

**Central European School  
on Physical Organic Chemistry**

**Modeling, molecules,  
processes and properties**

**Przesieka, 26-30 of May 2014**

**organized by  
Faculty of Chemistry, University of Wrocław,  
Section of Physical Organic Chemistry  
of the Polish Chemical Society**

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Edited by:  
Marina Lopatkova  
Alicja Wolny,

Faculty of Chemistry University of Wrocław  
2014

# Programme

## Monday, 26.05.2014

- 15:00 *The conference office (in Przesieka) is open*
- 16:00 *Conference bus departs from the front of the Chemistry Department (Joliot-Curie 14, Wrocław), close to 16.30 at the airport*
- 18:30 *The bus arriving to Przesieka*
- 19:00 *Dinner*
- 20:00 *Get-together party*

# Tuesday, 27.05.2014

7:30-8:30      *Breakfast*

*Morning session*

*Chairman: Andrzej Katrusiak*

9:00-9:45	<b>Celia F: Guerra</b>	<i>Supramolecular chemistry based on halogen bonding</i>
9:45-10:30	<b>Irena Kulszewicz-Bajer</b>	<i>Organic magnetic materials for spintronics: design, synthesis and physical characterization</i>
10:30-11:00	<b>Katarzyna Sadecka</b>	<i>Novel hybrid materials for photonics manufactured by crystal growth methods</i>
11:00-11:30		<i>Coffee break</i>
11:30-12:15	<b>Poul E: Hansen</b>	<i>Protic ionic liquids, their constitution, properties and use: A NMR, IR, DFT study</i>
12:15-12:45	<b>Grażyna Bator</b>	<i>Structure and tunneling splitting spectra of methyl groups in the molecular complexes containing tetramethylpyrazine</i>
12:45-13:50		<i>Presentation of posters 1-21</i>
13:50-14:30		<i>Lunch</i>

*Afternoon session*

*Chairman: Poul E. Hansen*

15:00-15:45	<b>Erich Kleinpeter</b>	<i>Application of NMR Spectroscopy to Tautomerism Studies.</i>
15:45-16:15	<b>Zofia Dega-Szafran</b>	<i>X-ray and DFT studies of the interactions between glycine derivatives and squaric acid</i>
16:15-17:00	<b>Peter Tolstoy</b>	<i>Solvent Dynamics and Proton Tautomerism in Strong Hydrogen Bonds</i>
17:00-17:30		<i>Coffee break</i>
17:30-18:00	<b>Mirosław Jaboński</b>	<i>Charge-inverted hydrogen bond as a new type of interaction</i>
18:00-18:30	<b>Marcin Palusiak</b>	<i><math>\pi</math>-Electron delocalization in charged cyclic hydrocarbons.</i>
18:30-18:45	<b>Justyna Dominikowska</b>	<i>On singlet state cations of polycyclic aromatic hydrocarbons</i>
18:45-19:00	<b>Lilianna Chęcińska</b>	<i>Hypercoordinated triorganosilyl cations stabilized by pincer type ligands: structures and bonding</i>
19:00-19:15	<b>Aneta Sieradzka</b>	<i><math>\pi</math>-Electron conjugation in polyenes</i>
19:15-19:30	<b>Agnieszka Rybarczyk-Pirek</b>	<i>The temperature-dependent polymorphism of an imidazole-N-oxide</i>
19:30-21:00		<i>Barbecue</i>

# Wednesday, 28.05.2014

7:15-8:45      *Breakfast*

*Morning session*

*Chairman: Peter Tolstoy*

9:00-9:45	<b>Klaus Wandelt</b>	<i>Properties and processes at metal-electrolyte interfaces: An atomic view</i>
9:45-10:30	<b>Robert Nowakowski</b>	<i>STM studies on 2D self-organization of thiophene-based organic semiconductors</i>
10:30-11:00	<b>Mirosław Szafran</b>	<i>Hydrogen bonds in complexes of betaines with phenols of the 1:1, 2:1 and 1:2 ratios</i>
11:00-11:30		<i>Coffee break</i>
11:30-12:15	<b>Andrzej Katrusiak</b>	<i>Pressure-modulated intermolecular interactions</i>
12:15-12:45	<b>Aleksander Koll</b>	<i>Application of dipole moments in modeling the structure of aggregates in solutions</i>
12:45-13:50		<i>Presentation of posters 22-42</i>
13:50-14:30		<i>Lunch</i>

*Afternoon session*

*Chairman: Mirosław Szafran*

15:00-15:45	<b>Boris Galabov</b>	<i>Electrostatic potential at nuclei: an accurate reactivity descriptor for organic compounds</i>
15:45-16:00	<b>Małgorzata Domagała</b>	<i>The influence of DFT functional on QTAIM calculations.</i>
16:00-16:45	<b>Zdzisław Latajka</b>	<i>Molecular system with intramolecular H-bonds - rigid or nonrigid: that is the question</i>
16:45-17:00	<b>Marina Lopatkova</b>	<i>Experimental and theoretical (DFT and TD-DFT) investigation of the ground and excited state of BODIPY dyes</i>
17:00-17:30		<i>Coffee break</i>
17:30-18:15	<b>Tadeusz Andruniów</b>	<i>Primary photoprocess of vision</i>
18:15-19:00	<b>David Djurado</b>	<i>Structure and Dynamics of Conjugated Polymers as Studied by Synchrotron Radiation and Neutron Scattering Measurements</i>
19:00-19:30		<i>Dinner</i>

# Thursday, 29.05.2014

7:30-8:45      *Breakfast*

*Morning session*

9:00-14:30      **Everybody**

*Semi-scientific chatters during a mountain walk*

14:30-15:30

*Lunch*

*Afternoon session*

*Chairman: Aleksander Koll*

15:45-16:30      **Gottfried Koehler**

*GR-signaling in HPA-axis fast non-genomic glucocorticoid processes studied by Fluorescence Correlation Spectroscopy*

16:15-16:45      **Andrzej Teisseyre**

*Putative future application of small-molecule organic inhibitors of voltage-gated potassium channels Kv1.3 in chemotherapy of some tumor diseases*

17:00-19:00

*Poster session*

20:00-1:00

*Conference dinner*

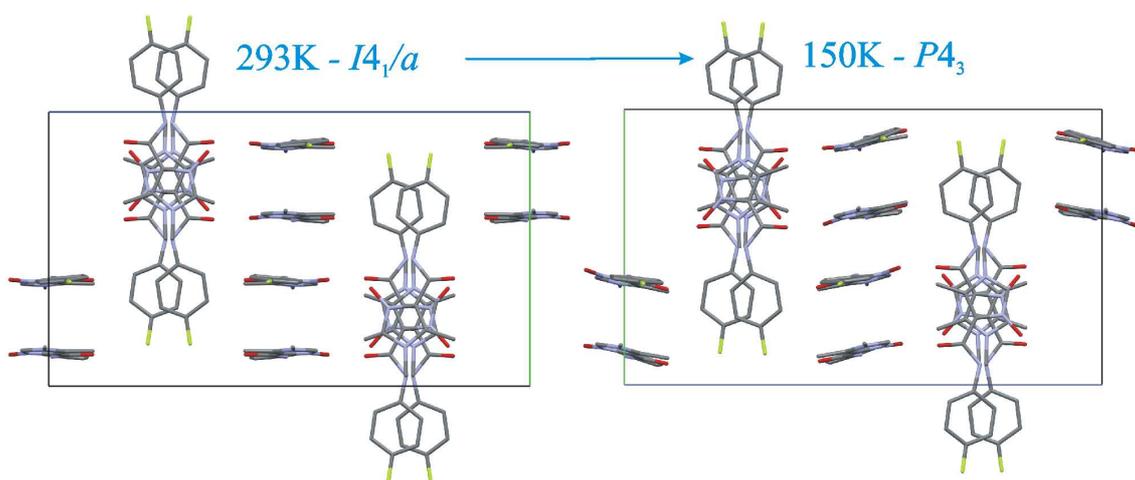
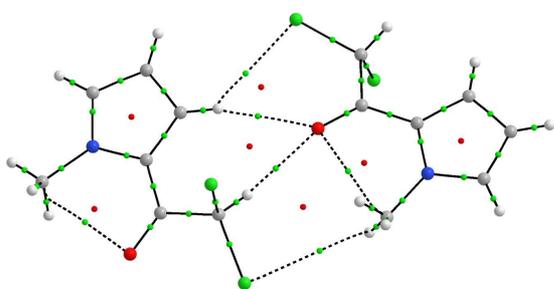
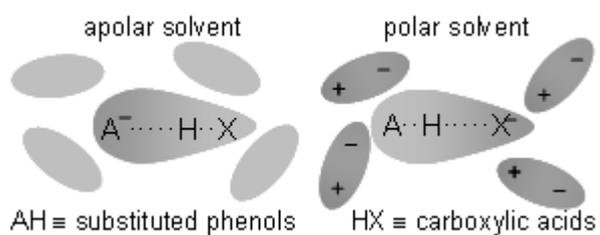
# Friday, 30.05.2014

7:30-8:30      *Breakfast*

9:00      *Depart to Wrocław (close to 12 at the airport, close to 13 at the railway/bus station)*

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# Lectures in chronological order



## Supramolecular chemistry based on halogen bonding

C. Fonseca Guerra

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Halogen bonds are shown to possess the same characteristics as hydrogen bonds: charge transfer, resonance assistance and cooperativity. This follows from computational analyses of the structure and bonding in N-halo-base pairs and quartets. The objective was to achieve understanding of the nature of resonance-assisted halogen bonds (RAXB), how they resemble or differ from the better understood resonance-assisted hydrogen bonds (RAHB) in natural DNA.

I will present an accurate physical model of the RAXB based on molecular orbital theory, which is derived from corresponding energy decomposition analyses and analyses of the charge distribution. I will show that the RAXB arise from classical electrostatic interaction and also receive strengthening from donor–acceptor interactions within the  $\sigma$ -electron system. Similar to the RAHB, there is also a small stabilization by  $\pi$ -electron delocalization. This resemblance lead to prove cooperativity in N-halo-guanine quartets originating from the charge separation that goes with donor–acceptor orbital interactions in the  $\sigma$ -electron system.

- [1] C. Fonseca Guerra, H. Zijlstra, G. Paragi, F. M. Bickelhaupt, *Chem. Eur. J.* 2011, 17, 12612.
- [2] C. Fonseca Guerra, T. van der Wijst, J. Poater, M. Swart, F. M. Bickelhaupt, *Theoret. Chem. Acc.* 2010, 125, 245.
- [3] T. van der Wijst, C. Fonseca Guerra, M. Swart, F. M. Bickelhaupt, B. Lippert, *Angew. Chem. Int. Ed.* 2009, 48, 3285.
- [4] C. Fonseca Guerra, F. M. Bickelhaupt, *Angew. Chem. Int. Ed.* 1999, 38, 2942.

