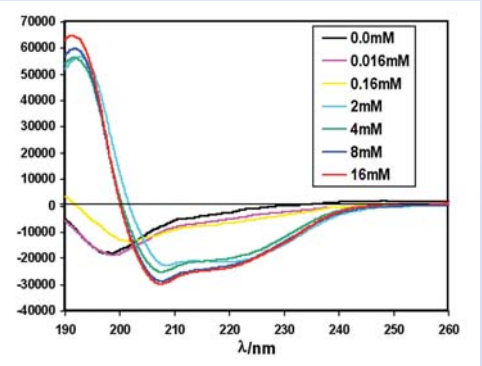
The growing resistance of pathogenic bacteria to conventional antibiotics has resulted in a search for new classes of antimicrobial agents with different modes of action than those of traditional antibiotics. Antimicrobial peptides (AMPs) identified in almost all forms of life offer new possibilities for developing drugs against resistant bacteria. We isolated and characterized novel AMPs from the venom reservoirs of Hymenoptera (wasps, bees, bumblebees, ants) and from the secretion of blowfly larva *Lucilia sericata*. Following the determination of peptide sequences by the methods of Edman degradation and mass spectrometry, the peptides were synthesized and tested for antimicrobial potency against Gram-positive and – negative bacteria, and for the toxicity to eukaryotic cells. Some of these peptides have cytostatic effect on different cancer cells and antifungal activity. Depending on the results of bioassays we have modified the structure of peptides to produce synthetic analogs with improved qualities in an effort to use them for the treatment of bacterial pathogens such as methicillin resistant *Staphylococcus aureus*. The secondary structures of these peptides were studied by CD-spectroscopy and NMR in the environment that mimics bacterial cell membrane. This was done in order to get insight into their mechanism of action.

Current grant support

Grant No. 203/08/0536 of the Czech Science Foundation, Research project No. Z40550506 of the Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic

Selected recent papers

1. Čeřovský V., Slaninová J., Fučík V., Hulačová H., Borovičková L., Ježek R., Bednárová L. New potent antimicrobial peptides from the venom of Polistinae wasps and their analogs *Peptides* **2007**, 29, 992-1003.
2. Čeřovský V., Hovorka O., Cvačka O., Voburka Z., Bednárová L., Borovičková L., Slaninová J., Fučík V. Melectin: Novel antimicrobial peptide from the venom of the cleptoparasitic bee Melecta albifrons. *ChemBioChem* **2008**, 9, 2815-2821.



UV-CD spectra of lasioglossin III in water and in the presence of various concentrations of SDS. The appearance of two minimum bands at 207 and 221 nm in the spectra reveals its α-helical structure at the concentration of SDS above 0.16 mM.

Irena Valterová

Senior research team in Natural Products Chemistry
e-mail: irena@uochb.cas.cz
www.uochb.cz/valterova

Chemical Ecology of Social Insects

The goal of the team is to deepen the understanding of the chemical ecology in two ecologically and economically important groups of social insects – bumblebees and termites. Using multidisciplinary approaches, combining analytical chemistry (two-dimensional gas chromatography/mass spectrometry, MALDI-TOF) with biology (electroantennography, scanning and transmission electron miscroscopy, bioassays) and molecular biology, the following topics are addressed: chemistry and biochemistry of lipids in relation to production of insect infochemicals; ontogenesis of the pheromonal glands as well as biosynthetic pathways of pheromone formation and enzymes involved; chemistry of male marking pheromone in bumblebees; pheromonal communication in termites, i.e. trail-following pheromones, alarm pheromones, sexual pheromones, primer pheromones involved in caste regulation; chemistry and biosynthesis of termite defensive substances.

Current grant support

Academy of Sciences of CR (Z40550506), Ministry of Education, Youth and Sports (2B06007, KONTAKT ME 860), Czech Science Foundation (203/09/1446, 203/09/1327, 525/08/1179), Grant Agency of the ASCR (IAA600550614).

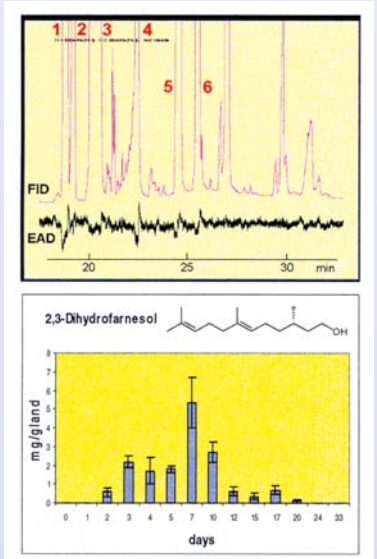
Selected recent papers

1. Šobotník, J., Kalinová, B., Cahlíková, L., Weyda, F., Ptáček, V., Valterová, I. "Age-dependent changes in structure and function of the male labial gland in *Bombus terrestris*." *J. Insect Physiol.* **2008**, *54*, 204-214.
2. Cvačka, J., Kofroňová, E., Vašíčková, S., Stránský, K., Jiroš, P., Hovorka, O., Kindl, J., Valterová, I. "Unusual Fatty Acids in the Fat Body of the Early Bumblebee *Bombus pratorum*." *Lipids* **2008,** *43*, 441-450.
3. Matoušková, P., Luxová, A., Matoušková, J., Jiroš, P., Svatoš, A., Valterová, I., Pichová, I. "A Δ9 desaturase from *Bombus lucorum* males: Investigation of biosynthetic pathway of marking pheromones." *ChemBioChem* **2008,** *9*, 2534-2541.
4. Piskorski, R., Hanus, R., Vašíčková, S., Cvačka, J., Šobotník, J., Svatoš, A., Valterová, I. "Nitroalkenes and sesquiterpene hydrocarbons from the frontal gland of three *Prorhinotermes* termite species." *J. Chem. Ecol.* **2007**, *33*, 1787-1794.
5. Šobotník, J., Hanus, R., Kalinová, B., Piskorski, R., Cvačka, J., Bourguignon, T., Roisin, Y. "(*E,E*)-α-Farnesene, an alarm pheromone of the termite *Prorhinotermes canalifrons*. *J. Chem. Ecol.* **2008,** *34*, 478-486.

Bombus lucorum males

Prorhinotermes simplex soldier

Irena Valterová, Assoc. Prof., PhD / Head of the Team
Michal Hoskovec, PhD / Scientist
Blanka Kalinová, PhD / Scientist
Aleš Svatoš, PhD / Scientist
Jan Šobotník, PhD / Scientist
Marie Zarevúcka, PhD / Scientist
Robert Hanus, PhD / Postdoc
Oldřich Hovorka, PhD / Postdoc
Anna Jirošová, PhD / Postdoc
Jiří Kindl, PhD / Postdoc
David Sillam-Dussès, PhD / Postdoc
Jana Dolejšová, MSc / PhD Student
Pavel Jiroš, MSc / PhD Student
Edita Kofroňová, MSc / PhD Student
Lucie Vaníčková, MSc / PhD Student
Klára Urbanová, MSc / PhD Student
Petr Žáček, MSc / PhD Student
Irena Červená, MSc. / Technician
Jana Mašková / Technician
Anna Nekolová / Technician
Jarmila Titzenthalerová / Technician



Electrophysiologically active compounds in the pheromonal gland of *B. terrestris* males (a) and quantitative changes in the content of 2,3-dihydrofarnesol, the main gland component in males of different age (b).

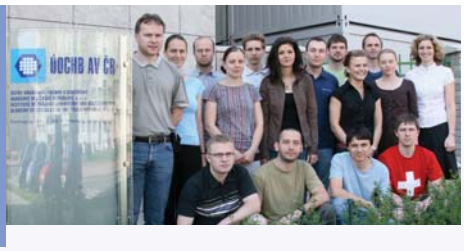
Michal Hocek

Senior research team in Bioorganic & Medicinal Chemistry

e-mail: hocek@uochb.cas.cz

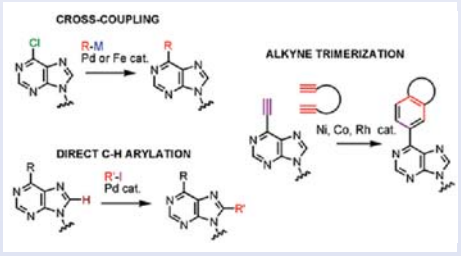
www.uochb.cz/hocek

Bioorganic Chemistry of Base-modified Nucleosides, Nucleotides and Nucleic Acids

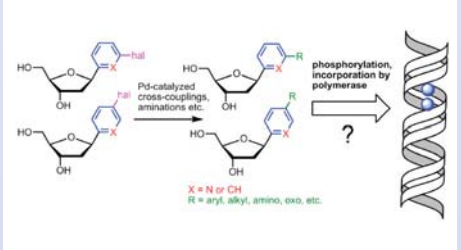


Michal Hocek, Assoc. Prof., DSc / Head of the Team
Hubert Chapuis, PhD / Postdoc
Robert Musiol, PhD / Postdoc
Petr Nauš, PhD / Postdoc
Jan Bárta, MSc / PhD Student
Igor Čerňa , MSc / PhD Student
Miroslava Čerňová, MSc / PhD Student
Zbyněk Hasník, MSc / PhD Student
Lubica Kalachová, MSc / PhD Student
Tomáš Kubelka, MSc / PhD Student
Hana Macíčková Cahová, MSc / PhD Student
Veronika Raindlová, MSc / PhD Student
Jan Riedl, MSc / PhD Student
Pavla Spáčilová, MSc / PhD Student
Martin Štefko, MSc / PhD Student
Satu Ikonen, MSc / Visiting PhD student
Kamila Havlíčková / Technician

Martin Kotora, Prof., PhD
Barbara Eignerová, MSc / PhD Student
Pavel Turek, MSc / PhD Student



Approaches to modification of purines and nucleosides



Modular synthesis of C-nucleosides and applications.

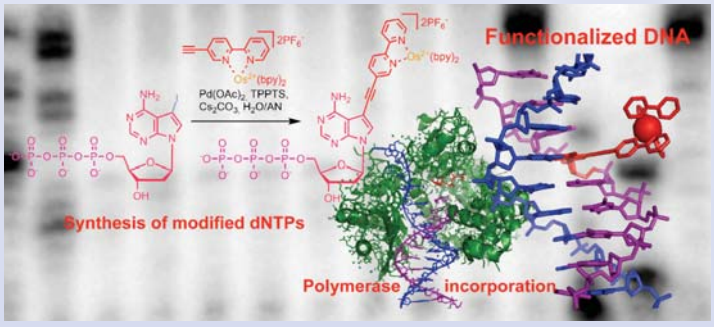
Novel types of modified derivatives and analogues of nucleobases, nucleosides, nucleotides and nucleic acids are designed and prepared for applications in all areas of biomedicinal sciences. Basic developments of methodology for the synthesis of purine nucleobases and nucleosides are performed largely using modern metal-catalyzed cross-coupling, C-H arylation and cyclotrimerization reactions. Cytostatic and antiviral activity of the novel compounds is systematically studied in collaboration with the pharmaceutical industry. Several collaborative projects address the chemical biology of nucleic acids (i.e. development of modular synthesis of C-nucleosides and study of DNA polymerase specificity and fidelity). The newest project deals with the polymerase construction of functionalized nucleic acids bearing diverse useful substituents and their applications in bioanalysis (e.g. diagnostics of mutations of DNA), chemical biology and nanotechnology. Appointed to this group is also independent *Laboratory of Prof. M. Kotora* (Charles University Prague) working in the field of applications organometallics in organic synthesis of natural products.

Current grant support

Academy of Sciences (Z40550506), Ministry of Education, Youth and Sports (1M0508, LC512, LC06077), Czech Science Foundation (203/09/0317), Grant Agency of the ASCR (IAA40040901, IAAA400550902) and by Gilead Sciences, Inc. (Foster City, U.S.A.).

Selected recent papers

1. Joubert, N.; Pohl, R.; Klepetářová, B.; Hocek, M. „Modular and Practical Synthesis of 6-Substituted Pyridin-3-yl C-Nucleosides" *J. Org. Chem.* **2007**, *72*, 6797-6805.
2. Čapek, P.; Cahová, H.; Pohl, R.; Hocek, M.; Gloeckner, C.; Marx, A. „An efficient construction of functionalized DNA bearing amino acid groups by cross-coupling reactions of nucleoside triphosphates followed by primer extension or PCR" *Chem. Eur. J.* **2007**, *13*, 6196-6203.
3. Cahová, H.; Havran, L.; Brázdilová, P.; Pivoňková, H.; Pohl, R.; Fojta, M.; Hocek, M. „Aminophenyl- and Nitrophenyl-Labeled Nucleoside Triphosphates. Synthesis, Enzymatic Incorporation and Electrochemical Detection" *Angew. Chem. Int. Ed.* **2008**, *47*, 2059-2062.
4. Hocek, M.; Fojta, M. „Cross-coupling reactions of nucleoside triphosphates followed by polymerase incorporation. Construction and applications of base-functionalized nucleic acids" *Org. Biomol. Chem.* **2008**, *6*, 2233-2241.
5. Čerňa, I.; Pohl, R.; Klepetářová, B.; Hocek, M. „Synthesis of 6,8,9-Tri- and 2,6,8,9-Tetrasubstituted Purines by a Combination of the Suzuki Cross-coupling, N-Arylation and Direct C-H Arylation Reactions." *J. Org. Chem.* **2008**, *73*, 9048-9054.



Polymerase construction of functionalized DNA

Ivan Rosenberg

Senior research team in Bioorganic & Medicinal Chemistry
e-mail: ivan@uochb.cas.cz
www.uochb.cz/rosenberg

Structurally Diverse Phosphonate Nucleotides and Oligonucleotides

The Group's principal interest consists in the synthesis and the biological and physico-chemical evaluation of novel, structurally diverse nucleoside phosphonic acids and corresponding phosphonate oligonucleotides containing isopolar *P-C* bridging internucleotide linkages. The main goals that we pursue, in general, are in bringing a new quality into the area of nucleoside/nucleotide antimetabolites, oligonucleotides interfering with gene expression, and those influencing natural cellular defence mechanisms.

More specifically, our research is aimed at the synthesis of
(i) nucleoside phosphonic acids with respect to their potential inhibition properties of important enzymes of the metabolism of nucleosides, nucleotides, and nucleic acids (thymidine, uridine and purine nucleoside phosphorylases, 5′ – nucleotidases, HCV and RSV RNA dependent RNA polymerase, and other polymerases),
(ii) chimeric phosphonate oligonucleotides in the *ribo* and *deoxyribo* series to evaluate the nuclease resistance, hybridization properties in connection with antisense effect, ability to elicit RNase H activity, cellular uptake, *etc.*, and
(iii) oligodeoxynucleotides with CpG motifs and short 5′ – phosphorylated 2′ – 5′ oligoadenylates containing isopolar phosphonate linkages as potential agonists/antagonists of TLR9 and ribonuclease L, respectively.

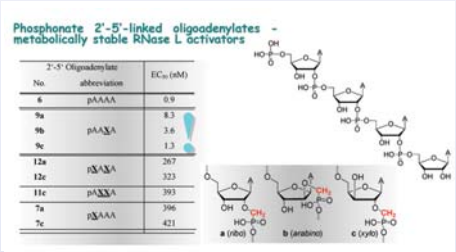
Current grant support

Academy of Sciences CR (Z40550506), Grant Agency of ASCR (KAN200520801), Czech Science Foundation (203/09/0820, 202/09/0193), Ministry of Education, Youth and Sports (LC06077, LC06061), 6th FW (EMIL – Centre of Excellence).

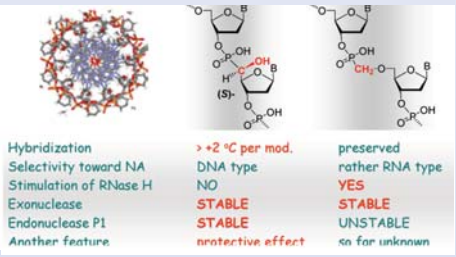
Selected recent papers

1. Rejman, D., Kočalka, P., Buděšínský, M., Barvík Jr., I., Rosenberg, I.. Stereospecific N-oxide-mediated monoprotection of trans-3,4-dihydroxypyrrolidine derivatives. *Tetrahedron Assymetry* **2007**, *18*, 2165-2174.
2. Točík, Z., Dvořáková, I., Buděšínský, M., Masojídková, M., Liboska, R., Rosenberg, I.. Electrophile-promoted addition of hydroxymethylphosphonate to 4′, 5′-didehydronucleosides: A way to novel isosteric analogues of 5′-nucleotides. *Tetrahedron* **2007**, *63*, 4516–4534.
3. Rejman, D., Kočalka, P., Buděšínský, M., Pohl, R., Rosenberg, I.. Synthesis of diastereomeric 3-hydroxy-4-pyrrolidinyl derivatives of nucleobases. *Tetrahedron*, **2007**, *63*, 1243-1253.
4. Páv, O., Barvík, I., Buděšínský, M., Masojídková, M., Rosenberg, I.. Ring Enlargement of Cyclic Acetals and Ketals: A Way to Seven-Membered Nucleoside Phostones. *Organic Letters* **2007**, 5469-5472.

Ivan Rosenberg, PhD / Head of the Team
Zdeněk Točík, PhD / Deputy of Team Head
Radek Liboska, PhD / Scientist
Magdalena Petrová, PhD / Scientist
Dominik Rejman, PhD / Scientist
Ivana Košiová, PhD / Postdoc
Natalya Panova, PhD / Postdoc
Ondřej Šimák, PhD / Postdoc
Ondřej Pačes / PhD Student
Soňa Kovačková / PhD Student
Eva Zborníková, MSc / Technician



The NMR and Raman spectroscopy, surface plasmon resonance, differential scanning microcalorimetry, and MDS and *ab initio* calculations are currently exploited to understand more clearly the role of nucleotide and oligonucleotide-related structural factors that control interactions with biological targets.



Tomáš Kraus

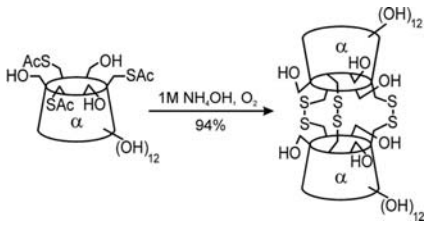
Junior research team in Organic Synthesis

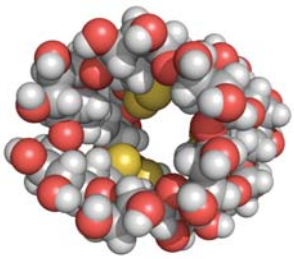
e-mail: kraus@uochb.cas.cz

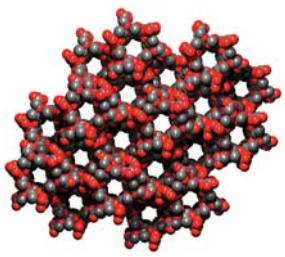
www.uochb.cz/kraus

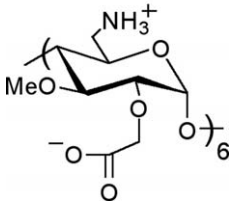
Chemistry of Macrocyclic Compounds

Tomáš Kraus, PhD / Head of the Team
Jana Hodačová, PhD / Scientist
Lukáš Kumprecht, MSc / PhD Student
Kristýna Bürglová / Student
Petr Koutník / Student
Vladimír Herzig / Student
Jiří Hlinka / Technician









Macrocycles are an important class of compounds found in natural products as well as in fully synthetic constructs. Our group is involved in projects spanning from the synthesis of new macrocycles to the use of macrocyclic building blocks for the construction of larger molecular scaffolds. As a „chemical glue" holding the building blocks together, non-covalent as well as dynamic covalent bonds are used.

