MINISTRY OF EDUCATION AND SCIENCE OF RUSSIAN FEDERATION
RUDN UNIVERSITY

NANOSCALE INTERDISCIPLINARY RESEARCH: PHYSICS, CHEMISTRY, BIOLOGY, MATHEMATICS

Book of abstracts
the First German-Russian Interdisciplinary Student Workshop

25–27 April 2017
Moscow, RUDN University

Moscow
Peoples' Friendship University of Russia
2017

УДК 53:54:57:51:001(063)
ББК 22.3+24+28+22.1+72
Н25

The event was financially supported by the Ministry of Education and Science of the Russian Federation (the Agreement № 02.A03.21.0008) and German-Russian Interdisciplinary Science Center (G-RISC) funded by the German Federal Foreign Office via the German Academic Exchange Service (DAAD)

Н25 **Наноразмерные междисциплинарные исследования: физика, химия, биология, математика = Nanoscale interdisciplinary research: physics, chemistry, biology, mathematics** : сборник тезисов первой немецко-российского междисциплинарного семинара студентов. Москва, РУДН, 25–27 апреля 2017 г. – Москва : РУДН, 2017. – 50 с. : ил.

The book of abstracts of the First German-Russian Interdisciplinary Student Workshop: “Nanoscale interdisciplinary research: physics, chemistry, biology, mathematics” which was held from 25 to 27 April 2017 based on the Faculty of Science of RUDN University includes abtracts of student`s, graduate`s, young scientist`s and invited lector`s reports.

The present publication was designed to demonstrate importance of Russian-German cooperation especially in a sphere of interdisciplinary research and to popularize scientific research activity in the field of chemistry and also to attract the most capable and concerned students to continue their studies in magistracy and postgraduate studies in RUDN University as a part of project for improving competitiveness of leading Russian universities among the world leading research and education centers (5-100).

The digest is intended for scientists, students, postgraduates and for wide range of readers interested in problems in chemistry, physics, biology and mathematics.

ISBN 978-5-209-07933-0

AeroNanoToxicology project

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In the 21st century - nanotechnology is seen as one of the key technologies. The previous industrial revolution has taught us that rapid technological change impacts on society in a variety of ways. Nanotechnology offers on the one hand various new properties and opportunities and on the other hand - brings new risks and uncertainties.

Sources of nanoparticles can be classified as natural or intentional and unintentional anthropogenic activities. Major natural processes that release nanoparticles in the atmosphere are forest fires, volcanic activities, weathering, formation from clay minerals, soil erosion by wind and water, or dust storms from desert. Man-made nanoparticles are released in the environment during various industrial and mechanical processes. The unfiltered exhaust gases from diesel engines contain large quantities of potentially harmful nanoparticles from the incomplete combustion of fuel. In the fireplace at home, fullerenes like buckyballs or buckytubes are formed when wood is burned. In industrial processes, coal, oil, and gas boilers release tons of nanoparticles unintentionally.

"AeroNanoToxicology" is a project which is intended to develop and introduce new cost-effective physical principles in large-scale production of the control devices and the use of nanoecology in the residential, office, laboratory and production facilities. The cooperation of the Peoples' Friendship University of Russia and the Vyatka State University has led to the elaborating of a new approach for determining the level of potential danger of nanoobjects using “Atmospheric modeling complex”.

Application of 3D printing in chemical research

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3D printing is an excellent tool to create multi-component chemical equipment directly in the laboratory without a manufacturing delay. Combination of computer-aided 3D modeling followed by printing can significantly speed up experimental studies in various research directions. The opportunities provided by 3D printing are of much importance for fundamental chemical research, as well as for applied and engineering projects. We believe that this innovation can be a valuable tool in the design of research equipment in chemical sciences.

Opportunities of 3D-printing and integration into everyday research in a lab will be highlighted. Evaluation of different 3D printing materials and examples of practical applications from our resent research will be presented and discussed (Figures 1 and 2) [1,2].

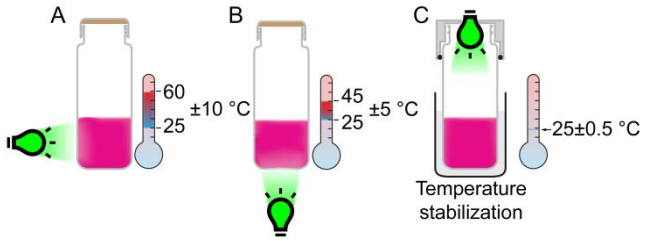

Figure 1. Design of photochemical reactor with temperature stabilization [2].

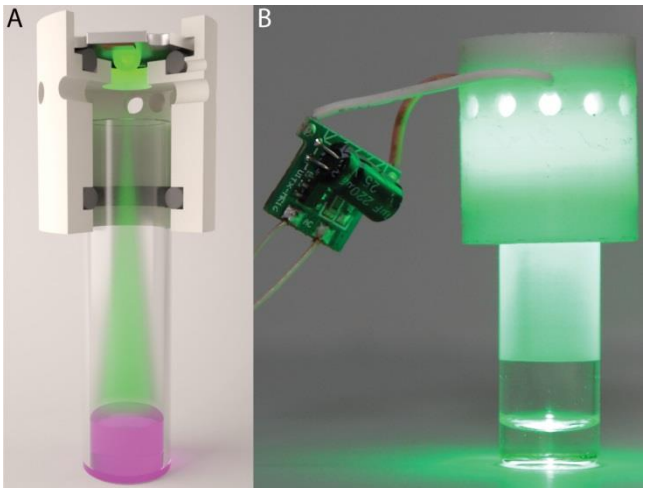

Figure 2. Construction of photochemical reactor with 3D-printing [2].

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Metal-free C-H bond functionalization

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C–H Bonds are ubiquitous in organic compounds and are among the least reactive bonds. Direct and selective methods of alkane functionalization are important and longstanding goals in chemistry. The direct transformation of C–H bonds into new carbon-carbon or carbon-heteroatom bonds is a fundamental challenge in organic chemistry. C–H bond functionalization is a straightforward and atom-economic process for the generation of pharmaceuticals and diverse other materials. Inspired by this green and sustainable chemistry, synthetic chemists have developed numerous methods for direct oxidative C–H functionalization.[1-3] Due to its low costs and the formation of environmentally acceptable by-products, this strategy is becoming more attractive, but is unfortunately associated with some limitations due to inertness of C–H bonds, regioselectivity issues and the necessity for additional amounts of sacrificial oxidants. Many of these methods are based on transition-metal catalysis, which is not universally acceptable in terms of either cost or toxicity. As an alternative, metal-free versions have become very important for avoiding expenditure and environmental issues. Substantial advancement in metal-free oxidative carbon-heteroatom bond-forming reactions has recently taken place. Direct oxidative carbon-heteroatom and carbon-carbon bond forming reactions will be discussed.

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An operator approach in investigation of partial differential equations involving the fractional derivative

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It is well-known that fractional derivatives have been successfully applied to problems in system biology, physics, chemistry and biochemistry (see, e.g., [1], [2], [3], [4], and the references given therein).

The role played by positivity property of differential and difference operators in Hilbert and Banach spaces in the study of various properties of boundary value problems for partial differential equations, of stability of difference schemes for partial differential equations, and of summation Fourier series is well-known (see, [5], [6], and [7]).

This is a discuss on results for fractional calculus and its applications. Its scope ranges from connection of fractional derivatives with fractional powers of positive differential and difference operators in a Banach space to well-posedness of various classical and nonclassical differential and difference problems for partial differential equations involving the fractional derivative. Finally, some problems and future plans are formulated.

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Synthesis of (1-chloro-3-(3-methylimidazolidin-1-yl)propan-2-yl diphenylphosphinite chloride) (chloro η4-1,5-cyclooctadiene rhodium(I))

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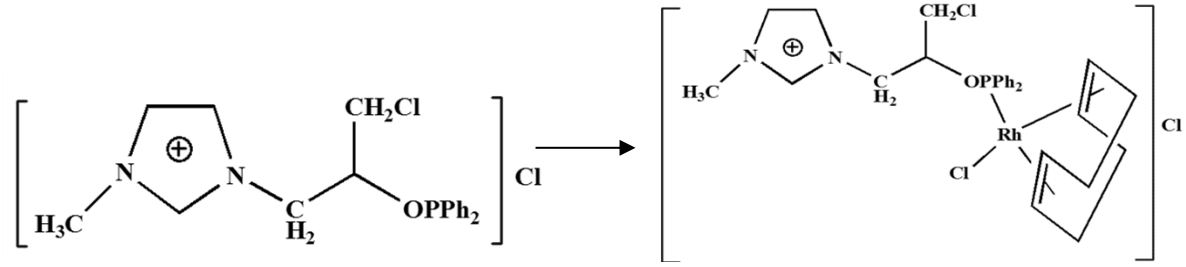
Transition metal complexes are powerful catalysts for organic transformations and when the suitable ligands are associated with the metal center, they can offer chemo-, regio- or stereo-selectivity under mild conditions [1]. A number of transition metal complexes are known to be effective catalysts for hydrogen atom transfer from an alcohol to a ketone, known as transfer hydrogenation (TH) [2].

Metal-containing ionic liquids are regarded as promising new materials that combine the properties of ionic liquids with additional intrinsic magnetic, spectroscopic, or catalytic properties, depending on the incorporated metal ion [3].

The synthesis of 1-(3-chloro-2-(hydroxypropyl)-3-methyl-imidazolium chloride, $[C_7H_{12}N_2OCl]Cl$, was accomplished in one step from the reaction of 1-methylimidazole and epichlorohydrin in ethanol at room temperature. Phosphinite ligand $[(Ph_2PO)\text{-}C_7H_{11}N_2Cl]Cl$, was synthesized from the starting material PPh_2Cl, in CH_2Cl_2 solution. The progress of this reaction was conveniently followed by $^{31}P\text{-}\{^1H\}$ NMR spectroscopy.

Reactions of $[Rh(\mu\text{-}Cl)(cod)]_2$ with $[(Ph_2PO)\text{-}C_7H_{11}N_2Cl]Cl$ in CH_2Cl_2 in a ratio of 1/2:1 at room temperature for 1 h gave micro-crystalline precipitate of complex (1-chloro-3-(3-methylimidazolidin-1-yl)propan-2-yldiphenylphosphinite chloride) (chloro η^4-1,5-cyclooctadiene rhodium(I))].



The synthesized rhodium complex was applied as a catalyst in the TH of ketones using alcohols as a source of hydrogen and appeared to be very promising catalyst of TH, giving high yield (up to 99%) of product.

This work was supported in part by the Ministry of Education and Science of the Republic of Kazakhstan, Grant 1318/GF4, 1752/GF4.

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Selective transition-metal-free vicinal cis-dihydroxylation of saturated hydrocarbons

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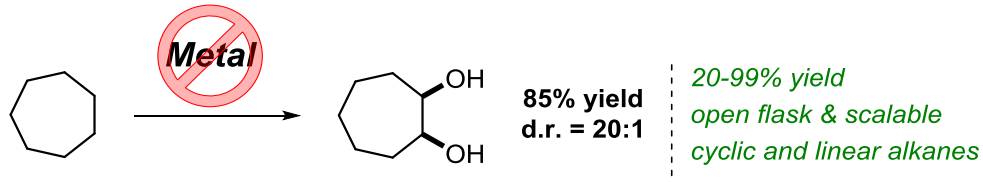
Transition metal-free *cis*-dihydroxylation of saturated hydrocarbons under ambient reaction conditions has been developed.[1] The described approach allows the direct and selective synthesis of vicinal diols. The new reaction proceeds thereby via radical iodination and a sequence of oxidation steps. A broad scope of one-pot dual C(sp^3)-H bond functionalization for the selective synthesis of vicinal *syn*-diols was demonstrated.



C-H bond functionalization of aliphatic hydrocarbons represents a longstanding goal in organic chemistry.[2] Selective functionalization of the chemical inert and ubiquitous C(sp^3)-H bond is a great challenge, since often high temperatures are required at the expense of controllability and economy of product formation.[3] State of art methods for diol synthesis are predominately based on dihydroxylation of alkenes in a metal-catalyzed or metal–free manner.[4] Despite the progress towards efficient and selective aliphatic C-H bond mono-functionalization, practical methods enabling the direct vicinal dihydroxylation of hydrocarbons are not known.

Inspired by the pioneer work of Barluenga and co-workers we considered the transient formation of iodoalkanes and further oxidation in a cascade reaction fashion as a promising approach for the synthesis of diols from saturated hydrocarbons.[5] Under optimized conditions different cyclic, linear and branched alkanes were successfully converted to vicinal diols in excellent to moderate yields.

Based on the results obtained during our studies, we visioned that the use of iodoalkanes offers the opportunity to selectively introduce vicinal diols into more complex substrates. In this process the iodine atom in iodoalkanes plays the role of a traceless directing group for metal-free dihydroxylation. Thereby, dihydroxylation of cholestane was achieved without the use of a metal-catalyst.

This work was supported by the Fonds der Chemischen Industrie e.V. (Chemiefonds-Fellowship to L. Bering).

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Finding drugs with DNA-encoded compound libraries

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The identification of bioactive compounds is a crucial step to initiate drug development programs, and also to develop probes for chemical biology studies. Target-based screening of DNA-encoded small molecule libraries (DELs) has emerged as a validated technology to interrogate vast chemical space. [1] DELs consist of chimeric molecules composed of low-molecular weight compounds that are covalently conjugated to individual DNA strands serving as identifier barcodes. DNA tagging of drug-like molecules allows for pooling of large compound libraries, and screening of these libraries by selection to identify "hits" (Figure 1). Screening of DELs has identified numerous bioactive compounds. Some of these molecules were instrumental in gaining a deeper understanding of biological systems, at least one compound has been progressed to clinical trials.