## Organic magnetic materials for spintronics: design, synthesis and physical characterization

Irena Kulszewicz-Bajer

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The search for organic materials exhibiting spins ordering is a great challenge nowadays. Among different classes of compounds studied to date special attention should be paid to arylamine oligomers and polymers which can form stable radical cations bearing electronic spins. An appropriate modification of conjugated systems of these compounds allows for tuning of their properties. Thus, oligomers and polymers containing *para*-phenylene units with extended  $\pi$ -conjugated systems show high electrical conductivity and are commonly used as conducting or efficient hole transporting materials in OLEDs and in solar cells. However, breaking the conjugation by synthesizing molecules (macromolecules) of special topologies, containing *meta*-phenylene units leads, to arylamine compounds with localized radical cations which are promising candidates for high-spin or magnetic organic materials.

We report on the synthesis, spectroscopic and magnetic properties of oligomers and polymers containing oligoarylamine units of different conjugation length. The  $\pi$ -conjugated systems of these compounds were intentionally broken by introducing 1,3-phenylene or 3,4'-biphenylene moieties. Oxidation of these arylamines derivatives yielded their radical cationic forms in which the created spins could be coupled *via* 1,3-phenylene or 3,4'-biphenylene in a ferromagnetic fashion. The spins interaction was studied by pulsed-EPR spectroscopy and magnetic properties were investigated by SQUID measurements which allowed to determine the exchange coupling constant  $J$ . In the compounds with alternating *meta-para*- bonding sequences, the formation of uncoupled spins with  $S=1/2$  with only a small fraction of coupled spins with  $S=1$  was detected. An increase in the conjugation length in compounds showing the *meta-para-para*- bonding sequence resulted in the formation of pure triplet states  $S=1$  in cyclic and linear dimers as well as in the linear polymer. The experimentally determined coupling constants  $J$  were equal to 18 K for the polymer, 35 K for the linear dimer and 57 K for cyclophane. The experimental  $J$  values were in perfect accordance with that estimated by DFT calculations. The modification of the polymer structure by incorporation of pendant oligoaniline chains or by creation a randomly branched polymer network lead to an increase of the spin multiplicity. It was found that in branched polymers spins interacted magnetically to form dominant quartet state  $S=3/2$  with  $J=8.7$  K. Detailed EPR studies showed that in the case of the polymer containing oligoaniline pendant chains quintet  $S=2$  state was reached. It should also be underlined that for the first time the high-spin state with  $S=3/2$  was obtained in linear compounds containing 3,4'-biphenyl moiety. This result is very promising in view of the design and synthesis of new linear polymers exhibiting magnetic ordering.

## **Novel hybrid materials for photonics manufactured by crystal growth methods**

K. Sadecka, M. Gajc, K. Korzeb, P. Osewski, A. Kłos, B. Surma, D. A. Pawlak

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Two novel bottom-up manufacturing methods of nanoplasmonic materials and metamaterials will be presented utilizing the crystal growth techniques: (i) directional solidification of eutectic composites [1], and (ii) direct doping of dielectric matrices with plasmonic nanoparticles (NanoParticles Direct Doping - NPDD) [2]. Eutectics are simultaneously monolithic and multiphase materials forming self-organized micro/nanostructures, which enable: (i) the use of various component materials including oxides, semiconductors, metals, (ii) the generation of a gallery of geometrical motifs and (iii) control of the size of the structuring, often from the micro- to nanoregimes. On the other hand, the novel method of direct doping of dielectric matrices with nanoparticles utilizing directional solidification provides three-dimensional nanoplasmonic materials enabling doping with nanoparticles of various chemical composition, various size and shape, as well as co-doping with other chemical agents. Materials with plasmonic resonances at visible and IR wavelengths, as well as materials with enhanced photoluminescence and with anomalous refraction [3] will be presented. Our new approach may lead to novel manufacturing solutions for photonic applications in areas such as metamaterials, plasmonics, as well as photovoltaics.

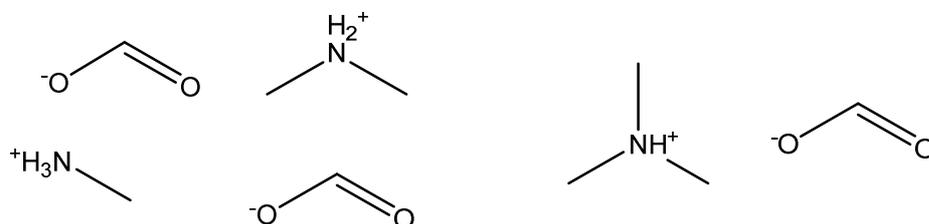
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- [2] M. Gajc, B. H. Surma, A. Kłos, K. Sadecka, K. Orlinski, A. E. Nikolaenko, K. Zdunek, Nanoparticle Direct Doping: novel method for manufacturing three-dimensional bulk plasmonic nanocomposites. *Adv. Funct. Mat.*, 2013, 23, 3443-3451.
- [3] A. Belardini, C. Sibilia, Evaluation of the negative refractive index by beam deviation measurements, *Optoelectron. Adv. Mater.-Rapid Commun.* 2013, 7, 184.

## Protic Ionic Liquids. A NMR, IR, DFT study.

Poul Erik Hansen, Jacob Krake, Jens Spanget-Larsen, Søren Hvidt  
and Torben Lund

*Department of Science, Systems and Models, Roskilde University,  
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The talk will introduce protic ionic liquids in general such as viscosity as a function of composition, conductivity, dependence of pH difference between acid and base, thermal stability, Walden plots etc. Use and limitations of the use of protic ionic liquids will be described and discussed.



Ionic Liquids?

Protic ionic liquids of the type an acid plus a tertiary amine are easy to make and have interesting properties. The composition of such simple ionic liquids will be discussed and a new composition for such ionic liquids will be presented. The importance of water will also be treated.

Hydrogen-bonding is investigated to reveal the structure of these ionic liquids. This is based on <sup>1</sup>H, <sup>13</sup>C NMR studies combined with deuterium isotope effects on chemical shifts, Infra Red measurements and DFT calculations.

The investigation reveals both strong traditional hydrogen bonds as well as equilibria.

The new findings are leading to a better understanding of why such simple mixtures are ionic liquids. The better structural understanding can be used to tailor new ionic liquids with specific properties.

## Structure and tunneling splitting spectra of molecular complexes containing tetramethylpyrazine (TMP)

G. Bator and L. Sobczyk

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In the presentation a review of the molecular complexes containing tetramethylpyrazine (TMP) will be presented. The experimental methods used will be described. In particular the methods concerning the neutron scattering will be taken into consideration. As the tetramethylpyrazine molecule may be mono- or double protonated the different examples will be shown and discussed.

Two complexes with TMP will be analyzed in details: TMP·CLA – tetramethylpyrazine with chloranilic acid<sup>i,ii</sup> and TMP·BRA – tetramethylpyrazine with bromanilic acid<sup>iii</sup>. Both complexes were studied by means of the single crystal X-ray, infrared and raman spectra as well as by the neutron methods (inelastic neutron scattering – INS). At low temperatures (below 50 K) TMP·CLA exhibits in the INS spectra so called tunneling peaks connected with the torsional vibrations of the methyl groups. The charge transfer from one molecule to the other modifies the potential to rotation of the CH<sub>3</sub> groups. The height of the rotational barrier may be treated as a measure of the charge transfer (CT) degree or the strength of the hydrogen bonds (HB) between the components.

In principle two effects are responsible for the height of the barrier. Besides the charge transfer or hydrogen bonds the packing of the crystal lattice plays an important role. The decrease in the electron density in the aromatic ring of the molecule causes the decreasing of the CH<sub>3</sub> rotational barrier. The steric hindrance results on the other hand in an increase of the barrier. The quantitative determination of these two competing contributions requires the systematic studies on the systems with different degree of the charge transfer and/or with different strength of the hydrogen bonds (with or without proton transfer as well). The complexes containing TMP are the ideal objects for such investigations since a variety of possible structures exists. Therefore on the basis of the comparison of the rotational potential parameters we intend to draw some conclusions about the main factors affecting the rotation of CH<sub>3</sub> groups at low temperature and the role of charge transfer in the reduction of the barrier to this rotation.

The results of the methyl group tunneling will be compared to those obtained from the <sup>1</sup>H NMR spin-lattice relaxation time measurements in a wide temperature range.

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[1] M. Prager, A. Pawlukojć, L. Sobczyk, E. Grech, H. Grimm, J. Phys.: Condens. Matter **17**, 5725 (2005).

[2] M. Prager, A. Pietraszko, L. Sobczyk, E. Grech, T. Seydel, A. Wischnewski and M. Zamponi, J. Chem. Phys. **125**, 194525 (2006)

[3] A. Piecha-Bisiorek, G. Bator, W. Sawka-Dobrowolska, L. Sobczyk, W. Medycki, G. J. Schneider, J.Phys.Chem., (2014) submitted.

## NMR Spectroscopic Study of Tautomerism in Solution and in the Solid State

Erich Kleinpeter

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My earlier overview of methods to study *tautomerism* in 2000 [1] included UV-VIS spectroscopy, diffraction methods and theoretical methodologies (both force field and ab initio MO/DFT treatment of tautomerism) which require separate chapters in a new book *Tautomerism – Methods and Theories* [2] (Chapters 2, 8, 10 and 13, respectively). The same is indicated for isotope effects in NMR spectroscopy for studying tautomeric equilibria owing to Poul Erik Hansen's continuous and great efforts with numerous collaborators (Chapter 5). So I will concentrate in the present report on *solution and solid state NMR spectroscopy* employing *chemical shifts* of magnetically active nuclei at our disposal and the *scalar couplings* between the latter; in few cases *dipolar coupling* was applied, however, in case of tautomeric equilibria fast on the NMR time scale, both spatial and dynamic information can be mixed and conclusions related to thermodynamics can be rather erroneous; *only unequivocal tautomerism evidences are given*.

The corresponding literature search (tautomerism/NMR) from 1997 up to now provided 200 to 300 references per year, thus, it is within the frame of this report impossible to consider the whole material. On the other hand, it is more than relieving that the designated groups of the topic, Alan R. Katritzky and José Elguero et al. [3,4], Branko Stanovnik [5] and Tony Lyčka [6] published reviews considering the state of the art. Some of the overviews are of same age as my former report [1] and employed methodologies were further applied by the groups or others. If new methodologies to study tautomerism by NMR were applied, they are given in this report. If anybody is interested in the methods and characteristic applications of <sup>15</sup>N NMR spectroscopy, a nucleus being of crucial importance in studying tautomerism, the reviews of Radek Marek et al. [7] can be recommended.

In solution, the most interesting topic beside the kind of tautomerism and structural influences proves to be the *solvent effects caused by intermolecular interactions solvent/solute* through hydrogen bonding and non-bonding interactions as are van der Waals forces, hydrophobic and hydrophilic dipole and  $\pi$  interactions. Solvent effects will not be especially covered, I will concentrate on nature of tautomerism and on the various methodologies to study the latter by NMR spectroscopy with special attention to the various nuclei which were employed.

In the solid state, solvent effects are replaced by packing forces in crystals and bulk effects in amorphous solids which are often of stronger influence on chemical shifts in the corresponding CP–MAS solid state NMR spectra than the solvent in solution spectra. For this reason, solid state structures (and solid state NMR spectra) may not be identical to those in solution. The specific solid state shift effects must be considered when comparing relevant tautomeric information in the two states. In the solid state, tautomeric structures could be frozen but also tautomerism could be still fast on the NMR time scale, even polymorphism and different tautomers in the unit cell could be observed. In the latter case, as in solution, low temperature measurements can complement tautomerism studies. Characteristic, representative examples will be given.