As an example, copper(I)-driven self-assembly of phenanthroline-containing macrocycles resulted in the formation of triangles and squares.

Cyclodextrin macrocycles are of special interest due to their capabilities of a forming inclusion complexes with other molecules. We have studied self-assembly of cyclodextrin macrocycles modified with pendant basic and acidic functions into nanotubular structure. Recently, we have developed synthetic methods for the preparation of tubular cyclodextrin duplexes connected by multiple disulfide linkages. These compounds are capable of forming highly stable complexes with shape-compatible guest compounds and can be cleaved by reducing thiols.

In collaboration with Institute of Chemical Technology (Dr. R. Cibulka), cyclodextrin macrocycles are used as chiral scaffolds for the synthesis of cyclodextrin-flavinium conjugates as organocatalysts for enantioselective sulfooxidation.

Current grant support

Grant Agency of the ASCR (IAA400550810); Czech Science Foundation (203/07/1246); Ministry of Education, Youth and Sports (OC 172).

Selected recent papers

1. T. Kraus, M. Buděšínský, J. Cvačka, J.-P. Sauvage: „Copper(I)-Directed Formation of a Cyclic Pseudo-Rotaxane Tetramer and Its Trimer Homologue." *Angew. Chem. Int. Ed.* **2006,** *45*, 258.
2. T. Kraus, M. Buděšínský, I. Císařová, J. Závada: „Per(6-amino-2-*O*-carboxymethyl-6-deoxy-3-*O*-methyl)-α-cyclodextrin: Helical Self-Assembly of the Polyionic Amino Acid into Nanotubes."*Angew. Chem. Int. Ed.*. **2002**, *41*, 1715.
3. L. Kumprecht, M. Buděšínský, J. Vondrášek, J. Vymětal, J. Černý, I. Císařová, J. Brynda, V. Herzig, P. Koutník, J. Závada, T. Kraus: „Rigid Duplex -Cyclodextrin Reversibly Connected With Disulfide Bonds. Synthesis and Inclusion Complexes." *J. Org. Chem.* **2009**, *74*, 1082-1092.
4. L. Krejčí, M. Buděšínský, I. Císařová, T. Kraus: "Tubular duplex alpha-cyclodextrin triply bridged with disulfide bonds: synthesis, crystal structure and inclusion complexes." *Chem. Commun.* **2009**, in press.

Ilya Lyapkalo

Senior Research Team in Organic Synthesis
e-mail: lyapkalo@uochb.cas.cz
www.uochb.cz/lyapkalo

New Methods in Synthesis & Catalysis

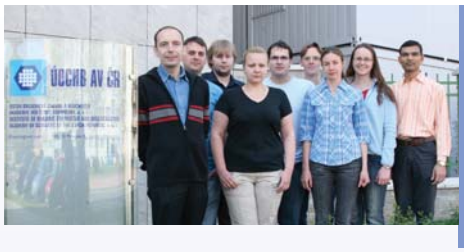
The research in our team is primarily involved with the invention of new reagents and synthesis techniques and in the application of these developments to the synthesis of naturally occurring and designed molecular structures. A continuing theme of the study in this laboratory is the relationship between structure, reactivity and selectivity in a variety of functional organic and organo-element systems. In recent years this interest has been focused on palladium catalyzed cross-coupling reactions with alken-1-yl perfluoroalkanesulfonates. Design and synthesis of new metal-free uncharged nitrogen bases, stable lipophilic organic cations as phase-transfer catalysts, asymmetric nucleophilic and Lewis-acid catalysis of carbonyl addition reactions are newly emerging areas of our activity.

Current grant support

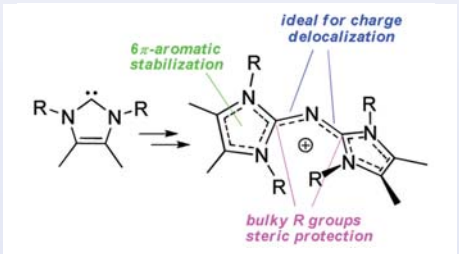
IOCB Internal Grant # 710/71

Selected recent papers

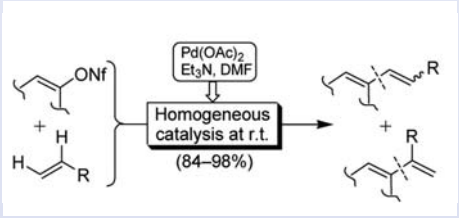
1. Cabirol, F. L., Lim, A. E. C., Hanefeld, U., Sheldon R. A., Lyapkalo, I. M.: Robust and Efficient, yet Uncatalysed Synthesis of Trialkylsilyl-Protected Cyanohydrins from Ketones. *J. Org. Chem.* **2008**, 73, 2446–2449.
2. Vogel, M. A. K., Stark, C. B. W., Lyapkalo, I. M.: A Straight-forward Synthesis of Alkenyl Nonaflates from Carbonyl Compounds Using Nonafluorobutane-1-sulfonyl Fluoride in Combination with Phosphazene Bases. *Synlett* **2007**, 2907–2911.
3. Cheng, S., Tjahjono, M., Rajarathnam, D., Chuanzhao, L., Lyapkalo, I. M., Chen, D., Garland, M.: Remote Monitoring of a Multi-Component Liquid-Phase Organic Synthesis by Infrared Emission Spectroscopy: The Recovery of Pure Component Emissivities by Band-Target Entropy Minimization. *Appl. Spectr.* **2007**, 61, 1057–1062.
4. Vogel, M. A. K., Stark, C. B. W., Lyapkalo, I. M.: An Expedient Variant of Heck Reaction of Alkenyl Nonaflates: Homogeneous Ligand-Free Palladium Catalysis at Room Temperature. *Adv. Synth. Catal.* **2007**, 349,1019–1024



Lyapkalo Ilya, PhD / Head of the Team
Sheshenev Andrey, PhD / Postdoc
Mašek Tomáš / Research Assistant
Boltukhina Ekaterina, PhD / Postdoc
Vavřík Jiří / Research Assistant
Volkov Sergey, PhD / Postdoc
Alexandrova Anastasia, PhD / Postdoc
Grishina Anastasia, MSc / PhD Student
Sonawane Manoj, MSc / PhD Student
Kunetskiy Roman, MSc / PhD Student



New extremely base resistant organic cations



First reliably proven homogeneous ligand-free Pd catalysis for organic sulfonates

Josef Michl

Senior Research team in Organic Synthesis

e-mail: michl@uochb.cas.cz

www.uochb.cz/michl

Molecular Electronics in the Broadest Sense of the Term

Josef Michl, Prof. PhD / Head of the Team
Ivan Stibor, Prof. PhD / Scientist
Lubomír Pospíšil, Assoc. Prof. PhD / Scientist
Jaroslav Vacek, PhD / Scientist
Michal Valášek, PhD / Postdoc
Jan Štursa, PhD / Postdoc
Felipe Luis Chazaro Ruiz, PhD / Postdoc
Dushant Khobragade, PhD / Postdoc
Abdul Wahab, PhD / Postdoc
Brian Stepp, PhD / Postdoc
Moise Dongmo / PhD Student
Kateřina Čmelová / Secretary

Our research group is engaged in molecular electronics in the broadest sense of the term.

- We prepare and characterize experimentally as well as computationally elements of molecular machines.
- We synthesize and characterize new types of molecular electron conductors, both for single-molecule studies and for bulk conduction.
- We investigate new means of attaching molecules to metal and other surfaces.

Our group comprises organic, inorganic, physical, and theoretical chemists and combines chemical synthesis with spectroscopic and other physical measurements. Some members actually work at the J. Heyrovsky Institute of Physical Chemistry, with whose electrochemists and other scientists we have a close collaboration.

Current grant support

ERC IDEAS 2009-2013 FP7: ERC-2008-AdG 227756-Dipolar Rotor Array Czech Grant Agency: 203/07/1619
Grant Agency of Academy of Sciences: IAA 400 550 708 and IAA 400 550 616
FUNMOL 213382
BASF cooperation

Selected recent papers (2007-8)

1. Pospíšil L., Varaksa N., Magnera T. F., Brotin T., Michl J.: Adsorption of Tentacled Tetragonal Star Connectors, C_4R_4-Co-$C_5(HgX)_5$, on Mercury. *Langmuir* 23: 930-935, **2007**.
2. King B.T., Körbe S., Schreiber P.J., Clayton J., Havlas Z., Vyakaranam K., Fete M.G., Zharov I., Ceremuga J., Michl J.: The Sixteen $CB_{11}H_nMe_{12-n}$• Anions with Five-fold Substitution Symmetry: Anodic Oxidation and Electronic Structure. *Journal of the American Chemical Society* 129: 12960-12980, **2007**.
3. Eriksson L., Vyakaranam, K., Ludvík J., Michl J.: Synthesis of the Isolable Biradicals •$(CH_3B)_{11}$C-C C-C(BCH3)11• and *trans*-•$(CH_3B)_{11}$C-CH=CH-C$(BCH_3)_{11}$• *Journal of Organic Chemistry* 72: 2351-2356, **2007**.
4. Vyakaranam K., Havlas Z., Michl J.: Aromatic Substitution with Hypercloso $C(BCH_3)_{11}$: a New Mechanism. *Journal of the American Chemical Society* 129: 4172-4174, **2007**.
5. Čárský P., Čurík R., Pezler B., Michl J.: Angular Distributions for Vibrationally Inelastic Nonresonant Scattering of Electrons by Molecules. *Journal of Physical Chemistry A* 111: 12216-12228, **2007**.
6. Caskey D.C., Yamamoto T., Addicott C., Shoemaker R.K., Vacek J., Hawkridge A.M., Muddiman D.C., Kottas G.S., Michl J., Stang P.J.: Coordination-Driven Face-Directed Self-Assembly of Trigonal Prisms. Face-Based Conformational Chirality. *Journal of the American Chemical Society* 130: 7629-7638, **2008**.
7. Vacek J., Caskey D.C., Horinek D., Shoemaker R K, Stang P.J., Michl J.: Pyridine Ligand Rotation in Self-Assembled Trigonal Prisms. Evidence for Intra-Cage Solvent Vapor Bubbles. *Journal of the American Chemical Society* 130: 7629–7638, **2008**

Ivo Starý

Senior research team in Organic Synthesis
e-mail: stary@uochb.cas.cz
www.uochb.cz/stary

Helical Aromatics, Functional π-electron Systems

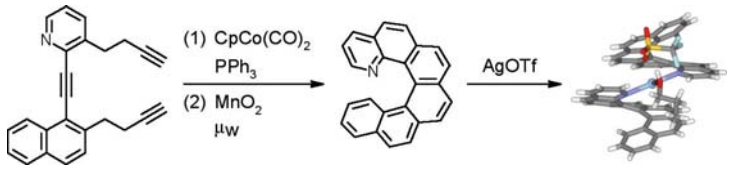
The team is focused on the chemistry and physics of helically chiral aromatics and other functional π-electron systems. [2+2+2] cycloisomerization of aromatic triynes under transition metal catalysis has extensively been used to prepare azahelicenes, extended helicenes and substituted helicenes. Furthermore, this methodology has been proven to be suitable for stereoselective synthesis of helicene-like compounds. The experimental and computational approaches go hand in hand with the design and preparation of synthetic targets exhibiting tailored physicochemical properties. Attention is paid also to π-electron macrocycles and multiple donor-acceptor interactions. The complex systems in solution as well as at interfaces are studied. We strive for unique applications in enantioselective catalysis, directed self-assembly, single-molecule electronics and on-surface chemistry and physics. Multi-disciplinary research is performed in close collaboration with experts in scanning probe microscopy, electrochemistry and mass spectrometry.

Current grant support

Academy of Sciences (ZZ40550506), Ministry of Education, Youth and Sports (LC512, Barrande 2-09-40, Kontakt ME09114), European Commission (FUNMOL 213382), Czech Science Foundation (203/07/1664, 203/09/1766) and Grant Agency of the ASCR (IAA400550704, IAA400550916, IAA400550919).

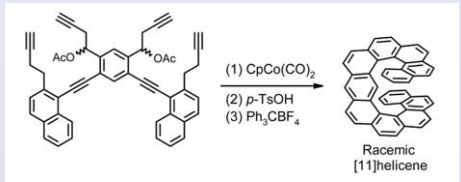
Selected recent papers

1. Míšek, J.; Teplý, F.; Stará, I. G.; Tichý, M.; Šaman, D.; Císařová, I.; Vojtíšek, P.; Starý, I. „A straightforward route to helically chiral N-heteroaromatic compounds: practical synthesis of racemic 1,14-diaza[5]helicene and optically pure 1-and 2-aza[6]helicenes" *Angew. Chem. Int. Ed.* **2008**, *47*, 3188-3191.
2. Sehnal, P.; Krausová, Z.; Teplý, F.; Stará, I. G.; Starý, I.; Rulíšek, L.; Šaman, D.; Císařová, I. „On the origin of diastereoselectivity in [2+2+2] cycloisomerization of chiral triynes: Controlling helicity of helicene-like compounds by thermodynamic factors„ *J. Org. Chem.* **2008**, *73*, 2074-2082.
3. Sehnal, P.; Stará, I. G.; Šaman, D.; Tichý, M.; Míšek, J.; Cvačka, J.; Rulíšek, L.; Chocholoušová, J.; Vacek, J.; Goryl, G.; Szymonski, M.; Císařová, I.; Starý, I. „An organometallic route to [11]helicenes, long helically chiral aromatics" PNAS (accepted).

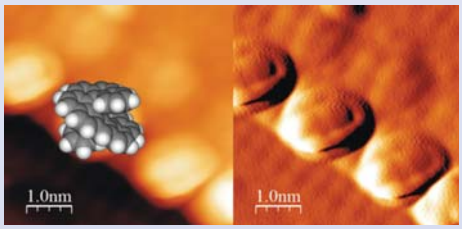


The tandem of Co'-catalyzed cyclotrimerization of triynes and microwave-assisted aromatization with MnO_2 is central to the practical synthesis of azahelicenes and their Ag' complexes.

Ivo Starý, PhD / Head of the Team
Martin Bělohradský, PhD / Scientist
Jana Chocholoušová, PhD / Scientist
Zuzana Krausová, PhD / Scientist
Petr Holý, PhD / Scientist
Jiří Rybáček, PhD / Scientist
Irena G. Stará, PhD / Scientist
Miroslava Šišková, MSc / Research Assistant
Jaroslava Perková / Technician
Olivier Songis, PhD / Postdoc
Angelina Andronova, MSc / PhD Student
Václav Dekoj, MSc / PhD Student
Andrej Jančařík, MSc / PhD Student
Šárka Lipnická, MSc / PhD Student
Petr Polášek, MSc / PhD Student
Michal Šámal, MSc / PhD Student
Jaroslav Žádný, MSc / PhD Student
Michal Buchta / Student
Jiří Klívar / Student
Karel Musil / Student
Jindřich Nejedlý / Student
Ondřej Palata / Student
Blanka Rejchrtová / Student
Tomáš Warzecha / Student
Václav Houska / Secondary School Student
Kateřina Čmelová / Secretary



Synthesis of racemic [11]helicene



UHV LT STM image of [11]helicene with submolecular resolution, which is deposited on the InSb(001) c(8 × 2) reconstructed surface

Jiří Šrogl

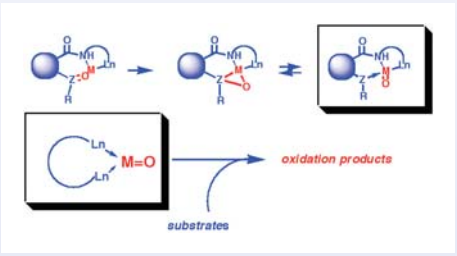
Senior research team in Organic Synthesis

e-mail: jsrogl@uochb.cas.cz

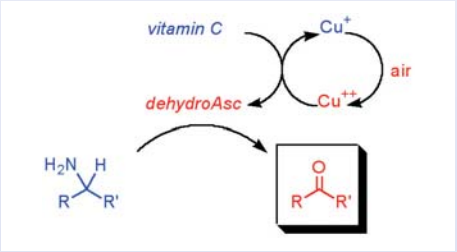
www.uochb.cz/srogl

Bio-mimetic Reactions in Organic Synthesis

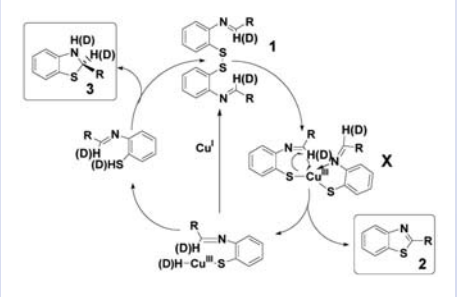
Jiří Šrogl, PhD / Head of the Team
Svatava Voltrová, PhD / Senior Scientist
Adam Henke, MSc / PhD Student
Jakub Hývl, MSc / PhD Student
Iva Štibingerová / Student
Michal Novotný / Student
Marek Martínek / Student
Erik Andris / Student



Metal mediated oxidation of organic substrates by sulfoxide derivatives.



Oxidation of amines by copper/ascorbic acid dyad.



Interaction of Cu(I) with disulfides.

The underlying topic of our research interests is bio-mimetic reactions in organic synthesis. In our research we try to apply the principles of biological chemistry to such diverse fields as materials engineering on one side, and organic synthesis on the other, in the hope of obtaining a Nature-like quality in a laboratory setting.

Our chief interest lies in the interactions of organosulfur moieties with transition and non-transition metals. Given the structural variety in sulfur based functional groups, the whole research theme has been separated into several subprojects: sulfur based oxidants in biomimetic oxidative reactions, sulfur based leaving groups in cross-coupling reactions, and disulfides and their derivatives in molecular recognition processes.

Disulfides, sulfoxides and their derivatives have been successfully introduced as viable oxidizing agents in a variety of metal catalyzed oxidative reactions.