DELs are synthesized through combinatorial strategies with alternating organic preparative synthesis and (enzymatic) DNA-encoding steps giving access to large numbers of compounds. We have synthesized a combinatorial DNA-recorded 27.000-membered library based on "privileged" scaffolds. [2]

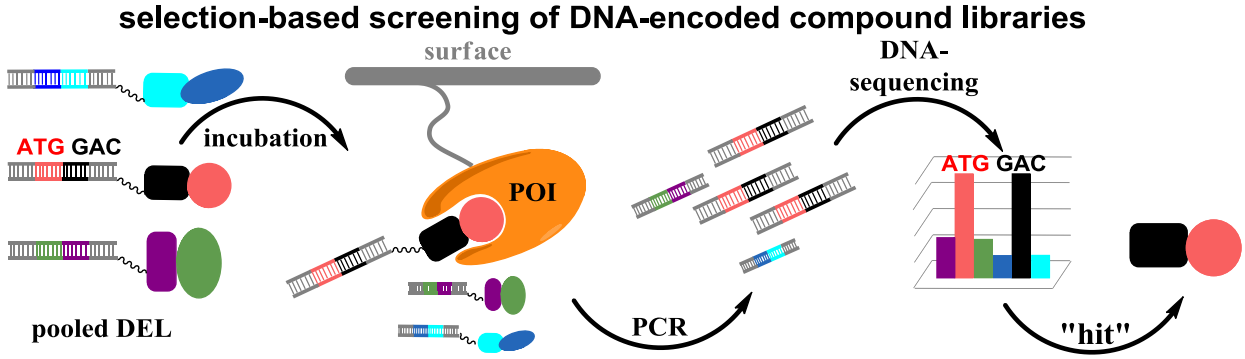

Figure 1. Selection-based screening of DNA-encoded libraries (DELs) allows for identification of bioactive compounds, so-called hits, from large pools of drug-like compounds in a single experiment. POI: protein of interest; PCR: polymerase chain reaction.

This work was supported by the German Federal Ministry of Education and Research (BMBF) Grant 131605.

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The impact of solvent structuring in organic synthesis

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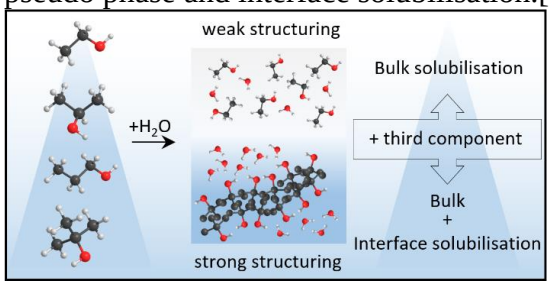
The choice of an appropriate solvent in organic synthesis is challenging and usually associated with a time-consuming screening of solvents and solvent mixtures. Solvent induced changes in reactivity still remain an unresolved issue. Within this context, we investigate binary mixtures of H_2O/alcohols and link the mesoscopic structuring of these mixtures with its impact on the efficacy of one particular chemical reaction.

To this purpose, the mesoscale solvent structuring of binary mixtures of ethanol(EtOH)/H_2O and *tert*-butanol(TBA)/H_2O is first linked to the solubilisation of poorly water miscible compounds (organic reactants, *e.g.* benzyl alcohol, limonene, *etc.*). No (or very weak) solvent structuring is found for EtOH/H_2O, whereas mesoscale compartmentation into water rich and aliphatic rich pseudo-domains (up to 6nm) are highly pronounced for H_2O/TBA mixtures. Such a solvent structuring leads to a high solubilisation power for poorly water miscible components (*e.g.* benzyl alcohol or limonene). The high solubilisation power of hydrophobic compounds in aqueous TBA mixtures is explained by an extension of the aliphatic rich pseudo-domains. In general, three different solubilisation mechanisms can be identified in mesoscopically structured liquids: bulk solubilisation in the aliphatic rich pseudo phase, bulk solubilisation in the water-rich pseudo phase and interface solubilisation.[1]



In this context, we also show that such mesoscale compartmentation in macroscopically homogeneous and transparent solutions has a huge impact on chemical reactivity.[2] We show with the help of a simple reaction that compartmentation of reactants may be the reason of a lower catalytic efficacy. Compartmentation of the catalyst and the organic reactant in the water-rich and aliphatic rich pseudo-phases in H_2O/TBA mixtures are caused by a difference in their hydrophilic/hydrophobic nature. Consequently, local separation of reactant/catalyst molecules leads to a lower contact probability and to a lower yield of the reaction product. With these studies on the relationship of solvent structuring/chemical reactivity, we open new insights in the field of solvent induced reactivity changes and provide new routes to replace organic solvents by mesoscopically structured binary solvents based on water and alcohols.

This work was supported by the the BFHZ (Bayerisch-französisches Hochschulzentrum) with the grant number FK41_15 and the DFG-project GRK1626 chemical photocatalysis.

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Employing ionic properties of organic compounds in drug development

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Modern pharmaceutics deals mostly with solid substances, which often suffer from low aqueous solubility and polymorphism. Accordingly, various ways for alleviating these issues have been developed during the last decades. The problem of low solubility can be solved by using salts of pharmaceutical ingredients (API). However, the issue of polymorphism still hinders the application of many drugs.

A recent new strategy of employing API in an ionic liquid form seems to be an efficient solution of the above-mentioned issues. Ionic liquids (ILs), or liquid salts, are unique systems, which find application in synthesis, catalysis, biomass conversion, biotechnology, etc. Initially, ILs have been supposed to become a 'green' alternative to common organic reagents. However, the emerged biological properties of ILs have been attracting much attention lately [1]. Thus, amino acid-based ILs were originally proposed to be non-toxic, but we showed that an introduction of an amino acid into ILs led to a significant increase of their toxicity [2]. Some of ILs have demonstrated anticancer and antimicrobial activities and have shown promising applicability in drug development [3].

Currently, API-containing ILs (API-ILs) are being studied actively. The strategy of API-ILs suggests using drugs in an ionic liquid form and allows uniting several API activities within one molecule. We designed model API-ILs containing salicylic acid (SA-ILs) in cation and/or anion and investigated their cytotoxicity in a human colorectal adenocarcinoma cell line and human fibroblasts [4]. Cytotoxic activity of SA-ILs was significantly higher than that of conventional imidazolium ILs and was comparable to that of SA. Notably, water solubility of SA-ILs was significantly improved in comparison with the pure SA. Therefore, incorporation of salicylic acid into an ionic liquid did not impair the biological activity of the drug and increased its bioavailability.

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Zeolites as nano-reactores - alkylation of phenol derivatives with methanol

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Zeolites have, because of their diversity, a high potential as selective heterogeneous catalyst. The alkylation of phenol derivatives towards 2,3,5-trimethylphenol is of great industrial interest, due to the fact, that it is one of the key products in the (all-rac)-α-Tocopherol (vitamin E) synthesis.[1] Starting from *m*-cresol 2,3,5-trimethylphenol could be obtained through the alkylation with methanol. Unfortunately, the number of byproducts, as dimethylphenols (DMP), trimethylphenols (TMP), tetramethylphenols (Tetra) or anisoles, is very high. Catalyst for this reaction can be zeolites with a well-defined structure as well as other acidic oxidic materials. Different catalyst and reaction conditions were applied in this work to evaluate the influence of the structural and chemical differences of the catalysts. The gas-phase reaction was carried out in a micro reactor equipped with an on-line gas chromatograph.

Results show the difficulty of the alkylation in the kinetically un-favored meta position, which is necessary for the formation of 2,3,5-trimethylphenol starting from *m*-cresol. Typically, multiple alkylation of one molecule is unlikely. This can be overcome with higher reaction temperatures. Therefore, *m*-cresol was substituted by 2,3-dimehylphenol as the starting material. Figure 1 shows the conversion and yields for the different catalysts. Surprisingly, *t*-ZrO_2 catalyst are more promising than zeolites like the H-Beta, *i.e.* expected form selective properties of zeolites do not dominate the reaction. This observation was also made for the conversion of *m*-cresol. Interestingly, Al_2O_3 has the highest measured conversion at 270 °C, as well as the highest selectivity (84.3%) towards 2,3,5-trimethylphenol at 220 °C. Al_2O_3 catalyzes the *ortho*-alkylation stronger than the alkylation in other positions. All tested catalysts deactivate very slowly.

Summarizing the results, the synthesis route to 2,3,5-trimethylphenole, as precursor for tocopherol, via alkylation of alkylphenols seems to be an promising approach for usage of cheaper feed.

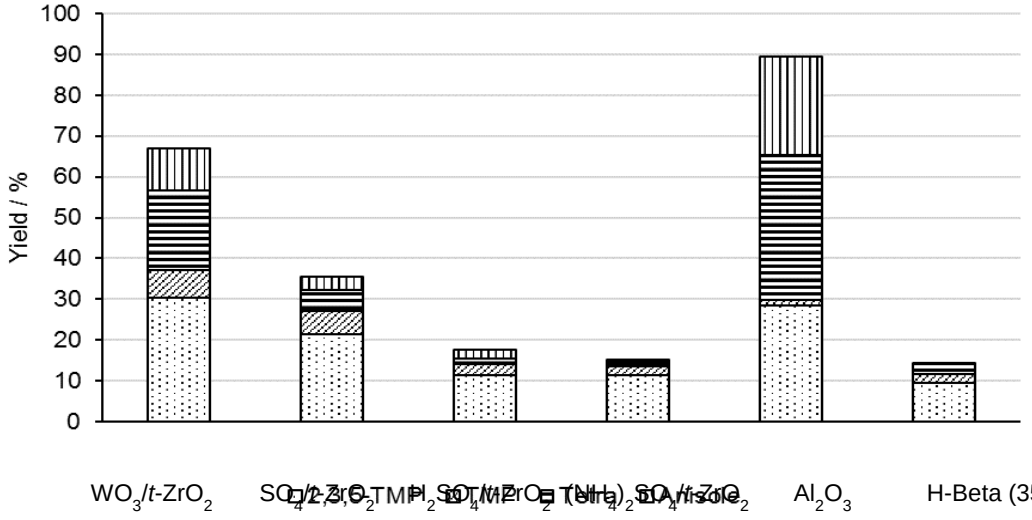

Figure 1: Comparison of different catalysts for the 3,5-DMP conversion, T= 270 °C, molar ratio 3,5-DMP:methanol 1:3

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A new method for the synthesis of benzofuran-2-one derivatives

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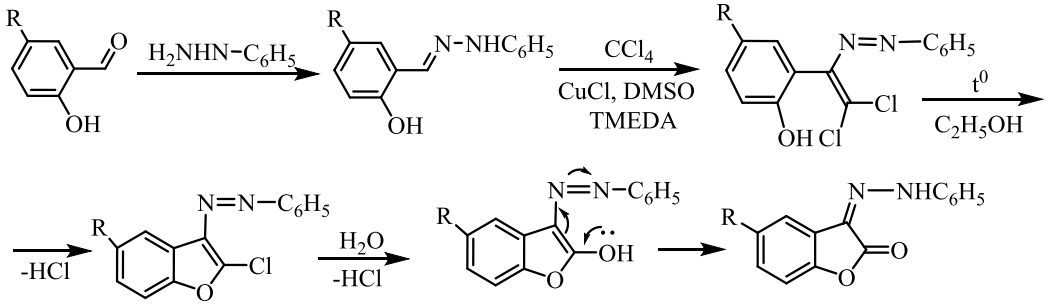
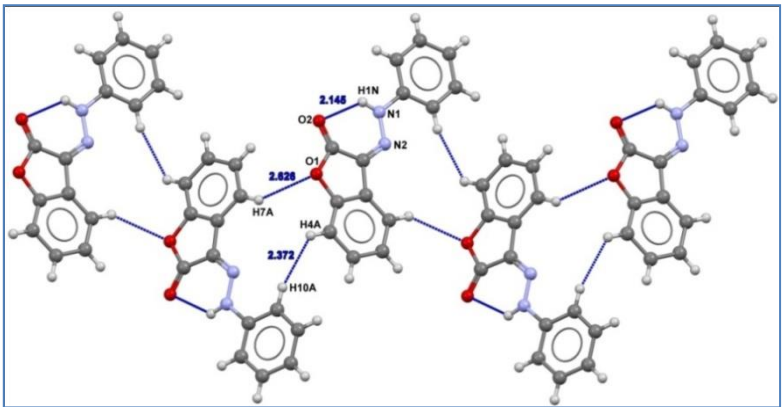
In previously published works we have described in detail methods for the preparation of various derivatives of dichlorodiazobutadienes by the reaction with CCl_4. Also, we have found that the presence of hydroxyl group in the structure of starting aldehyde opened new potential opportunities for this reaction, in particular, a new simple method for producing of benzofuranone-2 [1].

Given the great similarity between the synthesized benzofuranones with allready known antibacterial drugs based on furan, we studied the antibacterial activity of the latter. It is found that they affect both on the gram-positive (Staphylococcus aureus), as on gram-negative bacteria (Escherichia coli, Pseudomonas aeruginosa, Rlebsiella pneumonia).