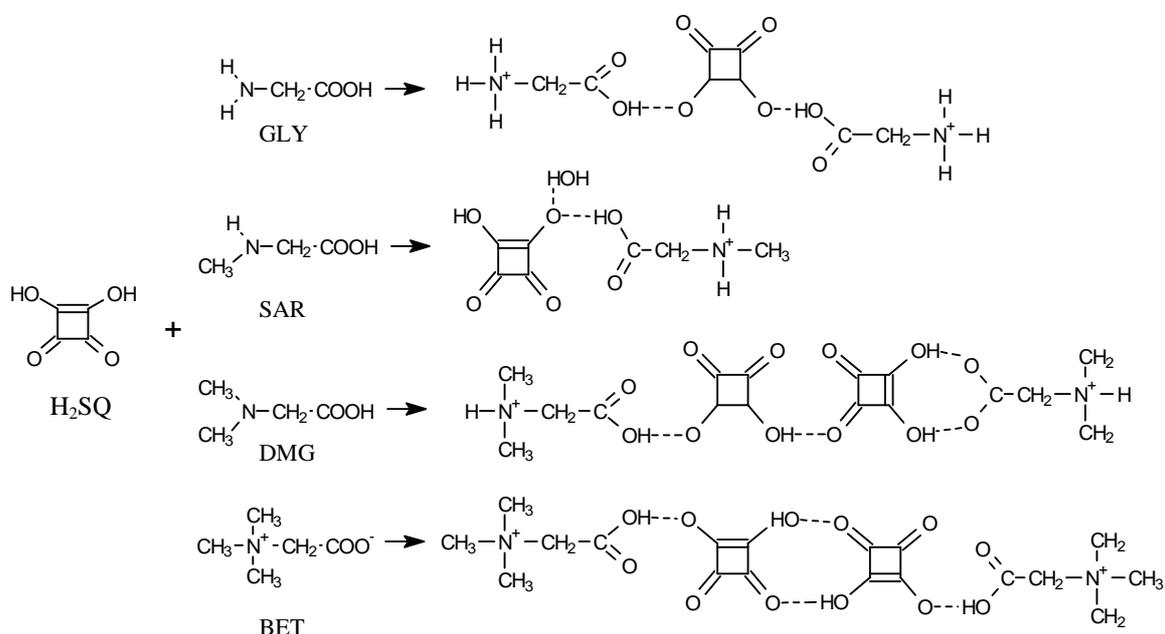
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- [3] (a) J. Elguero, A. R. Katritzky and O. V. Desisko, *Adv. Heterocycl. Chem.* **2000**, 76, 1-84; (b) R. M. Claramunt, J. Elguero and A. R. Katritzky, *Adv. Heterocycl. Chem.* **2000**, 77, 1-50; (c) W. Friedrichsen, T. Traulsen, J. Elguero and A. R. Katritzky, *Adv. Heterocycl. Chem.* **2000**, 76, 85-156; (d) V. L. Minkin, A. D. Garnovskii, J. Elguero and A. R. Katritzky, *Adv. Heterocycl. Chem.* **2000**, 76, 157-323.
- [4] R. M. Claramunt, C. López, M. D. Santa María, D. Sanz and J. Elguero, *Progr. NMR Spectr.* **2006**, 49, 169-206.
- [5] B. Stanovnik, M. Tishler, A. R. Katritzky and O. V. Denisko, *Adv. Heterocycl. Chem.* **2006**, 91, 1-134.
- [6] A. Lyčka, *Ann. Rep. NMR Spectroscopy* **2000**, 42, 1-57.
- [7] (a) R. Marek and A. Lyčka, *Current Org. Chem.* **2002**, 6, 35-66, and references therein; (b) R. Marek, and V. Sklenář, *V. Ann. Rep. NMR Spectrosc.* **2005**, 54, 201.

## X-ray and DFT studies of interactions between glycine derivatives and squaric acid

Zofia Dega-Szafran, Michalina Anioła, Andrzej Katrusiak, Mirosław Szafran

Faculty of Chemistry, Adam Mickiewicz University, Poznań, Poland  
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Four new hydrogen-bonded complexes of a simple amino acid glycine (GLY) and its methyl derivatives – sarcosine (N-methylglycine, SAR), dimethylglycine (DMG) and betaine (N,N,N-trimethylglycinium, BET) with squaric acid (3,4-dihydroxy-3-cyclobuten-1,2-dione, H<sub>2</sub>SQ) have been synthesized and characterized by X-ray diffraction, FTIR and NMR spectra. The complexes differ in a stoichiometry, interaction with H<sub>2</sub>SQ and hydrogen-bonding system.



Depending on methylation of glycine in its co-crystals with squaric acid, its dianions, monoanions, neutral and mixed forms have been stabilized. This process has been correlated with the number of N-H...O bonds to the oxygen atoms of squaric acid and the N-H donors capability of glycine derivatives. The effect of the presence of methyl groups on the proton and carbon-13 chemical shifts has been studied. The DFT calculations have been performed for one unit of complexes and suggested stable zwitterionic structures of SAR, DMG and BET in the complex with H<sub>2</sub>SQ, except GLY unit, which appears as an uncharged (neutral) form.

## Aprotic Polar Solvent Dynamics and Proton Tautomerism in Strong Hydrogen Bonds. NMR, UV-vis and MD Study

P.M. Tolstoy,<sup>a</sup> S.A. Pylaeva,<sup>b</sup> B. Koeppe,<sup>c</sup> E.Yu. Tupikina,<sup>b</sup> C. Allolio,<sup>d</sup>  
D. Sebastiani,<sup>d</sup> G.S. Denisov,<sup>b</sup> H.-H. Limbach<sup>e</sup>

<sup>a</sup> St. Petersburg State University, Dep. of Chemistry, St.Petersburg, Russia

<sup>b</sup> St. Petersburg State University, Dep. of Physics, St.Petersburg, Russia

<sup>c</sup> Humboldt University of Berlin, Berlin, Germany

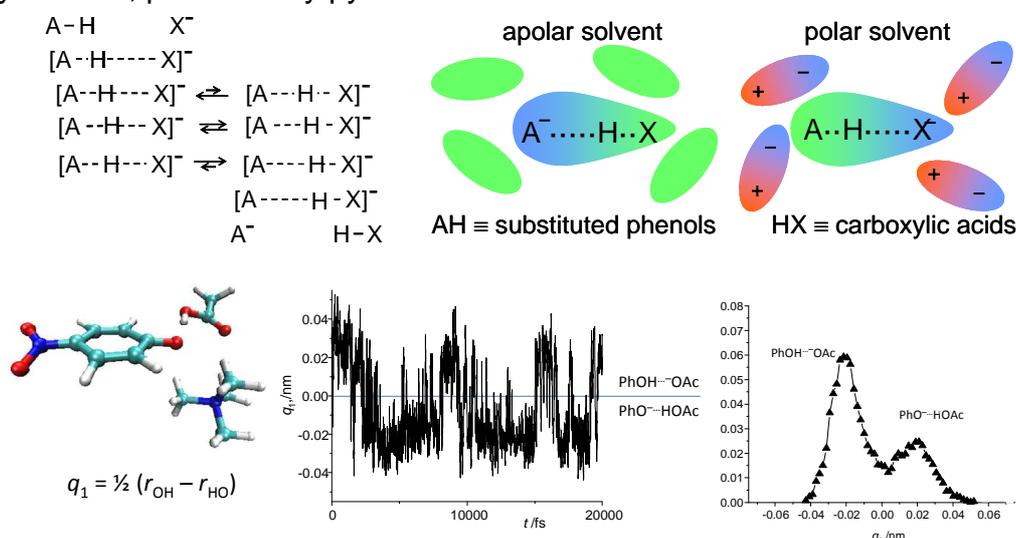
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Geometries of strong H-bonded complexes in solutions are quite susceptible to various weak solvent-solute interactions. Thermal fluctuations of the immediate surroundings lead to re-arrangement of the H-bond geometry. As a result, a distribution of rapidly interconverting structures of a complex is created. The process of interconversion of individual configurations is usually fast on the NMR time scale and slow on the optical time scale.

In this work we present the results obtained for two model systems: neutral (OHN) and anionic (OHO<sup>-</sup>) strong H-bonded complexes dissolved in polar aprotic solvents (CDF<sub>3</sub>/CDF<sub>2</sub>Cl, CD<sub>2</sub>Cl<sub>2</sub>) by means of low-temperature NMR, combined NMR/UV-Vis, some IR spectroscopy and MD simulations. Interacting partners include carboxylic acids, phenols any pyridines.



Analyzing the H-bond geometries we reconstruct an “adiabatic” proton transfer pathway (scheme in figure, top left), attempt to identify the essential solvent-solute interactions which could explain the experimentally observed trends (cartoon in figure, top right) and effects of thermal fluctuation of the solvent on the proton transfer processes (example based on MD simulations in figure, bottom).

*This work was partially funded by RFBR grant 14-03-00111-a, as well as by the German-Russian Interdisciplinary Science Center (G-RISC) funded by the DAAD.*

## Charge-inverted hydrogen bond as a new type of interaction

M. Jabłoński

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By performing ab initio calculations for a wide range of dimers with various types of interactions involving a hydridic hydrogen atom (hydride hydrogen bond, dihydrogen bond, agostic bond, etc.) we show that the recently proposed charge-inverted hydrogen bond (CIHB)<sup>[1-6]</sup> should indeed be investigated as a new type of interaction. This conclusion is obtained on the basis of formal definitions of relevant interactions as well as on the quantum theory of atoms in molecules<sup>[7]</sup> and the hybrid variational-perturbation scheme of the decomposition of the interaction energy<sup>[8]</sup>. Particular attention is paid to comparison of CIHB with agostic-type interactions. Additionally, it is shown that CIHB is somewhat similar to strong dihydrogen bonds. The origin of this finding is also presented.

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## $\pi$ -Electron delocalization in charged cyclic hydrocarbons

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Polycyclic aromatic hydrocarbons (PAHs), as systems fulfilling the magic Huckel  $4n+2$  rule, exhibit several properties being characteristic of aromatic systems. Although unsubstituted PAHs and their various derivatives are very common in chemistry, their isolated cationic and dicationic counterparts (which, in fact, are not  $4n+2$  pi-electron systems!) are practically unavailable in experimental conditions due to extreme reactivity of such chemical species. However, increasing attention has recently been paid to positively charged PAHs, among others, due to the fact that such compounds are supposed to be widespread in the interstellar space. [1,2] Also recent spectroscopic studies indicates that in specific conditions dicationic forms of some PAHs may be more stable than their parent neutral counterparts [3] Recently it was also demonstrated that charged PAHs may act as intermediate system in pi-type communication between substituents. [4] The above and other results of recent studies on charged PAHs will be presented and the observations will be discussed in the context of similarities and differences between neutral and charged counterparts.

