Technical University of Denmark

Annual Report 2013

Department of Chemistry

The Audacity to Break New Ground

I am pleased to report, that 2013 was a very good year for DTU Chemistry. Our Department continued to deliver superior academic results both in education, solutions to society and in publications with a high impact in leading journals.

I would like to express my appreciation for the hard work and dedication of the entire DTU Chemistry: The scientific leadership demonstrated by our Section Coordinators, the tireless effort of our Study Board, our innovative scientists, our skilled support units and not least the team spirit in all areas. Thanks to this unique blend and a unified drive towards excellence, DTU Chemistry is in a strong position to take on the challenges of 2014.

Attractive and relevant

2013 was the year when our outreach efforts paid off. More than 200 students began a chemistry related education at DTU. The success is mainly due to the combination of competent communications professionals, excellent educations and a focused dialogue with the entire "food chain" from high school to master level. I'm pleased to note, that DTU Chemistry is attractive and highly relevant in the eyes of future generations of chemical engineers.

Furthermore, we have enrolled 25 PhD students in 2013, many of them in partnerships with our industrial collaborators. I think it is safe to say, that we make a noticeable contribution to the creation of the next generation of top level researchers. Looking ahead, attracting the right talent at all levels is pivotal, if we are to continue our successful development.

In pursuit of excellence

The goal is to establish a robust setup allowing for unique combinations of talent and facilities needed in order to achieve scientific excellence. Through the years we have been successful in attracting a wide range of funding for research projects and been able to continuously upgrading our laboratories and equipment.

The VILLUM FOUNDATION has just granted DKK 16 million to a new NMR facility. With that generous donation we can build a strong NMR instrument infrastructure servicing the entire DTU with cutting edge equipment for studies of organic molecules.

Building strength

In this year's report you'll find testimony to new alliances and stronger synergies within the Department, across DTU and in collaboration with academic and industrial partners. We have become better at knowledge sharing. I'm pleased to see my colleagues inspire each other to have the audacity to break new ground and still keep the overall goals in sight. We have an increasing activity in innovation and entrepreneurship at DTU Chemistry. This is a living proof, that we have succeeded in our efforts to bridge the gap between basic and applied sciences.

Strengthening the team is an ongoing effort. We started 2014 with the appointment of two new professors in Chemical Biology, a fast growing area with great potential. You can find more about the work of Professor Mads H. Clausen and Professor Thomas E. Nielsen in the articles *New Center is Raising the Bar* and *DTU Chemistry LEADs the Way.*

2014 and beyond

The vision for 2014 is to raise the bar further. We want to address the tough and demanding challenges of chemistry for the future. We need people with the passion, attitude and aptitude to lead the way. DTU Chemistry aims to build a reputation as the team that always reaches for the most rewarding and exciting fruits all over the tree.

– Erling H. Stenby

DTU Chemistry Management Group

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DTU Chemistry Annual Report 2013

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Layout:
Graphic designers, We Love People

Photos:
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Print:
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DTU Chemistry's trademark is scientific expertise founded in fundamental research in applied chemistry. The research at the Department is organized into three areas each with underlying research groups. The work covers a wide range of scientific topics.

The Inorganic Chemistry Section consists of the Centre for Catalysis and Sustainable Chemistry (CSC) and the research groups on Metalloprotein Chemistry and Nano Chemistry. The Section covers a broad range of topics, from developing novel chemistry and improving industrial processes over focus on metals roles in biological systems to design of re-combinatory metalloproteins in genetic engineering. Recent years have shown increasing interaction between Inorganic Chemistry and the research in biological systems. Classic catalysis chemistry is mixing with nano-scale medicine and the Inorganic Chemistry has an important role to play in that development. In 2014 the Section Coordinator Professor Rasmus Fehrmann is on sabbatical for six months:

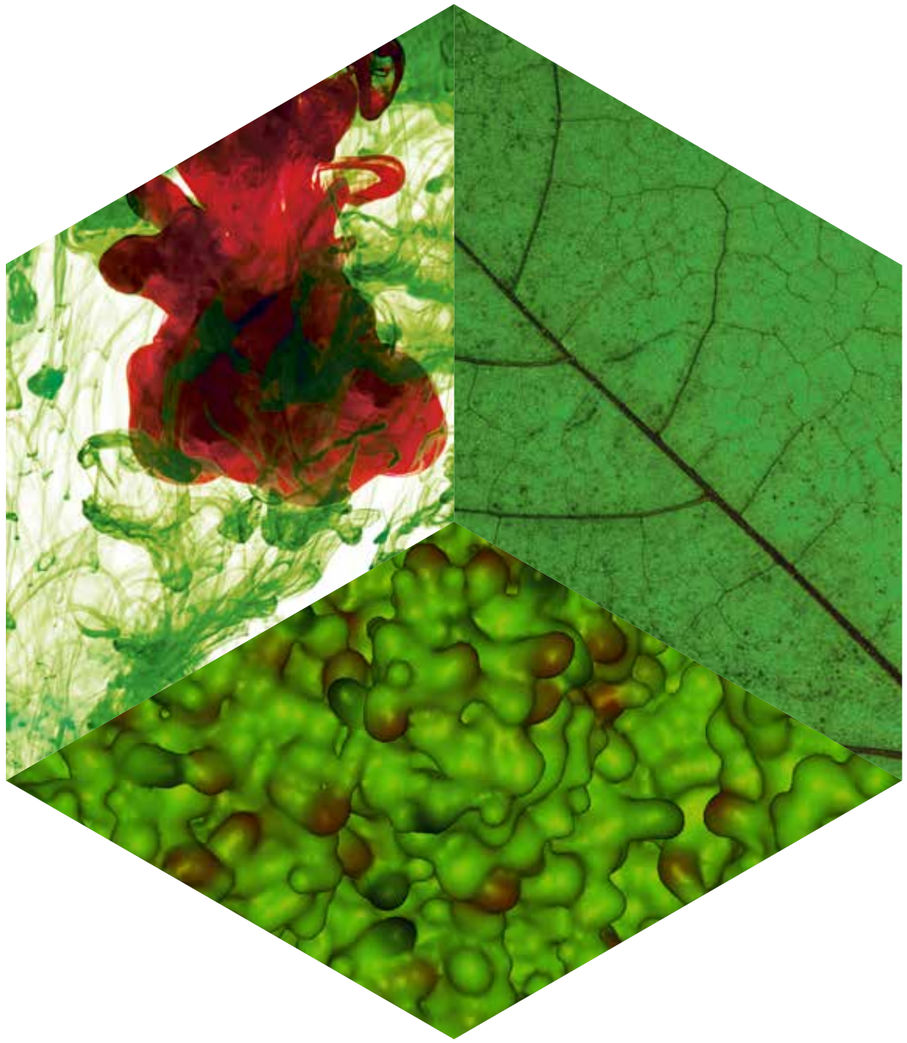
I'm looking forward to have the opportunity to seek new inspiration regarding fundamental and applied chemistry of ionic liquid based catalysts, absorbers of flue gas components and pharmaceuticals. My stays in France and the US may also pave the way for intensified exchange of scientists and students in the future between the research centers involved.

The Organic Chemistry Section's main strength is organic synthesis, with focus on catalysis and chemical biology. The two areas are highly integrated and several faculty members have projects in both fields. In chemical biology, organic chemistry is used as a tool to learn more about biological systems with the ultimate goal of suggesting new drug candidates for treatment of bacterial infections and cancer. Homogeneous metal catalysts are able to improve a number of chemical processes, making them more efficient, sustainable and environmentally sound. The aim is to design even better catalysts, which are able to convert simple and easily available precursor substances into more advanced molecules. The section also has strong expertise in NMR spectroscopy, a vital analytical technique for all projects.

Organic Chemistry is an area with great synergy and multiple internal cooperation, which ensures a "critical mass" for our research efforts and places the Section in a strategically strong position. Close collaboration with external partners in both academia and industry is also an important facet of our research activities, says the Section Coordinator, Professor David Ackland Tanner.

The Physical Chemistry Section focuses on biophysical chemistry and femtosecond chemistry. This is complemented by analytical chemistry and spectroscopy. In biophysical chemistry, metalloproteins related to different neurological diseases are being synthesized in-house or in collaboration with DTU Chemical Engineering and DTU Systems Biology. The roles of the metal ions are scrutinized through combination of crystallography, X-ray scattering (SAXS) and spectroscopy (XAFS), and in silico modelling. The ultimate goal is to provide the basis for a fundamental understanding of the biophysical processes and to create new generations of drugs. Femtosecond chemistry is in between chemistry and physics. Applied quantum mechanics are used to describe atomic movements, fundamental to chemical reactions, in a timeframe of femtoseconds and to find ways of controlling them.

Physical Chemistry wants to be a strong link between DTU and the new large facilities MAX-IV and ESS being built in Lund, Sweden. These facilities will open up completely new possibilities within life sciences and materials science, which we want to be part in, explains Section Coordinator, Associate Professor Kenny Ståhl.



Single-molecule Coordination Chemistry

For the first time, the coordinative bonding forces in a transition metal complex have been investigated at the single-molecule level. The observations should add new insight to our understanding of the physicochemical nature of coordinative bonds. The method is expected to apply generally to a range of transition metal complexes and to make impacts on coordination chemistry and related areas broadly.

Transition metals have become highly important over the last few decades as catalysts in both organic and inorganic chemistry. This trend has renewed the scientific interest in coordination chemistry. Practically all transition metal containing compounds consist of coordination complexes, meaning complexes where a central atom is surrounded by an array of bound molecules (or ligands). A joint international effort led by DTU Chemistry has for the first time produced a method capable of studying the metal-ligand interactions at the single-molecule level directly aqueous media.

Associate Professor Qijin Chi, from the Nano Chemistry Group at DTU Chemistry, has recently reported the results in an article in Nature Communications (4(2013), 2121). The overall approach demonstrated in this work represents a remarkable advancement in studying coordination chemistry at a new level.

Osmium, an important transition metal used for many catalytic purposes, was chosen as the metal, while the ligand was terpyridine. Terpyridine, or "terpy" for short, is an organic compound known to be highly stable and therefore a well known ligand in coordination chemistry. The coordination and bond breaking between terpy and osmium was followed by electrochemically controlled atomic force microscopy (AFM) at the single-molecule level.

Surprisingly weak bonding

A new finding revealed by the innovative setup is the fact that the metal-ligand coordinative bonding strength was found to be only about 5 % of that for a covalent bond. A covalent bond, in which two atoms share two electrons simultaneously, is the strongest type of bond in chemistry.

"Traditionally, chemists have viewed coordinative bonds as a special type of covalent bonds. Thus, it would be surprising if they may in fact be much weaker. However, this could be explained by the coordinative bond breaking representing ligand substitution in aqueous solution rather than simple dissociation," says Associate Professor Qijin Chi.

If, as it seems, coordinative bonds are quite weak at the single-molecule level, a natural question is what accounts for the well-known coordination chemistry strength at the larger scale.

"We could speculate that the strength comes from the compound being very stable or from the interface with the surrounding material where terpy is only partially coordinated, but really that should be the subject of further research. At this point the main thing is that we have shown some very basic chemistry to be quite different from what was anticipated. I think people need a little time to accept this. And once they do, I am sure we would begin to see new science that can explain the mechanisms behind our findings," Qijin Chi remarks.

Academic resources were pooled

Another remarkable finding from the study was the fact that the redox state of osmium had a clear effect on the strength of the coordinative bonding to terpy. The setup allowed control of the redox state of the transition metal complex and record of force spectra simultaneously. The data showed higher bonding strengths for Os(III) than for Os(II).

"The DFT computation has proven the experimental observation. However, the exact reasons behind this difference are not yet fully understood. The overall approach demonstrated in the project has raised several interesting questions. After all, our experiments have shown what happens at the single-molecule level, but not why it happens. Hopefully, our observations will spur further insight into the physiochemical nature of coordinative bonds."

Research groups from State Key Laboratory of Electroanalytical Chemistry (China), Chalmers University of Technology (Sweden), DTU Physics and DTU Chemistry have joined forces to achieve the breakthrough.

"It is hopeful that single-molecule studies would give you new findings. Therefore, several groups – including our own – have tried to accomplish such studies before, but the efforts were unsuccessful until we gained our academic resources together," explains Qijin Chi.

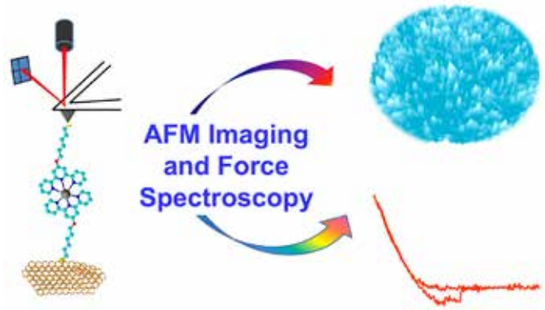
"The method is expected to apply generally to other transition metal complexes and to impact coordination chemistry and related areas broadly. And while this is fundamental research, it is highly possible that such findings will spur development of more efficient compounds for use in catalysts, for instance in energy production, organic chemistry and other applications."