R = H, Br, NO_2, OCH_3



Molecular structure of (z)-3-(2-phenylhydrazono)benzofuran-2(3H)-one

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Magnetically recoverable ruthenium nanocatalysts based on microporous organic polymers for transfer hydrogenations.

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Microporous organic polymers (MOPs) that are magnetized by incorporated carbon-coated cobalt (Co/C) nanobeads represent a potent platform for the immobilization of catalytically active metal nanoparticles (NPs) like ruthenium. Ruthenium NPs have been shown to be efficient catalysts for the transfer hydrogenation of aromatic carbonyl compounds [1] and thus the synthesized catalysts show high activity as well as good recyclability due to the supporting effects of the polymer. The polymer can have a size controlling effect on the NPs and also help to prevent their agglomeration during the catalysis reactions. [2]

The polymers used for the catalysts are built up from crosslinked arenes, polymerized by consecutive Friedel-Crafts-reactions. [3] The effect of the polymer on the catalytic properties as well as the recyclability of the material was studied by varying the arene monomers and the stoichiometry of the applied external crosslinker.

Different methods for the synthesis of ruthenium nanoparticles were tested and compared with respect to incorporation into the polymer and catalytic activity. The optimized catalyst was used for the transfer hydrogenation of a number of aromatic carbonyl compounds and showed good activity and recyclability for several runs.

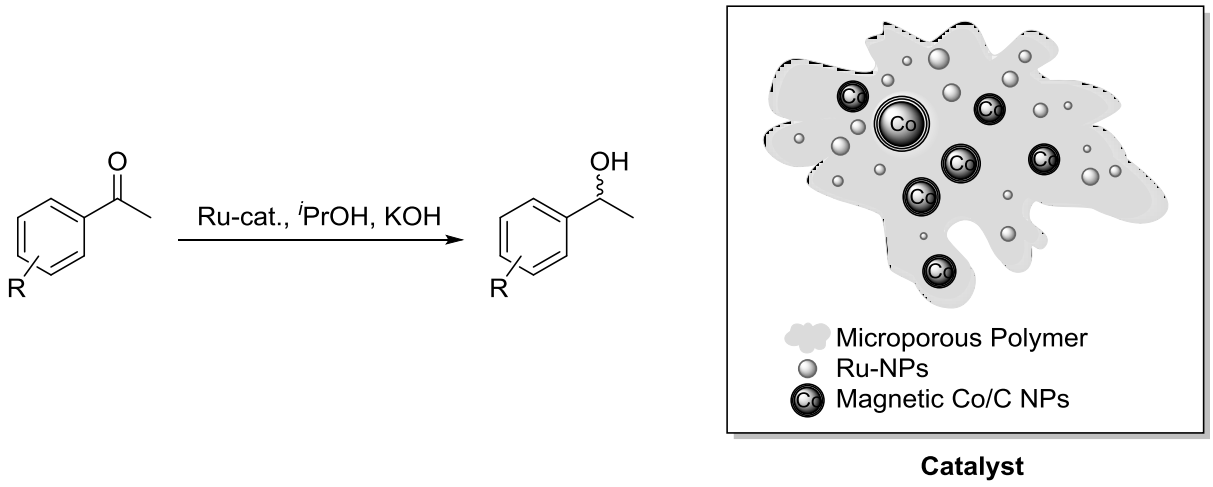

Figure 1: Transfer hydrogenation of aromatic carbonyl Compounds using Ru-NPs.

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Direct observation of the microstructure of reaction mixtures by scanning electron microscopy

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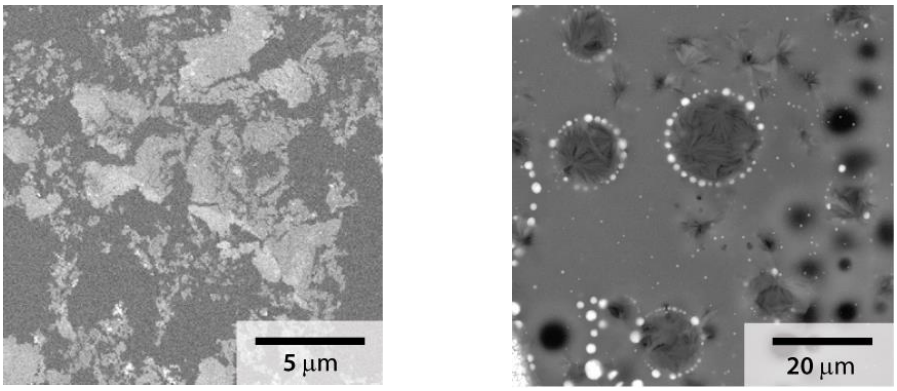
Scanning electron microscopy (SEM) is a simple and convenient method for the direct observation of the micro- and nano-structure of various objects which has proven itself to be a reliable characterization tool in the field of materials chemistry, nanotechnology, biology and so on.

At the current time considerable attention is paid to electron microscopy in non-standard environments, particularly in the liquid phase. In spite of the notable progress in this field, the number of the examples of electron microscopy utilization for the characterization of the reaction mixtures is limited.

In our study we used two approaches for the SEM studies of liquid systems: the use of ionic liquids, which are stable under harsh conditions of the electron microscope, as solvents and the use of low temperature SEM (cryo-SEM) technique in the case of conventional organic solvents. Acid-catalyzed conversion of fructose to 5-HMF and Cu-catalyzed carbon-sulfur bond formation reaction were chosen as model systems (Figure 1).



(a) (b)

Figure 1. SEM images of the reaction mixtures for the fructose conversion to 5-HMF (a) and C-S cross-coupling (b) obtained with the use of liquid SEM and cryo-SEM, respectively.

With the use of SEM in liquid phase the influence of the water on the acid-catalyzed fructose conversion to 5-HMF in ionic liquids at micro-level was established [1]. Cryo-SEM in the combination with X-ray microanalysis allowed to reveal the nature of the active form of the catalyst in Cu-catalyzed C-S cross-coupling reaction [2].

This work was supported by the Russian Science Foundation (RSF grant № 14-50-00126).

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Multifunctional magnetic iron-containing nanocomposites based on natural polysaccharide arabinogalactan

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Magnetic nanocomposite materials with metal particles are widely used in modern electronics, solar cell production, in biology, the preparation of catalysts, medicines and others. Among received nanosubstances special interest biocompatible nanocomposites based on a variety of polysaccharides, and in particular, arabinogalactan (AG), received from siberian larch, with a complex of catalytic, magnetic, optical and biological - antimicrobial, immunomodulatory and cytotoxic properties. Unusual magnetic, in particular paramagnetic, and thermostable properties of the nanocomposites largely determine their uniqueness and wide application.

It was made the study of thermal stability of multifunctional iron composite based on the natural polysaccharide AG and iron oxides and their paramagnetic properties change with temperature. We have shown that the magnetite nanoparticles of Fe_3O_4, being coated with a shell of natural high molecular polymer, form aggregate stability of magnetic nanomaterials. Nanocomposites study was performed in a linear temperature rise process by the methods of synchronous thermal analysis to 1000°C, and by EPR to 400°C. The results indicate that the nanocomposites have a temperature resistance up to 180-200°C. EPR method shows that all composites to some extent possess ferromagnetic properties at room temperature, which was confirmed by measurements of their magnetization. The similar nature of the FMR spectra investigated nanocomposites, which are asymmetric broad absorption lines, shows small changes in size and shape of the resulting nanoparticles with varying iron content in the nanocomposite from 1 to 12%. Trends destruction ferroarabinogalactan observed directly in the EPR spectrometer resonator. The EPR characteristics of change of *g*-factor and linewidth signal showed the presence of critical points on reaching 200°C – thermal degradation of the nanocomposite. Introduction of magnetite nanoparticles in polysaccharide matrix greatly lowers the activation energy of thermal degradation process, thereby reducing the degradation of the nanocomposite temperature range compared to the initial polysaccharide. On exotherm effect in ranging 220-290°C due to the thermal degradation of AG, superimposed very intense effect in the temperature interval 250-400°C, due to oxidation of iron oxide (II), which is part of the magnetite. Thus, this process lead to obtaining of the novel nanosystems with controlled magnetic properties. Prolonged storage nanocomposites bounded by external impact has shown that metal nanoparticles exist stably in the matrix, at least for one year, while maintaining the unchanged EPR characteristics.

Synthesis of nanosized mucoadhesive pectinic hydrogel for local anesthesia

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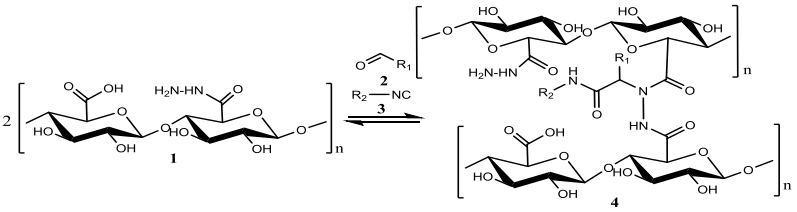
The dental treatment usually requires preoperative anesthetic and postoperative analgesic, so to prevent dental pain in effective and light way is an actual task for modern dentistry, especially in pediatric case [1]. The current advances in carbohydrate science have resulted in a novel type of drug delivery systems based on cross-linked biopolymers. They conjoin the advantages of natural materials, such as biocompatibility, low toxicity, biodegradability and market availability, with positive properties of synthetic polymers, such as workability, stability and reproducibility [2]. The aim of this investigation was to design a patient-friendly transmucosal drug delivery system based on natural polysaccharide nanoscaled hydrogel loaded with novocaine.

We chose high-methoxyl apple pectin (Herbstreith & Fox GmbH) with the 62 mol % degree of esterification due to already displayed mucoadhesive properties [3]. For further process natural polymer was modified by hydrazide groups and purified from low-molecular additives. Using original approach developed our research group and based on the Ugi multicomponent condensation (U-4CR) in diluted colloidal suspensions (0.1 m/v %) [4]. The wide range of cross-linked polysaccharide derivatives were synthesized according to reaction scheme. Various isocyanides (aliphatic, alicyclic and aromatic) and aldehydes with short aliphatic chains were used here.



The structures of the products were confirmed by the ^{1}H NMR-spectroscopy. The size distributions and polydispersity indexes of particles were determined by dynamic light scattering with the meaning 90-350 nm. Mucoadhesive properties of the hydrogels were evaluated by mucin adsorption method [5]. The derivative with basic properties showed extremely high level of mucosa affinity in 92 % that is comparable with the best known mucoadhesive carriers. The cytotoxicity of the modified polysaccharides was determined against HeLa cells by the MTT assay where they were evaluated as non-cytotoxic (cell viability near 80 %) with statistical significance. Three of the synthesized carriers were loaded with novocaine. The drug entrapment efficiency and rate of drug release were investigated by dialysis with UV-detection. The results of 84-92 % active compound loading and consistent release rate during 4 hours allows considering the developed form as a potential medicine for local anesthesia.

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Preparation of novel nanoscaled delivery system based on proliposomes

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The development of drug delivery systems is an innovative approach towards solving pharmaceutical tough issues associated with medicine toxicity and low therapeutic efficiency. Lipid-based nanomedicine has already proved their capability to improve bioavailability of encapsulated active compounds both hydrophilic and hydrophobic nature. However there are a number of clinical limitations for liquid liposomal forms due to poor physical and chemical stability related to leakage, sedimentation, aggregation, fusion and degradation reactions such as oxidation and hydrolysis. In order to overcome the stability problems a novel method to prepare liposome using the concept of proliposome was introduced. Proliposomes are defined as dry, free-flowing powders that immediately form liposomal vesicles when contact with aqueous phase [1]. Because of the solid properties, long-term stability of liposome can be achieved simultaneously with high entrapment efficiency, narrow size distribution and protective properties.

This study reports an improved design and a comparison of proliposomes obtained with various micronized species [2], such as sucrose, lactose and cellulose. The specified amounts of phosphatidylcholine, lecithin, cholesterol and additives were dissolved in chloroform. This solution was adsorbed onto micro-carriers (sieved crushed sucrose, lactose Pharmatose 100 M, microcrystalline cellulose Pharmacel 101), and the excess solvent was removed to obtain dry powder. Following hydration and size reduction using sonication led to stable nano-vesicles. These proliposomes were compared with conventional liposomes prepared by thin-lipid film technique with following extrusion in terms of liposome size, zeta potential and drug entrapment efficiency using rimantadine as a model drug.

Comparison of two approaches has shown that proliposome formation technique tended to yield liposomes smaller than the corresponding vesicles downsized via extrusion (ultrafiltration membrane 100 nm). In the first case all size measurements were in the range of 93.8–112.9 nm and pdI 0.205-0.285, meanwhile for the common liposomes the hydrodynamic diameters were 158.9-192.3 nm and pdI 0.125-0.223 for the same lipid mixtures. Obtained liposomes had positive or negative surface charge depending on their composition. The data indicate that the investigated technique of proliposomes was appropriate to obtain nanoscaled vesicles for different lipid types. Moreover the rimantadine entrapment efficiency in proliposomes was found to increase in comparison with thin-lipid film method that allows reaching the high drug entrapment efficiency (96.7±0.5%) for rehydrated liposomes.

In general, we have reported a reliable production method of nano-liposomes based on widely applicable industrial technologies such as micronized base coating, hydration and sonication. Moreover, sucrose and lactose can perform as a carrier in the proliposome formulations and as a cryoprotectant during future freeze-drying.

