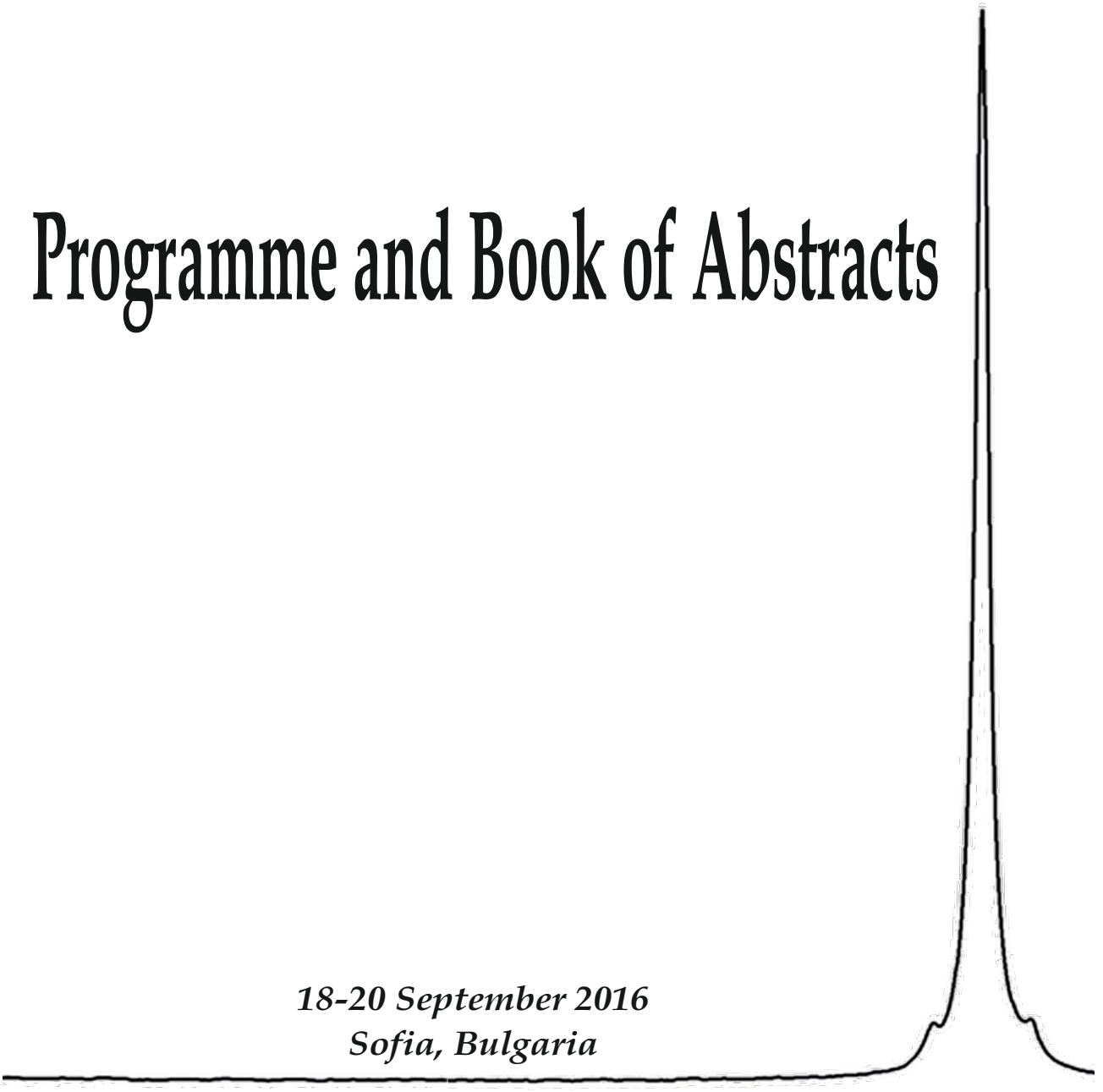
18th Central and Eastern European NMR Symposium & Bruker Users' Meeting