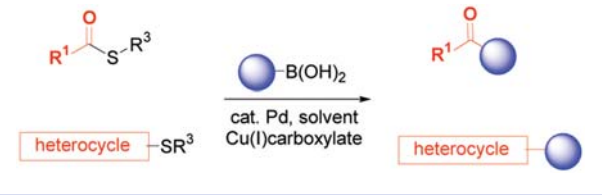
An alternative metal mediated cross-coupling protocol employing thioorganic moieties instead of more frequent halides and sulfonates have been introduced. The diverse pool of substrates has been studied with the aim of developing a universal methodology, which would allow for the formation of a carbon-carbon bond under mild, ambient condition.

Current grant support

Grant Agency of the ASCR (203/08/1318), AS CR (M200550907 and M200550908).

Selected recent papers

1. Srogl, J., Hývl, J., Révész, A., Schröder, D. Mechanistic Insights into a Copper-Disulfide Interaction in Oxidation of Imines by Disulfides *Chem. Commun.* **2009,** 3463-3465
2. Srogl, J.; Voltrova, S.Copper/Ascorbic Acid Dyad as a Catalytic System for Selective Aerobic Oxidation of Amines *Org. Lett.,* **2009,** *11,* 843-845.
3. Henke, A., Srogl, J.Thioimides: New Reagents for Effective Synthesis of Thiolesters from Carboxylic Acids *J. Org. Chem.,* **2008,** *73* (19), 7783–7784.
4. Voltrova, S., Srogl, J. Reaction of thiolesters with nitrogen ylides *Eur. J. Org. Chem.,* **2008,** *10,* 1677-1679.
5. Villalobos J. M., Srogl J., Liebeskind L. S. A New Paradigm for Carbon-Carbon Bond Formation: Aerobic, Copper-Templated Cross-coupling. *J. Am. Chem. Soc* . **2007**, 129(51); 15734-15735.



Liebeskind-Srogl cross-coupling protocol

Petr Beier

Junior research team in Organic Synthesis
e-mail: beier@uochb.cas.cz
www.uochb.cz/beier

Organic Chemistry of Fluorine, Phosphorus and Silicon New Methodology Development and Organocatalysis

The development of new methodologies in organo-fluorine, phosphorus and silicon chemistry is carried out by our group. Novel building blocks such as phosphonates, allenes, trifluoromethyl and difluoromethyl containing compounds are synthesized. Nucleophilic fluorination reactions, enantioselective reactions and organocatalytic processes are studied. In collaborative projects novel fluorine containing bioactive compounds are synthesized and their activity is evaluated. Utilization of perfluorinated solvents in enzymatic reactions and oxidations is also under investigation.

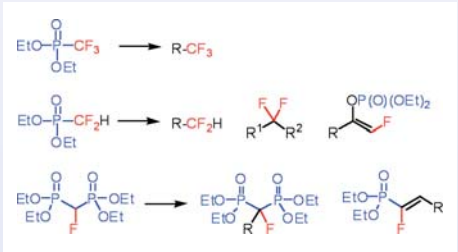
Current grant support

Grant Agency of the Czech Republic (203/08/P310).
Academy of Sciences (Z40550506)

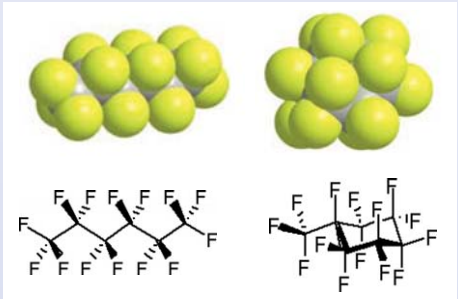
Selected recent papers

1. Alexandrova, A. V.; Beier, P. "Nucleophilic Difluoromethylenation of Aldehydes and Ketones Using Diethyl Difluoro(trimethylsilyl)methylphosphonate" *J. Fluorine Chem.* **2009**, *130*, in press.
2. Beier, P.; Pohl, R.; Alexandrova, A. V. "An Efficient and Highly Selective Synthesis of (*Z*)-Fluoroenol Phosphates from Hydroxy Difluorophosphonates" *Synthesis* **2009**, 957-962.
3. Beier, P.; Alexandrova A. V.; Zibinsky, M.; Prakash G. K. S. "Nucleophilic difluoromethylation and Difluoromethylenation of Aldehydes and Ketones Using Diethyl Difluoromethylphosphonate" *Tetrahedron* **2008**, *64*, 10977-10985.
4. Babiak, P.; Němcová, A.; Rulíšek L.; Beier, P. "On the Miscibility of Ethers and Perfluorocarbons. An Experimental and Theoretical Study" *J. Fluorine Chem.* **2008**, *129*, 397-401.

Petr Beier, PhD / Head of the Team
Tomáš Bezděk / Student
Katarina Hlat-Glembová / Student
Prabhakar Cherkupally, MSc / PhD student
Norbert Vida / Student
Pavel Weber / Student



Nucleophilic fluorinations using phosphonates.



Perfluorocarbons – novel reaction media.

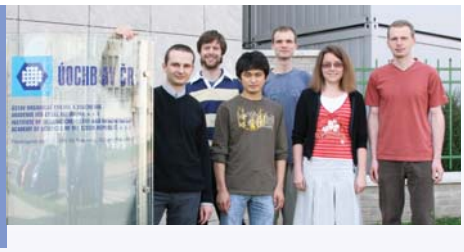
Filip Teplý

Junior research team in Organic Synthesis

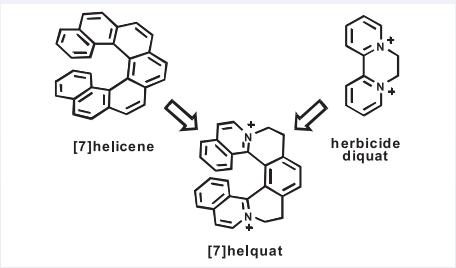
e-mail: teply@uochb.cas.cz

www.uochb.cz/teply

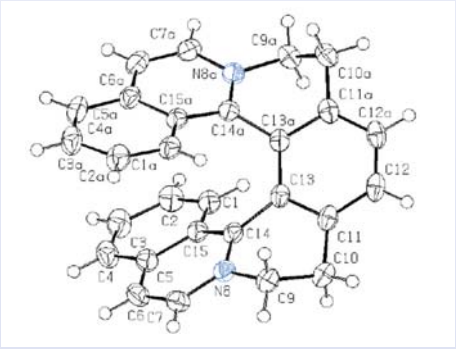
Chemistry of Nitrogen-based Organic Cations



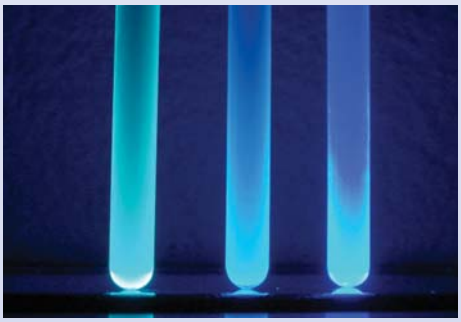
Filip Teplý, PhD / Head of the Team
Louis Adriaenssens, PhD / Postdoc
Tynchtyk Amatov, MSc / PhD Student
Martina Čížková, MSc / PhD Student
Jan Vávra, MSc / PhD Student
Lukáš Severa / Student
Nina Sarvašová / Student
Pavel Švec / Student



The priviledged pedigree of [7]helquat.



X-ray crystal structure of [7]helquat.



Fluorescence of various helquats.

Nitrogen-based organic cations constitute a field rich in remarkably diverse applications holding great promise for the future. In the Teplý group we strongly believe that one who can design and prepare novel cationic species also holds the key to a range of attractive and unexplored research topics.*

Inspired by the application wealth of this class of compounds, the group has recently introduced helquats (helical extended diquats), compounds representing the missing structural link between helicenes and viologens.[1] Bridging these renowned, yet until now separate, areas is anticipated to open up unknown scientific territories. Some of the currently pursued topics include design of novel materials for advanced optics and organocatalysis. Notably, all reactions within the synthetic sequence towards helquats are exclusively skeleton building, making the approach exceptionally step-economic. Furthermore, introduction of the three-step route to helquats displays the outstanding utility of the [2+2+2] cycloaddition strategy in the rapid assembly of intriguing organic cationics.

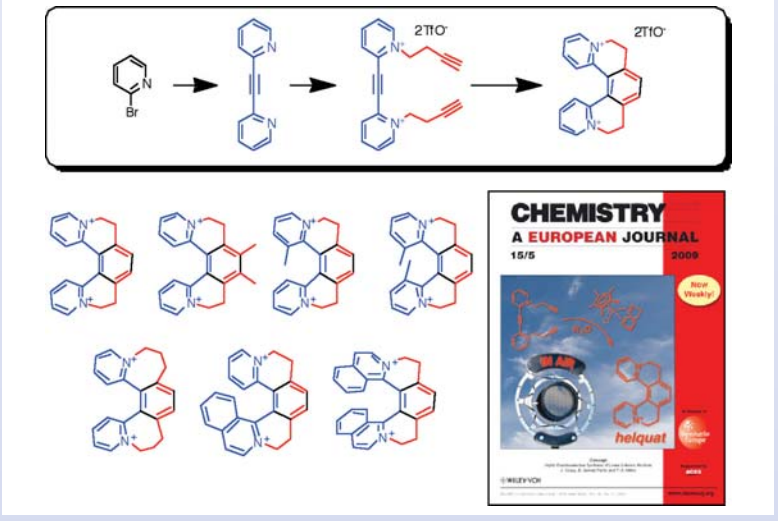
*This is best demonstrated in the very first issue of a new flagship journal *Nature Chemistry (April 2009 Vol 1 No 1)* featuring three articles where nitrogen-based cationics play a key role in demonstrating exciting and visionary research concepts (Cronin *et al.*, Kuimova, Ogilby *et al.*, Anzenbacher, Jr. *et al.*).

Current grant support

Academy of Sciences (Z40550506), Czech Science Foundation (203/09/1614), Czech Science Foundation (203/09/0705).

Recent paper

1. Adriaenssens, L.; Severa, L.; Šálová, T.; Císařová, I.; Pohl, R.; Šaman, D.; Rocha, S. V.; Finney, N. S.; Pospíšil, L.; Slavíček, P.; Teplý, F. "Helquats: A Facile, Modular, Scalable Route to Novel Helical Dications." *Chem.-Eur. J.* **2009**, *15*, 1072-1076.



Three-step synthesis of a family of helquats.

Petr Bouř

Senior research team in Spectroscopy & Physical Organic Chemistry
e-mail: bour@uochb.cas.cz
www.uochb.cz/bour

Molecular Spectroscopy

The team is oriented towards various spectroscopic techniques used for molecular structural studies. It develops advanced interpretation methods enabling the team to obtain extended information about molecular structure, dynamics and interactions. Although the primary target is basic research, we also solve concrete problems in organic chemistry and molecular biology, such as those associated with peptide folding, behavior of nucleic acids and fullerenes' dynamics. Traditionally, our group specializes in optical activity spectroscopy (electronic and vibrational circular dichroism, Raman optical activity) and nuclear magnetic resonance. The team also provides service measurements for the Institute and other institutions.

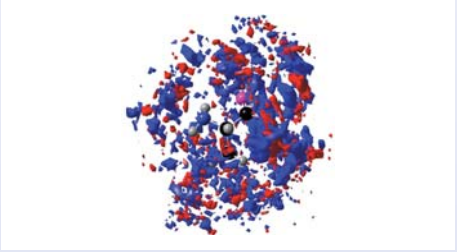
Current grant support

The Czech Science Foundation (grants Nos. 203/06/0420, 203/09/2037 202/07/0732), and the Grant Agency of the Academy of Sciences (A4005507020, IAA400550701), Marie Curie ERC Grant (PERG03-GA-2008-230955), Human Frontier Science Program.

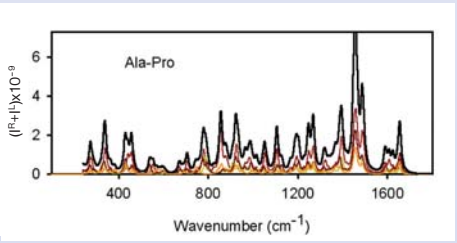
Selected recent papers

1. Kaminský, J.; Šebek, J.; Bouř, P. "Molecular Dynamics with Restrictions Derived from Optical Spectra" *J. Comput. Chem.* **2009**, *30*, 983-991.
2. Dračínský, M.; Kaminský, J.; Bouř, P. "Relative importance of first and second derivatives of nuclear magnetic resonance chemical shifts and spin-spin coupling constants for vibrational averaging." *J. Chem. Phys.* **2009**, *130*, 094106.
3. Andrushchenko, V.; Bouř, P "Infrared Absorption Detection of Metal Ion Deoxyguanosine Monophosphate Binding: Experimental and Theoretical Study." *J. Phys. Chem. B* **2009**, *1*, 283-291.
4. Andrushchenko, V.; Bouř, P. "Circular Dichroism Enhancement in Large DNA Aggregates Simulated by a Generalized Oscillator Model." *J. Comput. Chem.* **2008**, *29*, 2693-2703.
5. Sychrovský, V.; Buděšínský, M.; Benda, L.; Špirko, V.; Vokáčová, Z.; Šebestík, J.; Bouř, P. "Dependence of the L-Alanyl-L-Alanine Conformation on Molecular Charge Determined from Ab Initio Computations and NMR Spectra." *J. Phys. Chem. B* **2008**, *112*, 1796-1805.

Petr Bouř, PhD / Head of the Team
Valery Andrushchenko, PhD / Postdoc
Lucie Bednárová, PhD / Scientist
Ladislav Benda, MSc / PhD Student
Helena Dlouhá / Technician
Pavel Fiedler / Scientist
Jan Horníček, MSc / PhD Student
Jakub Kaminský, MSc / PhD Student
Petr Maloň, PhD / Scientist
Miroslava Otrubová / Technician
Michal Straka / Postdoc
Vladimír Sychrovský, PhD / Scientist
Martin Šafařík / Technician
Jaroslav Šebestík, PhD / Scientist
Zuzana Vokáčová, MSc / PhD Student
Soňa Vašíčková / Technician
Zbigniew Zawada, MSc / PhD Student



Water oxygen (red) and hydrogen (blue) probability distributions around alanine as obtained from quantum dynamics. The distribution significantly affected the NMR data.



Simulated decomposition of the Raman spectra enabled to accurately estimate the various forms of the Ala-Pro dipeptide in the sample.

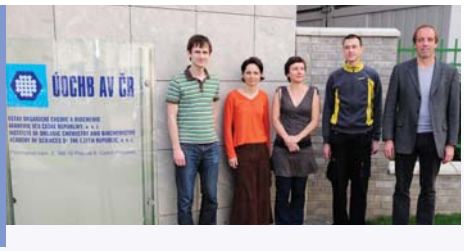
Detlef Schröder

Senior research team in Spectroscopy & Physical Organic Chemistry

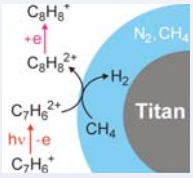
e-mail: schroeder@uochb.cas.cz

www.uochb.cz/schroder

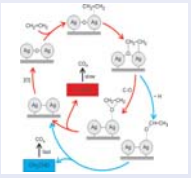
New Horizons in Mass Spectrometry



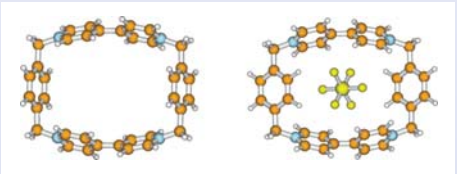
Detlef Schröder, PhD / Head of the Team
Jana Roithová, PhD / Scientist
Ján Tarábek, PhD / Scientist
Milko Petr / PhD Student
Marek Remeš / PhD Student
Králová Anna / Research Assistant
Šádek Vojtěch / Student



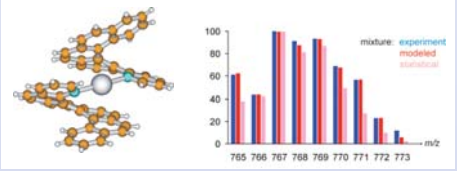
Model for the growth of hydrocarbons in the ionosphere of Saturn's moon Titan
(*Chem. Eur. J.* **2008**, 14, 4779-4783)



A three-atom model for a megaton process: Epoxidation of ethylene on silver contacts
(*J. Am. Chem. Soc.* **2007**, 129, 15311-15318)



Stoddart's tetrapyridinium tetracation and its counterion inclusion complex first detected as free polycations
(*J. Am. Chem. Soc.* **2007**, 129, 10411-10418)



Molecular recognition: Preferential formation of homochiral dimers between azahelicenes and Ag^+
(*Coll. Czech. Chem. Commun.* **2009**, 74, 323-333)

The group for Gas-Phase Chemistry at the IOCB serves as one of the points of linkage between the synthetic and biological groups of the Institute on the one hand and the theoretically oriented scientists on the other. Specifically, we conduct all kinds of experimental studies in the field of organic and inorganic ion chemistry, ranging from fundamental studies of the energetics of diatomic molecules over the wide area of organic chemistry, organic reaction mechanisms, and transition-metal catalysis all the way to enzyme models or atmospheric studies. To this end, we apply contemporary mass-spectrometric methods in conjunction with isotope labeling, ion spectroscopy, and state-of-art computational investigations. The pictures on the left show some examples of how gas-phase chemistry can contribute to extraterrestrial phenomena, catalyst research, supramolecular chemistry, and chiral recognition. The results of the research are published in leading scientific journals, and the group is recognized as one of the leading teams in the field, as demonstrated by invitations to reviews, feature articles, and lectures at international conferences. Connections to applied chemistry are reflected in consulting requests of chemical companies such as Arkema, Bayer, BASF, or Nestlé. Quite recently, Dr. Schröder has been awarded with an Advanced Grant of the European Research Council for the proposal „New Horizons in Mass Spectrometry" (HORIZOMS).

In addition, the group aims towards the improvement of the public understanding of science and actively communicates the fundamental research conducted in the group to a broader audience, such as interested adults, scholars, and kids. Whoever might be interested in a „lab-tour" for school classes or short-term practical courses is kindly requested to contact us.

Current grant support

Consiglio Nazionale delle Richerche (Italy), European Commission, European Research Council (ERC), Grant Agency of the Academy of Sciences of the Czech Republic, Grant Agency of the Czech Republic, Royal Chemical Society (United Kingdom)

Selected recent papers

1. Roithová J.; Schröder D. "Theory meets experiment: Gas-phase chemistry of coinage metals" *Coord. Chem. Rev.* **2009**, 253, 666-677.
2. Schröder D. "Gaseous rust: Thermochemistry of ionic and neutral iron oxides and hydroxides in the gas phase" *J. Phys. Chem. A* **2008**, 112, 13215-13224.
3. Schröder D.; Schwarz, H. "Gas-phase activation of methane by gaseous transition-metal cations" *Proc. Nat. Acad. Sci.* **2008**, 105, 18114-18119.
4. Ascenzi D.; Tosi P.; Roithová J.; Schröder D. "Gas-phase synthesis of the rare-gas carbene cation $ArCH_2^+$ using doubly ionized bromomethane as a superelectrophilic reagent" *Chem. Commun.***2008**, 34, 4055-4057. **„Hot article"**
5. Ricketts, C. L.; Schröder D.; Alcaraz, C.; Roithová J. "Growth of larger hydrocarbons in the ionosphere of Titan" *Chem. Eur. J.* **2008**, 14, 4779-4783.