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Topical drug delivery with nanoparticles: Science fiction or reality

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The requirements on nanoparticles for use in cosmetics and in dermatology are very different. While nanoparticles widely applied in sunscreens, like TiO_2 and ZnO, shall remain on the skin surface or in the upper cell layers of the stratum corneum, nanoparticles intended for drug delivery shall penetrate through the skin barrier to the target structures in the living cells.
At the Charité - Universitätsmedizin Berlin various laser scanning microscopy methods are used to investigate the penetration and storage of nanoparticles in the skin, hair follicles being in the focus of attention. Human hair follicles are ideal target structures for drug delivery. Hosting both the stem and dendritic cells, they are surrounded by a dense network of blood vessels. Investigating nanoparticles of different size and materials, it was found that particles of approximately 600 nm diameter penetrate most efficiently into the hair follicles and can be stored there for approximately 10 days. Their retention time in the hair follicles exceeds that in the stratum corneum by almost one order of magnitude.

No experiment had shown, however, that particles of 40 nm-1 μm in diameter penetrated from the hair follicle into the living tissue if the skin barrier was intact. This is plausible as the hair follicle has its own barrier. The moving hair is assumed to act as a gearing pump under in vivo conditions, pushing the particles deeply into the hair follicles.

Only if the barrier was disturbed artificially or by illness, nanoparticles of 40nm in diameter had penetrated into the living tissue. For more than 20 years, academic and industrial research has been intensely focusing on the utilization of nanoparticles for drug delivery through the intact skin. However, a commercial product providing this effect is still missing.

Taking into consideration that non-particulate substances poorly penetrate into the hair follicles, but once arrived there are capable of passing through the follicular barrier unto the living cells, whereas particulate substances do penetrate well into the hair follicles but cannot pass the follicular barrier, the triggered release of substances from nanoparticles in the hair follicle presents a promising field of research. Thereby nanoparticles are loaded with drugs which penetrate into the hair follicles nearby the target structures. Once the release of the drug from the nanoparticle has been triggered by a signal, the drug penetrates the last microns through the follicular barrier without assistance.

Stereoelectronic chameleons: new examples

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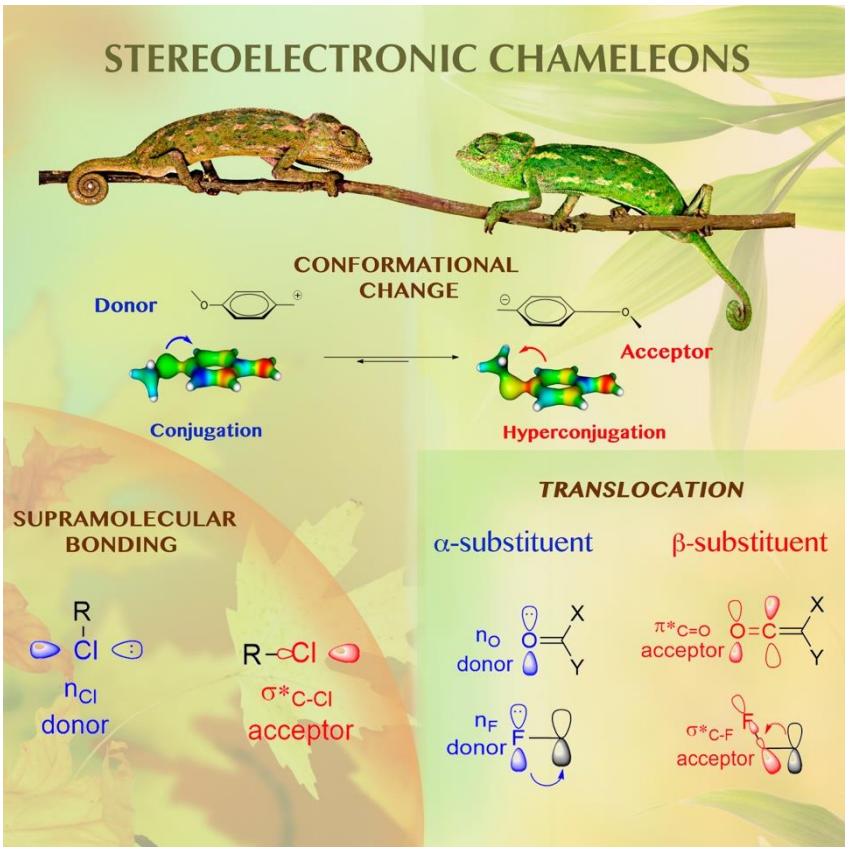
In order to change a donor into an acceptor, a chemical transformation is usually required. However, subtler and interesting situations exist where the donor/acceptor properties of substituents and, hence, chemical reactivity are controlled by their orientation in space in respect to the rest of the molecule [1].

The focus will be on a more nuanced stereoelectronic "conversion" of donors into acceptors (and vice versa) caused by either a conformational change or insertion of an additional atom between two functional groups. Such changes can lead to interesting consequences in stability, reactivity, spectroscopy etc.



The stereoelectronic nature of chemical interactions imparts a variety of reactivity patterns, sometimes strikingly different, to the majority of chemical groups and compounds, for example, imino, azido and ylides, cycloalkynes or nitroxides, as well as to the respective excited states. Chameleonic behavior inherent to the number of functional groups could result in new pathways in organic synthesis.

This work was supported by RSF (grant № 16-13-00114).

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Rectifier properties of hydrocarbons

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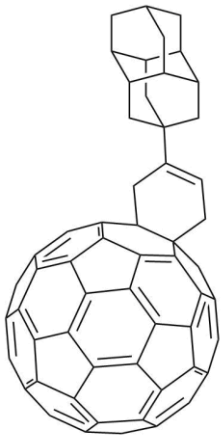
Molecular rectifiers are a bottom-up approach for the construction and fine-tuning of junctions between conducting materials.

To achieve rectification, electron transfer between molecular orbitals, which show an asymmetric probability amplitude is involved. Therefore a large dipole moment is necessary, which is rather unusual in hydrocarbons. In order to obtain this for the molecules demonstrated, a electron donor is combined with an electron acceptor. Adamantane and its higher homologues with their negative electron affinity serve as an electron donor. For their intramolecular counterpart fullerenes and aromatic components like pyrenes possess suitable electron acceptor capabilities.



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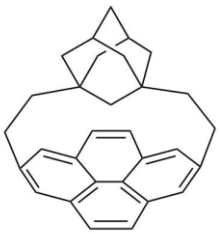

2

The strongly dipolar diamondoid-fullerene hybrid **1** was used to form a self-assembled monolayer on a Gold surface. The electronic properties were investigated by scanning tunneling microscopy.[1] The molecule showed current-voltage characteristics, that differed intensively from its individual components and therefore achieved the goal to work as a rectifier. On the down-side it is thermally unstable and its ability to form monolayers was less pronounced than that of pure fullerenes.

This initial investigation lead to the development of the Adamantanopyrenophane **2** and its synthesis was achieved recently.[2] The molecule is thermally very stable and depicts a strong dipole moment, whereas the dipole vector is perpendicular to the pyrene plane. Despite its promising properties the electronic characteristics have not been investigated yet.

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Kinetics and mechanism of allyl alcohol epoxidation to glycidol with hydrogen peroxide at titanium silicalite

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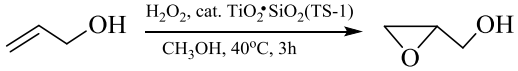
Oxygen-containing heterocyclic compounds (oxides olefins, cyclic acetals, etc.) are important products and intermediates of the basic and fine organic synthesis [1]. Great practical interest is the glycidol oxide of allyl alcohol. It is a valuable intermediate product in the manufacture of surfactants, plasticizers, textile dyes, photographic chemicals, drugs, pesticides, some rubbers, paints, thermosetting resins and plastics [2]. One of the most promising methods for producing glycidol is the epoxidation of allyl alcohol by hydrogen peroxide on the titanium-containing catalyst.



It was studied the epoxidation mechanism of allyl alcohol using titanosilicate zeolite (TS-1) at 40°C by means of procedures for the nomination and discrimination of mechanism hypotheses.

The hypotheses were carried out using the literature data and the preliminary experiment results. Discrimination hypothetical mechanisms implemented on the basis of the univariate results of the kinetic experiment, varying concentrations of allyl alcohol, hydrogen peroxide and glycidol.

The most probable mechanism involves the hydrogen peroxide and allyl alcohol adsorption at the catalyst active centers and the glycidol formation at a reversible stage in the interaction of the adsorbed molecules of the reactants. Considered hypotheses include a different sequence of interaction of the reactants with active catalyst centre. In addition, hypotheses take into account the formation of intermediate compounds as well as inactive products of the interaction of substances present in the reaction system, with the active centers on the silicalite surface. For each hypothesis, it was formulated the corresponding system of differential equations and carried out the estimation of the rate constants. The quality of the experimental data description was judged by the residual sums of squared deviations and correlation coefficients.

The best results are obtained for the hypothesis involving the hydrogen peroxide and allyl alcohol adsorption at the two active catalyst centers with subsequent interaction of the resultant intermediates between them, with the formation of glycidol adsorbed on one center, free catalyst centre and molecule of water. Formation of free glycidol occurs at a reversible stage. A significant part of the active centers of the catalyst increasing the concentration of glycidol is associated with it. This is the main reason for the decrease of the reaction rate, apart from reducing the concentration of the reactants.

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Diversity-oriented synthesis of intensively emissive 3-ethynyl- and 2-triazolylquinoxalines by MCR sequences

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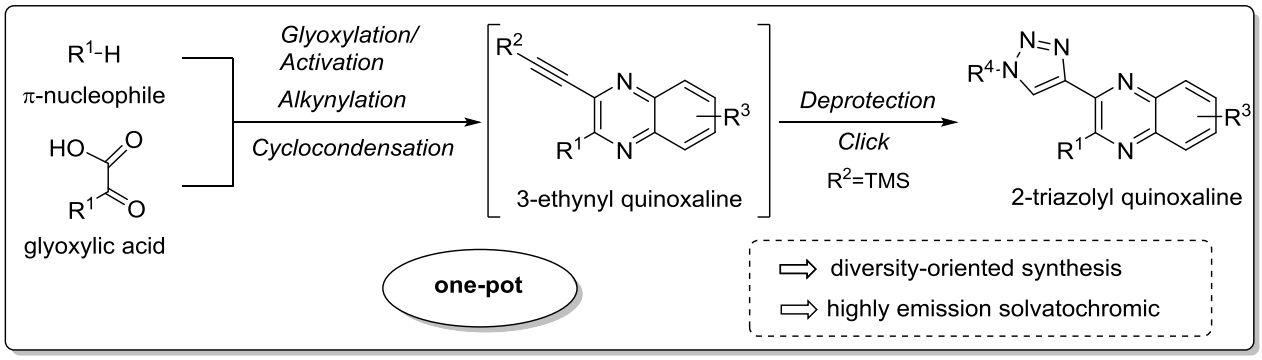
Especially in today's times the concept of one-pot and multicomponent reactions (MCR) adopts a central position in modern synthetic chemistry. Particularly the formation of fluorophores and chromophores *via* a rapid and elegant MCR approach remains a paramount challenge for organic and materials chemists. Ultimately with adequate reflection of this issue a crucial aspect of the one-pot fashion is the diversity-oriented nature. With the aid of this methodology substance libraries can be set up. These conceptual approaches has already found its way into the construction of highly luminescent and stable heterocycles. For this purpose, our group has recently developed a set of complementary one-pot syntheses of fluorescent and solvatochromic 3-ethynyl quinoxalines and 2-triazolyl quinoxalines (Scheme 1)[2] based on intermediary ynediones.[3]



Scheme 1: Diversity-oriented multi-component one-pot procedures for the synthesis of 3-ethynyl- and 2-triazolyl quinoxalines.

Further varied structural changes of the triple bond are conceivable.[4] Consequently, we set out to investigate the reaction scope as well as the photophysical and chemical properties of the synthesized compounds.

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Diversity-oriented multicomponent synthesis of fluorophores

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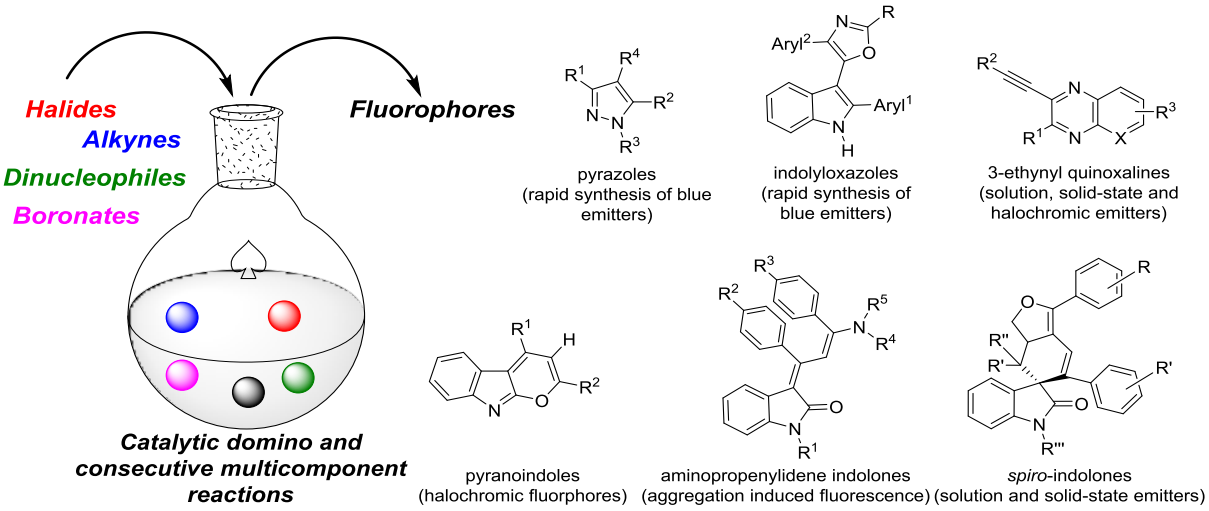
Multi-component and domino reactions are efficient and effective methods in the rapid and diversity-oriented synthesis of heterocycles. In particular, transition metal catalyzed multi-component sequences have recently gained a considerable interest.[1] In the past years functional π-electron systems[2] have been increasingly addressed by multicomponent reactions,[3] among them fluorophores in general,[4] and blue emitters[5] and aggregation-induced emissive chromophores in particular.[6]

In this tutorial lecture the concept of diversity-oriented chromophore syntheses, in particular multi-component and domino reactions as reactivity based reaction design, and principles of transition metal catalysis initiated multicomponent syntheses of heterocycles will be outlined and the photophysical properties of the obtained novel fluorophore class will be discussed.