Coordination Chemistry

A coordination complex consists of a metal atom or ion and a surrounding array of bound molecules or anions. Many metal containing compounds, and practically all transition metal containing compounds, consist of coordination complexes. Coordination chemistry has been a consistently active branch of chemistry since Alfred Werner's seminal theory of coordination compounds inaugurated in 1893, with the central focus on transition metal complexes. However, nearly all aspects of coordination chemistry, including metal-binding free energies and enthalpies, and bond association/dissociation kinetics so far have been based on average ensemble information.

How it was done

Terpyridine (terpy) was derivalized with an alkanethiol linker group. Thiol derivation enables terpy to self-assemble onto gold (Au(111)) surfaces and gold-coated atomic force microscope (AFM) tips. The self-assembled monolayers (SAMs) of terpy on an Au(111) surface with or without osmium (Os) coordination were studied by electrochemistry, electrochemical scanning tunnelling microscopy (ECSTM), and electrochemical AFM.



When the atomic force microscope (AFM) tip approaches the sample, tip-bound terpy interacts with Os-terpy on the substrate surface to form the complex. Retraction of the tip results in dissociation of the Os-terpy bond but does not break the Au-S bond, which is much stronger than the coordinative bond. Force-distance curves for the Os-terpy ligand dissociation process can thus be recorded.

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MIND the Gap

"The basic research in the understanding of structure-function relationship of metalloproteins might be highly relevant for the discovering of new drugs that might change the life for patients suffering from serious diseases – the basic research focus not associated with any specific diseases is critical to perform academic breakthrough discoveries".

Kim Andersen, Vice President at Lundbeck A/S

The research network MIND provides an excellent educational environment for students. Located at DTU Chemistry, the students are exposed to an interdisciplinary research approach.

MIND is an interdisciplinary basic research network established to understand how metalloproteins function. The main aim of the network is to provide a collaborative platform for investigating the structure-function relationship of metalloproteins involved in neurological disorders, with the long-term goal of understanding how these protein properties cause disorders and how they can be remedied. The five members - Associate Professors Hans E. M. Christensen, Pernille Harris, Kasper P. Kepp, Günther H. Peters and Kenny Ståhl - of the reserach network wish to collaborate and share their findings and enable the pharmaceutical industry to come up with treatments for these disorders – that put such severe and personal strains on afflicted individuals and their families.
The network was newly formed in 2013 by the five scientists at the Department of Chemistry. The team has collaborated individually in the past – and decided to pool their collective and complementary competences and experience into one focused research network capable of analysing and understanding this complex area through in-depth basic research. The five strongly believe in the strengths and advantages of bringing together and utilising different disciplines – to shed new light on the problem from all angles and combine the collective skills and knowledge to come up with enhanced and better solutions. Between them, they can design and produce proteins (Hans E.M. Christensen), measure and analyse proteins using crystallography and spectroscopy (Kenny Ståhl and Pernille Harris), and perform in-silico modelling of proteins (Günther Peters and Kasper P. Kepp). Thus, they hold the building blocks of expertise to put together the pieces in the puzzle of understanding metalloproteins – and fill the gaps in our knowledge.

The ultimate driver

The ultimate driver is to help alleviate a growing problem of immense human cost. The team puts its fundamental research of metalloproteins into a wider perspective. "We wish to provide fundamental research knowledge that can help the pharmaceutical industry unveil the causes of neurological disorders and eventually alleviate these. The costs of these disorders are huge – not just in terms of cost to society – the neurological diseases put a tremendous strain on the families, both personally, health wise and financially! And the problem is a growing one, in Denmark as well as globally," explain the five scientists. Thus, neurological disorders, like e.g. Alzheimer's and Parkinson's are diseases that attack a growing number of people – and in particular, as more and more people reach high age. In Denmark, 87,000 people suffer from dementia – and of these, more than 50% suffer from Alzheimer's disease. Only 2-3% of these cases are estimated to be genetically linked – and for the remaining part, the causes are not clear.

Classic causality dilemma

However, it is generally accepted that metals play a role in the neurological diseases. Increased or decreased levels of metals can be observed in relation to these diseases – and in particular, copper and zinc are in focus. The question, however, is whether the imbalance in the metals trigger the diseases or whether the diseases cause this imbalance. "This is the classic what came first question. The chicken or the egg?" the team wonders.

Unveiling the properties of metalloproteins and understanding how they work will combine both experimental and theoretical aspects and various research disciplines. To this end, the established network will provide an excellent platform for national and international collaboration. Furthermore, the network provides an excellent educational environment for students since they are exposed to an interdisciplinary research approach – which is precisely the environment they will find in the pharmaceutical industry.

MIND
Metallo-proteins in Neurological Disorders

MIND - Metalloproteins in Neurological Disorders

The current members of the network are Associate Professors Hans E. M. Christensen, Kenny Ståhl, Pernille Harris, Günther H. Peters, and Kasper P. Kepp.

The main aim of the network is to provide a collaborative platform for investigating the structure-function relationship of metalloproteins involved in neurological diseases, with the long-term goal of understanding how these protein properties cause diseases and how they can be remedied.

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Further information scan the code:
kemi.dtu.dk/english/Research/Mind

The Terahertz Dance

Shedding light on macroscopic systems one molecule at a time is the mission for DTU Chemistry's Assistant Professor René Wugt Larsen. With the prestigious Sapere Aude Grant he has set out to build a novel experimental platform for complementary spectroscopic experiments at DTU.

Assistant Professor René Wugt Larsen from DTU Chemistry became one of the chosen few when he received the Sapere Aude grant from The Danish Council for Independent Research Programme for the project entitled "Shedding Light on Macroscopic Systems One Molecule at a Time: Spectroscopy of Weakly Bound Cluster Molecules". The grant was given to support his efforts in shedding light on macroscopic systems one molecule at a time, an almost poetic mission considering that Kant coined the old quote Sapere Aude or "Dare to Be Right" as the essence of the Enlightenment.

"It is a great honor to receive this Sapere Aude Grant", René Wugt Larsen states. "It gives me the opportunity to found a research group with young, talented researchers and build a novel experimental platform for complementary spectroscopic experiments at DTU Chemistry."

New Spectroscopy Laboratory

The research group consists so far of René Wugt Larsen and PhD students Jonas Andersen and Denise W. Mahler. A Post Doc arrives early 2014. They are setting up a new laboratory dedicated to studies of weakly bound molecular assemblies by a variety of novel experimental approaches based on THz and IR spectroscopy.

"One of the major challenges in the physical sciences is to explore how remarkable macroscopic properties of condensed bulk phases, materials and biological systems emerge from hydrogen bonding, dispersion interactions and steric repulsion between molecules at the microscopic level. The interplay between these classes of non-covalent forces emerges already on the nanoscopic scale of isolated molecular assemblies" says René Wugt Larsen.

"Dancing" Molecules

When two or more molecules approach one another they might eventually end up in a chemical reaction. However, in the course of their interaction the molecules will start vibrating collectively at THz frequencies and every such "THz dance" by a specific assembly of molecules has its own unique characteristics. This kind of characteristic intermolecular vibrational motion provides a wealth of information about the non-covalent interactions between the molecules and can help to describe similar, but structural more complex supramolecular systems e. g. natural gas hydrates, functional polymers and enzyme-substrate complexes of relevance to the energy, materials and life sciences.

"Modern quantum mechanical methodologies are able to describe these non-covalent interactions, but the methods scale fast with the number of electrons involved," René Wugt Larsen explains. In consequence, an accurate description of many relevant supramolecular systems is out of reach - even with the largest computer facilities. But if one can isolate and characterize the smallest molecular constituents on the nano scale level, molecule by molecule, it becomes possible to describe and spectroscopically characterize the specific forces involved.

And this is where the cluster spectroscopy research group rushes to the rescue. "In popular terms, we are going to shed light on macroscopic systems one molecule at a time," the group explain.

Building Solutions

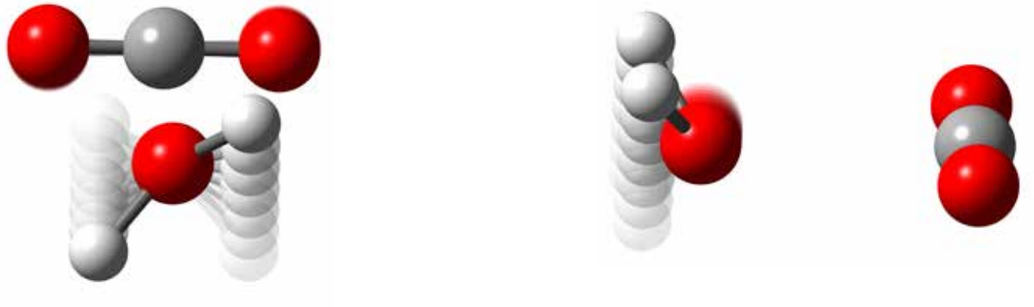
In a current collaboration with Universität Göttingen, René Wugt Larsen and his group investigate the microscopic origin of the thermodynamical anomalies observed for bulk alcohol/water mixtures. It is well-known, that significant heat is released when mixing alcohol and water with a larger heat release for water-rich mixtures. They have been able to demonstrate spectroscopically that these macroscopic anomalies, to a large extent, originate from the relative stability of smaller hydrogen-bonded assemblies of alcohol and water molecules in the bulk liquids.

International Network

With a background in elite research groups at UC Berkeley, MAX-lab Storage Ring and Universität Göttingen, René Wugt Larsen has a strong network, and he intends to use the new cluster spectroscopy platform to strengthen DTU's international contacts even more:
"An important part of this project is to transfer knowledge of novel experimental facilities from Germany and Sweden to DTU Chemistry. The goal is to build up a variety of experimental setups, where weakly bound molecular assemblies can be trapped in inert cryogenic matrices or adiabatically cooled in supersonic free jet expansions at ultra-low temperatures," he explains. "In this way we are able to "freeze" the molecules' internal degrees of freedom and let them interact under controlled conditions synchronized with the spectroscopic experiment."

Since his days as a PhD student in Lund, René Wugt Larsen has maintained strong connections and a close collaboration with the MAX-lab Storage Ring in Lund. MAX-lab is a world-class facility for research based on highly brilliant synchrotron radiation. The facility is now to be extended with MAX IV, which will place Lund at the very top of international research and technology.

"I hope very much to establish a firm relationship and network between our cluster spectroscopy research group and the international research hub at MAX IV and the research community that will grow around it," says René Wugt Larsen.



Dancing molecules: The large-amplitude intermolecular vibrational motion associated with torsional motion, out-of-plane wagging and in-plane rocking of one single H_2O molecule interacting with one single CO_2 molecule.

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New Center is Raising the Bar

Audacity to go after the most intriguing scientific problems and the willingness to engage in original thought without losing sight of the stakeholders needs will be the key drivers in the new DTU Center for Nanomedicine and Theranostics, according to DTU Chemistry's newly appointed Professor Mads H. Clausen and his colleagues.

Established in January 2012, the Center is a multidisciplinary cooperation between DTU Chemistry, DTU Nanotech, DTU Nutech and DTU Vet.

The Head of the DTU Center for Nanomedicine and Theranostics is Professor Thomas L. Andresen

"It is our vision that our research will result in new important technologies for the benefit of patients. The involvment of DTU Chemistry is important because it gives the Center a unique research platform to design and synthesize novel drug delivery systems and the ability to characterize the molecular interactions in such systems, which allows for rational development of new technologies," says Thomas L. Andresen.

from DTU Nanotech. Within this Center he and his team will put DTU on the map as a significant international player in the research of nanomedicine.

The Center focuses on advanced biomaterial technology and drug delivery where nanoparticles are used to shuttle drugs into cells to improve drug availability in the body. Theranostics, a combination of the two words therapeutics and diagnostics, refers to such nanoscale technologies where both diagnostic and therapeutic functionalities used for drug delivery and –release are combined in one carefully designed solution.

Killing Cancer

Associate Professor Esben Thormann from DTU Chemistry arrived at the Center in June 2013 and is a fine example of the Centers multidisciplinary layout. With a background in colloid chemistry, he works with polymers and how colloid particles interact with each other and with material surfaces.

"I design responsive systems containing polymers that can be used to control drug delivery. It is not classical "cancer-cure" research, but it might be a very powerful tool in the battle against tumors," he states.

"If I design stimuli responsive polymer particles that encapsulate a drug, and if I can get these particles to accumulate in a tumor, I can specifically target the cancer cells and minimize the side effects of traditional cancer treatment. The trick is to find a physical or chemical condition which is specific for the tumor and then design the drug carrier to respond to this condition – this can be local variations in temperature, pH, ion composition or high concentration of specific enzymes," Esben Thormann explains.

Cancer is very much in focus at the Center, but Professor Mads H. Clausen expects that other areas will be targeted in the years to come.

"We have made a strategic decision to focus on the characteristics of biomaterials and the way they will interact with biological systems because we have unique expertise in these two areas and they are important in applications for drug delivery," he explains.