Tomáš Macek

Senior research team in Natural Products Biochemistry
e-mail: tom.macek@uochb.cas.cz
www.uochb.cz/macek

Regulation of Activity of Selected Proteins and Enzymes by Low Molecular Weight Organic Compounds

The main task of the Joint Laboratory of IOCB and the Department of Biochemistry and Microbiology, Faculty of Food and Biochemical Technology of the ICT Prague is to influence the biological activity of selected synthesizing and degradative enzymes and some other proteins. Results of previous years led to discovery of some groups of effectors of studied enzyme activities (oxysterols, monoterpenes, flavonoids). Oriented immobilization of these low molecular weight organic ligands gave bioaffinity chromatography carriers that allowed isolation and identification of proteins binding these ligands. Among them is RuBisCO, the most abundant enzyme of the biosphere, converting inorganic carbon dioxide into sugars. Search for binding sites and activity regulation by ligands and their analogs included recently also crystallographic studies and modeling.
Several collaborative projects also address also proteins involved in detoxification of environmental pollutants and preparation of transgenic organisms for environmental protection (e.g. within Research Center for Functional genomics and proteomics in plant breeding, project Biobrom, project Metagenom).

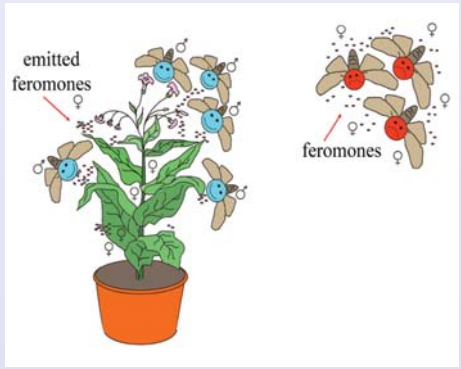
Tomáš Macek, Assoc. Prof., PhD, / Head of the Team
Marek Kamlar, MSc / PhD Student
Jan Rezek, MSc / PhD Student
Martina Nováková, MSc / PhD Student
Ondřej Uhlík, MSc / PhD Student
Simona Hybelbauerová, MSc / PhD Student
Blanka Vrchotová, MSc / PhD Student
Iva Doležílková, MSc / PhD Student
Jitka Najmanová, MSc / PhD Student
Tereza Neubauerová, MSc / PhD Student
Marcela Holečková, MSc / PhD Student
Věra Laudová, MSc / Scientist
Kateřina Bínová / Technician

Current grant support

Academy of Sciences (Z40550506), Ministry of Education (1M06030, 2B06151, 2B08031

Selected recent papers

1. Macek, T., Kotrba, P., Svatoš, A., Demnerová, K., Nováková, M., Macková, M.: Novel roles for GM plants in environmental protection. *Trends Biotechnol.* 26 (**2008**), s. 146-152.
2. Rezek, J., Macek, T., Macková, M., Tříska, J., Růžičková, K.: Hydroxy-PCBs, methoxy-PCBs and hydroxy-methoxy-PCBs: Metabolites of polychlorinated biphenyls formed *in vitro* by tobacco cells, *Environ. Sci. Technol.* 42 (**2008**), s. 5746-5751.
3. Uhlík, O., Kamlar, M., Kohout, L., Ježek, R., Harmatha, J., Macek, T.: Affinity chromatography reveals RuBisCO as an ecdysteroid-binding protein. *Steroids* 73 (**2008**), s. 1433–1440.
4. Macek, T., Uhlík, O., Kamlar, M., Harmatha, J., Kohout, L.: Method of increasing of the photosynthetic carbon dioxide assimilation yield. EU patent PCT/CZ2008/000044, 23. 10. **2008**, WO 2008/125069 A2
5. de Cárcer, D., Martín, M., Macková, M., Macek, T., Karlson, U., Rivilla, R.: The introduction of genetically modified microorganisms designed for rhizoremediation induces changes on native bacteria in the rhizosphere but not in the surrounding soil. *ISME Journal* (Nature Publishers) 1(3) (**2007**), s. 215-223.
6. Macková, M., Vrchotová, B., Frančová, K., Sylvestre, M., Tomaniová, M., Lovecká, P., Demnerová, K., Macek, T.: Biotransformation of PCBs by plants and bacteria, consequences of plant-microbe interactions. *Eur. J. Soil Biol.* 43 (**2007**), 233-241.



GM plants emitting insect pheromones

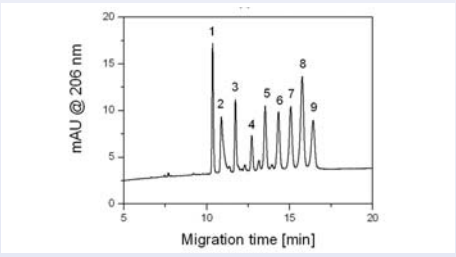
Research – Service teams

Václav Kašička

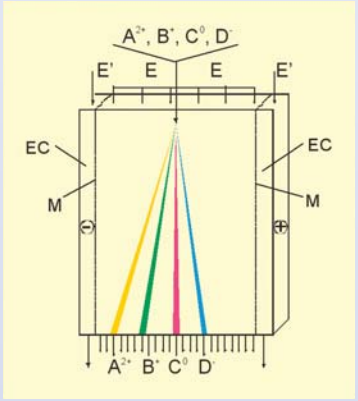
Research-Service Team
e-mail: kasicka@uochb.cas.cz
www.uochb.cz/kasicka

Electromigration Methods

Václav Kašička, PhD / Head of the Team
Sille Ehala, PhD / Postdoc
Dušan Koval, PhD / Postdoc
Petra Sázelová, PhD / Scientist
Veronika Šolínová, PhD / Postdoc
Hana Mikysková, Bc / Student
Miloslava Vítovcová, Bc / Student
Věra Lišková / Technician



Capillary electrophoretic separation of homologous series of insect oostatic peptides (dipeptide to decapeptide).



Principle of free-flow electrophoresis.

The team is engaged in the research and development of high-performance capillary electrophoresis (HPCE) and free-flow electromigration methods and their application to separation, analysis, purification and physicochemical and biochemical characterization of biomolecules.

Current Projects

HPCE with multidimensional separation and detection

A new HPCE device with multidimensional separation and detection of biomolecules is being constructed. It is based on on-line combinations of different separation principles performed in two in-series joined capillaries or in a single capillary with different selectivity sections.

Affinity capillary electrophoresis and electrochromatography and their use for investigation of biomolecular interactions

New procedures are being developed to investigate non-covalent interactions of biomolecules (amino acids, peptides, nucleotides) with various ligands, such as oligopyrrole macrocycles, cyclodextrins, metal ions and proteins.

New electrolyte systems and (pseudo)stationary phases for HPCE

New background electrolytes (strongly acidic, basic and isoelectric buffers), and (pseudo)stationary phases (chiral selectors, nanoparticles) are being developed in order to increase the selectivity and separation efficiency of HPCE methods.

Conversion of capillary microscale separations into preparative free-flow electrophoresis scale

Conversion is based on the correlation between capillary zone electrophoresis (CZE) and free-flow zone electrophoresis (FFZE), two instrumental format of the same separation principle (zone electrophoresis).

Current grant support

Academy of Sciences (Z40550506, bilateral projects ASCR-CSIC (Spain), ASCR-BAS (Bulgaria)), Czech Science Foundation (203/08/1428, 203/09/0675).

Selected recent papers

1. Sázelová, P.; Kašička, V.; Koval, D.; Prusík, Z.; Fanali, S.; Aturki, Z. "Control of electroosmotic flow in capillary electrophoresis by different ways of application of radial electric field" *Electrophoresis* **2007**, *28*, 756-766.
2. Šolínová, V.; Kašička, V.; Sázelová, P.; Barth, T.; Mikšík, I. "Separation and investigation of structure-mobility relationship of gonadotropin-releasing hormones by capillary zone electrophoresis in conventional and isoelectric acidic background electrolytes" *J. Chromatogr. A* **2007**, *1155*, 146-153.
3. Kašička, V. "Recent developments in CE and CEC of peptides" *Electrophoresis* **2008**, *29*, 1 (2008) 179-206.
4. Ehala, S.; Míšek, J.; Stará, I.G.; Starý, I.; Kašička V. "Determination of acid-base dissociation constants of azahelicenes by capillary zone electrophoresis" *J. Sep. Sci.* **2008**, *31*, 2686-2693.
5. Koval, D.; Busnel, J.-M.; Hlaváček, J.; Jiráček, J.; Kašička, V.; Peltre, G. "Evaluation of carrier ampholyte-based capillary electrophoresis for separation of peptides and peptide mimetics", *Electrophoresis* **2008**, *29*, 3759-3767.

Tomáš Elbert

Research-Service Team
e-mail: elbert@uochb.cas.cz
www.uochb.cz/elbert

Laboratory of Radioisotopes

The primary task of the laboratory is to provide commercialy non-available radioactively labeled compounds to biochemical research teams of the institute. At present we use mainly radionuclides ^{125}I and ^{3}H. We plan to expand our activities on ^{14}C.

For the receptor studies with biologically active peptides very high specific activities are needed. As amino acids tyrosine and histidine are very often present in the peptide chain, the introduction of carrier free radioactive iodine by electrophilic aromatic substitution on activated tyrosin benzene ring or imidazol ring of histidine is a very convenient way to achieve specific activities over 2 000 Ci/mmol of peptide. We are steadily optimizing the reaction conditions as every new peptide poses new challenges due to its specific qualities. The resulting mixture of the starting peptide and its monoiodinated and diiodinated derivatives is separated using radio-HPLC. Recently we prepared the following labeled peptides: [^{125}I]W-peptide-NH_2, [^{125}I]CART(61-102), [^{125}I][d(CH2)51, Tyr(Me)2, Thr4, Orn8, Tyr-NH29]vasotocin.

[^{3}H]Pregnenolone-3-O-sulfate ammonium salt and 3 -hydroxy-[^{3}H]pregnanolone 3-O-sulfate ammonium salt were prepared with specific activities 47.5 Ci/mmol and 40 Ci/mmol, respectively. The receptor binding experiments with these labeled steroids gave unexpected results.

α-5-Aza-2′-deoxy-[6- ^{3}H]cytidine with specific activity 19.2 Ci/mmol was prepared by CESG method.

The structures of ^{3}H-labeled compounds and their specific activities are checked by ^{3}H NMR.

The project aiming the preparation of ^{3}H-labeled brassinosteroids with specific activity higher than 60 Ci/mmol is under way.

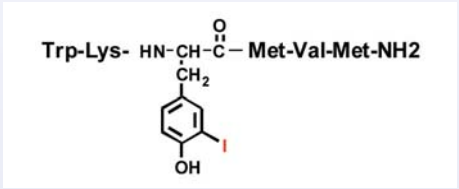
Current grant support

Academy of Sciences (Z40550506) Grant Agency of the ASCR (IAA400550801).

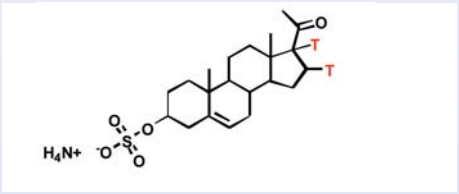
Selected recent papers

1. Elbert T.; Černý B. "Preparation of alpha-5-aza-2′-deoxy-[6- ^{3}H]cytidine" *Collection of Czechoslovak Chemical Communications*. **2008,** *73*, 701-704.
2. Elbert T.; Slaninová J.; Chodounská H.; Šaman D. "Labelling of steroid 3-O-sulfates by tritium and their binding to guinea pig cortical cell membranes" *Journal of Labelled Compounds and Radiopharmaceuticals* **2007**, *50*, 574-575.
3. Maletínská L.; Maixnerová J.; Matyšková R.; Haugvicová R.; Šloncová E.; Elbert T.; Slaninová J.; Železná B. "Cocaine- and amphetamine-regulated transcript (CART) peptide specific binding in heochromocytoma cells PC12" *European Journal of Pharmacology* **2007,** *559*,109-114.
4. Maixnerová J.; Hlaváček J.; Blokešová D.; Kowalczyk W.; Elbert T.; Šanda M.; Blechová M.; Železná B.; Slaninová J.; Maletínská L. "Structure-activity relationship of CART (cocaine- and amphetamine-regulated transcript) peptide fragments" *Peptides* **2007**, *28*,1945-1953.

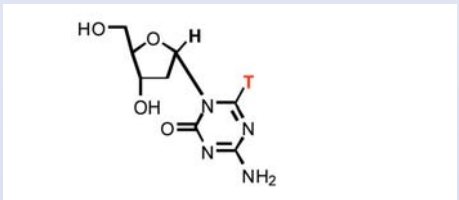
Tomáš Elbert, Assoc. Prof., PhD / Head of the Team
Petr Hezký, MSc / Scientist
Iva Veselá, MSc / Scientist



[^{125}I]W-peptide-NH_2,



[^{3}H]pregnenolone-3-O-sulfate ammonium salt



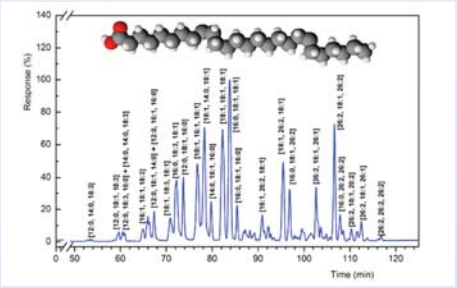
α-5-aza-2′-deoxy-[6-^{3}H]cytidine

Josef Cvačka

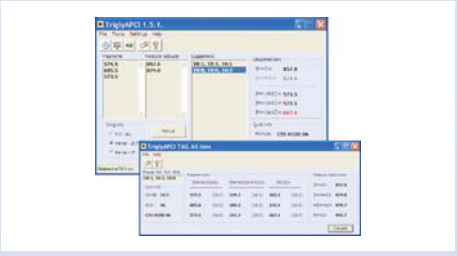
Research-Service Team
e-mail: cvacka@uochb.cas.cz
www.uochb.cz/cvacka

Mass Spectrometry of Organic Compounds

Josef Cvačka, PhD / Head of the Team
Vladimír Vrkoslav, PhD / Postdoc
Filip Kaftan, MSc / PhD Student
Radka Míková, MSc / PhD Student
Miloslav Šanda, MSc / PhD Student
Anna Březinová, MSc / Research Assistant
Kveta Kertisová, MSc / Research Assistant
Kateřina Nováková, MSc / Research Assistant
Jana Jersáková / Student
Daniela Janechová / Student
Marie Krásová / Student
Martina Háková / Student
Petra Macháčková / Student
Eva Mikolášová / Technician



HPLC/APCI-MS chromatogram of triacylglycerols from bumblebee *B. pratorum* and structure of unusual (*Z,Z*)-9,19-hexacosadienoic acid identified in the sample.



Screenshots of *TriglyAPCI* software developed for interpretation of APCI mass spectra of triacylglycerols.

The research is focused on mass spectrometry (MS) and its use for structure elucidation and identification of organic substances. The target compounds are mostly natural products with known or expected important biological functions, e.g., semiochemicals, metabolites, lipids, peptides or proteins. In addition to classical approaches, new methods are being developed. They are mostly based on direct sample analysis by MS or their coupling with thoroughly optimised chromatographic separations (GC/MS or LC/MS). The recent projects are centred on analysis of lipids in tissues. Lipids are either extracted and analyzed or detected in situ, which allows visualization of their spatial distribution (MALDI imaging). An effort is also made to locate position(s) of double bond(s) in intact lipids and to develop software for automated mass spectra interpretation.
The team also performs routine MS analyses for the local scientific community, maintains open-access instruments and provides collaborative support.

Current grant support

Academy of Sciences (Z40550506), Czech Science Foundation (203-09-0139), Ministry of Education, Youth and Sports (MEB 080863)

Selected recent papers

1. J. Cvačka, O. Hovorka, P. Jiroš, J. Kindl, K. Stránský and I. Valterová: Analysis of triacylglycerols in fat body of bumblebees by chromatographic methods. *J. Chromatogr. A*, 1101, 226-237 (**2006**).
2. J. Cvačka, P. Jiroš, J. Šobotník, R. Hanus, A. Svatoš: Analysis of Insect Cuticular Hydrocarbons using Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry *J. Chem. Ecol*. 32, 409-433 (**2006**)
3. J. Cvačka, E. Krafková, P. Jiroš, I. Valterová: Computer-assisted interpretation of atmospheric pressure chemical ionization mass spectra of triacylglycerols. *Rapid Commun. Mass Spectrom*. 20, 3586-3594 (**2006**).
4. J. Cvačka, E. Kofroňová, S. Vašíčková, K. Stránský, P. Jiroš, O. Hovorka, J. Kindl, I. Valterová: Unusual Fatty Acids in the Fat Body of the Early Nesting Bumblebee, *Bombus pratorum*. *Lipids*, 43, 441-450 (**2008**).
5. M. Buděšínský, K. Vokáč, J. Harmatha, J. Cvačka: Additional minor ecdysteroid components of *Leuzea carthamoides*. *Steroids* 73, 502-514 (**2008**).

Hana Chodounská

Research-Service Team
e-mail: chodounska@uochb.cas.cz
www.uochb.cz/chodounska

Chemistry of Medicinal Steroids

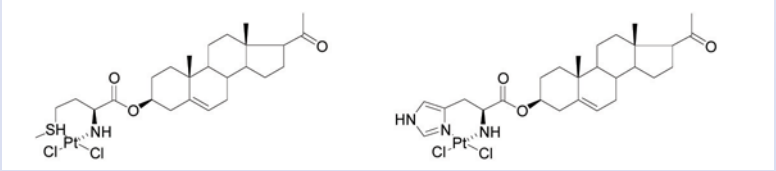
The ability of steroids to penetrate the hematoencephalic barrier and to act fast on the receptors for neurotransmitters designates these compounds for the affecting of processes in the neuronal system. We are engaged in the design and synthesis of such derivatives that can act as the natural neurosteroids. In addition, they enable to study processes in the neural system, which could eventually be utilized in clinical diagnosis and treatment.
Such compounds are synthesized by steroid chemistry procedures in combination with methods of modern organic synthesis, e.g. metal catalyzed coupling reactions or reactions using organocatalysis.
The next topic of our research is based on the fact that the selective transport of steroid hormones can be utilized for the targeted delivery of some active agents.