This work was supported by the Fonds der Chemischen Industrie, the Deutsche Forschungsgemeinschaft, and Evonik Industries.

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Protein-templated fragment ligations – from molecular recognition to drug discovery

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The understanding and manipulation of molecular recognition events is the key to modern approaches in drug discovery. Protein-templated fragment ligation is a concept to support drug discovery and can help to improve the efficacy of already existing protein ligands. Protein-templated fragment ligations are chemical reactions between small molecules ("fragments") that utilize a protein´s surface as a template to combine and to form a protein ligand with increased binding affinity.[1] The approach exploits the molecular recognition of reactive small molecule fragments by proteins both for ligand assembly and for the identification of bioactive fragment combinations. Chemical synthesis and bioassay are thus integrated in one single step. In this presentation we discuss the biophysical basis of reversible and irreversible fragment ligations and the available methods to detect protein-templated ligation products. The scope of known chemical reactions providing templated ligation products is reviewed and the possibilities to extend the reaction portfolio are considered. Selected recent applications of the method in protein ligand discovery are reported.[2-6] Finally, the strengths and limitations of the concept are discussed and an outlook on the future impact of templated fragment ligations on the drug discovery process is given.

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Mag(net)ic nanaocatalysts and reagents - applications for sustainable organic synthesis

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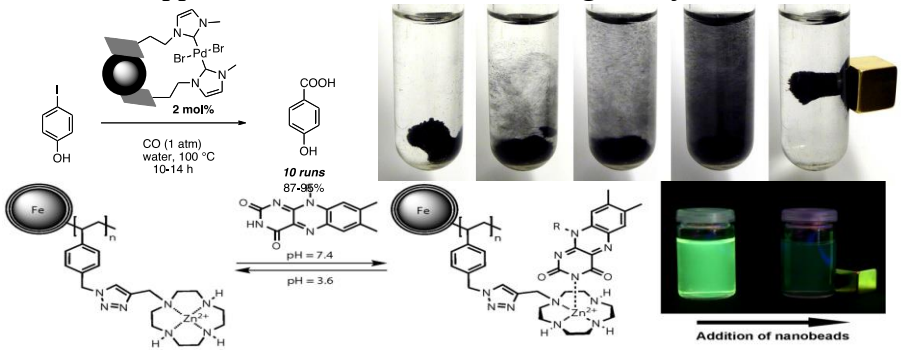
Sustainability is the edifice for the development of efficient chemical processes. Catalytic transformations are especially attractive owing to the generally mild and selective reaction conditions and the reduction of waste byproducts. Nevertheless, even catalysts need to be efficiently removed from a reaction mixture, often down to the ppm levels due to the toxicity of some transition metals that are being used. In this workshop I would like to introduce magnetic nanoparticles as platforms for catalysts and reagents, which can be rapidly and quantitatively removed with the aid of an external magnet. Choosing examples from our research group, strategies for covalent and non-covalent immobilization of catalysts,[1] reagents,[2] and functional materials,[3] as well as applications in various areas of organic synthesis will be discussed.



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Endothelial Notch1 activity facilitates metastasis

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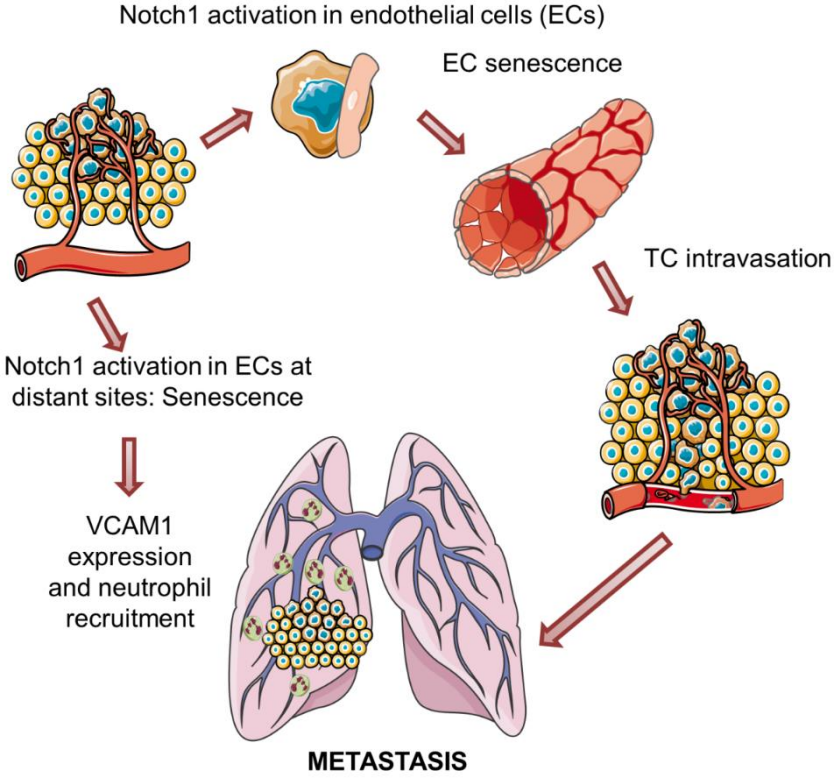
Endothelial cells (ECs) provide angiocrine factors orchestrating tumor progression. Tumor cells need to cross the endothelial barrier to spread throughout the blood vessels in order to colonize new organs. Notch signaling pathway provides a cell-to-cell communication system, widely used by different cell types. This signaling pathway is responsible for the development of different organs, and different tissues within organs. It consists in a series of ligands and receptors that define the cell functions at a molecular level.

Here we show that Notch1 receptors are frequently activated in ECs of human carcinomas and melanoma, suggesting a role of the Notch receptor activation in tumor endothelial cells. Tumor cells do not metastasize to any spot in the organ. A metastatic spot needs to acquire certain characteristics to promote tumor cell colonization. This is called premetastatic niche. We found that ECs of the pre-metastatic niche in mice had a higher Notch1 receptor activation. EC Notch1 activation in melanoma correlated with shorter progression-free survival, thus Notch1 activation in ECs is a risk factor for metastasis. Taken together these results indicate that EC Notch1 activation could increase metastasis. Sustained Notch1 activity induced EC senescence, expression of chemokines and the adhesion molecule VCAM1. Notch1 activation also promoted neutrophil infiltration, TC adhesion to the endothelium, intravasation, lung colonization and postsurgical metastasis. Thus, sustained vascular Notch1 signaling facilitates metastasis by generating a senescent, pro-inflammatory endothelium. Consequently, treatment with Notch1 or VCAM1-blocking antibodies prevented Notch-driven metastasis, and genetic ablation of EC Notch signaling inhibited peritoneal neutrophil infiltration in an ovarian carcinoma mouse model.



London dispersion enables the shortest intermolecular hydrocarbon H•••H contact

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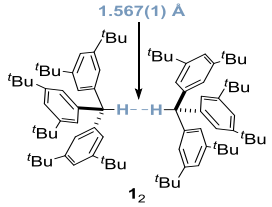

1$_2$

Intermolecular interactions are described by Morse potentials and feature a steep raise in energy for closed shells interaction, namely Pauli repulsion. While rather steep at the repulsive end, there is space for contacts closer than the sum of the vdW-radii. The shortest published record holder for H···H contacts determined indirectly from an X-ray crystal structure (XRD) in conjunction with density functional theory (DFT) computations a Si–H···H–Si distance of ~1.57 Å, underscoring the former record[1] by –0.05 Å and the sum of the vdW-radii by –35%.[2]

We found the hydrocarbon tri(3,5-di-*tert*-butylphenyl)methane **1** to crystallize as a dimer in an unusual head-to-head fashion **1**$_2$. Neutron diffraction (NRD)[3] revealed a short H···H contact of 1.567(1) Å – the shortest experimental H···H contact determined to date. Unlike all other reported structures, the short contact in **1**$_2$ is *intermolecular*. Large deformations of bond angles and distances are not present. Periodic solid state HSE-3c DFT computations are in excellent agreement with the NRD structure. Comparison to the gas phase structure at the same level of theory revealed only 4% H···H distance shrinkage due to crystal packing. Energy decomposition analysis (B3LYP-D3^{ATM}(BJ)/def2-TZVPP) and symmetry-adapted perturbation theory (SAPT(0)/aug-cc-pVDZ) reveal London dispersion interactions to predominantly enforce this close contact. The ^{t}Bu groups were found to be crucial, as the truncation of these groups result in a loss of the close contact and bindig energy.

Dimer **1**$_2$ is the formal hydrogenation product of the weak central C–C bond in all-*meta tert*-butyl hexaphenylethane **2**.[4] The weak bond in **2** dissociates in solution and presumably the corresponding radicals are hold together by the cage effect;[5] an earlier investigation predicted a second dispersion bond radical complex (traditionally called a vdW-complex).[6] This "frustrated" complex appears to be very similar to frustrated lewis pairs (FLPs), which in fact can split H_2. Unfortunately, treatments of solutions of **2** with H_2 show no sign of H_2 splitting.

The remarkable short H···H contact of 1.567(1) Å is the first example of such close intermolecular contacts and is enabled by the surrounding ^{t}Bu groups acting as "dispersion energy donors".[7]

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Activation of ammonia on Fischer-Tropsch-catalysts

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The Fischer-Tropsch (FT) synthesis is a polymerization reaction between carbon monoxide and hydrogen to generate products such as paraffins, olefins and oxygenated compounds including aldehydes, alcohols, ketones and carboxylic acids on iron, cobalt or ruthenium catalysts. The addition of ammonia to the synthesis gas (CO, H_2) leads to an extended product spectrum. Beside the typical Fischer-Tropsch products, it is feasible to obtain valuable organic N-containing compounds such as amines, nitriles and amides [1-3].

Based on these results it is important to understand the mechanisms and the principle of the interaction of ammonia during the Fischer-Tropsch process as this could present a new pathway for the production of nitrogen-containing chemical compounds using a different feedstock than crude oil.

The experiments with ammonia-containing synthesis gas were conducted in a fixed-bed and slurry reactor at pressures between 4-5 bar using cobalt and potassium promoted iron catalysts. The catalytic performance was studied as function of reaction temperature, synthesis gas composition, residence time and ammonia concentration.

Additional co-feeding experiments with oxygenates and N-containing compounds were carried out in order to get an insight onto the reaction behaviour during the formation of N-containing products. The product stream was analyzed online and offline using different gas chromatographic techniques. Organic compounds were identified by means of one- and two-dimensional gas chromatography equipped with mass spectrometers (GC-MS, GCxGC-TOF).

In the absence of ammonia, the formation of conventional FT products such as paraffins, olefins and oxygenated compounds was observed. The addition of ammonia leads to the formation of nitrogen-containing compounds including amines, nitriles and amides. It was noted that the formation of alcohols, aldehydes and carboxylic acids was suppressed upon ammonia co-feeding.

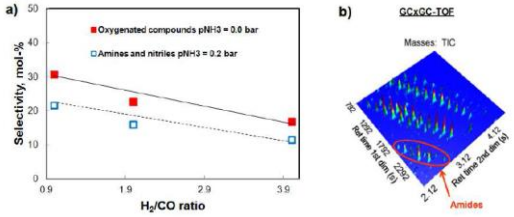

Fig.:
a) Selectivity to oxygenated compounds, amines and nitriles.
b) Amides analyzed by means of GCxGC-TOF.

Moreover, while terminal amines and nitriles were obtained during the experiments in a fixed-bed reactor, N-alkylated amines were predominant using a slurry reactor. In addition, it was feasible to control the selectivity to amines and nitriles with different reaction temperatures, synthesis gas compositions, residence times, ammonia concentrations and reactor types during the experiments. However, the mechanism of formation of N-containing products is still under discussions, since an un-catalyzed reaction of O-containing compounds with ammonia cannot excluded at the actual state of investigation.