Assistant Professor Jonas Rosager Henriksen from DTU Chemistry is also part of the Center and he holds some of the core competences in design and characterization of biomaterials, that Mads H. Clausen talks about. In recent years he has worked with design of liposome based PET tracers used for screening of the proper liposome based drugs for individual patients.

Creative Power

To Mads H. Clausen the Center is as an opportunity to meet researchers he wouldn't meet otherwise.

"I get to work with people I wouldn't meet if the Center didn't exist. It inspires new ideas and a greater creativity for all of us. It is definitely helping us raise the bar", he says.

Jonas Rosager Henriksen strongly agrees. "We have facilities and in-house competences covering everything from synthesis of new compounds, their characterization to in vitro and in vivo tests in animal models. You can't do that in small companies and it's difficult to organize in larger corporations. Our knowledge pool and facilities offer a huge advantage to our partners," he explains.

But the Center is more than a platform for scientific creativity and audacious research. It is also a strong unified effort to reach out to industrial partners and future students. Visibility and accessibility are natural benefits from a one-point-entry initiative as for the DTU Center for Nanomedicine and Theranostics, and indeed this is very much a part of the Centers overall strategy:

"I have no doubt that we with this initiative strengthen our ability to attract highly talented students and researchers as well as interesting new partners," Mads H. Clausen states.

Strong Industrial Partners

The new Center is born with strong pharmaceutical partners, but the scientists are very aware that further initiatives are necessary in the highly competitive fields of nanomedicine and theranostics. Workshops involving industrial partners showing off the centers united capabilities and exploring new opportunities are the first step on the road to a stronger profile among future stakeholders. "They like the talent and the candidates we produce, but we also need to show them the quality of our work in a broader perspective. We are actually very good at what we do, and we need to get that message across to a wide range of stakeholders in the next two or three years," Mads H. Clausen explains.

"Within the next six months, we are fully consolidated and ready to meet the industry and other stakeholders. In five years' time, I think we will see an energetic and creative research hub with a lot of interesting nanomedicine projects in the pipeline. We will have solid interaction with our industrial partners and a band of bright Master- and PhD students coming out. And to achieve that, we need to engage our partners and create awareness. Visibility and scientific outreach are the primary challenges in 2014," says Professor Mads H. Clausen.

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DTU Chemistry LEADs The Way

DTU Chemistry is one of 30 partners in The European Lead Factory, a novel pan European consortium and platform for innovative drug discovery based on crowd sourcing. The European Lead Factory was launched in February 2013 with a budget of 196 million Euros.

The 30 partners were carefully chosen in an effort to combine the agility of the small and medium sized enterprises with the experience of the pharmaceutical companies and the innovation of academia. Danish participants include DTU and H. Lundbeck A/S.

"I'm much honored that Professor Mads H. Clausen's and my team at DTU Chemistry participate in this consortium," Professor Thomas E. Nielsen admits. "This is a very big and entirely unique initiative from seven major pharmaceutical companies. Our early involvement and participation in the project confirms that our efforts and the resources DTU Chemistry invested in chemical biology were wisely spent."

Pharmaceutical companies rely on high-throughput screening of large compound collections in the search for new drugs. One problem is that each company traditionally guards its compound library in the ongoing battle for the next blockbuster drug. As each company has well-defined focus areas and tends to design their search for new drug candidates accordingly, many compound libraries have not yet been fully exploited.

The European Lead Factory will change this rather counterproductive stalemate through shared compound libraries. Access to a sufficiently large stock of small molecules is the starting point for researchers in the drug development businesses. In the world's first compound-crowdsourcing effort around 300.000 industrial research compounds have been contributed by the seven founding pharmaceutical companies. Over time, the collection will be expanded by an additional 200.000 new compounds designed through the collaborative forces of the universities and SME's in the consortium, totaling an unprecedented 500.000 compounds library. And all these compounds will be accessible to the members of the Consortium.

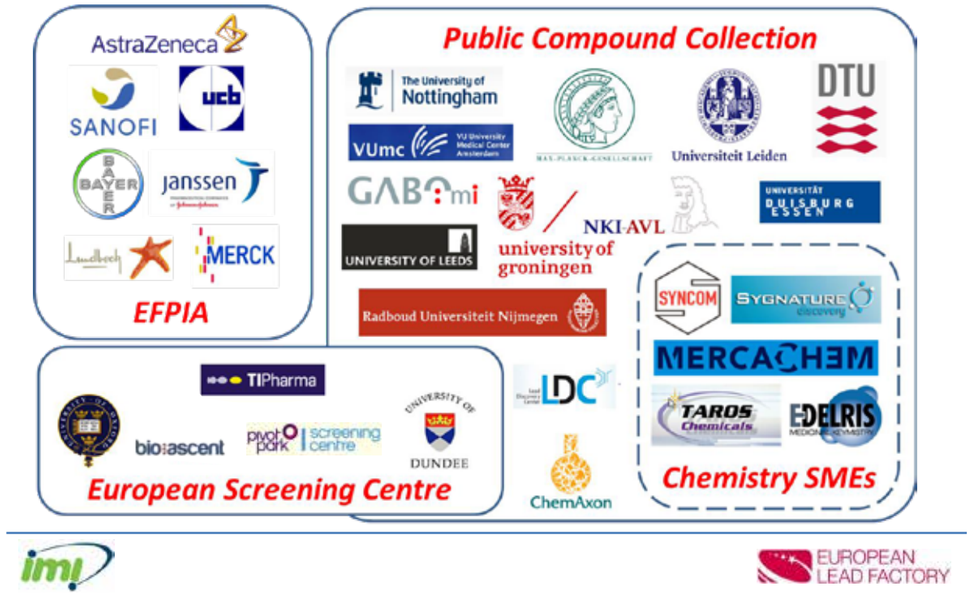
Role model for future drug development

According to Thomas E. Nielsen, The European Lead Factory might very well be the role model for future drug development, but it is also a big experiment. "It's the first time in Europe, that this way of pooling resources across the board has ever been tried, and we don't know how crowd sourcing works at this level" he explains.

But the need for innovative thinking is very acute. For decades the pharmaceutical companies have been in a situation, where productivity is declining and the costs of bringing a new drug to the market keep rising. "The industry is challenged and everybody is looking for new ways to identify the drugs of the future – this initiative might give a push forward", Thomas E. Nielsen hopes.

Building a large compound library is only the first step on the path to boost European drug discovery. Another aspect is the actual screening of the compound collection. The European Lead Factory will develop and fund this screening in state-of-the-art facilities based in Scotland and the Netherlands. The screening centers take responsibility for compound logistics, characterization, data analysis and program management. At the same time the screening centers function as a marketplace to foster new public-private partnership programs between the pharmaceutical companies and public partners.
European academia and SMEs on the search for bioactive compounds in the pursuit of a target receive a qualified hit list with up to 50 chemical structures of compounds per target program from the screening centers. Each of the pharmaceutical companies can use the created compound collection in 4 screening campaigns per year.

Consortium with 30 Public and Private Partners



*30 Public and Private Partners. 150 employees combining **agility** of SME's, **experience** of Pharma and **innovation** of Academia.*

DTU Chemistry's contribution

Professor Thomas E. Nielsen and DTU Chemistry's contributions to the European Lead Factory comprise the design and validation of innovative strategies to be used by SME's in the consortium to produce compound libraries. "We are well through the curve on this one" he states. "In 2013 we designed and received approval for 11 proposals. We have validated four of these proposals and our partner SME (Edelris, France) has synthesized more than 1000 compounds. This is an impressive achievement for the hardworking and dedicated chemists working with us."

2013 was Year One for the European Lead Factory. At DTU Chemistry this meant staffing up with 4 Post Docs and starting out at full speed. "We have some very tough deliverables" Thomas E. Nielsen explains. "This is not trivial, it's hard work and we have to keep up momentum. Yes, we have validated 4 proposals already and the funding for the next year is in place. But we have to remember that we, the public partners of The European Lead Factory, have to deliver 200.000 compounds in five years. That is no small task, but we are confident that we'll make it".

The research leading to these results has received support from the Innovative Medicines InitiativeJoint Undertaking under grant agreement n° 115489, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in kind contribution.
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PhD from DTU Chemistry

A PhD at DTU Chemistry is a diverse research education in modern chemistry. It is a core activity for the Department. The topics range from basic research to projects in collaboration with industry as well as innovative projects that can lead to start-up companies. With a duration of 3 years the PhD projects contribute to the development of cutting edge science at the Department. At the same time, a PhD project qualifies the candidate to become a scientist or to work in a similar function in industry.

DTU Chemistry takes pride in educating PhD's, that are not just excellent scientists, but are also able to communicate their work. A cornerstone in this regard is the annual PhD Symposium at which stake-holders from the industry are invited to attend both oral presentations and a postersession by the Departments PhD students. In the following you will find the PhD Defences 2013. You can get the full thesis as a pdf by scanning the QR-code for a specific project - if you want more than the following appetizers.

Smarter Synthesis in Organic Chemistry

In this project a new method for ruthenium catalyzed dehydrogenative coupling of alcohols and amines to form imines is presented.

Agnese Maggi, PhD

"Metal-Mediated Couplings of Primary Alcohols with Amines and Carbohydrates."

Supervisor:
Robert Madsen

Funded by:
DTU

The Danish Council for Independent Research - Technology and Production Sciences

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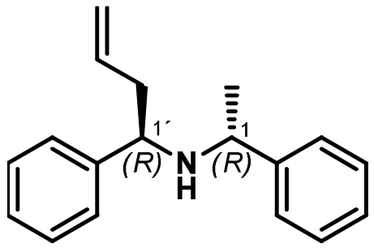
Imines are common ligands in coordination chemistry, in other words they are important organic chemistry tools. In this thesis, a method for direct (one step) synthesis of imines from alcohols and amines is presented. The method provides quick and extended access to structurally diverse and synthetically important imines.

In a separate, second part of the thesis novel synthetic methods for assembling oligosaccharides are presented. Such methods are essential tools for the emerging fields of glycobiology and glycomics.

Both projects have metal-mediated couplings of primary alcohols with amines and carbohydrates as a common denominator.



Synthesis of imines via dehydrogenative coupling of alcohols and amines has recently become of great interest mainly for its broad applicability and environmental friendliness. In 2008, Madsen and co-workers performed the amide synthesis with an in situ generated Ru-NHC catalyst. The present project builds on this work.

In this project a new method for the dehydrogenative coupling of alcohols and amines to form imines is presented. The reaction is catalyzed by the ruthenium N-heterocyclic carbene complex [$RuCl_2$(IiPr)(p-cymene)] in the presence of the ligand DABCO and molecular sieves. The method can be applied to a variety of primary alcohols and amines and can be combined with a subsequent addition reaction.

The second, separate project is focused on tin mediated regioselective 6-O-glycosylations of unprotected glycopyranosides acceptors. The development of efficient synthetic methods for assembling oligosaccharides has become an essential tool for the emerging fields of glycobiology and glycomics.

A key area in glycobiology is cell surface molecules. These play a key role in numerous biological processes such as cell recognition events including cell adhesion, host-pathogen interactions, cancer progression, spermatogenesis, and development of the nervous system. The growing interest in these molecules has increased the demand for structurally defined oligosaccharides, as these constitute a major class of cell surface molecules.

Even though a vast number of synthetic methods is available, the assembly of complex glycans is still an intricate process and the development of easier and more efficient procedures remains a primary goal. The major constraint of oligosaccharide synthesis is the extensive use of protecting groups. Thus, approaches to reduce the number of steps connected to chemical synthesis are highly important.

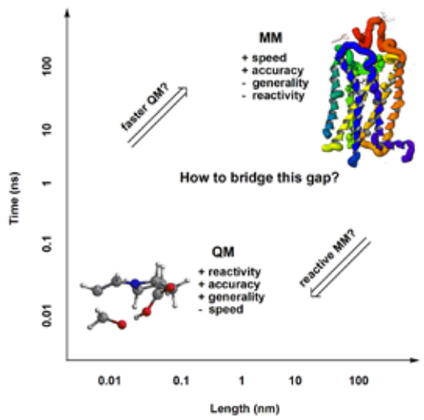
In this thesis thioglycosides deriving from D-glucose, D-galactose, and D-mannose were coupled with different bromide donors to afford the corresponding 1-6 linked disaccharides in good to moderate yields. Furthermore, it has been shown that these disaccharides can act as glycosyl donors for subsequent tin mediated glycosylation reactions.

Green Chemistry: Computers to the Rescue

In this project, a novel ReaxFF force field, ProtReaxFF, has been developed, optimized and applied to enzyme catalysis reactions.

Enzymes are biological nano-machines that catalyze almost all chemical reactions within biological cells. It is widely accepted, that enzyme catalysis can be applied in a large number of industrial contexts, spurring a green chemistry revolution, as enzymes are obtained from renewable resources, are biodegradable, and are generally non-toxic. Further, their selectivity is a great advantage in chemical industry batch processes because it will require far less work to refine the end product. However, the complexity of enzymatic reactions constitutes a problem, since it is difficult to model and predict the outcome of novel enzyme-catalyzed reactions by the same methods that are applied to traditional forms of catalysis. This thesis presents a tool for overcoming this barrier.