Programme and Book of Abstracts



18-20 September 2016
Sofia, Bulgaria

Organized by the Bulgarian NMR Centre and Bruker Biospin GmbH

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09:45	**Ruediger Weisemann** *Probe news*
10:00	**Fabrice Moriaud** *Solutions for routine analytics: SmartDriveNMR, CMC-assist and Fusion-SV*
10:30	***Coffee break***
11:00	**Daniel Mathieu** *Broadband Homonuclear Decoupling*
11:30	**Stefan Steuernagel** *Solid State NMR news*
12:00	**Venita Decker** *TopSolids – Where Expertise meets Convenience*
12:30	**All** *Q&A*
12:45	***Lunch***
14:00	**Daniel Mathieu** *BioNMR made easy*
14:30	**Wiktor Koźmiński** *New NMR experiments for intrinsically disordered proteins*
15:00	***Coffee break***
15:30	**Fabrice Moriaud** *Simplifying special NMR tasks: fragment based screening and potency determination of APIs*
16:00	**Pavleta Shestakova** *Solid state NMR characterization of zeolite beta based drug formulations*
16:30	**Free discussion**
17:00	**Closing remarks and best poster awards for young scientists**
17:30	***Visit to the Bulgarian NMR Centre***

Lectures **L-10**

Solid state NMR characterization of zeolite Beta based drug formulations containing Ag and sulfadiazine

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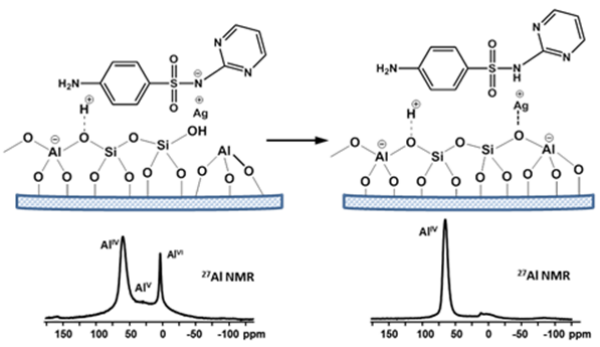
Solid state NMR (^{1}H, ^{13}C, ^{29}Si, ^{27}Al and ^{1}H-^{29}Si CP-HETCOR) was applied for characterization of zeolite Beta-based (HB) dual drug formulations with antibacterial properties, containing Ag, sulfadiazine (SD) and silver sulfadiazine (AgSD).[1] A mechanism for transformation of octahedral defect framework Al sites and encapsulation of the extraframework Al (EFAl) present in the parent Beta material into framework tetrahedral species as a result of the drug loading procedure is proposed. The nature of the drug-carrier interactions and the location of the drug molecules inside the pores and/or on the crystallite surface are discussed.



The ^{27}Al NMR spectra showed that the loading of SD, Ag or AgSD resulted in a reinsertion of the EFAl into the zeolite matrix of the parent HB carrier. ^{1}H spectra suggested that the mechanism of EFAl inclusion involves exchange between the zeolite protons and H^{+} or Ag^{+} cations, originating from SD and AgSD respectively, that play a role of charge compensating species. The comparison of onepulse and CP ^{29}Si spectra in combination with ^{1}H spectra, suggested that the loaded drug (SD, AgSD) is predominantly localized in the vicinity of Si(0Al) groups and a larger amount of it is most probably embedded within the zeolite pores. The amount of the SD drug confined into the pores of HB zeolite is higher than that included into the Ag modified carrier. ^{1}H-^{29}Si HETCOR spectra of SD/AgB and AgSD/HB samples show similar correlation patterns, evidencing the analogous localization of the drug into the zeolites. Comparison of T_1 and T_2 relaxation times of pure drugs and drug loaded formulations indicate that the drug incorporated into the pores of the zeolite matrix is in amorphous form.

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1. Shestakova P., Martineau C., Mavrodinova V., Popova M., *RSC Adv.* **5**, 81957-81964 (2015).

Acknowledgements: *The financial support by Bulgarian Science Fund (UNA-17/2005 and DRNF-02/13/2009) is acknowledged.*

Posters **P-6**

Structural/morphological transformations of core-shell particles based on Polystyrene/Polyether block copolymers studied by Diffusion Ordered NMR Spectroscopy and TEM

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The aim of the present work was to investigate the structural transformations and size changes of amphiphilic block copolymer particles induced by addition of hydrolytic agents to their solutions. Aggregates were prepared by dissolving a series of diblock copolymers consisting of hydrophobic polystyrene (PS) with randomly distributed short diene moieties and hydrophilic polyether or polyglycidol (PEO or PG) blocks in selective solvents. Attempt to induce structural changes of the preformed aggregates was made by addition of strong acid and ferric salt to the system. The structure and size of the PS/PEO and PS/PG block copolymer core-shell particles were investigated by conventional and Diffusion Ordered NMR Spectroscopy (DOSY). The broadening and disappearance of the PS signals in ^{1}H NMR spectra upon increase of water content in mixed organic/water solutions, evidenced possible reversal of the core-shell structure. The DOSY spectra indicate an increase of particle size in parallel with the increase of water content and upon addition of strong acid and ferric salt. More detailed information on morphology transformations, shape and size distribution of the aggregates was provided by TEM. For comparison, the change of the particle size under identical conditions for objects of preliminary stabilized core-shell morphology was monitored as well. In addition size exclusion chromatography (SEC) was used to follow the changes in copolymer molecular weight and molar mass distribution, while dynamic light scattering (DLS) was applied as complementary technique for particles size determination.