Current grant support (selected)

Academy of Sciences (Z40550506), Czech Science Foundation (203/08/1498), Agency of the ASCR (KAN 200200651).

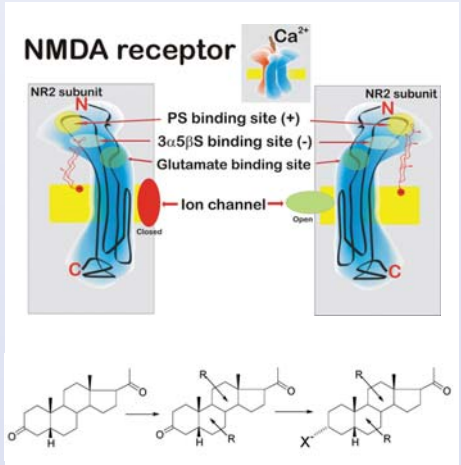
Selected recent papers

1. Kasal A., Krištofíková Z., Buděšínský M.: „7-Aza-allopregnanolone - a pure substitute for allopregnanolone." *Tetrahedron* 63: 11355-11362, **2007**.
2. Matyáš L., Pohl R., Kasal A.: „Neighboring group participation in 12,20-dioxopregnanes." *Nat. Prod. Commun.* 2: 1091-1094, **2007**.
3. Kvasnica M., Budesinsky M., Swaczynova J., Pouzar V., Kohout L.: „Platinum(II) complexes with steroidal esters of L-methionine and L-histidine: Synthesis, characterization and cytotoxic activity." *Bioorg. Med. Chem.* 16: 3704-3713, **2008**.
4. Herrmann P., Kvíčala J., Pouzar V., Chodounská H.: „Synthesis of fluorinated steroids using a novel fluorinating reagents tetrabutylammoniumdifluorodimethylphenylsilicate (TAMPS)." *Collect. Czech Chem. Comunn.* 73: 1825-1834, **2008**.
5. Sedlacek M., Korinek M., Petrovic M, Cais O., Adamusova E., Chodounska H., Vyklicky L.: „Neurosteroid modulation of ionotropic glutamate receptors and excitatory synaptic transmission." *Physiol. Res.* 57 (Suppl.3): S49-S57, **2008**.



Examples of cis-platin transporting steroid conjugates.

Hana Chodounská, PhD / Head of the Team
Ivan Černý, PhD / Scientist
Alexander Kasal, DSc / Scientist
Vladimír Pouzar, DSc / Scientist
Miroslav Kvasnica, MSc / Postdoc
Libor Matyáš, PhD / Postdoc
Miroslav Šíša, PhD / Postdoc
Eva Šťastná, PhD / Postdoc
Jaroslava Hniličková, MSc / Research Assistant
Barbora Slavíková, MSc / Research Assistant
Alena Slavíčková, Bc / Student
Lukáš Vidrna / Student
Daďka Hybšová / Technician
Lenka Kloučková / Technician
Michaela Sedláčková / Technician



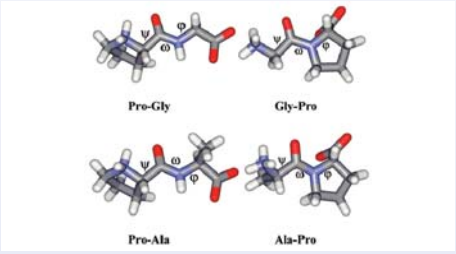
Synthesis of negative modulators of NMDA receptors.

Miloš Buděšínský

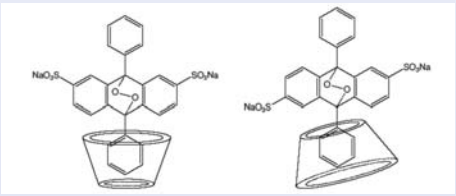
Research-Service Team
e-mail: budesinsky@uochb.cas.cz
www.uochb.cz/budesinsky

Nuclear Magnetic Resonance Spectroscopy

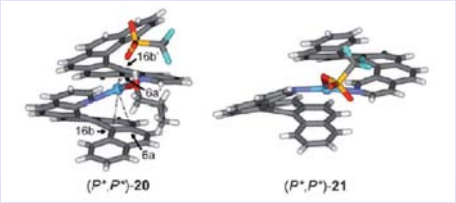
Miloš Buděšínský, PhD / Head of the Team
David Šaman, PhD / Scientist
Radek Pohl, PhD / Scientist
Martin Dračínský, PhD / Scientist
Lenka Slavětínská, PhD / Scientist
Milena Masojídková, MSc / Assistent
Marie Snopková / Technician



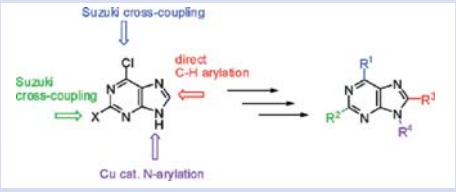
Model dipeptides – quantitative conformer analysis by NMR and ROA [1]



NMR study of host-guest complexes of disulfonated endoperoxides of 9,10-diphenylanthracenes with cyclodextrins [2]



NMR analysis of aza[6]helicenes [3]



NMR analysis of purine regioisomers [5]

NMR is a unique spectroscopic method for structure elucidation and provides information about the constitution, configuration and conformation of studied compounds. Our research is focused on structural study of both synthetic compounds originating in laboratories of the IOCB and those isolated from natural sources. We utilize modern onedimensional and multidimensional NMR techniques and then obtained NMR parameters are subsequently used for structure elucidation of nucleosides, nucleotides, peptides, steroids, saccharides, pheromones, helicenes and other classes of compounds.

Chirality is an important property of many biologically significant compounds and knowledge of absolute configuration is necessary for structure-activity relationship evaluation. NMR enables determination of enantiomeric purity, enantiomeric excess and absolute configuration using chiral shift reagents and chiral derivatizing reagents for *in-situ* reactions in NMR tubes.

Our research is also focused on the study of nonbonding interactions of supramolecular systems, mechanism and kinetics of deuterium exchange of pyrimidine C(5)-H using NMR and *ab initio* quantum chemical calculations.

Quantum chemical calculations of NMR parameters (shielding tensors and indirect nuclear spin-spin coupling constants) are found to be useful for prediction and interpretation of experimental NMR data. Our research is focused on calculation of these NMR parameters using *ab initio* methods for model compounds (peptides, nucleotides) and understanding and explaining of relationships between structural factors and calculated NMR parameters.

Current grant support

Grant Agency of the Czech Republic (203/09/1919)
Grant Agency of the Czech Academy of Sciences (KJB 400 550 903)

Selected recent papers

1. Buděšínský M., Daněček P., Bednárová L., Kapitán J., Baumruk V., Bouř P.: Comparison of quantitative conformer analyses by nuclear magnetic resonance and raman optical activity spectra for model dipeptides. *J. Phys. Chem. A* 112, 8633-8640, **2008**.
2. Slavětínská L., Mosinger J., Dračínský M., Pošta M.: NMR study of host-guest complexes of disulfonated derivatives of 9, 10-diphenylanthracene and corresponding endoperoxides with cyclodextrins. *J. Inclusion Phenomena and Macrocyclic Chem.* 61, 241-250, **2008**.
3. Míšek J., Teplý F., Stará I.G, Tichý M., Šaman D., Císařová I., Vojtíšek P., Starý I.: A straightforward route to helically chiral N-heteroaromatic compounds: Practical synthesis of racemic 1,14-diaza[5]helicene and optically pure 1- and 2-aza[6]helicenes. *Angew. Chem. Int. Ed.* 47, 3188-3191, **2008**.
4. Česnek M., Holý A., Masojídková M., Kmoníčková E., Zídek Z.: Synthesis of guanidino analogues of PMPDAP and their immunobiological activity. *Bioorg. & Med. Chem.* 16, 965-980, **2008**.
5. Čerňa I., Pohl R., Klepetářová B., Hocek M.: Synthesis of 6,8,9-Tri- and 2,6,8,9-Tetra-substituted Purines by a Combination of the Suzuki Cross-coupling, N-Arylation, and Direct C-H Arylation Reactions. *J. Org. Chem.* 73, 9048-9054, **2008**.

Pavlína Řezáčová

Research-Service Team
e-mail: rezacova@uochb.cas.cz
www.uochb.cz/rezacova

Structural Biology

The structural biology team carries out structural studies on various proteins of biological or medicinal interest. Among them, HIV protease (HIV PR) takes a prominent position. The HIV protease research is focused on development of novel potent inhibitors as well as on understanding the structural basis of drug resistance acquired by mutations in HIV PR. Emergence of drug-resistant strains of HIV remains a severe problem and therefore continued research effort is required to develop more potent antivirals. Our recent collaborative research project is focused on development of novel treatment strategies targeting cellular co-factors of HIV nuclear import and integration.

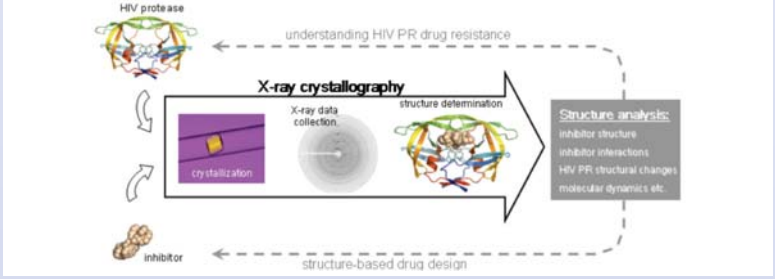
The team maintains an X-ray diffraction station for macromolecular crystallography and provides assistance with protein crystallization and collaboration for structure determination. Service for small molecular crystallography is also provided.

Current grant support

Commision of the European Communities (HEALTH-F3-2008-201032), Ministry of Education Youth and Sports of the Czech Republic (ME08016)

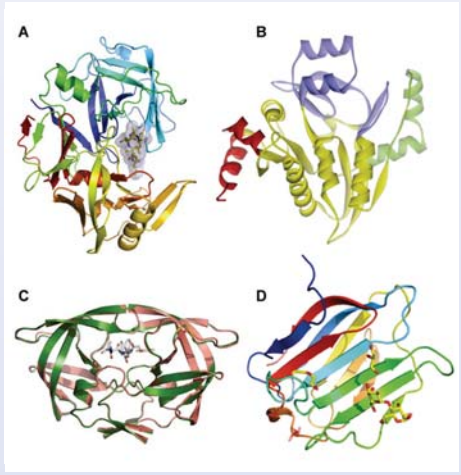
Selected recent papers

1. Dostál J., Brynda J., Hrušková-Heidingsfeldová O., Sieglová I., Pichová I., Řezáčová P.: The crystal structure of the secreted aspartic protease 1 from Candida parapsilosis in complex with pepstatin A. *J. Struct Bilogy* (**2009**) *in revision*
2. Gratz-Šašková K., Kožíšek M., Lepšík M., Brynda J., Řezáčová P., Václavíková J., Kagan R.M., Machala, L., Konvalinka, J. Molecular Mechanism of Reduced Susceptibility of HIV Protease to the Protease Inhibitor Lopinavir Conferred by the I47A Mutation. *Protein Science* (**2008**) 17:1555-64
3. Krejčiříková V., Fábry M., Marková V., Malý P., Řezáčová P., Brynda J.: Crystallization and preliminary X-ray diffraction analysis of mouse galectin-4 N-terminal carbohydrate recognition domain in complex with lactose. *Acta Cryst F* (**2008**) 64:665-7.
4. Řezáčová P., Kožíšek M., Moy S.F., Sieglová I., Joachimiak A., Machius M., Otwinowski Z.: Crystal structures of the effector-binding domain of repressor CggR from Bacillus subtilis reveal ligand-induced structural changes upon binding of several glycolytic intermediates. *Mol. Microb.* (**2008**) 69: 895-910
5. Kožíšek M., Šašková K., Řezáčová P., Brynda J., van Maarseveen N.M., De Jong D., Boucher Ch., Kagan R., Nijhuis M., Konvalinka J.: Ninety Nine is Not Enough: Molecular Characterisation of Drug-Resistant HIV-Protease Mutants with Insertions in the Flap Region Yielding Resistance to Protease Inhibitors. *J. Virol (**2008**),* 82 (12): 5869-5878.



Schematic of structural studies of HIV PR-inhibitor complexes.

Pavlína Řezáčová, PhD / Head of the Team
Jiří Brynda, PhD / Scientist
Irena Sieglová, MSc / Research Assistant
Blanka Klepetářová, MSc / Research Assistant
David Kredba, MSc / Research Assistant
Jitka Kredbová / Technician
Kateřina Čermáková / Student
Jana Písačková / Student



Selected protein crystal structures published in 2008/2009: **A**. Secreted aspartic protease from Candida parapsilosis [ref. 1], **B**. the effector-binding domain of repressor CggR from Bacillus subtilis [4], **C**. HIV-1 protease with insertion E35EE [5], **D**. mouse galectin-4 carbohydrate recognition domain [3].

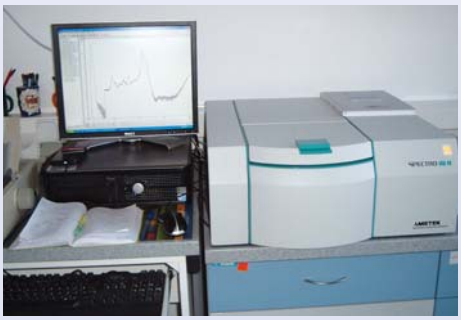
Service Departments

Stanislava Matějková
Service Department
e-mail: matejkova@uochb.cas.cz
www.uochb.cz/matejkova

Analytical Laboratory

Stanislava Matějková, MSc / Head of Analytical Laboratory
Lucie Holasová, MSc / Vice-head of Analytical Laboratory
Štefan Štanga, MSc / Technician
Magdalena Hošková / Technician

Perkin Elmer – CHN



Spectro iQ – XRF

Autopol IV – OR

The standard analytical services provided to the staff of the IOCB include elemental analyses, optical rotation measurements of organic compounds and some other analytical determinations using volumetric analyses or ion selective electrode.

In 2008, a **new simultaneous energy-dispersive X-ray fluorescence spectrometer SPECTRO iQ II** was purchased for our analytical laboratory to provide sufficiently sensitive and nondestructive analysis of sulphur, phosphorus, chlorine, bromine and iodine. This replaced classical time and sample consuming titrimetric determinations. Additionally, both qualitative analyses and quantitative determinations of many other elements extended services of our laboratory. In fact, we can develop methods for determination of any element from sodium to uranium (except palladium), but we need appropriate standards with a known (certified) content of the element to be determined. The limits of detection are different depending on individual elements; typically they are in a range from one to tens ppm. In addition to S, P, Cl, Br and I, determination methods for potassium and silicon in methanol solutions, in toluene/oil matrix, and platinum in aqueous medium have been established in the previous months. In the future, we plan to develop various quantitative methods in several other non-volatile solvents with proper elemental compositions (water, ethanol, etc.). Considering the minimal requirements on sample preparation for X-ray fluorescence analysis and the nondestructivity of the technique, the major part of the sample will be given back to the client.

Elemental analysis of organic compounds (EA) – The laboratory provides analytical capabilities for measuring content of hydrogen, carbon, nitrogen, fluorine, chlorine, bromine, iodine, phosphorus and sulphur in organic compounds. An automated CHN analyzer **(PE 2400 Series II CHNS/O Analyzer)** is used in C, H and N mode. Fluorine content is determined by use of and **ion selective electrode**. The determination of other mentioned elements is based on either volumetric methods or X-ray fluorescence spectroscopy **(SPECTRO iQ II).**

Measurement of optical rotation / specific rotation (OR) – The ordinary optical rotation of plane polarized light can be measured in the UV/Vis range at six different wavelengths (365 nm, 405 nm, 436 nm, 546 nm, 589 nm and 633 nm) using the polarimeter **Autopol IV**. The sample cells for 0.5, 1.5 and 2.8 mL are available.

Karel Ženíšek

Service Department
e-mail: karelz@uochb.cas.cz
www.uochb.cz/zenisek

Development Engineering Workshops

Topics of Development Workshops include maintenance of scientific instruments, development and production of simple apparatuses according to the requirements of the individual scientific laboratories and development and production of unique scientific equipment.
The number of the IOCB service orders exceeds 1100 per year. An *in vitro* model of an *in vivo* human digestive tract type GOLEM has been developed and realized in cooperation with Zentiva a.s. (2008).
An automatic multiple peptide synthesizer type AVSP -2 has been developed and realized for Institute of Macromolecular Chemistry of the ASCR, v.v.i. (2008).

Current grant support

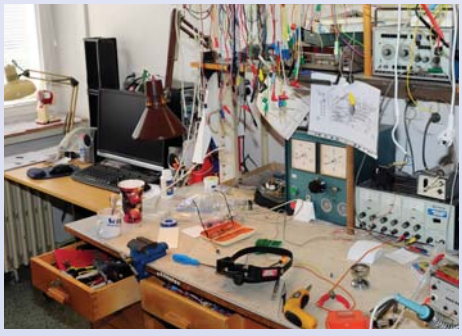
Grant Agency of the Academy of Sciencies of the Czech Republic ident. Code IAA400550919, Ivo Starý
Electronic transport in single molecule junctions
(2009-2012)

Karel Ženíšek, MSc
/ Head of Development Workshops
Petr Mudra, MSc / Vice-head
Pavel Poncar
/ Vice-head of Mechanical Workshops

Technicians:
Jiří Smrž, MSc
Václav Pešek, MSc
Vít Pokorný, MSc
Zdeněk Barták
Olga Karpíšková

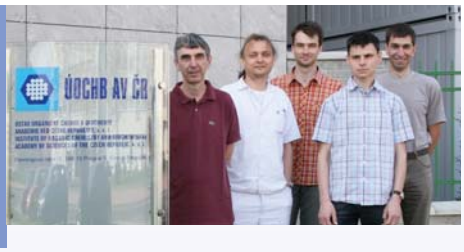
Secretary:
Věra Bláhová

Qualified workers:
Daniel Kolaja
Miroslav Bok
Jaroslav Bárta
Oldřich Spáčil
František Vávra
Vladimír Šprdlík
Jan Všetečka



Ivan Černý
Service Department
e-mail: cerny@uochb.cas.cz
www.uochb.cz/cerny

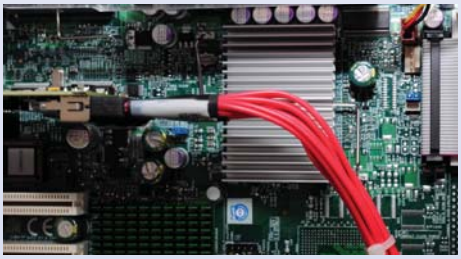
Information Technology



Černý Ivan, PhD / Head of IT group
Babovák Miloš, MSc / Vice-head of IT group
Klusák Vojtěch, MSc / IT
Kulhavý Vladimír, Bc / IT
Liboska Radek, PhD / IT

The main objectives of the Department of Information Technology are to provide convenient and secure access to information sources and services for IOCB employees. Our small team is responsible for the maintenance and development of basic network infrastructure, for the management of institutional servers (network services and databases), and for assistance in desktop computer related problems. We provide support for workstation installations, network configuration, multi-license software administration, security incidents handling, and network printing.