Ideally, techniques based on Quantum Mechanics (QM) should be applied to enzymatic reactions, since QM applies to conditions at the atomic level. However, for a biological system this would involve far too many variables for our present computer power to handle. One of the major problems in relation to proteins is calculating the electronic energy for a given nuclear configuration to give a potential energy surface.



The project builds on efforts by the Goddard group at the California Institute of Technology. The group has developed a simplified model, the ReaxFF (reactive force-field), which bridges the gap between quantum chemistry methods and the ordinary force-fields of classical molecular mechanics methods. Thereby, chemical reactions can be described properly with bond-forming and bond-breaking events during the simulation time.

In this project, a novel ReaxFF force field, ProtReaxFF, has been developed, optimized, and applied to enzyme catalysis reactions. It is shown that the current version of ProtReaxFF can be used to perform molecular dynamics simulations of biomolecules. The developed method is complementary to the more well-known QM/MM method, the inventors of which were awarded the Nobel Prize in chemistry 2013. Although the preliminary results using the developed ProtReaxFF are encouraging additional work is needed for the method to fully mature as a computational tool.

Alessandro Corozzi, PhD

"Computational Enzymology, a ReaxFF Approach"

Supervisor:
Peter Fristrup

Funded by:
DTU

The Danish Council for Independent Research - Technology and Production Sciences.

The project included an external stay in the group of Dr. Susanna Monti, ICCOM-CNR, Pisa, Italy.

Scan the QR-code and get the thesis as a pdf.

Successful Synthesis of a Plant Carbohydrate

The thesis presents strategies for chemical synthesis of linear and branched oligosaccharide fragments of rhamnogalacturonan I (RG I).

Alexandra Zakharova, PhD

"Synthesis of Oligosaccharide Fragments of the Pectic Polysaccharide Rhamnogalacturonan I"

Supervisor:
Mads H. Clausen
Robert Madsen

Funded by:
The EU Marie Curie initial training network Lean-GreenFood.

Scan the QR-code and get the thesis as a pdf.

Pectin is the common name for a family of plant polysaccharides. Pectin plays an important role as a functional food ingredient, serving as a stabilizing and thickening agent in jam, jellies, yoghurts, fruit juice, and confectionary products. It is also used in biodegradable films, surface modifiers for medical devices, materials for biomedical implants, and for drug delivery. The wide range of practical applications has spurred interest in developing chemical synthesis of pectic oligosaccharides. This thesis contributes to this task.

Understanding pectin structure, function, and biosynthesis is essential for understanding, and potentially modifying cell wall structure. This can lead to new "designer" pectins with improved properties. Structurally defined oligosaccharide fragments of pectin can find a wide application for studying plant cell wall structure and function as well as plant cell wall acting enzymes. Pectic oligosaccharides can be obtained either by controlled chemical or enzymatic degradation of pectin followed by fractionation or by chemical synthesis. Of these methods, chemical synthesis promises production of structurally diverse oligosaccharides of excellent purity and in sufficient amount.

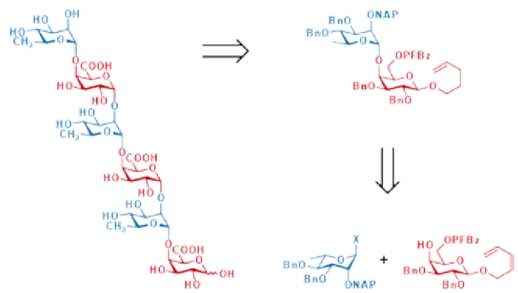
However, although modern carbohydrate chemistry has an extensive arsenal of methods to assemble virtually any oligosaccharide molecule, each case is an individual and often laborious task. Unlike in peptide and nucleic acid chemistry, in carbohydrate synthesis there is yet no universal approach.

The project focusses on rhamnogalacturonan I (RG I), which is one of the main structural classes of pectic polysaccharides. RG I is the second most abundant class of pectic polysaccharides. It has a complex chemical structure with a backbone of alternating α-(1→4)-linked L-rhamnose and α-(1→2)-linked D-galacturonic acid units with numerous branches of arabinans, galactans, or arabinogalactants positioned at C-4 of the rhamnose residues, with substantial structural variation within these branches.

The thesis presents strategies for chemical synthesis of linear and branched oligosaccharide fragments of RG I.

The first successful synthesis of a fully unprotected linear hexasaccharide fragment of the RG I backbone was accomplished. The strategy employs a highly modular approach which takes advantage of the armed-disarmed effect to generate the key n-pentenyl disaccharide donor in a chemoselective fashion.

Two protected n-pentenyl tetrasaccharide intermediates bearing the digalactan and the diarabinan side-chains have been synthesized. The suitably protected mono- and disaccharide donors have been utilized in the chemoselective glycosylations. The protective group pattern is designed to allow the assembly of larger branched RG I fragments.



Biomass Conversion in Ionic Liquids

The kinetics of cellulose hydrolysis and the simultaneous 5-hydroxymethylfurfural (HMF) formation was investigated using a range of catalysts.

Andreas Jonas Kunov-Kruse, PhD

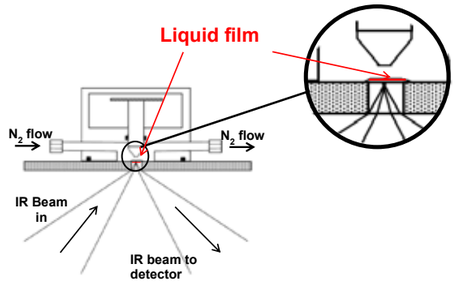
"Biomass Conversion in Ionic Liquids – in-situ Investigations."

Supervisor:
Rasmus Fehrmann
Anders Riisager

Funded by:
The Danish Ministry for Science, Innovation and Higher Education's initiative "Catalysis for Sustainable Energy" (CASE).

Scan the QR-code and get the thesis as a pdf.

Biofuels obtained from conversion of straw and other agricultural and forestry waste products is known as second generation biofuels. For economic and ethical reasons, second generation biofuels have preference over first generation biofuels which are derived from agricultural products that could also serve as food. Conversion of cellulose is a key challenge in this respect. The thesis investigates catalytic conversion of cellulose into sugars and the important platform chemical 5-hydroxymethylfurfural (HMF).



Several concepts for cellulose conversion catalysis are available. The project focusses on ionic liquid (IL) catalysts. ILs are salts that melt at relatively low temperatures, typically comprising a bulky organic cation and a smaller inorganic anion. They are very tunable solvents and a wide range of properties can be achieved by combining different cat- and anions. Some ILs have been shown to dissolve cellulose in rather high amounts, as the IL anions are able to break up the crystalline structure of the cellulose crystals. When cellulose is dissolved, the glucoside bonds become exposed and can easily be hydrolyzed by acidic catalysts. The cellulose can also be precipitated from the IL by addition of small amounts of water, yielding amorphous cellulose, which is significantly easier to hydrolyze enzymatically. Such pre-treatment could become commercially attractive in future second generation biofuel plants.

In the project, the kinetics of hydrolysis and the simultaneous HMF formation was investigated using sulfuric acid, solid acids and Lewis acidic chromium(III)chloride as catalysts. A new in-situ Fourier Transform Infrared (FTIR) spectroscopic method successfully determined activation energies for hydrolysis to be 92-96 kJ/mol regardless of the catalyst used. The activation energies of HMF formation could be determined to 84 and 102 kJ/mol for Brønsted and Lewis acidic catalysis, respectively. The low activation energies suggest that the IL acts co-catalytic by stabilizing an oxocarbenium transition state.

Further, conversion of glucose with chromium(III)chloride or chromium(II)chloride as catalysts was investigated. The Cr(III) catalyst exhibited high initial conversion rates but suffered from pronounced product inhibition. Activation energies were found to be 100-102 kJ/mol. For Cr(II) the initial rates were around 8 times lower but the activation energy was identical. Notably, the Cr(II) showed no sign of production inhibition and followed an apparent first order kinetics, which resulted in high conversion at longer reaction times compared to Cr(III). In a proposed mechanism, this was suggested to be due to a Cr(II)/Cr(III) synergy involving electron transport between the Cr centers .

A kinetic model based on active monomeric $[CrCl_3]^{3-}$ species was proposed showing that the product inhibition resulted in second order like kinetic behavior. The thesis identifies product inhibition as a major challenge for the utilization of chromium catalysts in biomass conversion.

More Efficient Chemical Reactions

In this project different transition metal C-H activations have been investigated by experiments and by computational chemistry.

Casper J. Engelin, PhD

"Investigations of Transition Metal Catalyzed C-H Activation".

Supervisor:
Peter Fristrup

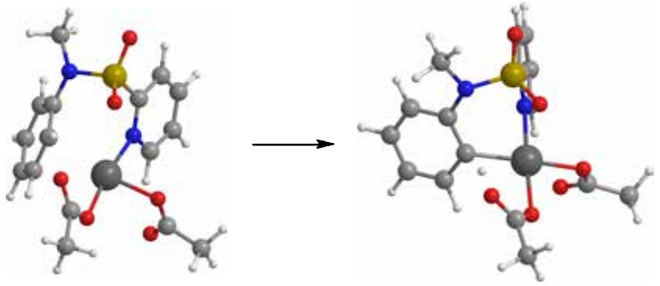
Funded by:
DTU

The project included an external stay with Prof. Jin-Quan Yu, Scripps Research Institute, San Diego, USA.

Scan the QR-code and get the thesis as a pdf.

Methods for performing selective chemistry on the carbon-hydrogen (C-H) bonds in alkanes would be highly beneficial for various chemical applications, such as fuel production, fine chemical production, and novel pharmaceutical products. Traditionally, C-H bonds have been thought of as inert, but progress in catalysis over the latest decades has shown that activation is indeed possible. This thesis investigates a number of C-H activation methods.

C-H activation is made possible by use of so-called transition metals, a group of basic chemical elements of which 23 are relevant to organic chemistry. A common feature for the transition metals is found in an electron sub-shell, the d-shell. For the transition metals the d-shell is not filled. This feature allows for one or more electrons from other compounds to reside temporarily in the d-shell. By "lending" electrons to the transition metal, these compounds will be able to engage in chemical reactions more easily. In other words, the transition metal can act as a catalyst, speeding up reactions between other compounds.

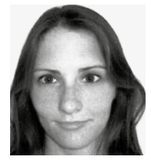


In this project different transition metal C-H activations have been investigated by experiments, computational chemistry or a combination thereof. The palladium-catalyzed allylic C-H activation was studied with a Hammett study, determination of deuterium kinetic isotope effect (KIE) and Density Function Theory (DFT) calculations. The Hammett study showed build-up of a partial negative charge in the reaction, supporting a proton abstraction mechanism. The determined KIE values indicated that the C-H activation step was the selectivity-determining step. Using DFT calculations, the transition states for various possible C-H activation mechanisms were determined. Comparison of experimental and theoretical KIE values supported a C-H activation mechanism where acetate plays a pivotal role either as an internal or external base and the results were published in ACS Catalysis.

A palladium-catalyzed N-(2-pyridyl)sulfonyl directed C-H olefination was studied with DFT calculations. A concerted metalation-deprotonation mechanism was found most favourable for the C-H activation step. The influence of electronic effects on the C-H activation mechanism was found to qualitatively fit reported experimental results. Comparable C-H activation energy barriers were determined for aniline, benzylamine, and phenethylamine derived substrates. During an external stay at The Scripps Research Institute, a novel ruthenium-catalyzed non-directed oxidative alkenylation reaction was investigated. Finally, the product-forming steps of the palladium-catalyzed chemoselective oxidation of glycerol and 1,2-propanediol were investigated with DFT calculations.

Towards an alternative Treatment of Diabetes

The thesis investigates different aspects of interactions between Glucagon-Like Peptide-1 (GLP-1) and its receptor (GLP-1R).



Christina Rye Underwood, PhD

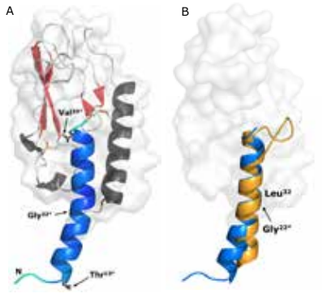
"Ligand Binding and Activation Mechanism of the Glucagon-Like Peptide-1 Receptor".

Supervisor:
Steffen Reedtz-Runge (Novo Nordisk), Günther H. Peters

Funded by:
Novo Nordisk (2/3) and DTU Chemistry (1/3).

Scan the QR-code and get the thesis as a pdf.

While insulin remains the dominant treatment for diabetes, in recent years have so-called incretin-based therapies become available for the treatment of type 2 diabetes (T2D). The "incretin effect" refers to the observation that insulin secretion increases substantially in response to orally ingested glucose compared to intravenous glucose administration. Especially as T2D continues to affect ever larger parts of the world's populations, it is highly desirable to have different regimes for treatment available. Also, to different patients, different treatments could be most suitable. Two main incretin hormones have been identified; one of these being Glucagon-Like Peptide-1 (GLP-1). The receptor for GLP-1 (GLP-1R) is the focus of this thesis.