Acknowledgements: *The financial support by Bulgarian Science Fund (UNA-17/2005 and DRNF-02/13/2009) is acknowledged.*

Posters **P-11**

A ^{1}H, ^{11}B and DOSY NMR STUDY OF COMPLEXES OF CHIRAL AMINOALCOHOLS AND THEIR SQUARAMIDES WITH $BH_3 \cdot SMe_2$

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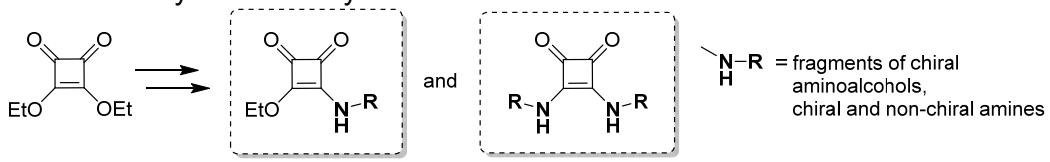
Chirally modified boron complexes have been object of significant interest in recent years due to their ability to induce enantioselectivity in asymmetric borane reduction ($BH_3 \cdot SMe_2$). Remarkable success has been achieved using chiral oxazaborolidines either formed *in situ* or prepared separately from natural compound-derived aminoalcohols such as amino acids, terpenoids etc. [1]. Interesting results have been reported recently in which squaric acid is used as a backbone to bind chiral aminoalcohol fragments [2].

We have prepared a series of compounds through combination of squaric acid and chiral amines or aminoalcohols. The squaramides and the corresponding free aminoalcohols were applied and compared as chiral ligands in enantioselective borane reduction of acetophenones, with the aim to investigate the contribution of the squaric acid core (bearing several chiral aminoalcohol moieties) on the degree of enantioselectivity achieved by the reduction of ketones.



The reactivity and stability of the *in situ*-formed borane complexes of chiral aminoalcohols and their squaric amides were investigated by 1D and 2D NMR. The ^{1}H and ^{11}B NMR spectra indicated that there was a coordination between the squaramide and $BH_3 \cdot SMe_2$, most probably through the N-atom from the ligand, however no definite structure was identified. Moreover the occurrence of destructive reactions resulting in disintegration of the ligand and the $BH_3 \cdot SMe_2$ was observed. The formation of complex between $BH_3 \cdot SMe_2$ and parent aminoalcohols was confirmed by ^{1}H diffusion ordered NMR spectroscopy (DOSY).

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Posters **P-17**

Detailed Mechanism of ATP Hydrolysis Promoted by a Binuclear Zr^{IV}-Substituted Keggin Polyoxometalate Elucidated by a Combination of ^{31}P, ^{31}P DOSY and ^{31}P EXSY NMR Spectroscopy

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The full reaction mechanism of adenosine triphosphate (ATP) hydrolysis in the presence of the binuclear Zr^{IV}-substituted Keggin type polyoxometalate $(Et_2NH_2)_8[\{\alpha\text{-}PW_{11}O_{39}Zr(\mu\text{-}OH)(H_2O)\}_2]\cdot 7H_2O$ (ZrK 2:2) at pD 6.4 and 50 °C was elucidated by a combination of ^{31}P, ^{31}P DOSY and ^{31}P EXSY NMR spectroscopy, demonstrating the potential of these techniques for the analysis of complex reaction mixtures involving polyoxometalates (POMs). ^{31}P and ^{31}P DOSY NMR measured for pure ZrK 2:2 and for the solution containing ZrK 2:2 and ATP at pD 6.4 shows that in the presence of ATP, ZrK 2:2 converts into the more active species ZrK 1:1 and this species is responsible for the hydrolysis of the phosphoanhydride bonds [1,2]. Two possible parallel reaction pathways were proposed on the basis of the observed reaction intermediates and final products. The ^{31}P spectrum of a mixture of 20.0 mM ATP and 3.0 mM ZrK 2:2 at pD 6.4 measured immediately after sample preparation, shows the formation of a complex I1A and I1B between ATP and POM. During the course of the hydrolytic reaction at pD 6.4 and 50 °C, various products including adenosine diphosphate (ADP), adenosine monophosphate (AMP), pyrophosphate (PP) and phosphate (P) were detected. In addition, several intermediate species representing ADP/ZrK 1:1 (I2), AMP/ZrK 1:1 (I3), P/ZrK 1:1 (I4) and PP/ZrK 1:1 (I5) complexes were also identified. ^{31}P EXSY NMR spectra evidenced slow exchange between ATP and I1A, ADP and I2, and PP and I5.