Network services at the institute have been provided since 1992 by network administrators. In 2003, the IT group was formed as part of the Scientific Information Centre of IOCB, and in 2007 the group became an independent department.



Petr Šimek

Service Department
e-mail: simek@uochb.cas.cz
www.uochb.cz/simek

Chemical Service Laboratories

The activities of the Chemical Service Laboratories can be separated into five basic areas:

1) Distillation of solvents
2) Purification of solvents (for example preparation of HPLC solvents or dry solvents)
3) Regeneration of solvents
4) Bulk synthesis
5) Collection and disposal of waste solvents

Distillation of solvents

In 2008, nearly 10 tons of solvents was distilled.

Purification of solvents

Main products are dry and high pure dichloromethane, which has been prepared 650 litres and HPLC methanol, which has been prepared 1000 litres.

Regeneration of solvents

The reason for regeneration of solvents is economic rather than ecological. That is why mainly chloroform is regenerated. In 2008, 2 tons of chloroform by regeneration was obtained.

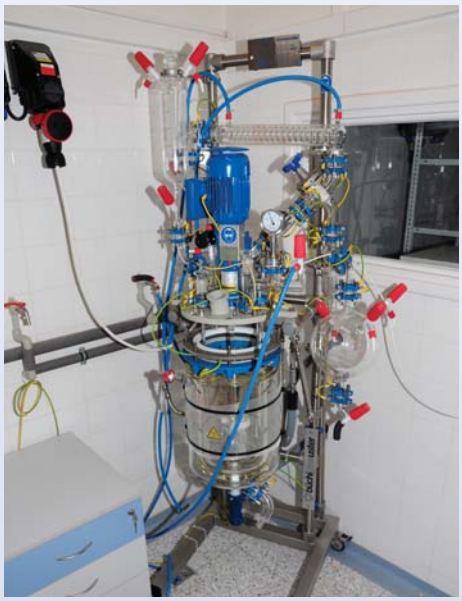
Bulk synthesis

This synthesis is performed usually in hundreds of grams. The compounds prepared are either expensive or commercially not available.
In 2008, a new chemical reactor, MiniPilot 10 equipped with a 10lt reaction vessel and thermostat (Julabo Presto LH50) was purchased for performing bulk synthesis.

Collection and disposal of waste solvents

Nearly 14 tons of waste solvents was collected in 2008 and transferred to specialized form for disposal.

Petr Šimek, PhD / Head of Service Laboratories
Jiří Erbs / Technician
František Pavlů / Technician
Vladimír Strnad / Technician



Miroslava Blechová
Service Department
e-mail: blechova@uochb.cas.cz
www.uochb.cz/blechova

Synthesis of Peptides

Miroslava Blechová, MSc
/ Head of Synthesis of Peptides
Martin Hradilek, PhD /Research Assistant
Aliaksandryna Prykhodzka / Technician

We are focused on synthesis of peptides in solid phase. The principle of solid phase peptide synthesis as conceived by R. B. Merrifield is based on the idea that if the synthesized peptide is bound to an insoluble support, then any unreacted reagents left at the end of any synthetic step can be removed by a simple wash procedure. And, such arrangement is amenable to automation. The peptides are synthesized by Fmoc chemistry. The reason is that the use of the base labile fluorenylmethyloxycarbonyl group (Fmoc) for α-amino group protection enables relatively mild deprotection and cleavage from the resin.
The peptide sequence is assembled by a solid-phase synthesizer ABI 433A (Applied Biosystems).
The peptide chemistry group provides peptides and related products for protein structure and activity studies. It includes chromogenic/fluorogenic substrates, peptides with special amino acids, peptidomimetics, and features side and/or main-chain modified peptides, peptides with secondary structure mimetics and inducers, de novo peptide structures, macropeptide structures, and reactive peptides. It involves Boc and Fmoc solid/solution phase synthetic methodology including combinatorial peptide libraries, peptide conjugation, disulfide bridges, complex peptides/peptidomimetics, special amino acids and their derivatives, phosphorylated/biotinylated structures, chromogenic/fluorogenic probes attachment, and solid phase/solution/segment coupling technologies.

Zdeněk Voburka

Service Department
e-mail: voburka@uochb.cas.cz
www.uochb.cz/voburka

Protein Analysis

The protein analysis department provides protein sequencing, amino acid analysis, and additional services for other groups, including administration, glass washing, and growth media preparation.

Protein Sequencing

The chemical process used in the Procise system is derived from the technique developed by Pehr Edman in the 1950's for the sequential degradation of proteins and peptides. In the Edman degradation, a protein's N-terminal amino acid is specifically reacted with phenylisothiocyanate (PITC). This derivatized amino acid is then selectively removed, leaving the rest of the peptide chain intact. Each cycle of the degradation removes the new N-terminal amino acid from the peptide chain. The resulting PTH-amino acids are analyzed sequentially [by RP HPLC] to determine the amino acid sequence of the protein or peptide.
The facility operates the Procise 491 HT Protein Sequencing System and the Procise 494 cLC Protein Sequencing System (high sensitivity analyses at sub-picomole level).

Amino Acid Analysis

Our facility conducts several hundreds of analyses of sample concentration, composition, and purity annually, thus aiding the research teams in their proteomics, protease inhibition, recombinant protein, and incorporation studies.
Typically, amino acids bound in peptide or protein are hydrolyzed in a vacuum for 20 hours by means of 6N HCl, the hydrolysate is vacuum evaporated, reconstituted in loading buffer (pH 2.2) containing the internal standard norleucine, and injected onto the Biochrom 20 Amino Acid Analyzer.
Amino acids are separated primarily according to their charge and secondarily according to their size and hydrophobicity. Effluent amino acids mix on-line with the ninhydrin detection reagent, react at elevated temperature, and their derivatives are detected photometrically at 570 and 440 nm.
Hydrolysis and analysis usually require about two business days. The estimated amount of protein required for an accurate analysis is 0.1 to 0.5 mg. Generally, pure samples are required as the presence of salts, buffers (phosphate, sulphate, amine buffers), carbohydrates, glycerol, and detergents is potentially deleterious. Samples containing heavy metals are unacceptable. The average internal error is between 5 and 10%.

Zdeněk Voburka, MSc
/ Head of Protein Analysis
Radko Souček, MSc
/ Vice-head of Protein Analysis
Věra Himrová / Technician
Jana Šípová, MSc / Secretary
Eva Círmanová/Technician

Zuzana Formanová

Scientific Information Centre/Library
e-mail: formanova@uochb.cas.cz
www.uochb.cz/library

Zuzana Formanová, MSc / Head of the Team
Kristina Doležálková / Reprography
Miluše Kalusová / Reprography
Miluše Kortusová / Book-binder
Marie Krahulcová / Librarian
Hana Pěknicová / Librarian
Michaela Sejková / Librarian
Michaela Záluská / Librarian

The library of IOCB was established with the foundation of IOCB. Since then, the library stock and the number of provided services have been enlarged step by step. The visitors of the library are mainly IOCB staff. Since the library was opened to the public in 2002, it has also provided special services to external visitors. Currently the existing department of SIC (Scientific Information Centre) is divided into three parts:

1/Library
2/Reprography
3/Bindery

SIC Collections:

The library collection is created from **50,073** items (as 2008). With the advancement of modern technology, the structure of services provided has changed. We offer **111** print journals and **7,500** fulltext on-line journals (ACS, Royal Society of Chemistry, Elsevier, Springer, Wiley, EBSCO, ASM, etc.) and thousands of other factographic, bibliographic and other information from databases like Web of Knowledge, Scopus, etc.

Services:

– Purchase of books and journals on demand for IOCB staff, planning of acquisitions, development and implementation of new services, reference services, editing Web sites, ISBN assignment (responsible person, Dr. Z. Formanová)
– Loan of books and journals, inter-library journal exchange, registration and claim of journals and reference services (responsible person, H. Pěknicová)
– Provide international inter-library loan services for visitors of library both in the classic form and through electronic document delivery systems, and granting inter-library loan services to other libraries. We cooperate mainly with libraries of The Academy of Sciences of The Czech Republic, The National Library, The National Medical Library, The Technical State Library and with university level libraries and schools (responsible person M. Záluská)
– Collect information about publication activities of IOCB scientists into the database ASEP ARL (RIV) (responsible person M. Krahulcová)
– Catalogue, revise and administer of stocks (responsible person M. Sejková)
– Reprography and print services (responsible persons K. Doležálková and M. Kalusová)
– Bindery services (responsible person M. Kortusová)

Miroslav Ledvina

Technology Transfer Team
e-mail: Ledvina@uochb.cas.cz
www.uochb.cz/ledvina

Bioorganic Chemistry of Saccharides, Glycoconjugates and Delivery Systems for Target Therapy

The team is presently engaged in two main areas: (a) basic research of glycomics and delivery systems; (b) transfer of research results achieved in the field of non-pyrogenic nor-muramic glycopeptides as immunotherapeutics to clinical practice. These compounds can be used as adjuvants in the construction of a new generation of vaccines (both recombinant and genetic) and as immunostimulants of innate immunity (antiinfection and antitumor) in the treatment of haemopoiesis caused by radio- or chemotherapy. This topic is solved in collaboration with the Imperial College London, with the Veterinary Research Institute – Brno and with ImuThes Limited – London. Results are subject to the submitted UK patent application and PCT application. Recently, a company spin-off has been established (Mendel Therapeutics, Ltd.). The research activities are focused on chemistry of saccharides, oligosaccharides, and glycoconjugates of hexosamine type, and the study of interactions of these structures with the recognition and regulatory systems in living organisms on a molecular level. The newly opened project is focused on the development of delivery systems for target immunotherapy and chemotherapy. Close attention is paid to self-assembly lipid structures and systems based on prospective properly functionalized carbon nanoparticles.

Current grant support

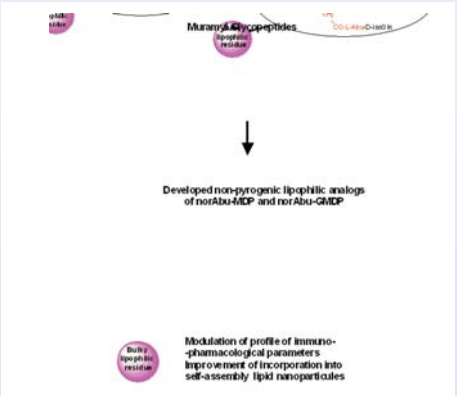
Academy of Sciences (Z40550506) and The Grant Agency of the Academy of Sciences of the CR ("Nanotechnologies for Society", KAN200520703 and KAN200100801).

Selected recent papers

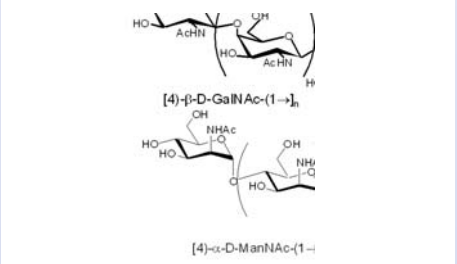
1. Turský, M.; Veselý, J.; Tišlerová, I.; Trnka, T.; Ledvina, M. "Synthesis of new type of D-mannosamine glycosyl donors and acceptor and their use for the preparation of oligosaccharides consisting of D-mannosamine units linked by (1 → 4) glycosidic bonds" *Synthesis* **2008**, 2610-2616.
2. Wang, X. F.; Birringer, M.; Dong, L. F.; Vepřek, P.; Low, P.; Swettenham, E.; Stantic, M.; Juan, L.H.; Zobalová, R.; Vu, K.; Ledvina, M.; Ralph, S.J.; Neužil J. „A peptide conjugate of vitamin E succinate targets breast cancer cells with high ErbB2 expression" *Cancer Research* **2007**, *67*, 3337-3344.
3. Veselý, J.; Rohlenová, A.; Džoganová, M.; Ledvina, M.; Trnka, T.; Tišlerová, I.; Šaman, D. "Preparation of Ethyl 2-azido-2-deoxy-1-thio-β-D mannopyranosides, and their rearrangement to 2-S-Ethyl-2-thio-β-D-mannopyranosylamines" *Synthesis* **2006**, 699-705.

Miroslav Ledvina, PhD / Head of the Team
Ludvík Streinz, PhD / Scientist
Jan Ježek, PhD / Scientist
Martin Flegel, PhD / Research Assistant
Daniel Zyka, PhD / Research Assistant
Anna Kovalová / Postdoc
Lukáš Werner / Postdoc
Martina Wernerová / Postdoc
Lukáš Drašar / PhD Student
Beata Jonsztová / Student
Radka Pavelová / Technician
Věra Součková / Technician

Non-pyrogenic lipophilic analogs of nor-muramic glycopeptides



Novel and versatile methods for synthesis of oligosaccharides of hexosamine type



The synthesis olidosacharides consisting from D-galactosamine and D-mannosamine units has received little attention so far.

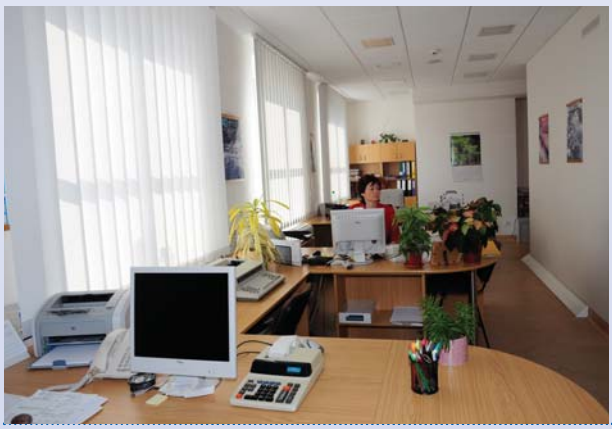
Economic & Technical Administration

Head: Božena Petschová
e-mail: petschova@uochb.cas.cz

Services – Finances and Administration:

Head: Božena Petschová

Marta Bassová
Jitka Bieberová
Eva Doležalová
Marie Dvořáková
Irena Eisenreichová
Jana Framberková
Ivana Hervertová
Ivana Janáčková
Svatoslava Janečková
Simona Juzlová
Štěpánka Kindlmannová
Jiřina Maršíková
Jarmila Mlejnková
Dagmar Oudrnická
Bronislava Šaffková
Ilka Tomášková
Dagmar Šimková
Zdeňka Gregorová
Eva Křížková



Services – Building Maitenance:

Head: Josef Šára

Karel Šobíšek
Jaroslav Hofman
Radoslav Kracík
Václav Mžourek
Leopold Cillich
Josef Dvořáček
Jan Hladký
Libuše Kalibová
Zdeněk Studený
Radka Faltová
Martin Autengruber
Daniela Fantlová
Hana Ederová
Václav Hrabák
Petr Heřman
Miroslava Fialová
Ludmila Baštová
Jan Janoušek
Petr Polák
Richard Jebavý
Jiří Mach
Jan Prachař
Jaroslav Slaba
Jiří Vytejček

Director's office

Head of the Secretariat:
Jakub Hošek
hosek@uochb.cas.cz

Secretary:
Olga Stanková
stankova@uochb.cas.cz

Human Resources:
Stanislava Opplová
opplova@uochb.cas.cz

IOCB Safety Officer:
Michal Pošta
posta@uochb.cas.cz

Grant Officer:
Renata Šroglová
sroglova@uochb.cas.cz

Public Relation:
Irena Krumlová
krumlova@uochb.cas.cz

Board of Institute

Chairman: *Jan Konvalinka* *IOCB AS CR, v.v.i.*
Vice – Chairman: Tomáš Kraus *IOCB AS CR, v.v.i.*

Internal Members:

Antonín Holý	*IOCB AS CR, v.v.i.*
Irena Valterová	*IOCB AS CR, v.v.i.*
Miloš Buděšínský	*IOCB AS CR, v.v.i.*
Lubomír Rulíšek	*IOCB AS CR, v.v.i.*

External Members:

Jitka Moravcová	*ICT Prague*
Hana Sychrová	*IP AS CR, v.v.i.*
Jana Hodačová	*ICT Prague*

Secretary:
Bohumír Koutek *IOCB AS CR, v.v.i.*

Board of Trustees

Chairman:
Jiří Rákosník *Academy of Sciences AS CR*

David Šaman	*IOCB AS CR, v.v.i.*
Helena Illnerová	*Council of Science AS CR*
Tomáš Chalupa	*Metropolitan District Prague 6*
Pavel Šebek	*Zentiva, a.s.*
Peter Šebo	*IMG AS CR, v.v.i.*

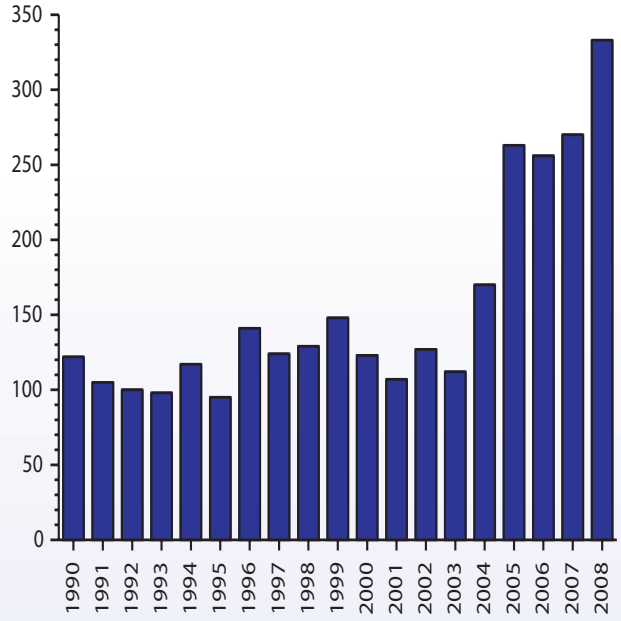
Secretary:
Bohumír Koutek *IOCB AS CR, v.v.i.*

International Advisory Board

Daniel Belluš (Switzerland)
Wilhelm Boland (Germany)
Erik De Clercq (Belgium)
Alan R. Katritzky (USA)
Pavel Kočovský (United Kingdom)
Burkhard König (Germany)
H.G. Kräusslich (Germany)
Michal Lebl (USA)
Jean-Marie Lehn (France)
Frank Tureček (USA)
Alexander Wlodawer (USA)

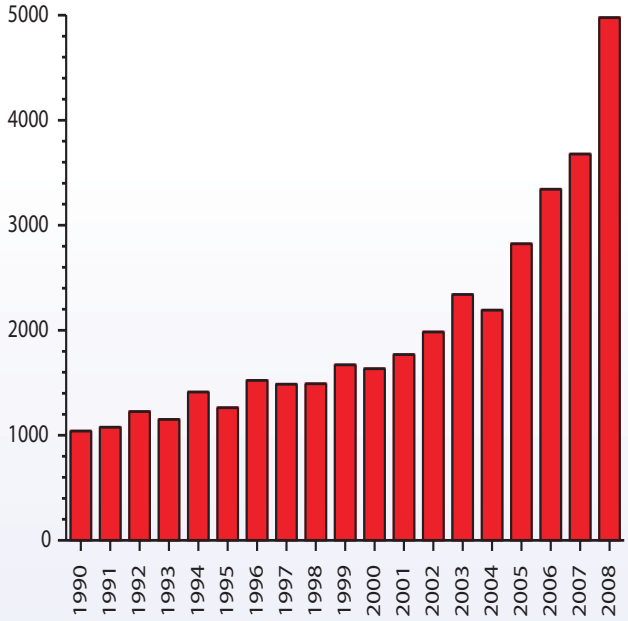
Publications

Number of Publications in Scientific Journals



The graph shows number of publications in scientific journals published or co-published by the IOCB employees each year. The increase of the published items is attributed to periodic evaluation of the scientific teams, increased motivation of the IOCB scientists and improved working conditions. Adapted from WoS (Thomson ISI).