GLP-1R is a G-protein coupled receptor (GPCR). Also known as seven-transmembrane (7TM) receptors, GPCRs constitute one of the largest families of proteins in the human genome. They have become important drug targets, which make elucidation of their molecular structure and functional domains increasingly important for designing new and better therapeutic agents.

The thesis investigates different aspects of GLP-1R interactions with GLP-1 and other receptor agonists.

Firstly, the crystal structure of GLP-1 in complex with the extracellular domain (ECD) of GLP-1R was established. The crystal structure solved in the project showed that GLP-1 is a continuous α-helix from Thr13* to Val33* when bound to the ECD, but the helix has a distortion of the backbone around Gly22*.

Secondly, a combination of crystallography and site-directed mutagenesis supported the existence of different binding modes of GLP-1 and exendin-4. The work demonstrated a ligand-supported effect of a Leu32-Ala mutation in the ECD of the full-length GLP-1R. Whether the ligand-specific effect is affected by a kink in the α-helix of GLP-1 remains to be investigated.

Thirdly, a cysteine-deprived and C-terminally truncated GLP-1R established that seven cysteine residues and more than half of the C-terminal tail are not required for GLP-1 binding or function.

Finally, real-time cAMP-measurements indicated that exendin-4 has a prolonged effect on GLP-1R compared to other peptide agonists; and receptor domains and specific residues involved in small molecule-mediated activation of GLP-1R were identified.

It is probable that these findings could help in improving the design and development of small molecule GLP-1R agonists that are suitable for oral administration. It is obvious that rational drug design, regardless of whether it is applied to peptide- or small molecule ligands, would benefit immensely from a crystal structure of the full-length GLP-1R. The results obtained with the cysteine-deprived and C-terminally truncated GLP-1R may guide the design of stable receptor constructs that can ultimately lead to structural characterization of the full-length GLP-1R.

Iridium Catalysts in Organic Chemistry

In the project an iridium-catalyzed degradation of primary alcohols, where hydrogen and carbon monoxide were liberated as gases, was developed.

Esben Paul Krogh Olsen, PhD

"Homogeneous Catalysis with Primary Alcohols."

Supervisor:
Robert Madsen

Funded by:
The Danish Council for Strategic Research, Nordic Energy Research (N-INNER).

Scan the QR-code and get the thesis as a pdf.

Homogeneous transition metal catalysis has revolutionized organic chemistry over the past 40 years. The fact that three of the last 12 Nobel Prizes in chemistry have been awarded to scientists in this field illustrates its importance. However, iridium has been in less focus in comparison with other transition metals. In this project a novel iridium-catalyzed pathway for degradation of primary alcohols was developed. The end product is mixed hydrogen and carbon monoxide, which is important in many industrial contexts.

In industry, the mixture of hydrogen and carbon monoxide is known as syngas. As carbon monoxide is a versatile carbon based feedstock, syngas is an interesting component in organic chemistry.

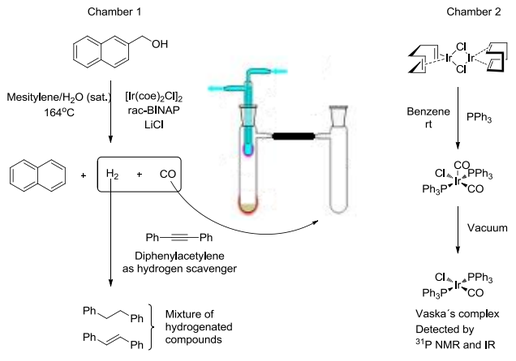
In the project an iridium-catalyzed degradation of primary alcohols, where hydrogen and carbon monoxide were liberated as gases was developed. The reaction was carried out with the complex $[Ir(coe)_2Cl]_2$ and the phosphine ligand BINAP in refluxing mesitylene. The catalytic system showed strong functional group tolerance as many different primary alcohols could be converted selectively. The reaction combined two known iridium-catalyzed transformations in the same sequence, i.e. dehydrogenation of an alcohol and decarbonylation of an aldehyde in independent catalytic cycles.

In a near stoichiometric reaction of $[Ir(cod)Cl]_2$, (rac-)BINAP and benzyl alcohol, the complex IrCl(CO)(rac)-BINAP was formed and isolated in high yield. The complex was catalytically active and kinetically very close to the in situ formed system. The complex was applied to study the individual steps in the catalytic cycles. The cod ligand had been shown to thwart KIE experiments due to scrambling. The premade catalyst was devoid of the cod ligand and could therefore be applied to determine a KIE of 1.0 in the decarbonylation cycle and 1.42±0.07 in the overall reaction.

The complex was also applied to synthesize expected catalytic intermediates such as the dihydride isomers $IrH_2Cl(CO)$(rac)-BINAP which were proven to reductively eliminate hydrogen under the reaction conditions. Furthermore, convincing results indicated that the carbon monoxide was liberated from a dicarbonyl complex.

An overall mechanism was suggested where HCl was formed in the dehydrogenation of the alcohol and could be oxidatively added to another IrCl(CO)(rac)-BINAP molecule forming $IrHCl_2$(CO)(rac)-BINAP.

The project also investigated a two-chamber method with promising results where syngas is released from the iridium-catalyzed reaction in one chamber and then reacted in a palladium-catalyzed transformation in the other chamber.



Enzymes, Catalysis and Surface Modification

This thesis investigates a number of issues related to synthesis and functionalization of liposomes with possible future drug delivery applications in mind.

Hélène Viart, PhD

"Organic Synthesis – Applications in Enzymatic Studies, Catalysis and Surface Modification."

Supervisor:
Mads H. Clausen

Funded by:
DTU

Lundbeck Foundation

Scan the QR-code and get the thesis as a pdf.

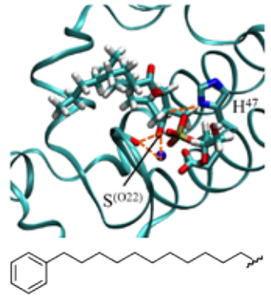
Despite advances in cancer treatment, side effects caused by the high toxicity of anti-cancer drugs towards healthy cells continue to be a major problem. A strategy to overcome this problem is the use of liposomes as drug delivery systems. Liposomes can be designed for specific purposes by altering their biophysical properties. Ideally, liposomes can encapsulate the active drug and only release it once the tumor has been reached. In practice this has not yet been achieved. This thesis investigates a number of issues related to synthesis of liposomes with possible future drug delivery applications in mind.

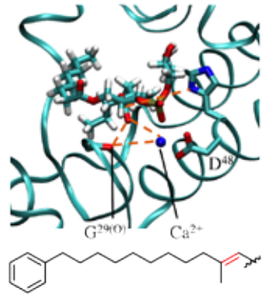
Firstly, a series of phospholipids were synthesized in order to perform a structure-activity relationship study of an enzyme, secretory phospholipase A_2 ($sPLA_2$) capable of hydrolyzing phospholipids in the sn-2 position specifically. This enzyme is over-expressed in several types of cancer and is under evaluation as a potential trigger for drug release from a new generation of liposomal drug delivery systems. Based on previous observations and MD experiments, we developed a theory to predict and explain the activity of the enzyme in engineered phospholipids. According to our theory, two aspects of the enzyme-substrate interactions are primordial for an effective hydrolysis to occur: the formation of a constructive Michaelis-Menten complex, and access of water to the hydrolysis site. The theory was confirmed by experiments.

Secondly, surface functionalization of liposomes was studied. The copper mediated [3+2] azide-alkyne cycloaddition has been successfully applied for this purpose by different groups, but no general optimization has been developed for the reaction on functionalized liposomes. Our results indicate that the reaction is most efficient when the liposome carries the alkyne functionality rather than the azide. We also investigated and developed a novel selective method for functionalizing liposomes, which has not yet been reported in the literature, based on the reaction between propargyl-amine decorated liposomes and isothiocyanate derived coupling partners that results in a coupling via formation of an iminothiazolidine.

Thirdly, the synthesis of sn-2 glyceryl 10,16-dihydroxyhexadecanoate is reported, in the context of the identification of the process of formation of the cutin polymer, one the primary reactive components of the epidermis of land plants.

Finally, a last section of the project differs greatly as it is not related to liposomes. Here, a *C3* symmetric phosphine oxide was synthesized. We intend to test it, after reduction to the phosphin, as a ligand in organometallic catalyzed reactions. The ultimate goal is to obtain enantioselectivity, introduced by the organization of aryl substituents around phosphorous in our ligand.





An affordable Alternative to Phthalates

"Towards an industrial synthetic route for producing sunflower oil based on plasticizer"

Helle Søndergaard, PhD

"Development of a synthetic Pathway for a sustainable Plasticizer."

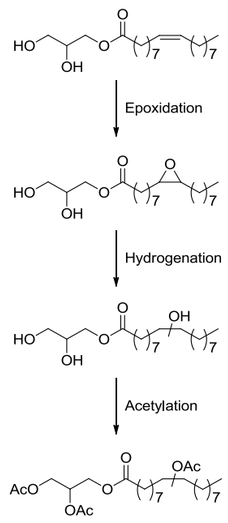
Supervisor:
Anders Riisager

Funded by:
The Danish Advanced Technology Foundation (Højteknologifonden).

The project was done in collaboration with DuPont Nutrition Biosciences Aps, Danish National Food Institute (DTU-Food), and Department of Engineering at Aarhus University (AU).

Scan the QR-code and get the thesis as a pdf.

Increasing health concerns in relation to use of phtalates as plasticizers have led to the discovery of the safer alternative Grindsted SOFT-N-SAFE (SNS) by Danisco A/S (now known as DuPont Nutrition Biosciences Aps). The main component of SNS is based on acetylated glycerol monostearate, originating from hydrogenated castor oil. Unfortunately, castor oil is too expensive and available in too small quantities for SNS to be a realistic, large-scale alternative to phthalates. This thesis presents a less expensive and more accessible alternative, namely the SNS-analogue (SNS-A) in which the starting material is glycerol monooleate originating from sunflower oil.



Plasticizers are added to polymers to increase fluidity. In the worlds' third mostly used plastic type polyvinyl chloride (PVC), mainly used in building and construction, phthalates continue to be used as plasticizers. The most widely used phthalate is di(2-ethylhexyl)phthalate (DEHP). SNS, released in 2005, is a 1-1 replacement alternative to DEHP. As SNS is made from vegetable oil, it is fully biodegradable and metabolizes like any other vegetable oil and is therefore fully digestible. SNS is thoroughly tested for environmental and health effects with no harmful effects found. For example, is the no-observed-adverse-effect level (NOAEL) in rats about 1,000 times higher for SNS than for DEHP.

However, a major concern about SNS is the price, as it is 3-4 times more expensive compared with DEHP. Thus, a cheaper alternative with the same safety features would be highly attractive. This has led DuPont Nutrition Biosciences Aps to take interest in the SNS-A from sunflower oil.

In this project a three step synthetic pathway consisting of epoxidation, hydrogenation and acetylation of glycerol monooleate was developed.

The pathway uses an ionic liquid (IL) as reaction media. ILs are salts that are liquid at ambient temperatures – often with melting points lower than 100 degrees C. ILs can act as solvents for chemical reactions and can have a dual function as both catalyst and solvent. Further, ILs have extremely low vapor pressure, which minimize solvent emission and thus makes it easier to reuse them efficiently.

Having considered several ILs the choice fell on trihexyltetradecyl phosphonium bis(trifluoromethylsulfonyl)amide which showed favorable phase separation properties allowing a homogeneous epoxidation and hydrogenation reaction. The method was shown to provide satisfying results, but additional development will be needed to establish an industrially viable process protocol. A patent has been filed for the process.

"Green" Synthesis of Amides

This project is focused at improving our understanding of the ruthenium-catalyzed process through a combination of experimental and theoretical work.

Ilya S. Makarov, PhD

"Ruthenium-Catalyzed Transformations of Alcohols: Mechanistic Investigations and Methodology Development."

Supervisor:
Robert Madsen
Peter Fristrup

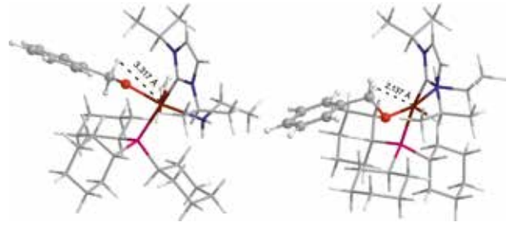
Funded by:
The Danish Council for Independent Research – Technology and Production Sciences.

The project included an external stay at Haldor Topsøe A/S.

Scan the QR-code and get the thesis as a pdf.

Amides are nitrogen-containing compounds which are important in biology and in organic chemistry. The amide bond is found in peptides, artificial polymers, drugs, and biologically active compounds. For example, 9 out of 53 small molecule drugs, whose sales exceeded 1 billion USD annually in 2003, contain an amide. This thesis contributes to the understanding of a novel, and environmentally benign pathway for the synthesis of amides.