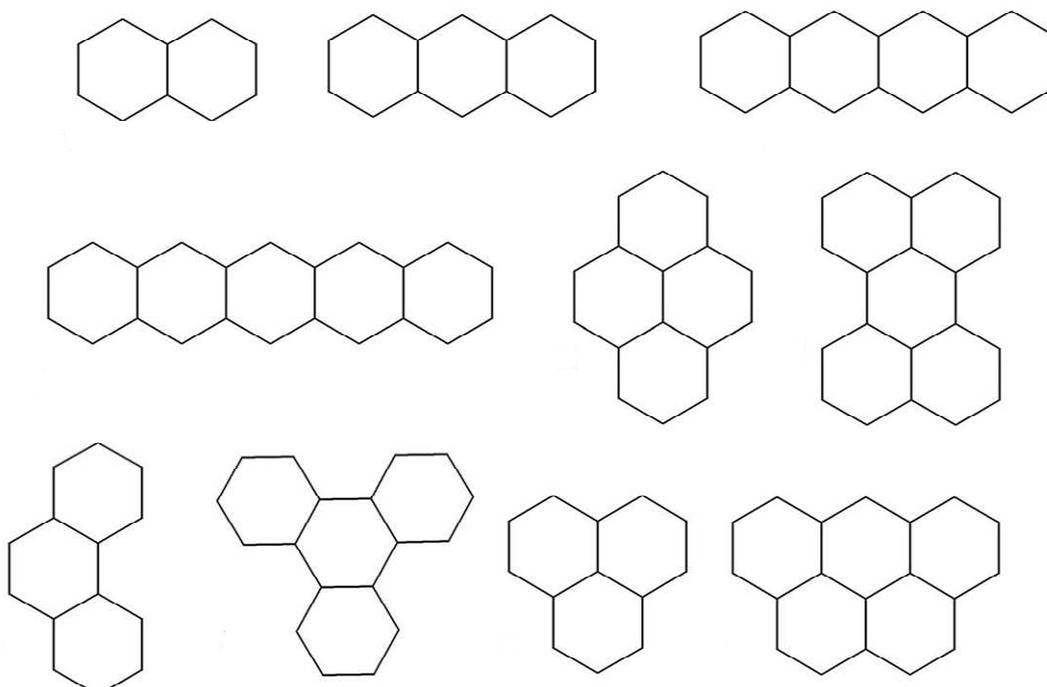
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## On singlet state cations of polycyclic aromatic hydrocarbons

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A theoretical study of singlet state cations of polycyclic aromatic hydrocarbons shown in the picture below is presented.



Appropriate symmetry suitable for calculations is chosen for each of the systems. The excitation states of such species are obtained by the time dependent DFT method.[1] The results obtained with the use of different basis sets are compared. The electronic transitions are described and the relationships for the lowest-lying transitions states of different species are delineated. The properties of in-plane and out-of-plane transitions are found. The TD-DFT results are compared with the experimental data[2] available.

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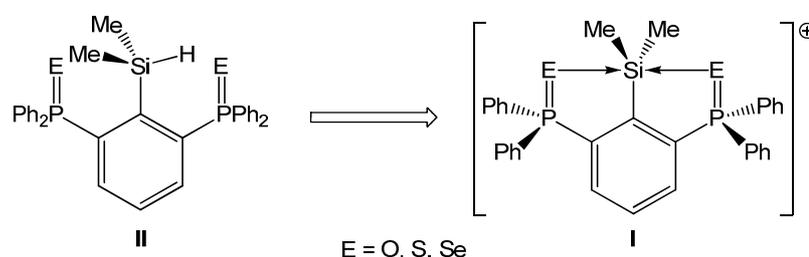
## Hypercoordinated triorganosilyl cations stabilized by pincer type ligands: structures and bonding

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Hypercoordinated triorganosilyl cations **I** stabilized by pincer-type ligands have been prepared by abstraction of hydride ions from the neutral precursors **II**. The stabilization of the cations is achieved by two intramolecularly coordinating P=E groups.



We report X-ray single-crystal structure determinations of precursors **II** and cations **I** studied. Based on their geometries from crystals the DFT calculations have been performed (full optimizations of geometry) at the B3PW91/6-311+G(2df,p) level of theory. The further investigation of the structurally relevant bonds based on various topological and integrated criteria deduced from theoretical calculations according to QTAIM theory [1] and ELI-D approach [2] has been performed. A combination of these two methods provides quantitative information about the nature of analyzed bonding C–Si, C–P, E–P and E–Si (where E = O, S, Se).

### Acknowledgements

We would like to thank the Deutscher Akademischer Austauschdienst (DAAD) for a two-month fellowship for L. Chęcińska.

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**$\pi$ -ELECTRON CONJUGATION IN POLYENES**

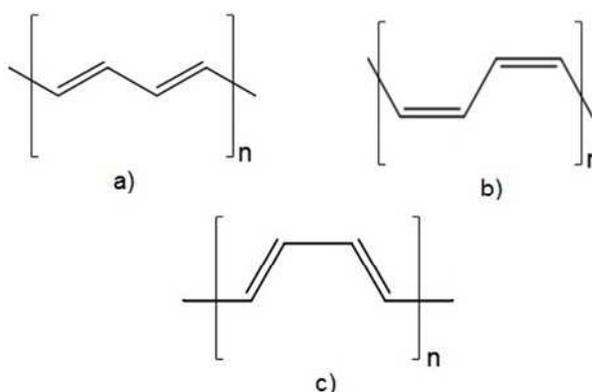
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One of the most important linear polymer is polyacetylene, which is the subject of many studies, both experimental and theoretical. Polyacetylene is composed of long chains, in which the carbon atoms are bonded with alternate double and a single bonds. It exists in two forms, *cis* and *trans*, of which there are two variations of the *cis* form, that is, *cis-transoid* and *trans-cisoid*.

The purpose of our study was to estimate the degree of delocalization of  $\pi$ -electrons in polyacetylene (in the form of an infinite chain) and its analogs with a finite number of bonds. In the first stage of the study the geometry optimization was performed in Gaussian09 program (DFT-B3LYP/6-31+G(d) level of theory), and then the degree of delocalization was estimated as a function of the length (number of C atoms) of the hydrocarbon chain (up to 42 carbon atoms). The measure used to calculate the degree of delocalization was the structural aromaticity index HOMA (Harmonic Oscillator Model of Aromaticity)<sup>[1]</sup>. The obtained energy parameters indicate the *trans* form as the one being the most stable (thermodynamically). When considering the two *cis* forms, it turned out that the more stable is the *cis-transoid* one.

The next step was to carry out the periodic calculations, which were performed using a B3LYP functional and a series of various basis sets. The use of different basis sets allowed to estimate the effect of level of calculations on the final result achieved. Obtained results are consistent with experimental data available in the CSD<sup>[2]</sup>.



*Isomeric forms of polyacetylene a) trans b) cis-transoid c) trans-cisoid.*

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## The temperature-dependent polymorphism of an imidazole-N-oxide

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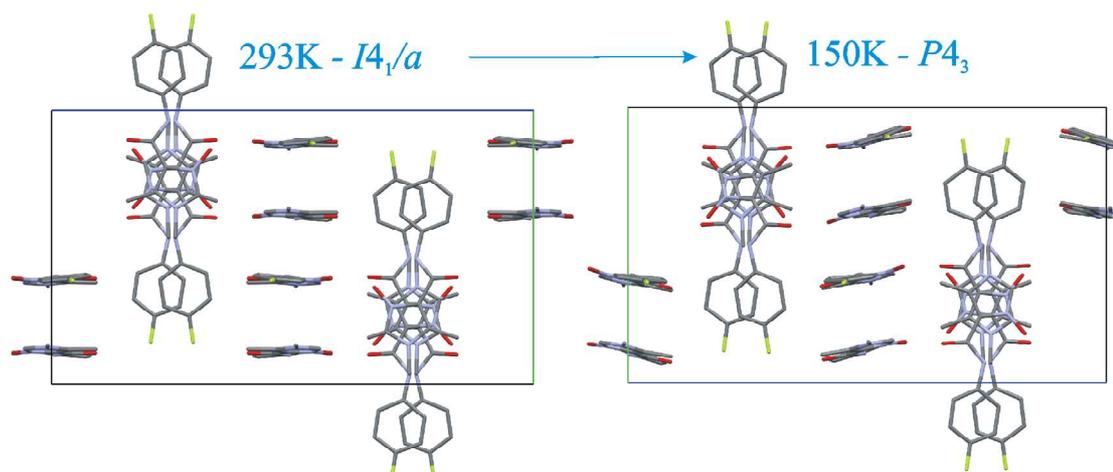
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Research on new imidazole and benzimidazole *N*-oxides and their applications in biology has focused particular interest in recent years as some of them exhibit biological activity, e.g. as insecticides, plant growth regulators, antiinflammatory and antiprotozoal agents [1,2]. There are also published some reports on imidazole derivatives containing amide or hydrazide groups as potential pharmaceuticals [3].

Herein we present results of X-ray studies on *N*-(4-fluorophenyl)-1,5-dimethyl-1*H*-imidazole-4-carboxamide 3-oxide, a compound which reveals the temperature-dependent polymorphism associated with the crystallographic symmetry conversion [4]. The observed crystal structure transformation corresponds to a symmetry reduction from  $I4_1/a$  (I) to  $P4_3$  (II) space groups. The phase transition mainly concerns the subtle but clearly noticeable reorganization of molecules in the crystal space, with the structure of individual molecules left almost unchanged.

The Hirshfeld surface analysis shows that various intermolecular contacts play an important role in the crystal packing, revealing graphically the differences in spatial arrangements of the molecules in both polymorphs. The *N*-oxide oxygen atom acts as a formally negatively charged hydrogen bonding acceptor in intramolecular hydrogen bond of N-H...O<sup>-</sup> type. The combined crystallographic and theoretical DFT methods demonstrate that the observed intramolecular *N*-oxide N-H...O hydrogen bond should be classified as a charge-assisted, closed-shell very strong non-covalent interaction.



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**An atomic view of metal electrolyte/interfaces:  
"Electrochemical surface science"**

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"Surface Science" in ultrahigh vacuum (UHV) based on a plethora of highly sensitive and surface specific methods has produced an incredibly detailed insight into properties and processes at well-defined single-crystal surfaces on the atomic and molecular scale. This knowledge is the essential basis for many – if not most – modern and future technologies.

Likewise modern "Electrochemical Surface Science". i.e. the in situ investigation of single crystal metal electrodes in electrolytic solutions, is able nowadays to provide the same detailed atomic-scale insight in the properties and processes at these metal/electrolyte interfaces which we are used to from UHV-surface science. This is again very important for the understanding and optimization of many "wet" technologies with a promising future, like electro-catalysis (fuel cells), materials science (plating, etching), nanotechnology (computer chips), etc..