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High-contrast ptychographic x-ray bio-imaging

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X-ray microscopy provides higher spatial resolution than conventional visible light microscopy due to the comparably short wavelength of X-rays. However, the choice of X-ray photon energies depends on the sample to be studied. For biological samples soft X-rays in the water window energy range between the absorption edges of carbon (284 eV) and oxygen (532 eV) is well suited for high-contrast imaging [1]. We show the results of a coherent x-ray diffractive imaging (CXDI) experiment performed at the coherent XUV beamline P04 at the PETRA III synchrotron radiation source in Hamburg. By means of ptychography [2, 3], a scanning variant of CXDI, a large field of view and quantitative high-contrast phase image was obtained from a fibroblast cell. Compared to conventional visible light microscopy we find the fibrous cytoskeleton resolved well below 100 nm [4]. With our experimental setup a variety of biological samples in dried or cryogenic environment can be studied with high-contrast ptychographic imaging.

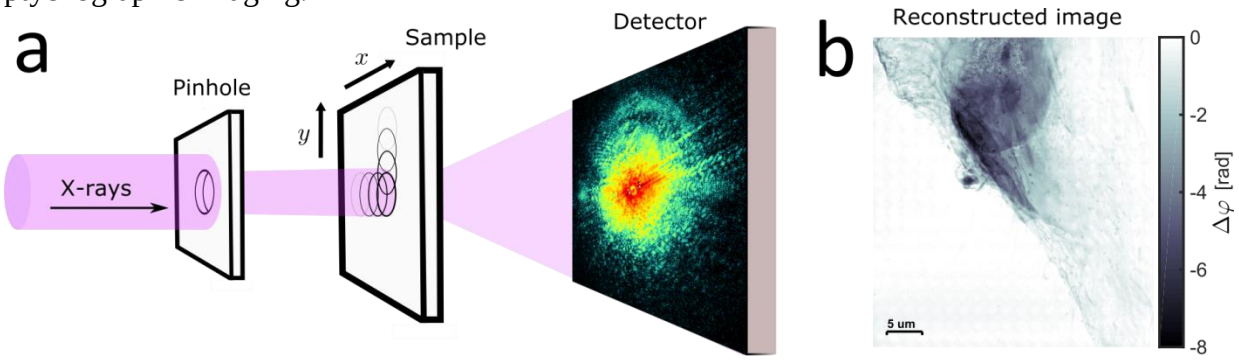

Fig 1: (a) Experimental coherent diffractive imaging geometry. (b) Reconstructed phase image from a series of coherent diffraction patterns.

This work was supported by BMBF 05K10VH4, the Virtual Institute VH-VI 403 and the Joachim Herz Foundation in cooperation with the PIER Helmholtz Graduate-School.

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Sensor properties of the silica gel materials prepared by different methods

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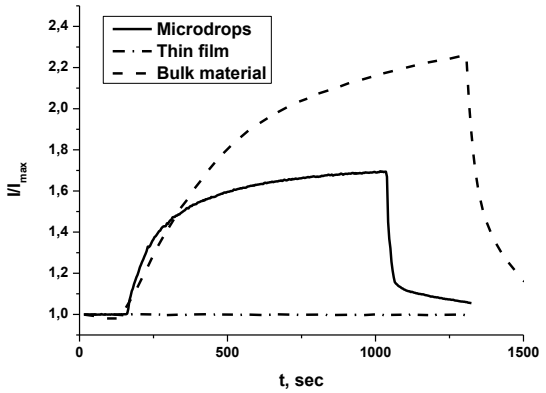
Fluorescent sensor materials for the volatile organic substances detection attracting high attention of the researchers because of their high sensitivity, high number of possible detectible analytes and simplicity of the sensor devices. One of the most important characteristics of sensor materials is time of response on the presence of analytes. As the fluorescent sensor material response time mainly depends of the diffusion speed of the analyte to the indicator molecule, one of the logical solutions is a decreasing of the volume or thickness of the material. От practice it means using of thin film or microdrops instead of bulk materials. Usually, the optical properties of thin film and microdrops are easily predictable on the base of bulk materials study, whereas sensor properties could be quite different.

To study the dependence of the silica gel materials sensor properties of the preparation technology the samples of thin films on the glass surface, ink-jet printed arrays of microdrops and bulk materials were prepared from the water soluble precursor, tetrakis(2-hydroxyethyl) orthosilicate in presence of well know fluorescent dyes Nile red and Rhodamine 6G. The choice of precursor was driven by longer gelation times compared with ordinary tetraethoxysilane. It allows to avoid solid phase formation inside the nozzle of ink jet printer. The characterization of fluorescent molecules surrounding in film films or microdrops by study of their fluorescence spectra showed no or very little deviations from bulk materials. To reveal a difference in sensor properties a set of different volatile analytes was applied.



It was shown the samples of bulk materials and microdrops are sensitive to the presence of acetone vapors, whereas thin film samples showed no response on the presence of acetone. As it was expected, the printed materials have much shorter response times comparing to bulk materials. But at the same time the relative fluorescence intensity change is also smaller than those of bulk samples. Based on the obtained data was proposed the differences in the behavior to be a result of smaller pore size of thin film samples. Indeed, the fluorescent response of thin films was detected by using of ammonia vapors allowing to roughly determine an upper limit of thin film samples pore size to be about 7.5 angstroms.

This work was supported by the Russian Science Foundation under grant № 15-13-00163.

Probing barriers in topical drug delivery into skin by label-free spectromicroscopy

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Topical drug delivery into skin is reported, as probed by label-free spectromicroscopy. This approach permits us to identify the barriers affecting drug penetration. Besides drug formulations the role of polymeric drug nanocarriers is evaluated regarding their role to overcome skin barriers. Selective and high resolution detection (spatial resolution: <100 nm) of drugs and drug nanocarriers is accomplished by X-ray microscopy.[1] We report on recent results on the penetration of the anti-inflammatory drugs dexamethasone and tacrolimus that are topically applied to *ex vivo* human or murine skin samples as well as reconstructed human skin by using drug solutions, formulations, as well as drug-containing nanocarriers (core-multishell nanocarriers[2] and pNIPAM-nanogels). The important barriers for drug penetration in the top skin layers are: (i) the stratum corneum; (ii) tight junctions in the stratum granulosum; (iii) the basal membrane; and (iv) the transfer from hydrophobic to hydrophilic regions, occurring e.g. in corneocytes. In contrast, the drug nanocarriers can only penetrate to the tight junction barrier. In the case of nanogels they facilitate drug penetration into corneocytes. In addition, damage to these barriers is investigated, which is either induced by mechanical impact (tape-stripping) or by inflammatory skin diseases (oxazolone induced psoriasis in murine skin). Detailed results are presented, allowing us to probe absolute drug concentrations penetrating human skin samples.[3] High spatial resolution studies permit to approach a molecular understanding of drug penetration processes.[2,3] These studies also allows us to determine the role of drug nanocarriers altering drug penetration properties.

Complimentary results from stimulated Raman microscopy are reported allowing us to derive 3-dimensional maps of the compounds under study. Focus of these studies was put on the distribution of lipids and proteins.[4] It is shown that proteins and lipids are affected by drug delivery processes depending on the drug formulation penetrating the skin samples.

Financial support by German Research Foundation and SFB 1112 is gratefully acknowledged.

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The regioisomers of di(benzothieno)thiazines – syntheses and electronic properties

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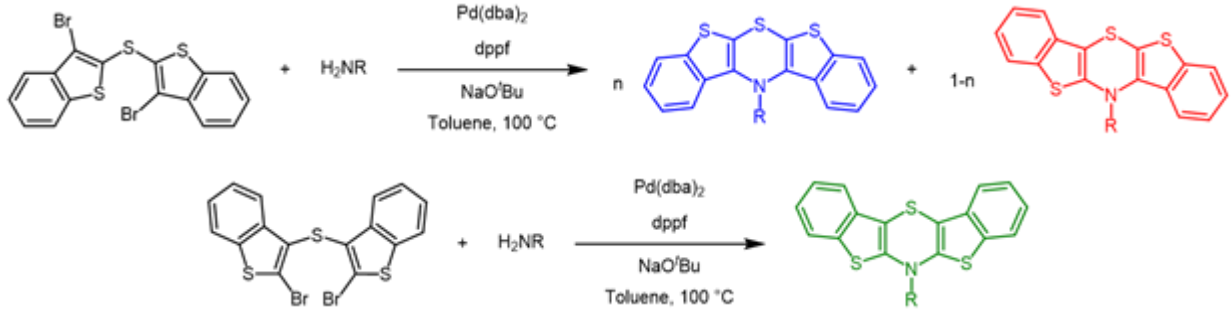
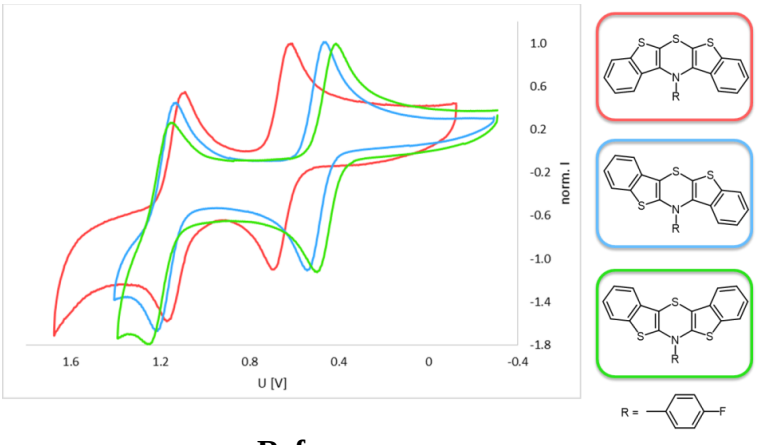
Di(benzothieno)thiazines are annelated derivatives of the parent system dithienothiazine [1]. Dithienothiazines are electron rich organic π-systems, which are reversibly oxidized to stable radical cations and dications. This stabilization results from fully conjugated planarized π-systems of the oxidized specimen. The variation of the substitution pattern should greatly influence the electronic properties of this new polyheterocyclic system. Thus, the first synthesis of the regioisomer of di(benzothieno)thiazine was performed in a similar manner as for dithienothiazines [2]. Surprisingly the ring closing *Buchwald-Hartwig* amination did not specifically lead to the expected *syn-syn* regioisomer but also to the formation of the *syn-anti* regioisomer. This unique isomer formation can be rationalized by a novel palladium catalysis reaction pathway.



Encouraged by the formation of the *syn-anti* regioisomer also the third possible regioisomer of di(benzothieno)thiazine was selectively prepared by using the same method [3]. The three regioisomers show different electronic properties, whereby the varied constitution has a significant influence on the oxidation potentials and the luminescence behavior.



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Palladium nanoparticles embedded in magnetic microporous organic polymers: highly active and recyclable catalysts for hydrogenation reactions

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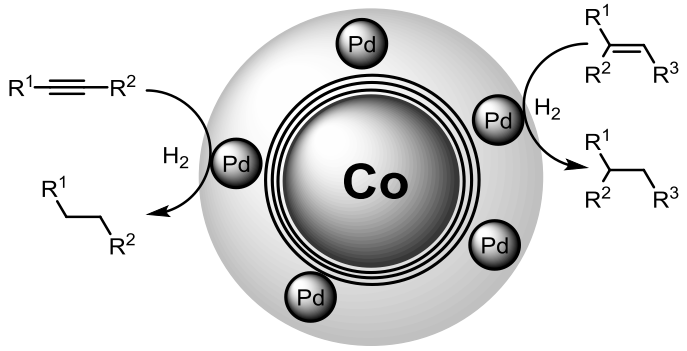
Palladium nanoparticles (NPs) embedded in microporous organic polymers (MOPs) are attractive for catalytic applications.[1,2] The MOPs prevent nanoparticles from agglomeration or deactivation,[2,3] while the NPs show high reactivity due to their high surface-area-to-volume ratio.[4] In this work, we present a strategy to grow MOPs on magnetic nanobeads, followed by incorporation of palladium NPs. Thus, the resulting catalysts can be easily recovered by the aid of an external magnet.

Starting from magnetic carbon-coated cobalt (Co/C) nanobeads, a MOP structure is readily grown on the carbon layer by Friedel Crafts polymerization of arenes crosslinked by formaldehyde. Subsequently, palladium NPs are embedded into the MOP structure.

Hydrogenation reactions were selected as model reactions to evaluate the activity and stability of our novel catalyst. The catalyst turned out to be highly suitable for the reduction of alkenes, alkynes, and also nitro groups. Removal and recycling of the catalyst from the reaction mixture could be easily achieved through magnetic decantation due to the high magnetization of the cobalt core of the catalyst without a decisive loss in activity for several consecutive runs.



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Azobenzene switches as tools to understand fundamental molecular interactions

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The application of azobenzenes as molecular switches which reversibly change their geometry from (*E*) to (*Z*) upon irradiation was already widely demonstrated.[1] The instability of the (*Z*)-isomer was generally explained by the steric hindrance of the two phenyl rings.[2] Recently, we could show that by increasing the bulkiness of electronically equal substituents in the *meta*-position the thermal stability of the (*Z*)-isomers is enhanced, which contradicts the also in textbooks commonly accepted reasoning.

We performed isomerization studies from (*Z*) to (*E*) supported by computations, which clearly indicate, that attractive intramolecular London dispersion interactions in the (*Z*)-form between the substituents outweigh their repulsive steric hindrance. As can be seen by the computational studies, the stabilizing London dispersion forces are mainly operative in the (*Z*)-isomer and almost negligible in the transition state and also in the (*E*)-isomer. The stabilization by London dispersion forces could be directly evaluated for specific substituents by the measured kinetic parameters.[3]

Therefore, not only the substitution pattern,[4] but also structural properties such as ring strain as well as symmetry[5] have to be considered for the design of molecular switches.