Given the vast importance of amides, it is not surprising that a range of alternative methods for amide synthesis have been developed. Most however, have the same problem: they require additional reagents which do not end up in the products. In chemical terminology, they are not atom-economical.



In 2008, Madsen and co-workers published their discovery of ruthenium-catalyzed dehydrogenative coupling of primary alcohols to form amides. This direct pathway is highly atom-economical and is also considered "green" since only a small amount of catalyst is needed to make the reaction work efficiently.

This project is focused at improving our understanding of the ruthenium-catalyzed process through a combination of experimental work and theoretical techniques. In the experimental part, deuterium-labeled alcohols and amines were used. This revealed that ruthenium-dihydride species are involved in the catalytic cycle.

These experimental results were compared to a Density Functional Theory (DFT) / M06 computational study and a plausible catalytic cycle was proposed.

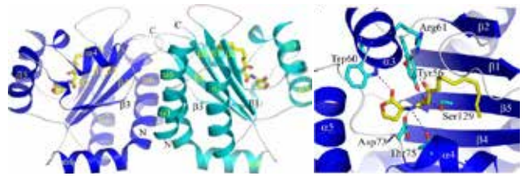
Further, this catalytic cycle was turned into a model which again would form the starting point for additional computer calculations. The aim of these calculations was to find even more effective carbene ligands. The study showed that ruthenium complexes with dimethoxyimidazolylidene and pyridilidene ligands could be more active than the $RuCl_2$(IiPr)(p-cymene) complex used in the original study by Madsen and co-workers.

Further experiments with a mixture containing a N-ethyl pyridilidene-substituted ruthenium complex afforded the amide in 38 % yield. This indicates that computer (in silica) ligand screening might be used for catalyst optimization.

An improved protocol was developed for the ruthenium catalyzed dehydrogenative self-coupling of primary alcohols to give esters. Addition of 16.7 mol% of Mg_3N_2 to the reaction mixture gave esters from aliphatic alcohols in similar yields but at lower temperature as compared with a previously reported catalytic system. The additive also suppressed the decarbonylation of aromatic alcohols. A previously unknown ruthenium catalyzed dehydrogenative Guerbet reaction with secondary alcohols to give ketones was discovered. It was found that only acyclic 2-methyl carbinols and simple cyclic alcohols underwent this transformation. It was shown that the reaction proceeded via an oxidation-aldol condensation-reduction pathway and that the active ruthenium species was a dihydride.

Towards New Cures for Hospital Infections

In this project, a number of small molecules capable of interfering with the quorum sensing (QS) system of *Pseudomonas Aeruginosa* were synthesized.



Mette Reimert Hansen, PhD

"Design, Synthesis and Biological Evaluation of Quorum Sensing Modulators."

Supervisor:
Thomas E. Nielsen

Funded by:
DSF Center for Antimicrobial Research

Scan the QR-code and get the thesis as a pdf.

Infection caused by bacteria resistant to most common types of antibiotics represents a growing global health problem. Research over the last few decades has shown that development of antibiotic resistance is related to the ability of bacteria to form so-called biofilms. Consisting mainly of an extracellular polysaccharide matrix, the biofilm embeds the bacterial cells and makes it difficult for the immune system as well as antibiotics to eradicate the bacterium. This thesis focuses on the prevention of biofilm formation. More specifically, the project investigates a series of novel, synthetic small molecules for their ability to perturb the intercellular communication system of bacteria related to biofilm formation.

The bacterium Pseudomonas aeruginosa was used as a model organism. P. aeruginosa is a pathogenic bacterium associated with the majority of hospital-aquired infections and patients suffering from cystic fibrosis. The microorganism uses an intercellular communication process termed quorum sensing (QS) to control the formation of drug-resistant biofilm and various virulence factors. The system is regulated by small signaling molecules, referred to as N-acyl homoserine lactones (AHLs).

Recent scientific advances have indicated the possibility of intercepting the QS system by synthetic non-native ligands and thereby lower the pathogenesis and antibiotic tolerance of bacterial biofilms. Furthermore, since QS is not directly involved in biological processes that are essential for bacterial survival, the modulation of the system does not impose selective pressure for the development of resistant mutants.

In this project, a number of small molecules capable of interfering with the QS system were synthesized. Virtual screening of N-dipeptido homoserine lactone libraries against target proteins responsible for QS control in P. aeruginosa identified a number of potential hits. The best hits were then synthesized using a solid-phase strategy, and subsequent biological studies revealed 17 compounds that activate the QS system of P. aeruginosa, with EC50 values in the low micromolar range.

Two "build/couple/pair" strategies for the synthesis of structurally diverse small molecules were developed. In the first strategy, the Petasis 3-component reaction of hydrazides was utilized to rapidly assemble a densely functionalized template. Diversification by "functional group pairing" was then applied to provide a range of cyclized products, thereby providing efficient access to oxazolidinone and oxadiazolone heterocyclic compounds. Ring-closing metathesis of alkene moieties appropriately positioned in Petasis-3CR products yielded a variety of cyclized products. In the second strategy, a number of alkyne- and azide-containing amino acid-derivatives were coupled, and macrocyclic peptidomimetics were obtained after intramolecular ruthenium-catalyzed azide-alkyne cycloadditions.

Many challenges around toxicity and other issues need to be solved before clinical applications of the compounds presented in the thesis can even be considered. However, the small molecules synthesized in this project may serve as chemical probes to provide further knowledge about bacterial QS systems and infectious disease.

Survival of the fittest Molecules

Thermochemical data for Myoglobin (Mb) mutants were merged with a new physiological model of O_2-transport and storage in muscles of deep-diving mammals.

Pouria Dasmeh, PhD

"Integrating Chemistry, Biophysics, and Physiology in the Evolution of Mammalian Myoglobins."

Supervisor:
Kasper P. Kepp

Funded by:
DTU

Scan the QR-code and get the thesis as a pdf.

Any change in living organisms is in principle caused by underlying changes in the molecular and cellular properties. Molecular evolution aims to relate natural variations in organisms and living systems all the way to the properties of their molecules. A possible application could be in improved design of enzymes and other industrially relevant molecules. The thesis describes the application of molecular evolution methodology to the study of the protein Myoglobin (Mb) in diving mammals such as sperm whales and Weddell seals.

Mb plays a key role in storage and transport of oxygen in mammals. Mb is present in both cardiac and skeletal muscles of vertebrates and in the body walls of invertebrates. The primary function of Mb is to increase the availability of O_2 in muscle cells and provide the oxygen for the energy-producing mitochondria. The importance of this function is evident from typically 10-20 times more abundant Mb in diving mammals, compared to their terrestrial relatives.

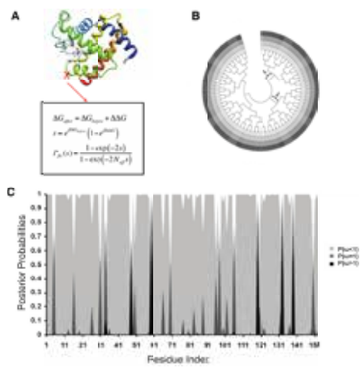
In the project, a large set of previously reported thermochemical data for Mb mutants was merged with a new physiological model of O2-transport and storage in skeletal muscle cells. It was shown that O2-storage and transport are distinct functions that rank mutants and wild type (WT) Mb differently depending on O_2 partial pressure.

Further, an integrated model of convective O_2-transport and O_2-affinity of mutant Mb was developed. The model quantifies the impact of mutations in Mb on the aerobic dive limits (ADL) of Weddell seals. This integration, the first quantitative relation from molecular properties to organism fitness, illustrates the superiority of WT Mb traits under specific physiological conditions that prolong the dive time, action radius, and thus fitness of the seals.

Thirdly, the observation of higher folding stabilities of cetacean Mbs compared to their terrestrial counterparts was investigated. Accelerated evolution in cetaceans was observed, and we identified seven positively selected sites in Mb. We showed that these sites contribute to Mb stabilization by favoring hydrophobic folding, structural integrity, and intra-helical hydrogen bonds.

Finally, a model that combines explicit evolution of Mb sequences, folding stability, and application of maximum likelihood (ML) estimation of evolution rate (ER) was developed. We found that ER predicted by ML methods is highly correlated with ER from simulations using the explicit sequence information by counting the number of synonymous and non-synonymous mutations fixed in the population. This agreement is strongest in the regime of high stability where proteins are mostly evolving neutrally.

Overall, this thesis provides one of the first evolutionary examples of a direct impact of changes in protein function and thermodynamic stability on the fitness of the organism. Moreover, the thesis provides a number of theoretical findings directly testable in future experiments.



DeNO$_x$ at Biomass Combustion Plants

A new efficient deNOx catalyst was made by sol-gel synthesis resulting in a catalyst comprising amorphous vanadia on a high surface area crystalline anatase carrier.

Steffen Buus Kristensen, PhD

"DeNOx Catalysts for Biomass Combustion."

Supervisor:
Anders Riisager
Jørgen Nørklit Jensen
Rasmus Fehrmann

Funded by:
The Industrial PhD program of the Danish Agency for Science, Technology and Innovation with DONG Energy and Vattenfall

Scan the QR-code and get the thesis as a pdf.

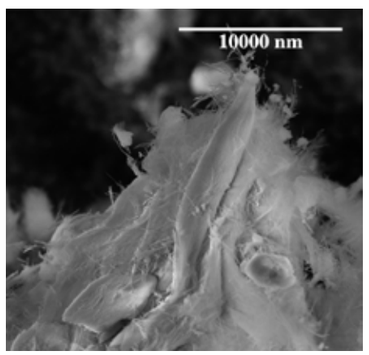
Practically all combustion processes create nitrogen oxides (NOx), which are problematic in various ways in relation to human health. For well-established combustion processes like coal-fired power plants and gasoline-driven cars, selective catalytic reduction (SCR) technology for post-combustion removal of NOx (or deNOx) has been developed and optimized. However, these catalysts are not ideal for deNOx at biomass combustion plants. The main problem is the content of alkali in biomass. Alkali severely deactivates traditional deNOx catalysts in a matter of weeks. Especially as many nations, including Denmark, plan to expand the use of biomass combustion, it is essential to develop suitable solutions to this problem. This thesis presents an optimized version of a new type of nanoparticular vanadia deNOx catalyst.

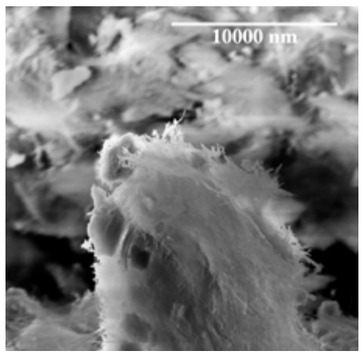
The nanoparticle catalyst was made through one-pot sol-gel synthesis resulting in a catalyst comprising amorphous vanadia on a high surface area crystalline anatase carrier. Due to the high surface area, loadings of 20 wt.% vanadia could be obtained without exceeding the vanadium oxide monolayer coverage. The catalyst proved highly active – corresponding to a factor of 2 compared to an industrial reference.

Even at high vanadia loadings the catalyst did not show any sign of increased SO_2 oxidation, compared with a low vanadia industrial reference catalyst. Furthermore, long-term activity measurements at normal operating temperature revealed that the catalyst did not display any sign of deactivation.

The catalyst showed very high resistance towards potassium poisoning maintaining a level of activity 16 times higher than an equally poisoned industrial reference catalyst, A catalyst plate was synthesized using 20 wt.% sepiolite mixed with nanocatalyst, supported by a silica-fibre mesh. Realistic potassium poisoning was performed on the catalyst plate by exposure in a potassium aerosol for 632 hours at 350 °C. Owing to physical blocking of potassium by sepiolite fibres, the composite catalyst showed a further increase in potassium resistance compared with the unsupported catalyst.

Finally, a refined mechanism was proposed for the nanoparticle catalyst explaining in-situ Fourier Transform Infrared (FTIR) observations. Most importantly, it indicated that the V=O bond did not break during the catalytic reaction, suggesting that another oxygen is responsible for the activity of the active vanadia site.





Casting Light on the Fundamentals of Energy Conversion

The project focusses on internal conversion by which electronic energy can be dissipated in conjugated molecules.

Thomas Scheby Kuhlman, PhD

"The Non-Ergodic Nature of Internal Conversion".

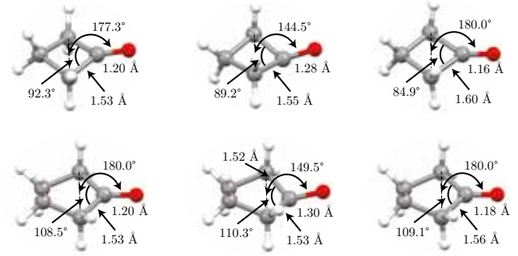
Supervisor:
Klaus B. Møller
Theis I. Sølling (University of Copenhagen)

Funded by:
DTU, Danish Ministry for Education, and the Idella Foundation

This thesis attracted the Organic Chemistry 2013 Award from the Danish Chemical Society, was granted the Springer Thesis Award by the international scientific publisher Springer, and was given the "Young Researcher Award" for the best thesis of the year at DTU.