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2. Luong T. K. N., Absillis G., Shestakova P., Parac-Vogt T. N. *Dalton Trans.* ***44***, 15690-15696 (2015).

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Posters **P-27**

Microgels of Poly(Acrylic Acid)/Polyacrylamide Interpenetrating Polymer Networks: Synthesis and Characterization

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Microgels are hydrogels within microscaled level which are currently extensively developed as drug delivery systems. Microgels of interpenetrating polymer networks (IPNs) possess a great potential in this field as they combine both phase-separated structure and possibility to vary the polymer components according to the nature of the drug to be delivered.
Microgels from poly(acrylic acid) (PAA)/polyacrylamide (PAAM) IPNs were prepared via inverse microemulsion polymerization. The sequential method for IPNs preparation was used to ensure a phase separated structure of the IPN at nanolevel. Thus formed PAA/PAAM microgels were separated via asymmetric flow field flow fractionation (AF4). The hydrodynamic radius of the particles as well as their pH and temperature responsiveness was studied by DLS. The smart behavior of the PAA/PAAM microgels as a function of pH and temperature was monitored by diffusion NMR proving their potential as smart drug delivery systems.

Acknowledgments: *This work is financed and supported by DAAD project DNTS Germany 01/12 and by Bulgarian Science Fund (UNA-17/2005 and DRNF-02/13/2009).*

Polyelectrolyte Complexes Based on Polysulfobetaines

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Zwitterionic polymers (PZI) provoke very low non-specific protein adsorption and thus possess very good haemo- and biocompatibility. These properties define many biomedical application as e.g. implants [1], systems for drug delivery [2], etc. The excellent performance of PZIs as biomaterials is explained by their specific structure defined by the presence of two opposite charges in the side chain of each monomeric unit [3]. Thus dipole-dipole interaction between PZI side chains is the widely accepted reason for these PZI specific performance. These interactions should also take place when PZI are in solution thus giving rise to a new type of polymer-polymer complexes.

The aim of the present study was to synthesize and study the behavior of polymer-polymer complexes formed between polysulfobetaines (PSBs) – PZI where the negative charge is carried by a sulfo group. The pH change and temperature were expected to modify the interaction between the PSBs side chains and hence to change their structure, and respectively, their properties. The PZI complexes were studied by conventional and diffusion NMR in order to reveal their structure-properties relationship and to follow the morphological transformations as a function of the temperature. In addition the behavior of thus formed complexes and their temperature and pH sensitivity were studied by dynamic light scattering (DLS).

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Posters **P-29**

NMR Characterisation of Novel Phosphorus- and Silicon-containing Polymers

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One of the most promising approaches to the development of new materials that combine the advantages of organic polymers with those of inorganic solids is to devise products that have a backbone of inorganic atoms to which are attached organic or organometallic side groups [1-3]. Such polymers are known as "inorganic-organic polymers", often abbreviated to "inorganic polymers". The inorganic backbone can provide heat-, fire-, or radiation- resistance. The side groups control properties such as solubility or resistance to solvents, liquid crystallinity or nonlinear optical behavior, hydrophobicity, hydrophilicity, adhesion, and biological compatibility [4]. Inorganic polymers find application in: catalysis; solid electrolytes; pharmacy (drug delivery); medicine (regenerative therapeutic materials); fuel cells; polymer modification (flame retardants; thermostabilizers; adhesives). In the present study a new type of inorganic polymer with a structure [-O-P(O)(H)-O-Si$(CH_3)_2$-] has been characterized by means of ^{1}H, $^{13}C\{H\}$, $^{31}P\{H\}$, and ^{31}P NMR spectroscopy in solution and under magic angle spinning conditions (MAS).

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