In this contribution the combination of classical electrochemical methods such as cyclic voltametry with in-situ scanning tunneling microscopy (STM), in-situ grazing incidence x-ray diffraction (XRD), in-situ infrared spectroscopy (IR), and ex-situ synchrotron-based X-ray photoelectron spectroscopy (XPS) will be used to study the specific adsorption of anions (e.g. Cl, I, SO<sub>4</sub> or S on Cu(100) and Cu(111)), the two-dimensional phase formation (e.g. CuI on Cu(100) and Cu(111), CdCl<sub>2</sub> on Cu(111) and CdS on Cu(111)), and the self-organization and reactivity of organic molecules (namely viologens and porphyrins) on Cu(100) and Cu(111) surfaces in solution with atomic resolution. The benchmark quality of the data is a reliable basis for theoretical model calculations.

## STM studies on 2D self-organization of thiophene - based organic semiconductors

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The important advantage of organic electronics is a wide possibility of precise tuning of electronic and optoelectronic properties of organic semiconductors by chemical modification of their molecular structure. However, the another factor which seriously influences the final properties of organic electronic devices (including charge transport, etc) is supramolecular organization of active material. It is evident that progress in this field can be achieved using methods which are able to afford not only an averaged information on the large area but also the detailed structure of the surface in 'real' space.

In this talk I will discuss ability of Scanning Tunneling Microscopy to study at molecular resolution the structural and electronic properties of ordered layers of thiophene-based organic semiconductors. Two examples of our investigations will be presented.

In the first part I will focus on ordering process of poly(dioctyl-2,2':5',2''terthiophene) monolayers deposited on HOPG. The structures of monomolecular layers processed from monodispersed fractions of different molecular mass have been compared for two derivatives with different position of alkyl side groups (3,3'' and 4,4''). The evidently observed differences in supramolecular organization of these oligomers enable to discuss two problems of crucial importance: how does this organization depend on the type of regioregularity? and how it evolves with increasing chain length.

The second example concerns new semiconductors of donor-acceptor-donor (DAD) type. The studied adsorbates are octyl derivatives of complex molecules consisting of an electron withdrawing central ring (thiadiazole, tetrazine) symmetrically attached to two dithiophene donor parts. In particular the effect of the electron-accepting unit and the alkyl substituent's position on the type and extent of 2D supramolecular organization of these semiconductors on HOPG substrate will be discussed. Finally, a comparative study of 3D organization, deduced from the X-ray diffraction patterns, will be also presented clearly confirming the polymorphism of the studied adsorbates.

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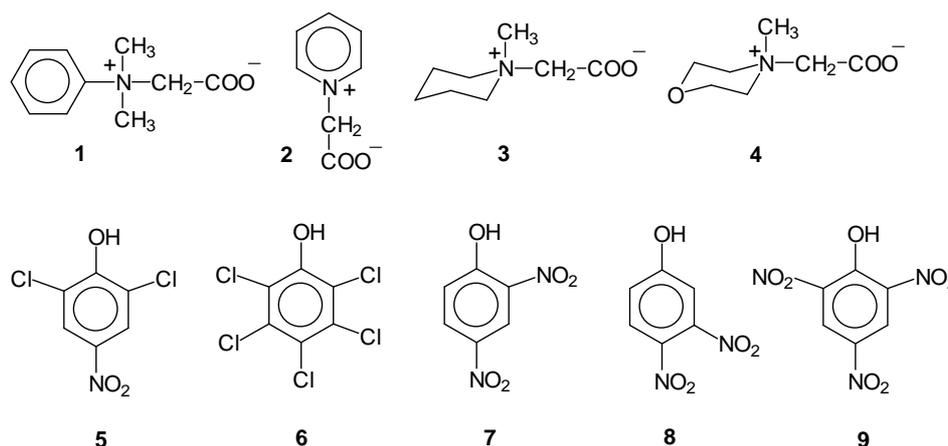
## Hydrogen bonds in complexes of betaines with phenols

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Zwitterions are compounds with oppositely charged centers and are often referred to as betaines, dipolar ions, salt-bridged-containing molecules and inner salts. This diverse nomenclature reflects the extraordinary importance of these species in biological transformations, organic synthesis, preparation of novel materials and as chromatographic supports [1-3]. Betaine ( $(\text{CH}_3)_3\text{N}^+\text{CH}_2\text{COO}^-$ ) is distributed in animals, plants, microorganism and is a significant component of many foods [4].

Betaines form 1:1 and 2:1 complexes with mineral and organic acids [5,6]. Interesting are complexes of betaines [dimethylphenyl betaine (**1**), pyridine betaine (**2**), N-methylpiperidine betaine (**3**) and N-methylmorpholine betaine (**4**)] with phenols [2,6-dichloro-4-nitro-phenol (**5**), pentachlorophenol (**6**), 2,4-dinitrophenol (**7**), 3,4-dinitrophenol (**8**) and picric acid (**9**)].



Pyridine betaine with **5** [7] and **6** [8] form 1:1 and 1:2 complexes. N-Methylpiperidine betaine with **7** form 1:1 complex, N-methylmorpholine with **9** form 1:1 and 2:1 complexes, while dimethylphenyl betaine interacts only with two molecules of **5** (1:2 complex). Molecular interactions between betaine and phenols were studied by X-ray diffraction, DFT calculations, FTIR and NMR spectroscopies.

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## Pressure-modulated intermolecular interactions

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Pressure can drastically affect intermolecular interactions, not only by compressing the contacts present at normal conditions, but also by favouring interactions of minor significance, for example CH...N and CH...O contacts. This pressure effect often leads to phase transitions of chemical compounds and their new forms, such as hydrates, solvates and even to chemical reactions and new products. [1-3]. It will be shown that such a pressure-promoted competition involving hydrogen bonds CH...O and OH...O induces a phase transition in sucrose, leading to a new polymorph of this compound. In other structures, the pressure drastically changes the preference of crystallization of compounds, favouring the formation of solvates unstable at normal conditions. We have also observed the pressure-induced formation of solvates to a certain pressure value, above which the neat unsolvated compounds are obtained again. The effect of pressure is relatively easy for studying by performing in situ crystallization in a diamond-anvil cell, and a short introduction to this experimental method will be presented along the results and their discussion.

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## **Application of dipole moments in modeling the structure of aggregates in solutions.**

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The presentation concerns the problem of selfaggregation of alkyl substituted ureas and thioureas, which play an important role in many biological processes, interacting with proteins. To understand the mechanisms of such interactions we have studied the process of the formation of selfaggregates of these compounds in function of concentration in a few non polar solvents. Our studies have been performed by simultaneous use of different complementary methods like an average molecular weight, dipole moments and IR spectra. Average molecular weight measurements allowed us to estimate the degree of aggregation. IR spectra gave the possibility for quantitative description the aggregation by determining the association constant. It was demonstrated that aggregation strongly depends on the symmetry of substitution and type of proton accepting groups. The dipole moments in principle can be used to estimate the structure of aggregates. It was found that dipole moments dependence on concentration differs between various types of derivatives. An approach to understand the obtained experimental characteristics was undertaken by using theoretical methods at DFT B3PW91/6-31+G(d,p) level. It appeared however, that results of calculations were not consistent with experimental tendencies. The calculated relative energies of states did not reproduce the experiment. It was shown, that using the model of simultaneous specific and bulk interactions with solvent molecules in building the dimers one is able to approach the experimental trend in dependence of dipole moments on concentration. In the present approach we try to find out what is the distribution of different forms of aggregates in dependence on concentration. Using such an information we are able more in detail apply the calculated dipole moments in interpretation of the experiment.

## Electrostatic Potential at Nuclei: an Accurate Reactivity Descriptor for Organic Compounds

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The lecture surveys mostly original work from our laboratory on the application of the electrostatic potential at nuclei (EPN) as a reactivity index in quantifying hydrogen bonding as well as different reactions of organic compounds. The EPN index was defined and introduced by E. B. Wilson in 1962. However, it was first applied as a reactivity index much later (Bobadova-Parvanova & Galabov, 1998; Galabov & Bobadova-Parvanova, 1999; Dimitrova, Ilieva, & Galabov, 2002). Numerous applications showed that the EPN index, an accurate quantum mechanical quantity, predicts with remarkable accuracy the energy shifts accompanying hydrogen bonding. The theoretically evaluated EPN descriptor correlates also excellently with experimental and theoretically evaluated kinetic parameters for a number of important organic reactions. Especially fruitful is the application of EPN in quantifying the reactivity of aromatic compounds. The reactivity patterns of several typical reactions of aromatic systems are considered. The performance of alternative reactivity descriptors, such as theoretical atomic charges, the Parr electrophilicity index, and the experimental Hammett constants, are considered as well. A computational approach for the evaluation of substituent constants is described.

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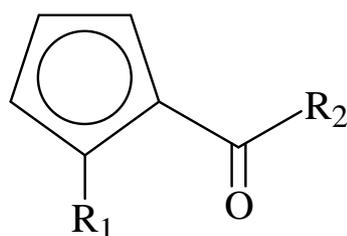
## The influence of DFT functional on QTAIM calculations

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All atomic and molecular properties are governed by the electron density distribution. Thus, the methods that deal with the analysis of the electron density distribution should have a particular appeal for chemists and help to understand the electron structure of molecules and thus interactions. Nowadays, the very powerful method in investigating inter- and intramolecular interactions is Quantum Theory of Atom in Molecules (QTAIM) introduced by Bader.[1]

In this presentation we investigate the influence of type of DFT functional on QTAIM calculations. For initial studies we chose model system taken from two crystal structures of pyrrole-2-yl-dichloromethyl ketone (Scheme 1). For complexes (dimers and tetramer) with geometry taken from experiment we performed DFT calculations using various functionals. Additionally, results of MP2 calculations were used as a reference data.



Scheme 1.  
Structure of the 2-substituted pyrroles

- I  $R_1=H$ ,  $R_2=CHCl_2$   
II  $R_1=CH_3$ ,  $R_2=CHCl_2$

Pyrroles are both important natural products and crucial starting materials for the synthesis of porphyrins. Nevertheless, a brief survey of the crystallographic literature shows that only a few crystal structures of aromatic N-unsubstituted monopyrroles have been reported [2]. In crystal structures of investigated compounds, we expected the existence of halogen and hydrogen bonds. X-ray structure determinations showed only the latter one.

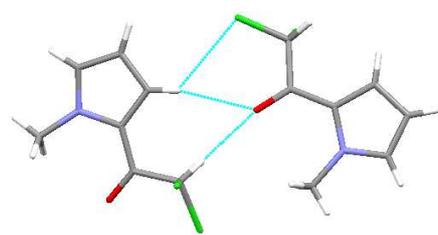


Figure 1.  
H-bond dimer motif in crystal structure of compound II

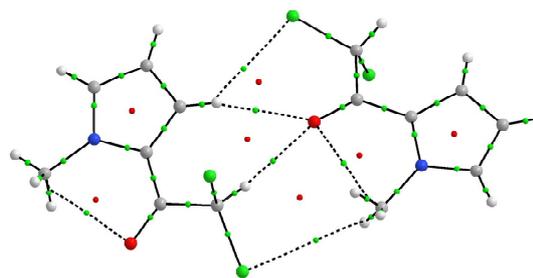


Figure 2.  
The molecular graph of dimer of compound II

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## Molecular systems with intramolecular H-bonds – rigid or nonrigid: that is the question

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Proton transfer in hydrogen bonds is one of the most important phenomena influencing dynamical behavior in many chemical and biological systems. In many living systems very fast proton transfer processes occur and moreover in many cases a proton behaves as a quantum particle tunneling through the energy barrier. Despite widespread importance of tunneling effects, the quantum character of proton transfer is not frequently used in theoretical models or is restricted only to the zero-temperature quantum effects in simple model systems with severe reduced dimensionality of considered systems.