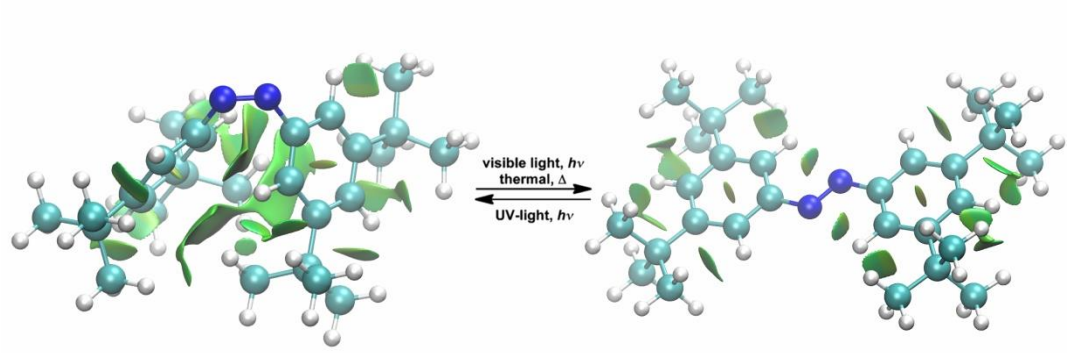

Fig 1. Non-Covalent Interactions (NCI) surfaces in the (*Z*)- and the (*E*)-form of all-*meta* *tert*-butyl substituted azobenzene [5]

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Synthesis of dichlorodiazobutadienes from nitrobenzaldehydes

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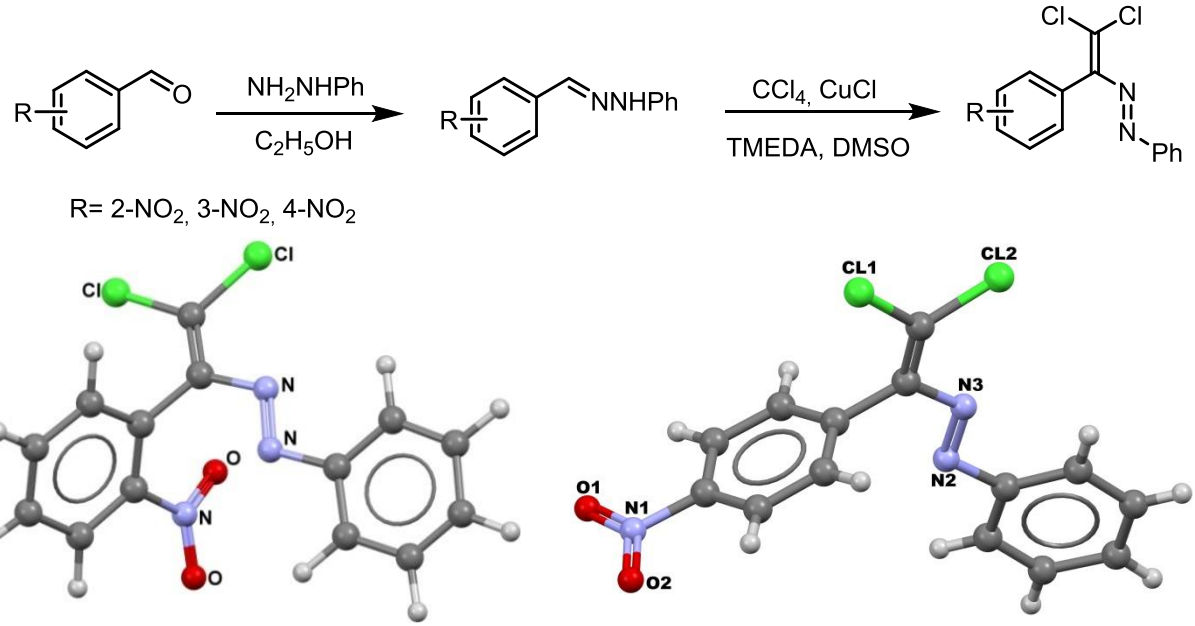
We studied the reactions of N-substituted hydrazones of nitrobenzaldehydes. The presence of conjugated π-electron system of dichloro-substituted carbon with acceptor azo group in obtained compounds, opens up new ways for the synthesis of various structures. At the same time, considering the fact that the synthesized products have chlorine atoms in the structure, they are of interest for the study of non-covalent halogen-halogen interactions[1]. The study of nature of non-covalent as the heteroatomic, and homoatomic halogen-halogen interactions and the ability to manipulate them, will allow to obtain the crystalline structures, which can be used for the construction of supramolecular structures. It is also known that a nitro group can be considered the main source of NO, which is one of the necessary and universal regulator of metabolic functions and unique signaling molecule, whereby the cells can exchange information. So research of these compounds as biologically active systems is of particular interest.



Molecular structures of ***(a)*** *(E)-1-(2,2-dichloro-1-(2-nitrophenyl)vinyl)-2-phenyldiazene,* ***(b)*** *(E)-1-(2,2-dichloro-1-(4-nitrophenyl)vinyl)-2-phenyldiazene*

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Modified mesoporous silica as basic hybrid materials

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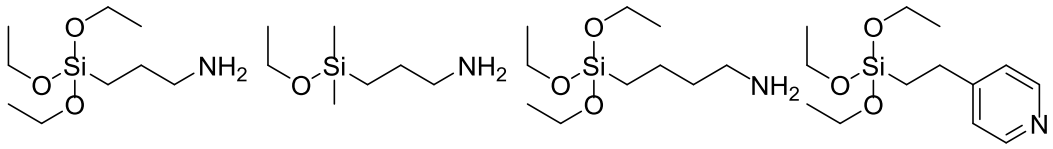
Porous materials with defined porosity and basicity are desirable for applications in heterogeneous catalysis and adsorption. An effective route to synthesize ordered mesoporous materials with a narrow pore size distribution is a surfactant templated synthesis. Using different surfactants and reaction conditions, the pore size as well as the three dimensional order of the pores can be tailored.

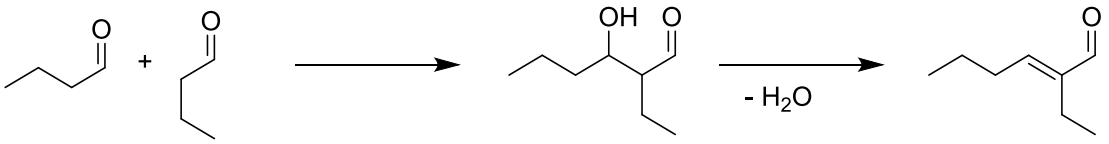
The corresponding silica-based ordered mesoporous materials are amorphous and contain silanol groups on their surfaces. These silanol groups offer the possibility for chemical modification *via* grafting with suitable organosilicon compounds.

This approach has been used to modify said porous silica materials of two different pore sizes (MCM-41 and SBA-15) with four different organic precursors comprising different types of basic functionalities.



Nitrogen adsorption measurements and XRD prove the high amount of ordered pores as well as the narrow pore size distribution both of calcined and modified materials. TGA and XPS measurements confirm the successful modification of nitrogen containing organic entities and give insight into their thermal stability.

Selected modified samples have been tested in the aldol condensation of *n*-butanal. Apart from the desired product 2-ethylhexenal, various byproducts, such as Tishchenko- or Cannizzaro-products can be observed. The aim of this study is to minimize all byproducts while obtaining a high yield of 2-ethylhexenal.



This work was supported by the German academic exchange service (grant № 57212311).

Novel drugs and targets for a selective treatment of cancer

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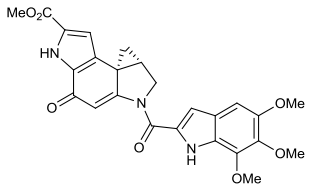
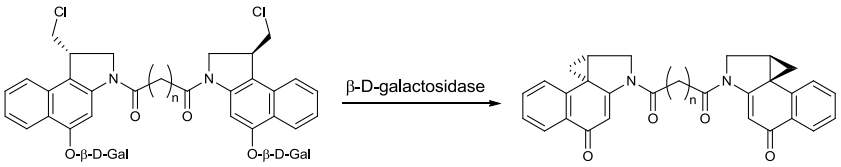
Anticancer therapy is hampered by an insufficient differentiation of normal and malignant cells by the known antiproliferant agents, resulting in severe side effects. Tumour-selective chemotherapy must therefore be based on the exploitation of phenotypic or genetic differences of malignant and normal cells.



Duocarmycin SA (**1**)



2 **3**

In the Antibody Directed Enzyme Prodrug Therapy (ADEPT) a non-toxic prodrug of a highly cytotoxic drug and a monoclonal antibody-enzyme conjugate are used to allow a selective liberation of the drug from the prodrug in the cancer tissue. We have recently developed novel glycosidic prodrugs **2** based on the natural antibiotic duocarmycin **1**, which are up to almost one million times less cytotoxic than the prodrugs **2** in the presence of galactosidase. The IC_{50}-values of the formed drugs **3** are as low as 150 fM. The mode of action of these compounds could be elucidated using mass spectrometry, CD-spectroscopy and X-ray crystal structure analysis. They do not attack DNA as found for **1** but aldehyde dehydrogenase as a new target in cancer therapy.

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Enantioselective total synthesis of dicerandrol C

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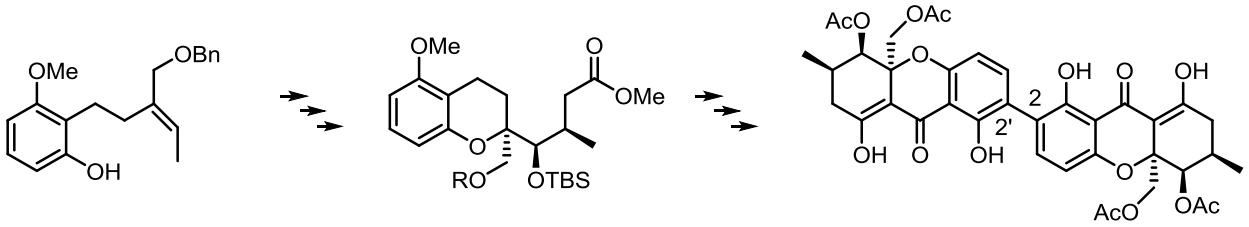
Dicerandrol C belongs to a group of natural mycotoxins containing a dimeric tetrahydroxantenone skeleton [1]. The dicerandrols have been isolated from the fungus *Phomopsis longicolla*, and their relative structure was elucidated by Clardy et al. [2] in 2001 and their absolute configuration has recently been determined by Proksch et al. using calculations [3].

We accomplished the first enantioselective total synthesis of natural dicerandrol C (**1**) as its enantiomer containing a dimeric tetrahydroxanthenone skeleton starting from the enantiopure chromane **3** [4] which was obtained from **2** through a Wacker-type cyclization in the presence of a BOXAX ligand with >99 % ee. This is not only the first synthesis of this type of natural product but it also proves the relative and absolute configuration of the dicerandrols.

After benzylic oxidation of **3** cyclization using $TiCl_4$ and $Ti(OiPr)_4$ led to the tetrahydroxantenone skeleton. Halogenation at the 2 position followed by a Susuki-Miyaura coupling gave the dimeric tetrahydroxantenone which after full deprotection was selectively acetylated to achieve dicerandrol C **1**.



2 **3** **1**

This work was supported by the Deutsche Forschungsgemeinschaft (DFG), the State of Lower Saxony, the VW-foundation and the Humboldt Foundation.

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Coherent x-ray imaging of nano- and bio-samples

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In my talk I will describe the basic features of the coherent x-ray diffraction imaging (CXDI) method [1]. This method use coherent x-ray beams produced by 3rd generation synchrotron sources as PETRA III at DESY in Hamburg. To produce an image of the sample instead of objective lenses powerful iterative methods are used to determine the phases of the scattered amplitudes. Such approach does not have limitations of conventional microscopes and could potentially lead to diffraction limited x-ray microscopy.

Two different scattering geometries will be presented: forward scattering geometry for non-crystalline samples and Bragg scattering geometry for crystalline samples. Results of CXDI applied to imaging of nanowires [2,3], colloidal crystals [4] and bio-samples [5] will be presented in this talk.