Number of Citations on the Articles Published by the IOCB



Number of citations on the articles published by the IOCB scientists each year. Increase of the number of citations reflects the increased number of publications produced by the IOCB employees and increased quality of the publications and scientific results. Adapted from WoS (Thomson ISI).

Scientific journal of IOCB

collection
of Czechoslovak Chemical Communications

Michal Hocek, Assoc. Prof., DSc
Editor-in-Chief
e-mail: hocek@uochb.cas.cz
http://cccc.uochb.cas.cz

Bohumír Valter, MSc
Managing editor
e-mail: valter@uochb.cas.cz
http://cccc.uochb.cas.cz

Collection of Czechoslovak Chemical Communications

Collection of Czechoslovak Chemical Communications is an international scientific journal founded in 1929. It has acquired a wide circulation and a high reputation in the world of chemical literature. The journal publishes original papers and reviews in English by authors from various countries. The journal covers not only traditional fields, such as organic, physical and inorganic chemistry and biochemistry, but also interdisciplinary areas ranging from chemical physics to bioorganic chemistry.

Invited Lectures

IOCB Invited Lectures 2007

February 19, 2007
Prof. Manfred T. REETZ
MPI für Kohlenforschung, Mülheim, Germany
Evolution in the Test-Tube as a Means to Create Functional Enzymes

March 30, 2007
Prof. Herbert WALDMANN
MPI of Molecular Physiology, Dortmund, Germany
Biology Oriented Synthesis (BIOS)

April 4, 2007
Prof. E. Peter KÜNDIG
Department of Organic Chemistry, University of Geneva, Switzerland
Advances in Transition Metal Lewis Acid – Mediated and Catalyzed Reactions

April 25, 2007
Prof. David N. REINHOUDT
Faculty of Science and Technology, University of Twente, Enschede, The Netherlands
Molecular Printboards

May 21, 2007
Prof. Sason SHAIK
Department of Organic Chemistry, The Hebrew University, Jerusalem, Israel
A Tale of Two States: From Iron Oxo Diatomic to Cytochrome P450 and Other Oxidation Catalysts

May 28, 2007
Prof. Colin NUCKOLLS
Department of Chemistry, Columbia University, New York, USA
Reaction Chemistry Meets Lithography

June 22, 2007
Prof. Douglas F. COVEY
Department of Molecular Biology and Pharmacology, Washington University School of Medicine, St. Louis, Missouri, USA
ent-Steroids: Chemistry and Biology

June 26, 2007
Prof. Klaus MÜLLEN
MPI for Polymer Research, Main, Germany
Putting the Molecules into Molecular Electronics

September 24, 2007
Prof. James M. TOUR
Chemistry Department, Rice University, Houston, Texas, USA
Organic Nanotechnology: Nanotubes, Molecular Electronics and Nanocars

October 8, 2007
Prof. Klaus MÜLLER-DETHLEFS
Photon Science Institute, University of Manchester, UK
Non-Covalent Interactions in Molecular Clusters: How Do We Compare Experiment and Theory?

October 22, 2007
Prof. Benjamin LIST
MPI für Kohlenforschung, Mülheim, Germany
New Concepts for Organocatalysis

October 29, 2007
Prof. Hisashi YAMAMOTO
Department of Chemistry, Chicago University, Illinois, USA
Acid Catalysis for Asymmetric Synthesis

October 31, 2007
Prof. Bruce H. LIPSHUTZ
Department of Chemistry and Biochemistry, University of California, Santa Barbara, CA, USA
Enabling Technologies Based on the Chemistry of Coenzyme Q10

November 6, 2007
Prof. Tamotsu TAKAHASHI
Catalysis Research Center, Hokkaido University, Sapporo, Japan
Carbon-Carbon Bond Cleavage and Formation on Titanocene

November 26, 2007
Prof. Ilan MAREK
Schulich Faculty of Chemistry, Technion-Israel Institute of Technology, Haifa, Israel
New Methods for the Preparation of Enantiomerically Pure all-Carbon Quaternary Centers in Acyclic System

December 3, 2007
Prof. Vlasta BONAČIĆ-KOUTECKÝ
Department of Chemistry, Humboldt University, Berlin, Germany
Tailoring Functionality of Clusters and their Complexes with Biomolecules by Size, Structures and Lasers

IOCB Invited Lectures 2008

February 19, 2008
Prof. Wolfgang LUBITZ
MPI für Bioanorganische Chemie, Mülheim, Germany
Light-Induced Water Splitting and Hydrogen Production in Nature: Structure and Function of the Enzymes Wateroxidase and Hydrogenase

March 4, 2008
Prof. Stephen L. BUCHWALD
MIT, Cambridge, Massachusetts, USA
Transition Metal-Catalyzed Carbon-Carbon and Carbon-Heteroatom Bond-Forming Processes: Progress, Applications and Mechanistic Studies

March 13, 2008
Prof. Paul KNOCHEL
Department of Chemistry, Ludwig-Maximilians-Universität, Munich, Germany
Functionalized Mg and Zn-Organometallics for Organic Synthesis

March 27, 2008
Prof. Eric T. KOOL
Department of Chemistry, Stanford University, Stanford, California, USA
Mimicking the Structure and Function of DNA

May 13, 2008
Prof. Albert PADWA
Department of Chemistry, Emory University, Atlanta, Georgia, USA
Cascade Reactions for Alkaloid Synthesis

May 19, 2008
Prof. Dieter SEEBACH
Laboratory of Organic Chemistry, ETH, Zurich, Switzerland
Lessons from Chemical and Biological Investigations of Peptides Built from Homologated Proteinogenic Amino Acids

May 27, 2008
Prof. Wes BORDEN
Department of Chemistry, University of North Texas, Denton, Texas, USA
Theoretical Studies of the Schizophrenic Effects of Geminal Fluorination on Organic Reactions: Explanations and Predictions

June 6, 2008
Prof. Jay S. SIEGEL
Organisch-chemisches Institut, Universität Zürich, Zürich, Switzerland
Novel Aromatics as the Core of Nano-Scale Materials

June 12, 2008
Prof. Alois FÜRSTNER
Max-Planck-Institut für Kohlenforschung, Mülheim, Germany
Catalysis for Total Synthesis

June 20, 2008
Prof. Marcel MAYOR
Department of Chemistry, University of Basel, Basel, Switzerland
Molecules: Nanoscale Functional Units

September 23, 2008
Prof. Shu KOBAYASHI
Graduate School of Pharmaceutical Sciences, University of Tokyo, Tokyo, Japan
Toward Truly Efficient and Powerful Organic Synthesis – New Dimension of Acid and Base Catalysis

October 16, 2008
Prof. Steven V. LEY
Department of Chemistry, University of Cambridge, Cambridge, UK
The Azadirachtin Story

Postdoctoral Projects

IOCB Postdoctoral Projects

Institute of Organic Chemistry and Biochemistry (IOCB), Academy of Sciences of the Czech Republic, v.v.i., is opening **postdoctoral positions in chemistry and biochemistry**. The IOCB will open up to 10 positions every year. The position is open for **one year**, with possible prolongation by **one more year**, if agreed by both parties. The applicant is expected **to have PhD** from foreign university.

The salary amounts to CZK 28,000 each month, plus possible premiums up to 10 % for exceptional performance, plus whatever complementary money can be obtained from research grants. The Institute also provides accommodation for around CZK 3,000, institute or academy housing. In case accommodation is not available, the IOCB will partly compensate the price of a private accommodation, up to the real price (reduced by CZK 3,000 of the applicant's contribution), but up to total amount of salary of CZK 34,000 in gross. In addition to the salary, the Institute will cover obligatory health and social insurance (about 2/3). The health insurance will be comparable to the one the permanent Czech employees have. The salary is subject to state tax.

The Institute is located in a desirable part of town with little traffic, about 20 minutes walk north from the Prague castle, and about 5 min walk from a subway terminal station (Metro). From the Metro station, downtown is 10 minutes away, with connections to other parts of town.

EU citizens will not need a work permit, non-EU citizens will need to get a work permit from the Czech Embassy in their home country. The Institute will provide the necessary documents for obtaining the work permit and assistance (at the expense of the applicant). To apply for IOCB postdoctoral position, applicants need to contact a scientist of the Institute, put together a postdoctoral project, and submit the proposal to the director of the Institute (e-mail address: uochb@uochb.cas.cz).

The application should include:

- Contact address
- Curriculum vitae
- Copy of PhD diploma
- List of publications
- Name of IOCB partner
- Description of the postdoctoral project
- Starting date
- Whether a work permit is needed
- Whether a accommodation is required
- Two letters of recommendation from respected scientists

The Selection committee will make the decision twice a year and will inform the applicant.

Postdoctoral Projects 2007

Louis ADRIANSSENS
Great Britain; Research team of Filip Teplý

Ivana KÓŠIOVÁ
Slovakia; Research team of Ivan Rosenberg

Angeles PULIDO-JUNQUERA
Spain; Research team of Pavel Hobza

Martina ZIKMUNDOVÁ
Czech Republic; Research team of Michal Mareš

Florence SZYDLO
France; Research team of Ivo Starý

Michael STRAKA
Czech Republic; Research team of Petr Bouř

Aurelie BOURDERIOUX
France; Research team of Michal Hocek

Sille EHALA
Estonia; Research-service team of Václav Kašička

Postdoctoral Projects 2008

David SILLAM-DUSSÉS
France; Research team of Irena Valterová

Dušan KOVAL
Czech Republic; Research-service team of Václav Kašička

Gloria HUERTA-ANGELES
Mexico; Research team of Ivo Starý

Ekaterina V. BOLTUKHINA
Russia; Research team of Ilya Lyapkalo

Hubert CHAPUIS
France; Research team of Michal Hocek

Dushant A. KHOBRAGADE
India; Research team of Josef Michl

Robert MUSIOL
Poland; Research team of Michal Hocek

Olivier SONGIS
France; Research team of Ivo Starý

Sabbatical Program

IOCB sabbatical visit program

The Institute of Organic Chemistry and Biochemistry (IOCB), Academy of Sciences of the Czech Republic, v.v.i. has introduced and will provide financial support for a new project entitled the „**IOCB Sabbatical Visit Program**„ for prominent foreign scientists. The aim of the program is to expand contacts between the Institute's employees and other scientists, to establish a framework for future cooperation, and to promote the Institute's activities.

Financial aid for the „**IOCB Sabbatical Visit Program**„ is granted based on an application made by a host. A guest's visit must last no less than six weeks and no more than one year. A guest must make a sworn statement that his/her parent organization has granted him/her a sabbatical leave and will not pay the guest's stay at the Institute of Organic Chemistry and Biochemistry ASCR, v.v.i. or that it will pay his/her stay to a limited extent only, describing the renumeration paid during the guest's stay at the Institute. Together with an application, the host must enclose the guest's CV, a list of his/her publications, and an agreement between the host and the guest regarding the topic of the guest's work and the organization of work conditions by the host. Further, the agreement must expressly state that publications created as a result of the guest's activities at the Institute will bear the name of the Institute and that the Institute will be entitled to the part of intellectual property created at the Institute.

Candidates for the „**IOCB Sabbatical Visit Program**„ will be selected by the Selection Committee for the „**IOCB Postdoctoral Project**„ at its regular semiannual meetings. In selecting candidates, the committee will use criteria based on the objectives of the program. The committee may recommend the maximum of three applicants for financial aid in one year.

The host is responsible for ensuring appropriate work conditions for a guest. Based on a preliminary budget, a host may request an increase in the applicable team budget to cover operating costs related to activities conducted by a guest, where such a sum may not exceed CZK 250,000 per year (or a commensurate portion of this sum depending on the length of stay).

The Institute provides financial aid in the following forms:

- Payment of per diems and reimbursement for accommodation expenses for guests who are not employed by the Institute, where an agreement on mutual exchange of employees is signed with their parent organization (Section 188[4] of the Labor Code). This financial aid is limited by the maximum length of stay at the Institute for three months. The maximum reimbursement for accommodation expenses totals CZK 15,000 per month, and it will only be paid by a transfer of funds to the account of the applicable facility providing accommodation.
- Payment of salary in the maximum gross amount of CZK 40,000 per month. As regards this form of financial aid, guests from countries other than EU Member States must arrange a work permit prior to their travel to the Czech Republic.

Financial aid will be reduced proportionately if a guest receives a partial reimbursement for expenses from his/her parent organization.

Granted Programs 2008

Prof. Hans LISCHKA

Institute for Theoretical Chemistry and Radiation Chemistry of the University of Vienna, Austria.

Research team of Prof. Pavel Hobza

Significant awards

Antonín Holý Prof., DSc, dr.h.c.mult.	Česká hlava	Project and synthesis of acyclic nucleosides	National prize of the Czech Government Česká hlava
Antonín Holý Prof., DSc, dr.h.c.mult.	Honorary Professorship of the University of Manchester	Life-work	University of Manchester
Antonín Holý Prof., DSc, dr.h.c.mult.	The John A. Montgomery Award 2008	Whole-life contribution in development of the chemistry of nucleic acid compounds	The Center for Drug Design, University of Minnesota
Antonín Holý Prof., DSc, dr.h.c.mult.	Doctor Honoris Causa	Life-work	University of South Bohemia in České Budějovice
Pavel Hobza Prof., DSc, FRSc	Česká hlava	Life-work and research in computational chemistry	National Prize of the Czech Government Česká hlava ČR
Pavel Jungwirth Assoc. Prof., DSc	Spiers Memorial Awards	Innovative computer simulation of surface processes	Royal Society of Chemistry, UK
Detlef Schroeder Assoc. Prof., DSc	Invited professor (cat. A)	Fundamental studies in ion chemistry	UPMC, France
Jiří Šrogl Assoc. Adj. Prof.	Associate Adjunct Professor	Scientific and pedagogical cooperation	Department of Molecular and Biomolecular engineering, North Carolina State university, Raleigh, USA
Ilya Lyapkalo PhD	Thieme Chemistry Journals Award 2008	Contributions to Thieme Journals	Editorial Boards of SYNTHESIS, SYNLETT and SYNFACTS
Filip Lankaš PhD	Fellowship J. E. Purkyně	Scientific work	Academy of Sciences CR
Petr Jansa MSc	2008 Gilead Sciences Fellowship	Scientific work	Gilead Sciences, Inc. (California, USA)
Vladimír Sychrovský PhD	Young Investigator Research Grant Award	Scientific work	Human Frontier Science Program, Strasbourg, France

Teaching Activities

Ab initio and density functional theory, *Sychrovský Václav,* Faculty of Mathematics and Physics, Charles University in Prague

Advanced methods of molecular dynamics, *Jungwirth Pavel,* Faculty of Mathematics and Physics and Faculty of Science, Charles University in Prague

Advanced Molecular Spectroscopy, *Sychrovský Václav,* Faculty of Mathematics and Physics, Charles University in Prague

Advanced practical course in biochemistry, *Konvalinka Jan,* Faculty of Science, Charles University in Prague

Bioorganic chemistry, *Břehová Petra,* Palacký University Olomouc

Bioorganic chemistry, *Hocek Michal,* Institute of Chemical Technology Prague

Computational simulations of molecule properties, *Bouř Petr,* Institute of Chemical Technology Prague

Determination of 3D structure of biomolecules, *Řezáčová Pavlína, Brynda Jiří,* Faculty of Science, Charles University in Prague

Electromigration methods, *Kašička Václav,* Faculty of Science and Faculty of Mathematics and Physics, Charles University in Prague; Institute of Chemical Technology Prague

General entomology, *Šobotník Jan,* Faculty of Science, Charles University in Prague

High performance liquid chromatography, *Cvačka Josef,* Faculty of Science, Charles University in Prague

Chemistry, *Blažek Jiří,* Secondary Technical School of Building and Business, Kladno

Chemistry of natural compounds I, *Hana Chodounská, Eva Šťastná, Miroslav Kvasnica, Vojtěch Kapras,* Faculty of Science, Charles University in Prague

Introduction to the methods of molecular dynamics and Monte Carlo, *Roeselová Martina,* Institute of Chemical Technology Prague and Faculty of Science, Charles University in Prague

Laboratory course in biochemistry, *Blažek Jiří,* Institute of Chemical Technology Prague

Mechanisms of organic reactions, *Stibor Ivan,* Institute of Chemical Technology Prague

Molecular biology and genetics II, *Konvalinka Jan,* Faculty of Science, Charles University in Prague

Natural compounds II, *Valterová Irena,* Faculty of Science, Charles University in Prague

Neurobiology, *Kalinová Blanka,* University of South Bohemian in České Budějovice

NMR II, *Dračínský Martin,* Faculty of Science, Charles University in Prague

Organic Chemistry, *Kotora Martin,* Faculty of Science, Charles University in Prague

Organic chemistry b, *Valášek Michal,* Faculty of Science, Charles University in Prague

Organic chemistry I, *Stibor Ivan,* Institute of Chemical Technology Prague

Organic Synthesis III, *Kotora Martin,* Faculty of Science, Charles University in Prague

Practical course in ethology, *Hanus Robert,* Faculty of Science, Charles University in Prague

Practical course in NMR I, *Dračínský Martin,* Faculty of Science, Charles University in Prague

Practical course in Organic Chemistry, *Kotora Martin,* Faculty of Science, Charles University in Prague

Regulation of biological processes by proteolysis, *Konvalinka Jan,* Faculty of Science, Charles University in Prague

Selected chapters of the chemistry of natural compounds I, *Pouzar Vladimír,* Institute of Chemical Technology Prague

Selected chapters of the chemistry of natural compounds II, *Pouzar Vladimír,* Institute of Chemical Technology Prague