The rapid development of computer power with efficient codes as well as theoretical models gives us an opportunity to study the dynamics of proton transfer processes with a great accuracy. The Car-Parrinello Molecular Dynamics (CPMD) is very efficient scheme for description of dynamics of molecular systems. In contrary to the classical molecular dynamics the CPMD calculations do not require an a priori determined model interaction potential because the internuclear forces for each configuration of nuclei are calculated from the first principle – the model Hamiltonian is defined in the Density Functional Theory formalism. The quantum behavior of proton from a hydrogen bridge as well as remaining heavy atoms can be taken by means of the Path Integration Molecular Dynamics (PIMD).

The chemical systems with strong single or double O-H...O hydrogen bonds are very common in many chemical and biological systems. In the lecture results of CPMD and PIMD calculations for the examples of proton transfer in strong intramolecular O-H...O and N-H...N hydrogen bonds in crystals will be presented. The classical and quantum nature of bridged proton will be discussed. Moreover, the results of CPMD and PIMD simulations for hydrogen maleate anion in different environments, starting with isolated anion, going through two crystal structures (sodium and potassium salts) then to an aqueous solution demonstrate that the mobility and the position of proton in O-H...O bridge is entirely related to the interaction with environment.

**Acknowledgements:** Calculations were performed at the Wrocław Centre for Networking and Supercomputing (WCSS) and the Academic Computer Centre in Gdańsk (CI TASK).

## Experimental and theoretical (DFT and TD-DFT) investigation of the ground and excited state of BODIPY dyes

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Quantum-mechanical research on fluorescent dyes of 4,4'-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) type was done. Investigation of the solvent influence in the wide range of solvent polarity, and substituents on the position of absorption and emission bands of BODIPY dyes by TD-DFT method was studied.

The calculations were carried out with the Gaussian09 program using PBE0, M062X functionals and 6-31+G(d,p) basis set (Figure 1). Ground and excited states of compounds were studied by DFT and TD-DFT methods respectively.

Polarizable Continuum Model (PCM) was used to investigate influence of solvent polarity effects on the ground and excited states of compounds. The contribution of solvent effects was studied within linear response (LR), and state-specific (SS) quantum mechanical approaches.

Agreement of experimental and theoretical data was shown.

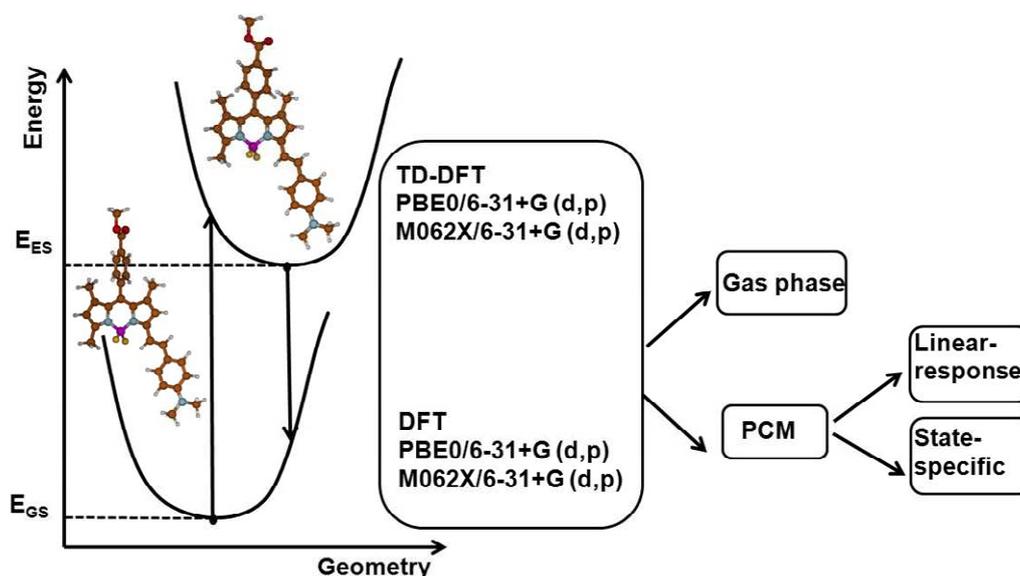


Figure 1. Representation of calculation scheme.

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## Primary photoprocess of vision

T. Andruniów

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The primary photochemical reaction in rhodopsin is the cis-trans isomerization of the retinal chromophore. It is characterized by an ultrafast speed, high selectivity, and high efficiency since 32-35 kcal/mol of the absorbed photon energy is stored in the primary photoproduct bathorhodopsin.

We report the results of the CASSCF/MM and CASSCF/MM MD calculations for the native and synthetic chromophores to investigate the effect of the chromophore distortion and substitution pattern on the effectivity of the photoreaction.

## Structure and Dynamics of Conjugated Polymers as Studied by Synchrotron Radiation (SR) and Neutron Scattering Measurements

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Conjugated polymers constitute a nowadays very important class of macromolecules due to their electronic properties. In their neutral form they can be used in devices as organic field effect transistors or photovoltaic devices while in their oxidized forms they can become true organic metals [1]. As expected, these properties are very dependent on the morphology, the local structure and the molecular dynamics prevailing in these polymers once processed as free standing films or thin layers. In particular the disorder (static and dynamical) effects will highly influence the value of the average mean free path of charge carriers in the molecular lattice since the energetic landscape opened to such an electrical transport mainly takes its origin in extended overlapped pi-conjugated orbital network.

Accordingly, the knowledge of the structure at different length scales and of the dynamics at different time scales is crucial for understanding the different parameters which may limit the performances of organic (opto)electronic devices based on these macromolecules. While many aspects can be studied with techniques available in the laboratory, through different examples we have studied, we will show how SR and Neutron scattering measurements could provide us with additional valuable knowledge. We will try to show, through these examples, what are the most important properties of these probes available in large facilities which permit to draw such a profit.

By doing incoherent quasielastic neutron scattering measurements we obtained pertinent information on the correlations between the electrical properties and the counter-ions dynamics in conducting films of the emeraldine salt form of polyaniline (PANI).

More recently we have investigated in details the structure of hybrid materials made of poly(3-hexyl-thiophene) (P3HT) mixed with CdSe nanocrystals to be used in solar cells. By analyzing grazing incidence SR X-rays diffraction measurements performed on thin layers (few dozens of nanometers) we will show how room temperature rubbed pure P3HT films of different molecular weights organize on a substrate and how the polymer mixed with CdSe nanorods are mutually aligned upon rubbing.

### Reference

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## GR-signaling in HPA-axis fast non-genomic glucocorticoid processes studied by Fluorescence Correlation Spectroscopy

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The hypothalamic-pituitary-adrenal axis (HPA axis) is a major part of the neuroendocrine system responsible for the regulation of the response to physical or mental stress and for the control of the synthesis of the stress hormone cortisol. Fast and slow glucocorticoid feedback mechanisms regulate the HPA axis response to stress signals in anterior pituitaries.

In this study we monitored changes of single molecules involved in glucocorticoid receptor (GR)-signaling and fast non-genomic feedback processes by a newly developed, highly sensitive Fluorescence Correlation Spectroscopy (FCS) Assay. Nanomolar changes of extracellular ACTH and Dexamethasone molecules as well as cytoplasmic Dexamethasone-bound GR-heterocomplexes were detected within seconds and minutes after CRH or dexamethasone administration to AtT20 anterior pituitary cells.

The quality of the data obtained by FCS allowed to study fast feedback mechanisms in the HPA-axis regulatory system and allowed to support the development of a mathematical model of that HPA-axis network. Mass action and Michaelis Menten enzyme kinetics were used to provide a mechanistic description of the feedback mechanisms within the pituitary gland cells by which cortisol inhibits its own production. A separation of the nucleus from the cytoplasm by compartments in our model enabled a differentiation between slow genomic and fast non-genomic processes and an extended dynamic repertoire in comparison to existing HPA models.

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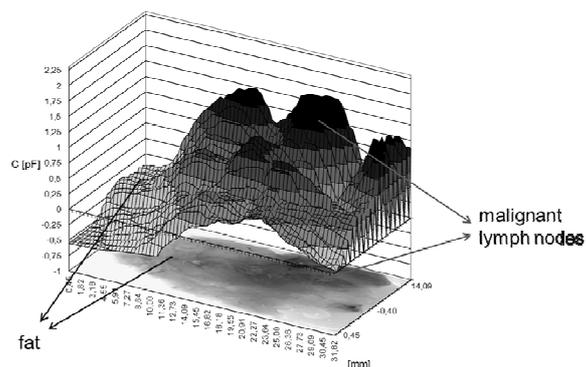
## **Putative future application of small-molecule organic inhibitors of voltage-gated potassium channels Kv1.3 in chemotherapy of some tumor diseases**

A. Teisseyre, J. Gąsiorowska, A. Uryga, K. Michalak

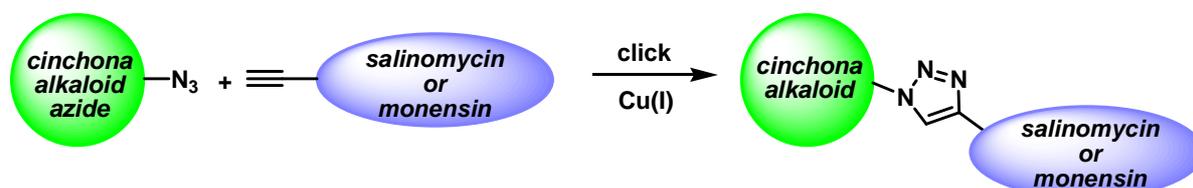
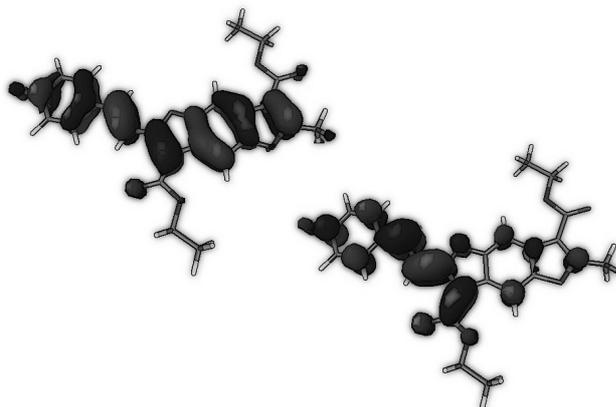
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Voltage-gated potassium channels Kv1.3 are integral membrane proteins, which are activated („open”) upon change of the cell membrane potential enabling a passive flux of potassium ions across cell membrane. The channels are expressed in many different tissues, both normal and cancer. Since 2005 it is known that the channels are expressed not only in the plasma membrane, but also in the inner mitochondrial membrane. Activity of Kv1.3 channels plays an important role, among others, in setting the cell resting membrane potential, cell proliferation, apoptosis and volume regulation. For some years, these channels are considered as a potentially new molecular target both in diagnostics and therapy of some tumor diseases. It was shown that blocking of Kv1.3 channels in the plasma membrane inhibited proliferation of cancer cells expressing Kv1.3 channels, whereas inhibition of the channels in the inner mitochondrial membrane induced apoptosis (programmed death) of these cells. Kv1.3 channels are inhibited by many chemically unrelated compounds, both inorganic and organic. Most promising candidates for a potential application in medicine are some small-molecule organic compounds, since they combine a high ability for selectively killing cancer cells with a good bioavailability and a low toxicity.