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Stereoelectronic chameleons: the donor/acceptor dichotomy of functional groups

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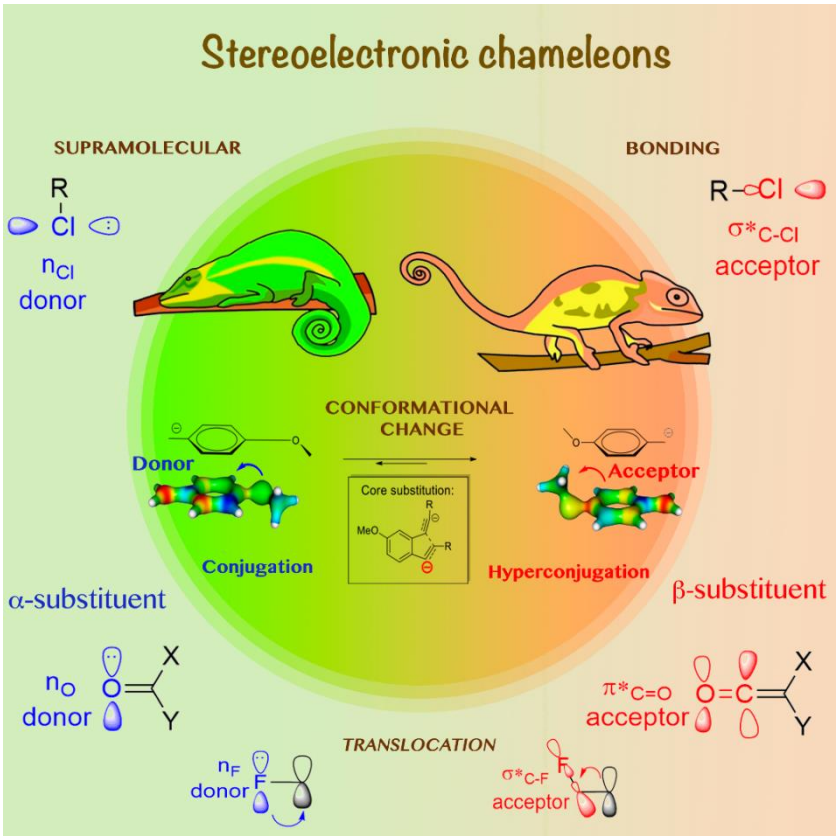
Stereoelectronic factors account for the apparent reversal of donor/acceptor properties of a variety of functional groups by a simple change of their orientation in space. The new reactivity patterns that arise from spatial anisotropy are associated with *chameleonic* behavior of common organic functionalities [1].



Because donor and acceptor properties are often engraved into our thinking about functional groups by the current educational paradigms, such a stereoelectronic "umpolung" can unlock useful ways of thinking about chemical reactivity and open new doors for reaction design. We are looking forward to new examples of stereoelectronic chameleons in control of structure and reactivity.

This work was supported by RSF (grant № 16-13-00114).

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Unprecedented effect of aryl alkyl ketones as a hydrogen peroxide stabilizers

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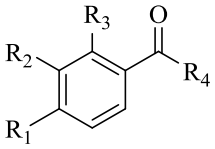
Hydrogen peroxide is one of large-scale products highly demanded in industry and laboratory chemistry. Scientific research related to hydrogen peroxide involves the following three areas of the study: preparation, application, and stabilization. A considerable progress has been achieved in the former two areas [1]. Less advances have been made in investigations concerning then stabilization of hydrogen peroxide, which still remains one of the key problems. Hydrogen peroxide decomposes on storage when exposed to light or high temperatures, and on contact with organic impurities and salts of metals of variable valence [2].

In the present work, when studying the synthesis of organic peroxides from carbonyl compounds and hydrogen peroxide, we unexpectedly found that aryl alkyl ketones would efficiently stabilize aqueous solutions of hydrogen peroxide. We tested aryl alkyl ketones **1–15** with σ-electron-donating, π-electron-withdrawing, and π -electron-donating substituents for the stabilization of hydrogen peroxide [3].



1: R_1 = H, R_2 = H, R_3 = H, R_4 = Me;
2: R_1 = *t*-Bu, R_2 = H, R_3 = H, R_4 = Et;
3: R_1 = Me; R_2 = H, R_3 = H, R_4 = Me;
4: R_1 = C(O)Me, R_2 = H, R_3 = H, R_4 = Me;
5: R_1 = H, R_2 = H, R_3 = COOH, R_4 = Me;
6: R_1 = OMe, R_2 = H, R_3 = H, R_4 = Me;
7: R_1 = OH, R_2 = H, R_3 = H, R_4 = Me;
8: R_1 = H, R_2 = H, R_3 = OH, R_4 = Me;
9: R_1 = OH, R_2 = H, R_3 = OH, R_4 = Me;
10: R_1 = H, R_2 = H, R_3 = Cl, R_4 = Me;
11: R_1 = Cl, R_2 = H, R_3 = H, R_4 = Me;
12: R_1 = Cl, R_2 = H, R_3 = Cl, R_4 = Me;
13: R_1 = H, R_2 = Br, R_3 = H, R_4 = Me;
14: R_1 = Br, R_2 = H, R_3 = H, R_4 = Me;
15: R_1 = OMe, R_2 = Br, R_3 = H, R_4 = Me.

Aryl alkyl ketones are proposed as new stabilizers of aqueous solutions of hydrogen peroxide. The efficient stabilizing effect is observed within 16–24 months for 33–37% H_2O_2 in the presence of a stabilizer in an amount of 0.005–0.5 wt% of the weight of the solution. Taking into account the large scale of application of hydrogen peroxide, as well as the commercial availability and low toxicity of aryl alkyl ketones, the results of the present study can find use in industry.

This work was supported by the Russian Foundation for Basic Research (grant № 16-33-00555).

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Pushing the frontiers in aromatic chemistry – substituted cycloparaphenylenes

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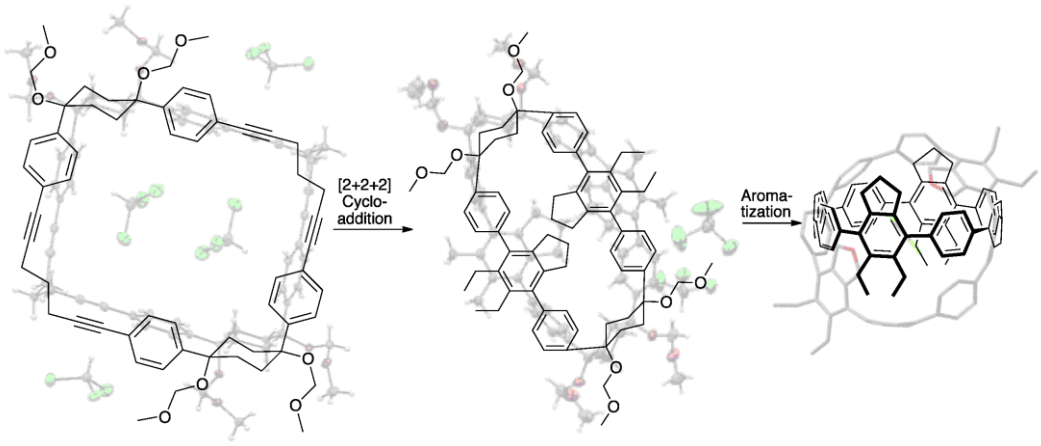
Cycloparaphenylenes (CPPs) have attracted the attention of chemists for over 80 years. Already in the early days, these esthetic compounds ignited fascination. The fact, that the textbook criterion of planarity for aromaticity is violated, further increased its attractiveness. With the era of carbon nanotubes (CNTs), CPPs promise an entry to novel synthetic pathways, which allow controlling all parameters of CNTs, especially diameter and chirality.

The main challenge of a CPP synthesis is the introduction of strain. We envisioned mastering this problem by relying on the gain of aromaticity in the [2+2+2] cycloaddition. In this presentation initial efforts , the final strategy as well as potential application of the methodology will be presented.[1-3]



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An anomalous behavior of the bond-orientational order parameters at the smectic-hexatic phase transition

Zaluzhnyy I.A.,[a,b] Kurta R.P.,[c] Sulyanova E.A.,[d] Gorobtsov, O.Yu.,[a] Shabalin A.G.,[a] Zozulya A.V.,[c] Menushenkov A.P.,[a] Sprung, M.,[a] Górecka E.,[e] Krówczyński A.,[e] Ostrovskii B.I.,[d,f] Vartanyants I.A.[a,b]

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In some thermotropic liquid crystals (LCs) the hexatic phase may occur, which is characterized by a short-range positional order and a sixfold long-range bond-orientational (BO) order. The BO order can be described by the set of the BO order parameters C_{6m}, where m is integer. X-ray scattering experiment was performed at Coherence beamline P10 at PETRA III. By means of angular x-ray cross-correlation analysis (XCCA) [1] we have measured precisely the values of the BO order parameters in the hexatic phase at different temperatures in three different compounds [2]. The temperature dependence of the BO order parameters in the vicinity of the hexatic-smectic transition was fitted by a conventional power law with a critical exponent $\beta \approx 0.1$ of extremely small value. We found that the temperature dependence of higher order harmonics of the BO order scales as the powers of the first harmonic, with exponent equal to harmonic number. This indicates a nonlinear coupling of the BO order parameters of different order. We demonstrate that compounds of various compositions display the same thermodynamic behavior in the hexatic phase and in the vicinity of the smectic-hexatic phase transition.

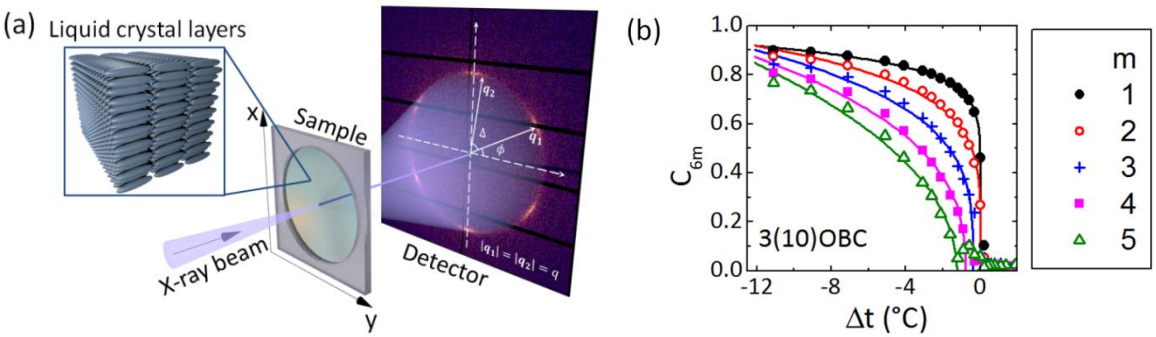

Fig. 1. (a) Scheme of the x-ray diffraction experiment and orientation of the LC molecules with respect to the incoming beam. (b) Temperature dependence of the BO order parameters C_{6m} and its fitting with power law for 3(10)OBC compounds.

This work was partially supported by Russian Science Foundation (grant № 14-12-00475).

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The synthesis of biogenic nanoparticles of various metal sulfides and their possible applications for the production of polymeric nanocomposite materials

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Over the past decade articles on the non-standard methods of biotechnological synthesis of producing nanoparticles of various metals and their salts are increasingly appear in scientific literature. The main components of these methods are biological objects: plant extracts, bacterial strains plurality of taxonomic groups, fungi, yeasts [1].

In addition to the narrow dispersion of biosynthesized particles, their form constancy, and simplicity of non-numerous stage approach of this process, these experiments are similar to "green synthesis" and provide a natural stabilization of the obtained nano-objects in aqueous solutions, which avoids the use of additional toxic surfactants.

This work is aimed at the physico-chemical studies of biogenic sulfide nanoparticles of some metals, incubated in the reaction mixture of sodium thiosulfate ($Na_2S_2O_3$) and nitrate salts of the corresponding metal in the presence of a metal-reducing electrogenic bacteria *Shewanella oneidensis* MR-1. This procedure for the preparation of above mentioned nanoparticles, as well as for nanoparticles of metallic gold, silver, palladium, is consecrated in literature [2 - 5].

As a result of transmission electron microscopy it can be concluded that these nanoparticles are round-shaped, low agglomerated and their average diameter is 7 ± 2 nm.

Knowing about the presence of the stabilizing protein / peptide layer on the metal surface [4], we were able to determine the molecular masses of the biocompounds and of their fragments included in its constituent. Protein analysis was performed by polyacrylamide gel electrophoresis. MALDI TOF/TOF mass spectrometry method was used to identify specific proteins secreted by a particular bacterium in a destructive effect of reaction salts.

The method of scanning electron microscopy confirmed the immobilization of biogenic sulfide nanoparticles on the surface of the amine-containing polyglyceridedimethylacrylate microspheres. Such a process is necessary to create a model polymer nanocomposite in order to find the probable applications of nano-objects of natural origin.

This work was partially supported by the Russian Foundation for Basic Research (grant № 16-04-00471).

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is a company, founded to develop the university project in the field of nanosafety named

AeroNanoToxicology

Development and commercialization of new physical principles for nanoecology control in habitable areas - the first and critical step in the creating of nanotechnology safety systems for population and staff of office, laboratory and production facilities. Sources of nanodanger are not only components and products of nanotechnology industry, but also emissions of household and office equipment, building materials, clothing and food. Currently nanoecology control can only be performed with the use of unique and expensive scientific equipment that does not resolve the general problem of nanosafety in the national scale.

AeroNanoToxicology is a project which is intended to develop and introduce new cost-effective physical principles in large-scale production of the control devices and the use of nanoecology in the residential, office, laboratory and production facilities.

Fields of research:

the study of the chemical nature of nanoobjects, research and development of nanoparticles formation mechanisms, the study of the propagation and behavior of nanoparticles in the atmosphere, modeling and prediction of accidents related to large-scale emissions of nanoparticles in the atmosphere in the residential areas, the possible penetration and impact on living organisms, development of standard equipment for nanosafety.

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Научное издание

НАНОРАЗМЕРНЫЕ МЕЖДИСЦИПЛИНАРНЫЕ ИССЛЕДОВАНИЯ: ФИЗИКА, ХИМИЯ, БИОЛОГИЯ, МАТЕМАТИКА

На английском языке

Издание подготовлено в авторской редакции

Дизайн обложки *Ю.Н. Ефремова*

Подписано в печать 17.04.2017 г. Формат 60×84/8.
Бумага офсетная. Печать офсетная. Гарнитура Таймс.
Усл. печ. л. 6,5. Тираж 80 экз. Заказ 631

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