Special spectroscopy, *Bouř Petr,* Faculty of Mathematics and Physics, Charles University in Prague

Structure and Reactivity II, *Starý Ivo,* Faculty of Science, Charles University in Prague

Theory of electron density, *Sychrovský Vladimír,* Faculty of Mathematics and Physics, Charles University in Prague

Theses Defended in 2007 and 2008

PhD theses

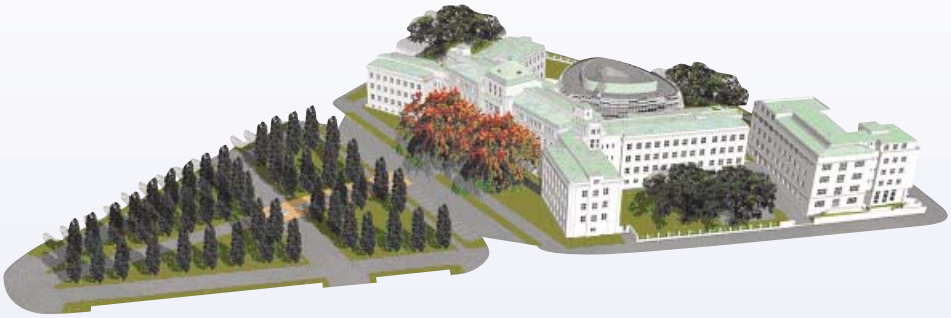
Petra Břehová	Synthesis and Properties of Chiral Acyclic Nucleoside Bisphosphonates and Phosphonomethylphospinates (Supervisor: Antonín Holý, Faculty of Science, Charles University in Prague)
Lucie Cahlíková	Isolation and identification of compounds affecting behaviour of hymenopteran insect (Supervisor: Irena Valterová, Institute of Chemical Technology, Prague)
Alice Ciencialová-Mášová	Study of immune response of flesh-fly larva Sarcophaga bullata (Supervisor: Jiří Jiráček, Faculty of Science, Charles University in Prague)
Petr Daněček	Anharmonic effects in vibrational spectroscopy (Supervisor: Petr Bouř, Faculty of Mathematics and Physics, Charles University in Prague)
Miroslav Hájek	Modulation of human telomerase activity by nucleoside and nucleotide analogues (Supervisor: Ivan Votruba, Faculty of Science, Charles University in Prague)
Jana Hýblová	Analysis of digestion process and its regulation in stock arthropoda contaminating food commodities (Supervisor: M. Mareš, Czech University of Life Sciences Prague)
Zuzana Krausová	Synthesis of Helical Molecules and their Application in Enantioselective Catalysis (Supervisor: Ivo Starý, Faculty of Science, Charles University in Prague)
Martin Kuchař	Synthesis of novel purine bases and nucleosides bearing functionalized ethyl or cyclopropyl groups in position 6 (Supervisor: Michal Hocek, Institute of Chemical Technology, Prague)
Babak Minofar	Structure and dynamics of ions at the air/water interface (Supervisor: Pavel Jungwirth, Faculty of Science, Charles University in Prague)
Jiří Míšek	On the Azahelicenes: Synthesis, Resolution, Properties and Application (Supervisor: Ivo Starý, Faculty of Science, Charles University in Prague)
Petra Mlčochová	Structure, activity and metabolism of human GCPII (Supervisor: Jan Konvalinka, Faculty of Science, Charles University in Prague)
Radim Nencka	Carbocyclic analogues of nucleosides and nonnucleoside inhibitors of thymidine phosphorylase (Supervisor: Hubert Hřebabecký, Faculty of Science, Charles University in Prague)
Miroslava Rovenská	Structural studies and tissue distribution of human GCPII and characterization of its rat and porcine orthologs (Supervisor: Jan Konvalinka, Faculty of Science, Charles University in Prague)
Jiří Rybáček	Synthesis of Complex π-Electron Systems (Supervisor: Petr Holý, Institute of Chemical Technology, Prague)
Jiří Šebek	Interpretation of peptide and porphyrin spectra (Supervisor: Petr Bouř, Institute of Chemical Technology, Prague)
Peter Šilhár	Synthesis and Transformations of Hydroxymethylated Purines (Supervisor: Michal Hocek, Institute of Chemical Technology, Prague)
Veronika Šolínová	Analysis, separation and physico-chemical characterization of peptide hormones by capillary electrophoresis (Supervisor: Václav Kašička, Faculty of Science, Charles University in Prague)
Václav Vaněk	Synthesis of prolinol-based phosphonate nucleotide analogues (Supervisor: Ivan Rosengerg, Faculty of Science, Charles University in Prague)
Milan Vrábel	Preparation of nucleosides, nucleotides and oligonucleotides bearing metal complexes for bioanalytical applications (Supervisor: Michal Hocek, Institute of Chemical Technology, Prague)
Luboš Vrbka	Theoretical studies of ions at phase interfaces (Supervisor: Pavel Jungwirth, Faculty of Science, Charles University in Prague)

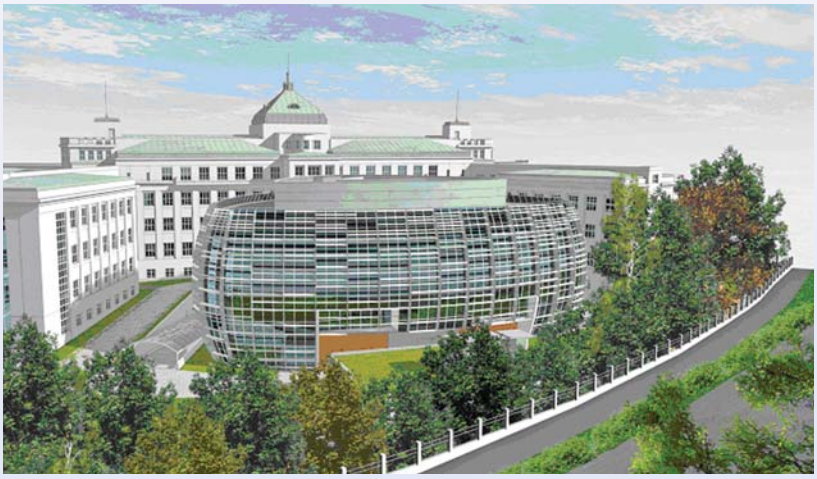
Diploma theses

Jiří Blažek	Synthesa sloučenin s možným biologickým účinkem a jejich převádění na proléčiva chemickými a enzymatickými metodami (Supervisor: Antonín Holý, Blanka Králová Institute of Chemical Technology, Prague)
Petra Buriánková	Analysis, characterization and separation of dipeptide derivatives of methionine-statine by capillary electromigration methods (Supervisor: Václav Kašička, Faculty of Science, Charles University in Prague)
Milan Dejmek	Syntéza nových konformačně uzamčených karbocyklických nukleosidů odvozených od 2-(hydroxymethyl)bicyklo[2.2.1]heptanu (Supervisor: Hubert Hřebabecký, Faculty of Science, Charles University in Prague)
Denisa Geffertová	Determination of acidity constants of cytosine and uracil derivatives by capillary zone electrophoresis (Supervisor: Václav Kašička, Faculty of Science, Charles University in Prague)
Ivona Hančlová	New truncated and untruncated insulin analogs with modifications in position B26 (Supervisor: Jiří Jiráček, Faculty of Science, Charles University in Prague)
Jan Heyda	Ion distribution on surfaces of hydrated proteins (Supervisor: Pavel Jungwirth, Faculty of Mathematics and Physics, Charles University in Prague)
Vojtěch Kapras	Synthesis of fluorescent-labelled neuroactive steroids (Supervisor: Hana Chodounská, Faculty of Science, Charles University in Prague)
Tomáš Knedlík	Mouse glutamate carboxypeptidase II: cloning, expression and activation (Supervisor: Jan Konvalinka, Faculty of Science, Charles University in Prague)
Michal Korf	Catalytic reductive cross-coupling of aryl iodides with disulphides. Study of mechanism and synthetic extent of the reaction. (Supervisor: Jiří Šrogl, Institute of Chemical Technology, Prague)
Šárka Lipnická	Oligophenylethynylenes with Electron-rich Substituents: Synthesis and Properties (Supervisor: Martin Bělohradský, Institute of Chemical Technology, Prague)
Resha Matyšková	Effects of CART peptide, cholecystokinine and neuropeptide Y on food-intake in mouse obesity model (Supervisor: Lenka Maletínská, Faculty of Science, Charles University in Prague)
Václav Navrátil	Human glutamate carboxypeptidase II and its paralogs (Supervisor: Jan Konvalinka, Faculty of Science, Charles University in Prague)
Adam Nekola	Male bumble-bees feromones and presumption for their formation from lipidic precursors (Supervisor: Irena Valterová, Faculty of Science, Charles University in Prague)
Tereza Schimperková	Determination of association constants of complexes of enantiomers of dipeptide β-Ala-D, L-Tyr and its derivatives with 2-hydroxypropyl-β-cyclodextrine by capillary electrophoresis (Supervisor: Václav Kašička, Faculty of Science, Charles University in Prague)
Alena Slavíčková	Synthesis of steroid carboxylic acids with expected biological activity (Supervisor: Hana Chodounská, Faculty of Science, Charles University in Prague)
Tereza Šálová	[2+2+2] Cycloaddition reaction catalysed by transition metal complexes as robust tool for synthesis of pyridine derivatives (Supervisor: Filip Teplý, Faculty of Science, Charles University in Prague)
Anna Šimková	Characterization and inhibition of mutant proteases from HIV virus resistant against protease inhibitors (Supervisor: Jan Konvalinka, Faculty of Science, Charles University in Prague)
Jan Tykvart	Expression and characterization of recombinant homolog of glutamate carbocypeptidase II (Supervisor: Jan Konvalinka, Faculty of Science, Charles University in Prague)
Veronika Zajícová	New ligands for anion complexations (Supervisor: Ivan Stibor, Technical University of Liberec)
Iva Žebrakovská	Expression and activation of cathepsin D (Supervisor: M. Mareš, Faculty of Science, Charles University in Prague)

Development of the IOCB Campus

The Reconstruction and New Construction of the IOCB Complex in Dejvice
After recent discussions, the plan for individual buildings in the IOCB complex to be reconstructed was altered. This resulted in a modification of the planned appearance and arrangement of the new Building B being to be constructed in the courtyard of the institute. After negotiations with the Council of the institute, it was decided to select one of two versions with three floors of organic synthesis laboratories. The overall view of the reconstructed complex, including the concept of the arrangement of the park in front of the institute, can be seen in the following picture. This is how the institute should look like sometime in 2014. The precise timetable is currently being prepared by project designers.



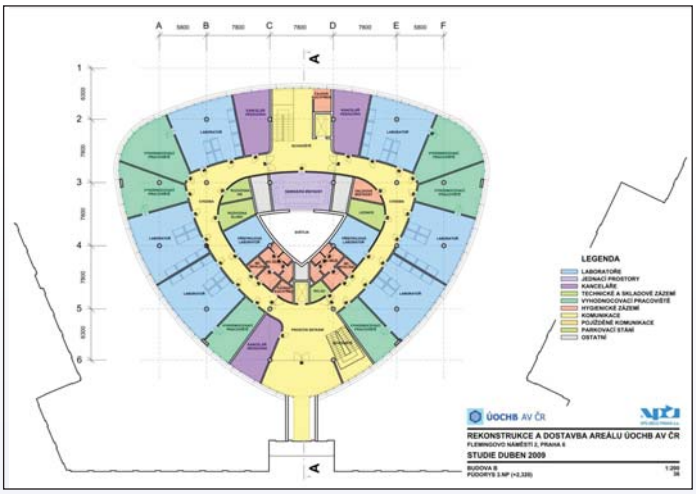


The following picture provides a view of Building B from Zelená Street.

Another view from the Architecture Building.

Development of the IOCB Campus

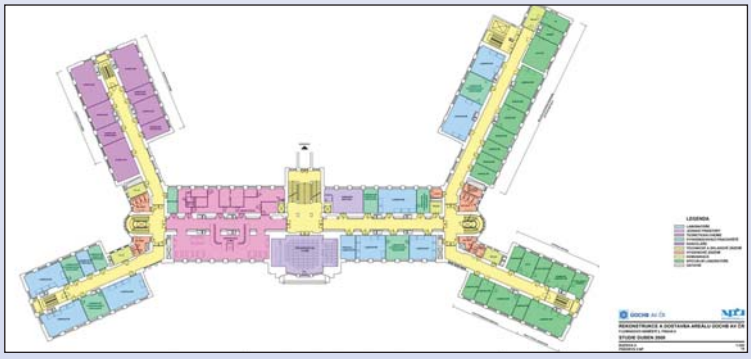
The new Building B will have library archives, areas for a computer cluster, a technological base, storage rooms for chemicals, and waste management in the lower, underground floors and ground floor, while the upper three floors will be reserved for organic synthesis laboratories. The following picture shows the first proposal of the layout of the organic floor. The final layout will be the subject of sub-sequent elaboration.



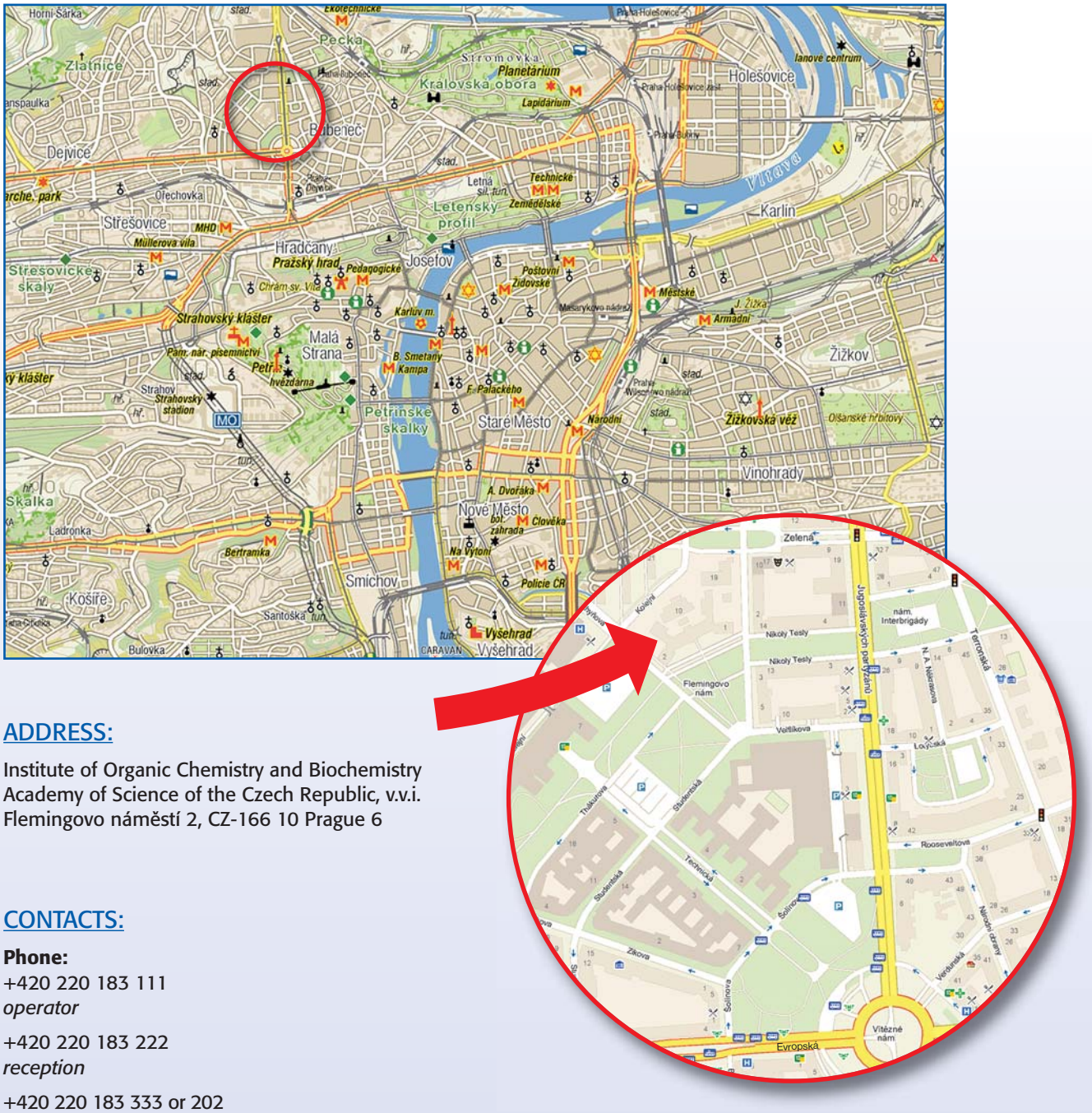
Building C, previously known as the New Building, will be used by biochemistry, specifically the GMO areas of biochemistry, and virological laboratory, which is being newly developed. The purpose of this building has not changed; the preparation of its reconstruction is in an advanced stage. Considering that the adaptation of this building does not require a zoning or planning decision and its project is in an advanced stage, we can proceed to the beginning of its reconstruction at the end of 2009 and beginning of 2010. The layout of a typical floor of Building C is shown in the following picture.

Building D, the annex of Building B, will not change. Its original purpose as well as division will remain the same. It will serve parts of administration and health facilities.

Building A, formerly called the Old Building, will have a newly modified meeting room, modernized and slightly expanded, in the existing area. On the same floor will be the gastronomical operations including canteen and cafeteria. These areas will provide the employees of the institute with the opportunity to meet informally. The basement of Building A will serve for the construction of necessary cloakrooms and a social base (by which we will also comply with existing regulations). The other areas will accommodate the remaining operations, including an area for theoreticians, who will finally join the institute and leave their exile on the Canon premises. Building A may also have two teaching laboratories for organic chemistry and for biochemistry and areas for further development.
The last picture shows the possible layout of the first floor of Building A.



How to Reach Us



ADDRESS:

Institute of Organic Chemistry and Biochemistry
Academy of Science of the Czech Republic, v.v.i.
Flemingovo náměstí 2, CZ-166 10 Prague 6

CONTACTS:

Phone:
+420 220 183 111
operator

+420 220 183 222
reception

+420 220 183 333 or 202
director's office

E-mail: uochb@uochb.cas.cz

PUBLIC RELATIONS:

Phone: +420 220 183 205 or +420 731 447 861
E-mail: krumlova@uochb.cas.cz

IMPRESSUM

PUBLISHED BY
Institute of Organic Chemistry and Biochemistry AS CR, v.v.i.

EDITORS
Irena Krumlová
Jakub Hošek
Devon Maloy
LAYOUT AND DESIGN
Venice Praha, s.r.o.
PICTURES AND CREDITS
IOCB Research Teams (Stanislava Kyselová, Michal Hoskovec)

PRINTED BY
Venice Praha, s.r.o.
July 2009