Scan the QR-code and get the thesis as a pdf.

The absorption of light by molecules can induce ultrafast dynamics of coupled electronic and nuclear vibrational motion. These dynamics take place on the femtosecond to picosecond timescale, which is the timescale of nuclear vibrational motion, and involve energy transfer processes which are fundamental to the very notion of chemistry. This thesis addresses the topic of intramolecular energy conversion using combined experimental and theoretical approaches.



More specifically, the project focusses on internal conversion by which electronic energy can be dissipated in conjugated molecules. By internal conversion the energy of an electronically excited state is given off to vibrational modes of the molecule. In other words, the excitation energy is transformed into heat.

As subject molecules were chosen seven cycloketones, three cyclopentadienes, and dithiane. These are all industrially relevant substances. For instance, several cycloketones are precursors for production of various polymers. All were investigated by time-resolved mass spectrometry and photoelectron spectroscopy supplemented by electronic structure calculations and quantum dynamics simulations.

The process of internal conversion was found to be non-ergodic. The ergodic hypothesis says that over a sufficiently long period of time, a particle will visit all regions within its phase space, and that the time spent by the particle in a given region is proportional to the volume of this region. However, for the processes investigated in the project it was shown, that the nuclear dynamics only sample a reduced space potentially resulting in localization of the dynamics in real space. In essence, this is a consequence of vibrational energy redistribution simply not being able to compete with the rate of internal conversion.

In the case of the cycloketones, the rate of internal conversion varies by more than an order of magnitude between the molecules. This non-ergodic process was found to primarily involve ring-puckering motion, and the different timescales observed could be rationalized on the basis of the vibrational frequency and the energy difference between the Franck-Condon and equilibrium geometries of the upper electronic state.

In the cylcopentadienes, the twisting of a single double bond is essential in reaching the conical intersection seam connecting the lowest excited state with the ground state. In dithiane, the coupling of stretching in the disulfide bond with torsion in the carbon backbone allows the molecule to repeatedly access the region near a conical intersection.

A common trait of the three types of molecules is that very few degrees of freedom participate in the investigated processes. By selectively modifying these modes, the rate of internal conversion can be significantly affected and the dynamics possibly tuned from non-ergodic to partly ergodic.

Closing in on Roots of Depression

The thesis presents an expression system for the enzyme dopamine ß-monooxygenase (DBM) which is a potential target for therapeutic treatment.

Trine Vammen Vendelboe, PhD

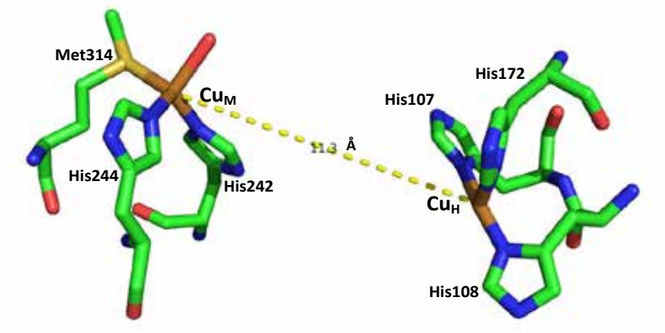
"Expression, purification and characterization of human Dopamine β-monooxygenase".

Supervisor:
Hans E. M. Christensen

Funded by:
DTU

Scan the QR-code and get the thesis as a pdf.

About 15 per cent of the Danish population will experience depression at least once in life. It is known that depression, and also several other diseases including hypertension, Parkinson's disease, and attention deficit hyperactivity disorder (ADHD), are linked to deficiency in the function of a key neurotransmitter, dopamine. Thus it has been suggested that enzymes related to dopamine conversion could be therapeutic targets. The thesis presents an expression system for one of these enzymes, dopamine β-monooxygenase (DBM). The lack of an efficient expression system for DBM has previously been a bottleneck for research on DBM as a potential target for therapeutic treatment.

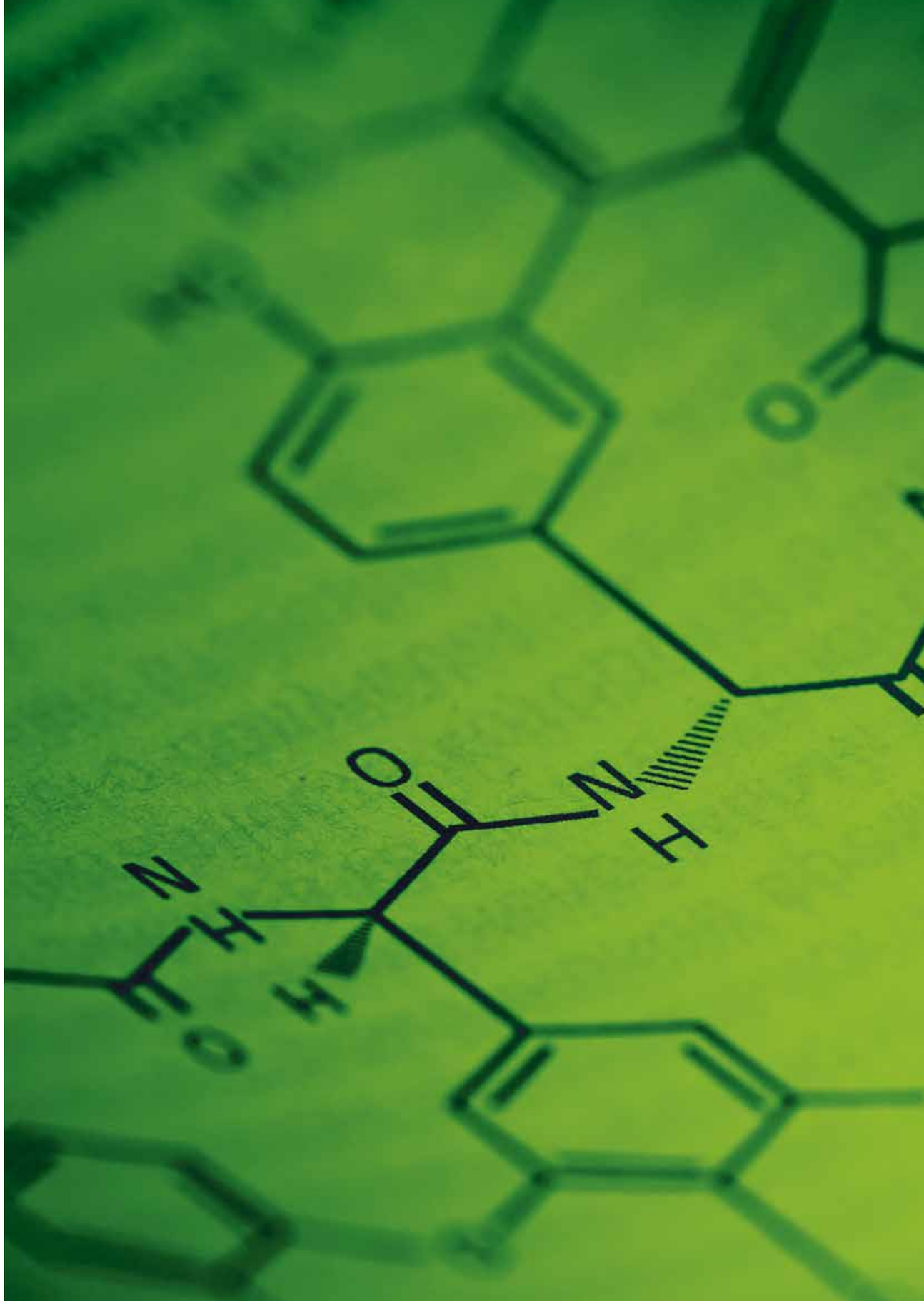


DBM catalyzes the conversion of dopamine into another neurotransmitter, norepinephrine (NE). In the reaction, an oxygen atom from molecular oxygen is inserted into dopamine whereby NE and water are formed. As it contains copper (Cu) in the active site DBM is a metalloprotein. Metalloproteins are involved in a number of key biological processes. Besides copper, DBM requires ascorbic acid in order to be active.

NE is a neurotransmitter in the sympathetic nervous system where it regulates the cardiac contractility and a hormone in the neurosecretory cells. Since DBM regulates the balance between dopamine and NE, the activity level of DBM is decisive and makes DBM an important therapeutic target. Several DBM inhibitors have been tested, but have side effects and are non-responsive to certain populations. The efforts have been troubled with the lack of an efficient expression system for human DBM (hDBM).

In the project, hDBM was successfully expressed in mammalian cells in a stable glycosylated form. Further, hDBM was expressed in large enough amounts for structural characterization using intact protein mass spectrometric analysis and X-ray crystallography. The protein exists in two homo-oligomer forms; a dimer and a tetramer. Both forms were glycosylated, pure, stable, and displayed activity.

*h*DBM in both the dimer and the tetramer was set up for crystallization and the dimer formed crystals that diffracted to 2.9 Å. This is the first structure of DBM and the structure revealed new unexpected features and a completely new reaction mechanism for this class of enzymes.



Master Theses 2013

Andreas Klinge Rønnest
Dynamics of Water and Lipid Molecules in Phospholipid (DMPG) Bilayers

Anita Godiksen
Desulfurization of Glycerol from Biodiesel Production

Anne Kathrine Nielsen
Metalloenzyme Characterization

Ann-Louise Nygård Christoffersen
Mental Understanding of the Impact of Acids on Alumina as Carrier for Hydrodesulphurization Catalysts

Casper Hoeck
Chemistry of Black Aspergilli

Daniel Michael Hinnerfeldt
Synthesis of New Antibiotics against Staphylococcus Aureus

Farnam Barimani
Viscosity Modeling of Hydrocarbon Systems Using Modified Lohrenz-Bray-Clark Models

Jacob Oskar Abildstrøm
Mesoporous Titanium-containing Zeolites for Catalytic Oxidation

Jascha Rosenbaum
Iridium-Catalyzed Decarbonylation of Alcohols

Katrine Hein Bünger
Characterization of Milk Proteins

Kim Thollund Mortensen
Synthesis of Hydroxylamine Derivatives Using a Novel Photolabile Protecting Group

Linda Maria Bruun
Synthesis of Human Milk Oligosaccharides

Line Loch Hesselholdt
Mechanistic Investigations of Ruthenium-catalyzed Amide Synthesis

Maria Mosbech Oettinger
Purification and Characterization of Novel Wild-type Lipases

Nanette Zahrtmann
Ionic Liquid Mediated Oxidative Carbonylation of Aniline

Pernille Sønderby
Albumin-protein Interactions Studied by Small Angle X-ray Scattering

Pifu Zhang
Chemical Preparation and Functionalization of Prisitine Graphene

Rebeca Sequera Pineda
Detection of Synthetic Cannabinoids in Biological Fluids within a Forensic Context

Yassine Kamal Lyauk
The Development of a Pharmacokinetic Model to describe the in vivo plasma concentration profiles of ZP1848 and active metabolites thereof, following repeated subcutaneous administration in healthy subjects and patients

Acknowledgement

DTU Chemistry highly appreciates the active involvement of our Advisory Board:

Kim Andersen	Lundbeck A/S
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Ole Kirk	Novozymes A/S
Jesper Nerlov	Haldor Topsoe A/S

DTU Chemistry has a wide cooperation with industry. Among the Department's industry partners are:

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Amminex A/S
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Arrayjet
Bayer
Bollerup-Jensen A/S
Carlsberg
Clauson-Kaas
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Danisco
Danish Power System ApS
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ExxonMobil
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OK a.m.b.a.
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QuantiBact A/S
Riemann
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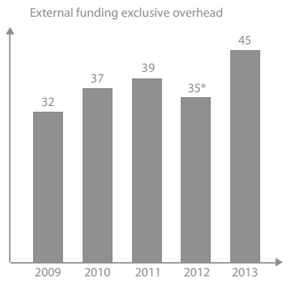
Vattenfall A/S
Veloxis
Wacker Chemie
Welltec

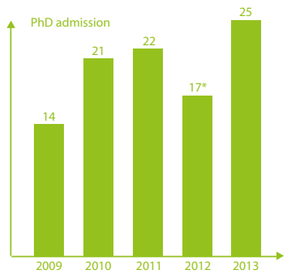
A Leading Research Institute

DTU Chemistry's position as a leading research institute was maintained in 2013. Once again the Department had a high success rate in applications for external funding, and we are pleased to confirm that the chosen setup has a very positive effect. The increase in external funding has also made it possible to increase our recruitment of PhD to a record level of 25 new PhD students.

Furthermore, we have had an exceptionally high number of applicants for the B.Sc. in Chemistry and Technology – 43 % more applicants than last year. The growth is due to both the progress in general on a national level as well as our constant focus of high quality education and strong marketing and recruitment efforts to attract the best students.



** the decline is solely due to that the Energy and material Science group is no longer part of DTU Chemistry but part of DTU Energy Conversion*



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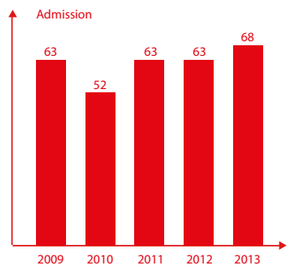


Publications 2013

DTU Chemistry performs well in the world of chemical science. This is reflected in all the publications produced every year. DTU Chemistry focuses on production of relevant science where quality is of the utmost importance.