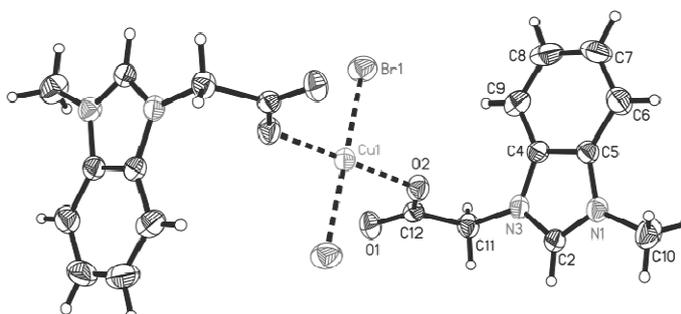
This presentation focuses on small-molecule organic inhibitors of Kv1.3 channels and their putative application in therapy of some cancers. In the last section, biologically-active plant-derived compounds from the groups of flavonoids, chalcones and stilbenes and their natural and synthetic derivatives that were tested in our Laboratory of Bioelectricity and appeared to be inhibitors of Kv1.3 channels in cancer cells are presented. A possible application of some compounds from these groups to support therapy of cancer diseases, such as breast and lung cancer, melanoma or chronic lymphocytic leukemia (B-CLL), is announced.



## Posters in alphabetical order



8 examples  
(49-82% yield)



**Dielectric properties of halloysite and halloysite – formamide intercalate**

Mariusz Adamczyk, Kazimierz Orzechowski

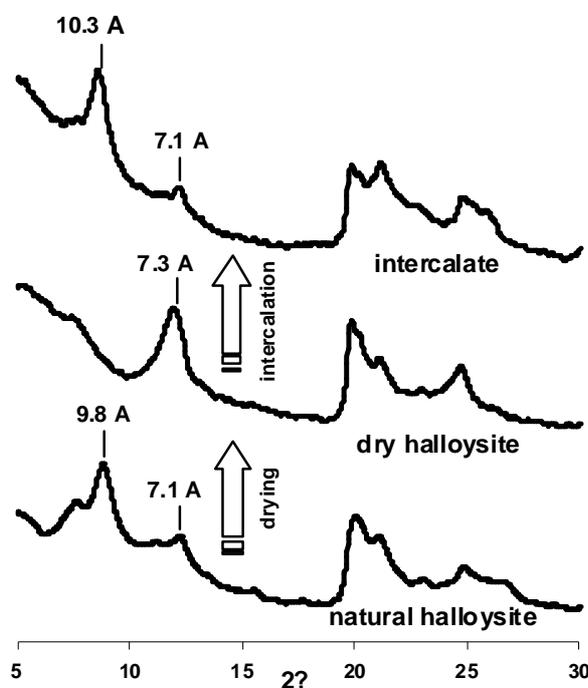
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Halloysite is a layered aluminosilicate and belongs to the kaolin group. Each layer contains the silicate ( $\text{Si}_2\text{O}_5$ ) and the gibbsite ( $\text{Al}_2(\text{OH})_4$ ) sheets. The layers are bound via hydrogen bonds between tetrahedral oxygens of silicate sheet and outer – plane hydroxyls of gibbsite sheet (from adjacent layer). The structure is similar to that of kaolinite, however, it is observed frequent replacement of  $\text{Al}^{3+}$  ions by  $\text{Fe}^{3+}$  in gibbsite sheet as well as a presence of interlayer water molecules.

The natural halloysite can exist as the mixture of hydro-halloysite (interlayer distance  $d_{001}=10\pm 0.2$  Å), containing weakly bonded interlayer water molecules, and halloysite (interlayer distance  $d_{001}=7\pm 0.2$  Å) without interlayering water.

We are looking for low - cost materials capable to absorb an electromagnetic wave. Natural halloysite could be a good candidate, as the material is slightly magnetic and effectively absorbs the electric component of an electromagnetic wave. Unfortunately, it is a very unstable material. We have demonstrated that the intercalation of halloysite (the process of introducing guest molecules into the mineral structure) makes it possible to recover the ability to absorb an electromagnetic wave and obtain a promising material for electromagnetic field shielding applications.

The samples were investigated with X-Ray diffraction, thermogravimetric analysis, scanning and transmission electron microscopy and dielectric relaxation spectroscopy.



## Monosubstituted benzyl amides of salinomycin – synthesis, structural and spectroscopic characterization as well as their biological activity

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Salinomycin (SAL, Figure 1) is an antibiotic belonging to a large group of polyether ionophores [1]. Sodium salt of SAL is commonly used in veterinary medicine as a non-hormonal growth promoting as well as coccidiostatic agent.

However, SAL caught the attention of scientists from around the world in 2009, when it was announced that this compound is nearly 100-fold more effective towards the breast cancer stem cells (CSCs) than the commonly used cytostatic drug – Taxol [2]. Since then, extensive research work has been undertaken to explain the unusual anticancer properties of this antibiotic.

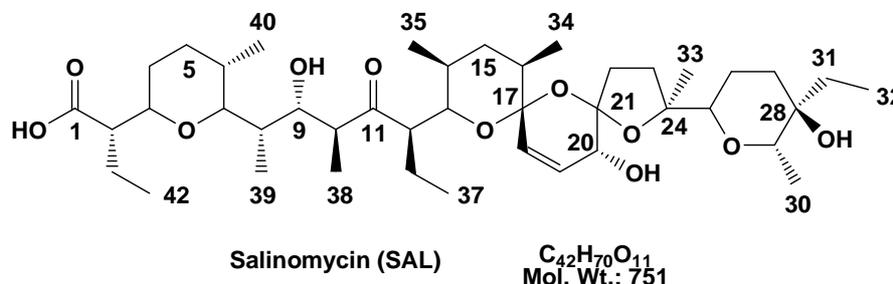


Fig. 1. Structure of salinomycin.

In this contribution we present an efficient synthesis method of 12 novel monosubstituted benzyl amides of SAL with fluorine, chlorine and bromine atoms as well as nitro groups in *-ortho*, *-meta* and *-para* position. The structure of these derivatives was characterized using spectroscopic and diffraction methods. Additionally, their ability to form complexes with mono- and divalent metal cations was determined using ESI mass spectrometry. Moreover, anticancer activity against drug-sensitive and drug-resistant human cancer cell lines as well as antibacterial activity against Gram-positive bacteria was also tested.

Financial support by grant of the Polish National Science Centre (NCN) – No. 2011/03/D/ST5/05884 is gratefully acknowledged

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## Complex of trifluoroacetic acid and methylethylketone. Spectroscopic study

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Trifluoroacetic acid (TFA) and ketones form quite strong hydrogen bounded complexes [1–3]. The energy of complexation of such systems is near 30 kJ/mole. As result the strong broad  $\nu(\text{OH})$  band is observing in IR spectra in 3500 – 1800  $\text{cm}^{-1}$  region. The ketone  $\nu(\text{C}=\text{O})$  band shifts to low frequencies also.

Here we report the spectrum of complex of TFA with asymmetric ketone methylethylketone (MEK). The spectrum was obtained from experimental spectra of mixtures of TFA and MEK in  $\text{CCl}_4$  at different concentration of components near  $10^{-2}$  mole/l at room temperature. The special attention was paid for the  $\nu(\text{OH})$  and  $\nu(\text{C}=\text{O})$  bands both ketone and acid in the complex and their difference from the bands of the monomers and TFA dimer.

The measurements at different temperatures ( $T = +30 - -18$  °C) were performed. It is allowed the estimation of some thermodynamic properties of complexation.

Acknowledgements. The spectra were recorded with apparatus of the Resource Centrum Geomodel of SPbGU. REA acknowledges the financial support of Russian Foundation for Basic Research (grant No. 12-03-00215-a)

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## Cobalt(II) complexes with pyrazine derivatives – chemical and antimicrobial properties

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Metal complex ions play an important role as bactericidal and fungicidal preparations [1-3]. However, the persistent increase in microbial resistance to drugs and other substances is forced to search for new antimicrobial compounds. Due to this, coordination compounds of Co(II) with 2,3-bis(2-pyridyl)pyrazine (dpp), pyrazine-2-amidoxime (paox), pyrazine-2-tiocarboxamide (ptca), and 2-amino-5-bromo-3-(methyloamino)pyrazine (abmap) were synthesized. These four coordination compounds were characterized by spectroscopic (<sup>1</sup>H NMR, IR, UV-Vis), potentiometric and other analytical methods.

Stability of Co(II) complexes were investigated in aqueous solution. Their values for all studied coordination compounds were determined using spectrophotometric titration method and recorded at room temperature. The ORIGIN and EQUID computer programs were used to calculate gradual and cumulative stability constants, respectively. The *in vitro* antimicrobial activities of the complexes studied were examined against antimicrobial strains of bacteria *Enterococcus hirae*, *Staphylococcus aureus*, *Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa* and fungus, *Candida albicans*.

The presented results have shown the way to obtain metal complex ions with pyrazine, where stoichiometry of metal : ligand was equal 1:1. The IR and UV-Vis spectra of the obtained complexes suggest octahedral nature of these compounds with didonor organic ligands inside. Based on the results of spectrophotometric titrations, the following arrangement proposed by increasing stability of the complexes:  $[\text{Co}(\text{ptca})(\text{OH}_2)_4]^{2+} < [\text{Co}(\text{paox})(\text{OH}_2)_4]^{2+} = [\text{Co}(\text{abmap})(\text{OH}_2)_4]^{2+} < [\text{Co}(\text{dpp})(\text{OH}_2)_4]^{2+}$ . Biological tests with a new compounds of Co(II) have shown much higher activity against fungus than bacteria. Complexes studied are selective towards *Candida albicans* fungus in aqueous solution. The values of minimal inhibitory concentration and the minimal bactericidal and fungicidal concentration were received (0.06-8 mg/ml).

This work was financially supported by BMN 538-8232-B345-14.