For a complete list of DTU Chemistry's publications in 2013, please scan the code or see: kemi.dtu.dk/Omos/Publikationer

Peak in Number of Bachelor Applications

As a whole, DTU has seen a steadily rising trend in the number of applications for some years. Even so, Chemistry stands out as very popular choice. The Bachelor of Science in Chemistry had 237 applicants for only 60 seats, and even with an exceptional extra uptake of 70 students, we were still able to pick the best from a pool of talented young people. That goes for the Bachelor in Chemical Engineering as well.

DTU Chemistry has become very attractive and highly relevant in the eyes of future generations of chemical engineers.

Chemical engineering at DTU has become a known brand associated with high quality education and very good job opportunities, and this awareness in the market attracts the talented young people we need.

DTU Chemistry Lectures

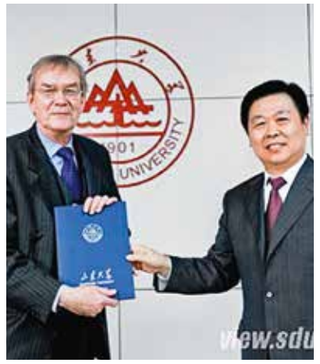
In 2013 DTU Chemistry introduced a new type of lecture – the DTU Chemistry Lecture. Twice a year prominent international scientists are invited to give a DTU Chemistry Lecture. **Professor Ben Feringa of the University of Groningen, the Netherlands,** kicked off the new type of event in April, as he lectured on Dynamic Molecular Systems. Ben Feringa is currently director of the Stratingh Institute for Chemistry and the Center for Systems Chemistry at the University of Groningen.

Professor Mario Amzel, Johns Hopkins University School of Medicine, USA, followed up in September on the topic of structure and mechanism of peptidylglycine-alpha-amidating monooxygenase (PAM). Mario Amzel is a renowned scientist in the field of structural biology, specifically X-ray crystallography, structural enzymology, and structural thermodynamics. Dr. Amzel was part of the group that first described and determined the structure of the Fab fragment of an antibody. Presently, his research focuses on how enzymes play a key role in all metabolic and cell-signaling processes.

DTU Chemistry Lectures can be viewed at kemi.dtu.dk

New Associate Professor in Nanomedicine

The Department's faculty was extended, as Esben Thormann was appointed Associate Professor. The position was created by the DTU management in support of the Center for Nanomedicine and Theranostics. Esben Thormann comes from a similar position at the Kungliga Tekniska Högskolen (KTH) in Stockholm, Sweden. His field is biophysics with a special emphasis on interface and colloid chemistry. You can find more about his work in the article *New Center is Raising the Bar.*



Honorary Professor at Shandong University

Professor Jens Ulstrup from DTU Chemistry has received the title of Honorary Professor at the Shandong University, China. Jens Ulstrup is head of the Nano Chemistry Group, which cooperates closely with their counterparts in China, especially within the field of nano-structures capable of acting as electrodes in electronics, in bio-electronics, in fuel cells, and in novel chemical and electro-chemical sensors.

Among other things, Shandong University is good at producing the materials and make certain types of characterization. Collaborating with Shandong University, DTU Chemistry will make other types of characterization and will be responsible for the electrochemical studies.

Copenhagen Conference on Femtochemistry

In July 2013, Copenhagen was the place to be for scientists in one of the hottest fields within the natural sciences. DTU Chemistry hosted the venue of the 11th edition of *The Femtochemistry Conference – Frontiers of Ultrafast Phenomena in Chemistry, Biology and Physics* with participants from more than 20 countries. With several large scale facilities opened or planned internationally over recent years, the study of chemical reactions and other ultrafast phenomena is blooming. The topics at the FEMTO11 included reaction dynamics, coherent control, structural dynamics, solvation phenomena, liquids and interfaces, fast processes in biological systems, strong field processes, attosecond electron dynamics and aggregates, surfaces and solids.

Spectroscopy for High School Chemistry Teachers

Associate professor Charlotte H. Gotfredsen from DTU Chemistry established a course on advanced spectroscopy, especially created for high school chemistry teachers. The course is mainly focused at the NMR technique, but also involves other types of analytical information such as mass spectroscopy and infrared (IR) spectroscopy. Having completed the course, a teacher will be able to carry out a project with his or her class, involving a visit and hands-on NMR experience at DTU. The first course was held November 2013 and will be repeated in 2014.

Chemistry Success at the Olympics

One silver medal and three bronze medals was the outcome for the Danish participants at the International Chemistry Olympics held in Moscow, Russia, in July 2013. The four Danish high school students – Ada Krzak, Frederik Nørfjand, Frederik Søndergaard-Pedersen and Theodor Lundberg – were actually honored twice, as they also took bronze, silver (2) and gold at the first Scandinavian Chemistry Olympics held at DTU Chemistry one week earlier.

Also the Swedish and Norwegian participants were able to profit from the experience gained in the Scandinavian event at DTU, as they took one silver medal and two honorable mentions in Moscow.

The Best PhD Thesis

PhD Thomas S. Kuhlmann was honored several times for his excellent PhD thesis. His thesis *The Non-Ergodic Nature of Internal Conversion* attracted the Springer Thesis Award (granted by the international scientific publisher Springer), the "Young Researcher Award" given to the best thesis of the year at DTU, and the Organic Chemistry 2013 Award from the Danish Chemical Society. Beside the awards, the thesis attracted a scholarship from the Danish Ministry of Education.

Today Thomas S. Kuhlman works as Associate Consultant at the Boston Consulting Group.

A summary of Thomas S. Kuhlman's thesis is found at page [33].

Sciencecamps for the Talents

In collaboration with the Danish Association ScienceTalents, DTU Chemistry welcomed talented Danish high school students for science camps on chemistry, oil exploration and pharma. The camps include intensive days of work and study at the Maersk McKinney Møller Videncenter in Sorø. The camps are part of the efforts to attract talented young people to DTU, and they are supported by leading companies in the fields.

The PharmaCamp was sponsored by Leo Pharma, while the PetroCamp was sponsored jointly by Maersk Oil and DONG Energy – the same two companies also sponsored the 2013 version of the Danish leg of the international PetroChallenge competition, in which high school classes compete against each other.

Steady Growth in Scientific Grants at DTU Chemistry

The Novo Nordisk Foundation has established a new type of grants for research related to synthesis and production in biotechnology. Both Professor Jens Ø. Duus and Associate Professor Günther H. Peters from DTU Chemistry applied successfully. The project of Jens Ø. Duus is titled *Development of new NMR methods for the elucidation of carbohydrate converting enzyme mechanisms and optimization of enzyme processes in future green synthesis*, while Günther H. Peters will head research in *Modulation of Enzymatic Activity and Stability in Organic Media by the Addition of Excipients*.

Generally, 2013 saw a rise in the level of scientific grants achieved at DTU Chemistry. Both Associate Professor Jingdong Zhang and Professor Rasmus Fehrmann received support from the Otto Monsted Foundation allowing them to invite a foreign scientist of their choosing for a stay as Visiting Professor at the Department in the near future.

Also has the Carlsberg Foundation contributed strongly to the Department's activity through generous support for a number of equipment purchases.

Two new Professors in Chemical Biology

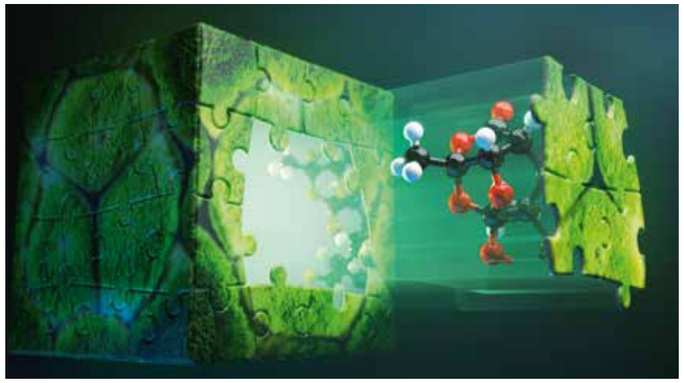
2014 has started out with the appointment of two new professorships in Chemical Biology, a fast growing area with a great potential. Congratulations to Professor Thomas E. Nielsen and Professor Mads H. Clausen.

Chemical Biology is a multidisciplinary area of research at the interface between chemistry and biology. Current focus for the area at DTU Chemistry is directed against cancer, infectious disease, drug delivery, and epigenetics, and research efforts are aimed at the development of new chemical probes, diagnostic tools, and lead compounds for drug discovery.

A central theme in the research of **Professor Thomas E. Nielsen** is organic synthesis as a tool to understand biological phenomena, such as cancer and antimicrobial infectious disease, including the development of miniaturized screening technologies.

The focus of **Professor Mads H. Clausen's** reserach is bio-organic chemistry and application of synthesis as a tool to answer biological questions, such as selective methods of cancer treatment as well as understanding of complex structures in plants and biomass.

You'll find more in depth information on the work of Professor Mads H. Clausen and Professor Thomas E. Nielsen in the articles *New Center is Raising the Bar* and *DTU Chemistry LEADs the Way*.



Gearing up on Entrepreneurship

DTU Chemistry has established a new project aimed at creating more spin-off companies from our research. The project, titled *Bridging the Gap*, is a joint effort with DTU Photonics. At DTU Chemistry it is managed by Special Adviser Majken Kramer Overgaard.

Bridging the Gap is inspired by a similar project in Finland, which has generated a number of new companies and entrepreneurship activities over just a few years. The project is supported by a 3 million DKK grant from the Danish Industry Foundation.

NMR: 16 million DKK from the VILLUM FOUNDATION

The VILLUM FOUNDATION has granted 16 million DKK for a new generation NMR at DTU Chemistry - a project involving the purchase of NMR cutting edge equipment for analyzing 3D molecular structures used in qualitative and quantitative measurements in drug discovery, materials sciences and other areas.

"We hope that this grant can support the set up of an ambitious new facility at DTU for interdisciplinary studies of organic molecules - from synthetic chemical compounds to large polysaccharides - in collaboration with leading national and international research partners ," states Kjeld Juel Petersen, the Director of the VILLUM FOUNDATION.

With the generous donation for the project *Structure to function in chemistry and biology – new generation NMR at DTU*, DTU Chemistry can now bring the NMR research at DTU in general at the forefront. NMR spectroscopy is one of the key techniques to study organic molecules and is therefore chosen to be a strategic commitment to DTU.

"I see great potential for the future of NMR at DTU. NMR spectroscopy has a strong position at DTU Chemistry, and we have come to a point where we can contribute significantly to the development of chemistry and biotechnology at DTU," explains Professor Jens Ø Duus, DTU Chemistry. Together with his colleague, Associate Professor Charlotte H. Gotfredsen, they are busy expanding their research group.

The Chemistry of Energy Resources

DTU Chemistry's involvement in the Center for Energy Resources Engineering (CERE DTU) increased in the past year, as several new activities related to oil and gas exploration were launched.

With faculty from five DTU departments, one of them being DTU Chemistry, CERE DTU addresses science relevant to exploration of oil and gas in the Danish part of the North Sea and other energy resources engineering topics.

Researchers from DTU Chemistry are active in several of CERE DTU's projects. This is especially true for the NextOil program, which addresses exploration of deep oil and gas fields. This is also known as HPHT (High Pressure, High Temperature) exploration. NextOil was initiated by late 2012 with DONG Energy, Maersk Oil, GEO and CERE DTU as partners.

Further, DTU Chemistry faculty members are active in two new JIP's (Joint Industry Projects) headed by CERE DTU. COMPPLEX is a new JIP dedicated to compositional reservoir simulations that not just calculate average oil properties (so called "black oil simulations"), but involve the phase behaviour of the main chemical components of the oil in question. This approach promises far more accurate simulations. Another effort will address the complex phase behaviour seen in carbon dioxide Enhanced Oil Recovery (EOR). Current industry partners are ConocoPhillips and ExxonMobil.

Finally, OPTION is a new JIP focussed at predicting flow and phase behaviour in relation to oil wells. The project promises new tools for optimizing the output from oil exploration not least in the Danish part of the North Sea. Industrial partners are Lloyd's Register Consulting and Welltec.

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The Annual PhD Symposium takes place every year in November with DTU Chemistry staff and external participants. In 2013 it was held at Mærsk McKinney Møller Videncenter in Sorø as a joint venture between the Department of Chemistry in collaboration with ScienceTalenter and Leo Pharma organizing a Pharmacamp for 24 of some of the most talented highschool-students.

The DTU Chemistry Support Unit

Innovating research, teaching, communication and consulting require the support of professional services. All the support units aim is to add value to the supply chain by offering the right support and complementary skills to the researchers in scientific and educational matters. Here they are all gathered a cold winterday in front of the Department.

Scan the QR-code and read more at kemi.dtu.dk