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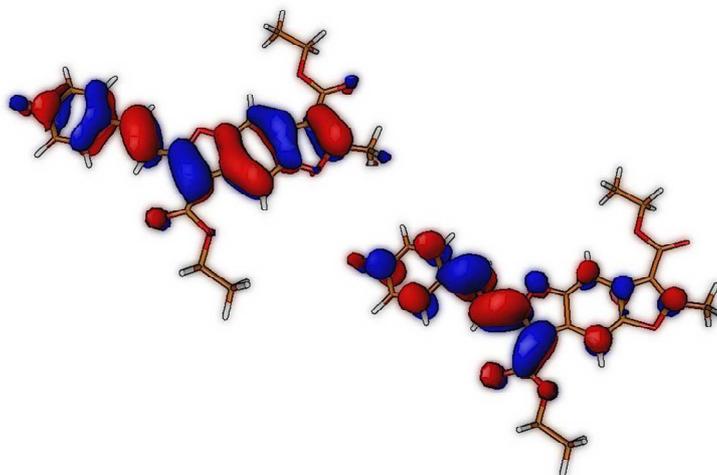
## Absorption and emission spectra of benzodifuran derivatives in dichloromethane – DFT computation

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Density Functional Theory computations of spectroscopic properties (absorption and emission spectra) of benzodifuran derivatives were performed. Several density functionals (BP, B3-LYP, CAM-B3LYP and PBE0) were tested and the results were compared with the experiment [1]. The influence of solvation model was investigated in the case of dichloromethane, which was used in the [1] work. PBE0 functional with polarizable continuum model applied proves to reproduce the experimental values the most correctly.

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## Synthesis, Spectroscopic and Theoretical Studies of New Quaternary Alkylammonium Conjugates of Bile Acids

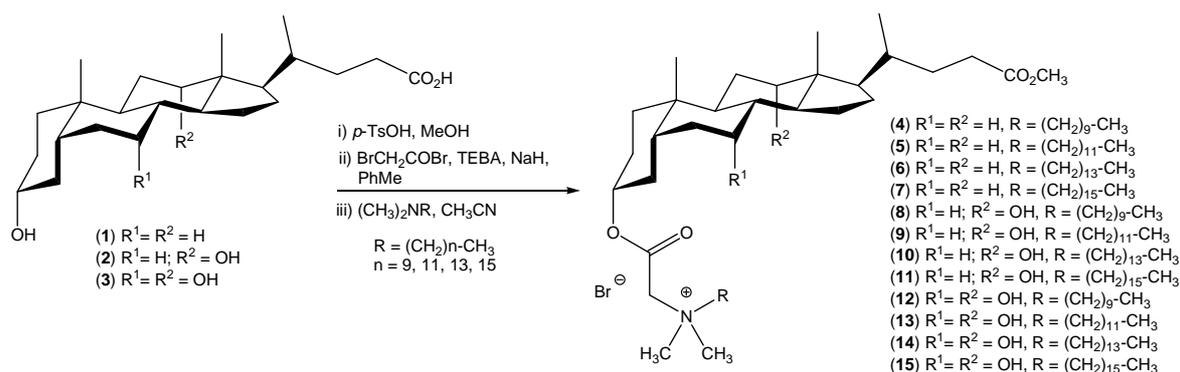
D. Czajewicz, T. Pospieszny, H. Koenig, I. Kowalczyk, B. Brycki

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Steroids are a large class of natural compounds and display very important roles in organisms e.g. constituents of the cell membrane in eukaryotes or they are main hormones [1,2]. Especially interesting are bile acids and their derivatives, because they have a large, rigid and curved skeleton. Therefore, they are good building material in supramolecular chemistry [3].

Quaternary alkylammonium salts exhibit excellent antimicrobial activity, and therefore they are used as antiseptics, bactericides and fungicides, as well as therapeutic agents. In general, quaternary alkylammonium salts with good antimicrobial activities contain one or two alkyl chains with lengths of the C<sub>8</sub>–C<sub>14</sub> range [4,5].

New quaternary 3-alkylammonium conjugates of bile acids were obtained and characterized by spectral, as well as theoretical methods (PM5, B3LYP, PASS).



A combination of aminoalkyl group and steroid substituent in ammonium salt structure, which contains positive charged nitrogen atom, will permit to obtain multifunctional compounds, proving antimicrobial activity and minimalizing possibility of increasing resistance of microorganisms [6-8].

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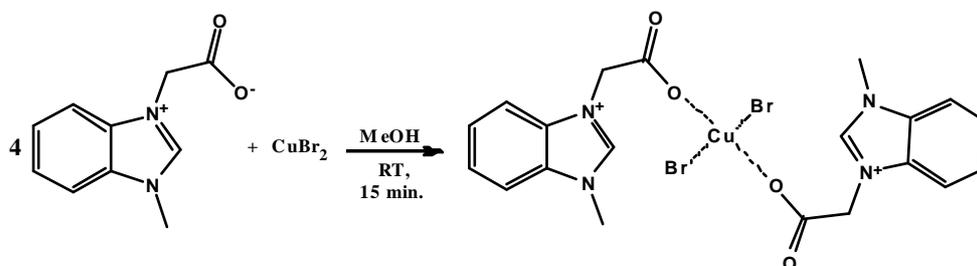
## Complex of 1-methyl-3-carboxymethyl benzimidazolium betaine with $\text{CuBr}_2$ . Structural and spectroscopic studies

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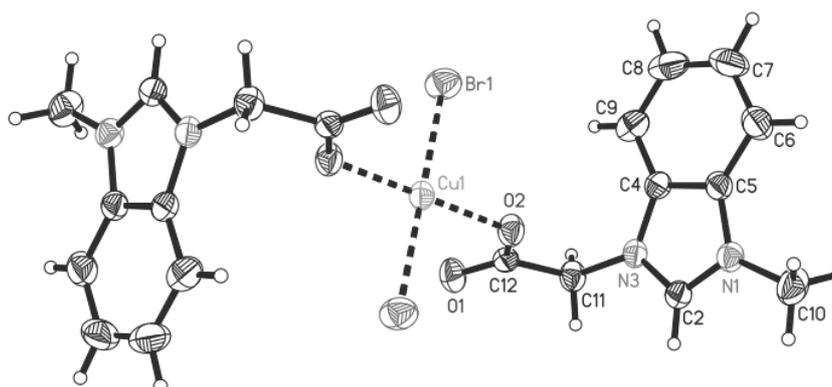
Complex of 1-methyl-3-carboxymethyl benzimidazolium betaine with  $\text{CuBr}_2$  was investigated by FT-IR and Raman spectroscopy and also by elementary analysis. Crystal structure was determined by X-ray diffraction.

The resulting complex was prepared by mixing of excess of 1-methyl-3-carboxymethyl benzimidazolium betaine with  $\text{CuBr}_2$  in methanol at room temperature. Precipitate was crystallized from water to give triclinic green crystals with space group  $P\bar{1}$ ; melting point 180 - 183°C.



Scheme 1. Synthesis of complex of 1-methyl-3-carboxymethyl benzimidazolium betaine with  $\text{CuBr}_2$ .

Cu atom lies on the special point on the center of symmetry. Carboxylate groups are twisted by  $77,5(2)^\circ$  from the plan of the benzimidazole rings which are almost planar.



Scheme 2. Crystallographic structure of complex of 1-methyl-3-carboxymethyl benzimidazolium betaine with  $\text{CuBr}_2$ .

The absorption band of the carboxylate group in FT-IR spectrum of complex is located at  $1626\text{ cm}^{-1}$ , and in free ligand at  $1616\text{ cm}^{-1}$ .

## Topological analysis of the electron density distribution in molecules of heteroaromatic thioketones

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Thioketones are sulfur analogues of ketones, characterized by the presence of the functional thiocarbonyl group C=S. Knowledge about them is limited to underscore their instability under standard conditions of organic synthesis [1]. Due to their high dipolarophilic reactivity thioketones were given the name *superdipolarophiles*. At present, very little is known about heteroaromatic thioketones, in which one or both aromatic rings are heteroaryl substituents, such as thiophene-2-yl, furan-2-yl, pyrrole-2-yl or pyridine-2-yl.

Considering the importance of heteroaryl fragments to obtain the desired material properties and high biological activity, a number of syntheses using Lawesson's reagent have been carried out and they resulted in corresponding new thioketone derivatives containing heteroaryl substituents [2].

The aim of the study was topological analysis of the electron density distribution in molecules of the newly obtained heteroaromatic thioketones and correlation with their electrochemical properties obtained by cyclic voltammetry. Additional AFM investigations showed that the Au surface had been modified after electroreduction.

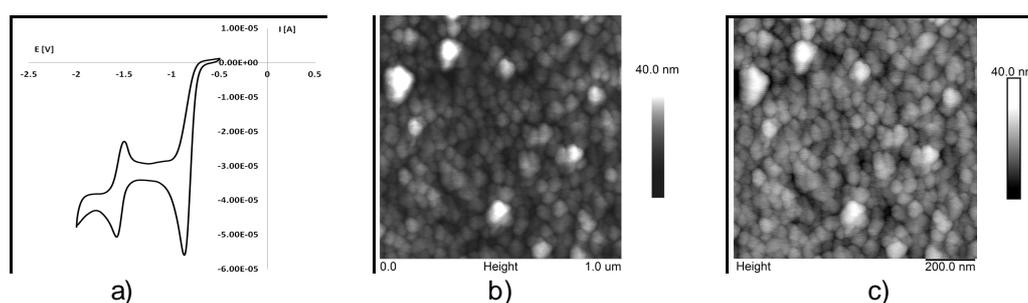


Figure 1. a) Voltammogram of furan-2-yl-selenophen-2-yl-methanethione (0.005 M) in 0.1 M  $Bu_4NClO_4/CH_3CN$  on Au vs. SCE; b) AFM image of Au surface before electroreduction; c) AFM image of Au surface after the electroreduction on Au.

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## NMR study of hindered internal rotation in $\beta$ -hydroxynaphthylamides

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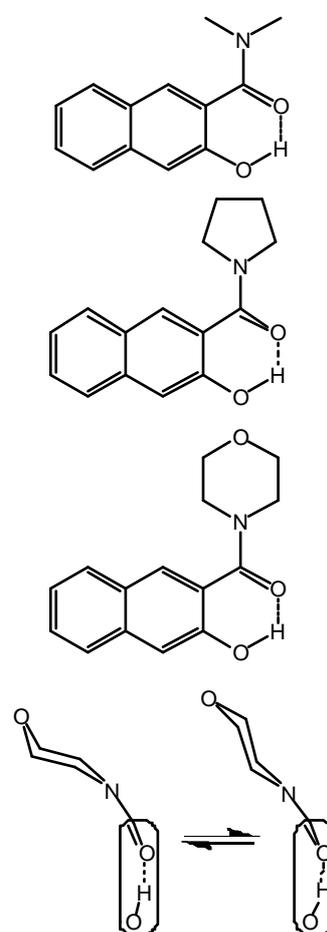
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Conformational research of amide group has been of significant scientific interest for many years because this type of formation composes fragments of the peptide bond in proteins and in DNA structure. However, despite a great number of papers dealing with conformational investigations of proteins, conformational research of ortho-hydroxyaryl-amides has not been given enough attention yet.<sup>1,2</sup>

In this work we have synthesized and studied a short series of  $\beta$ -hydroxynaphthylamides (see structures in the Figure). Molecules were dissolved in organic solvents ( $(\text{CD}_3)_2\text{CO}$ ,  $\text{CDCl}_3$ ,  $\text{CD}_3\text{OD}$ ,  $\text{THF-}d_8$ ) and investigated by variable-temperature  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy (measurements were performed at the Center for Magnetic Resonance of St.Petersburg State University). The resulting spectra confirmed that molecules undergo a hindered internal rotation around C-N bonds in amide groups. Line shape analysis allowed us to estimate energy barriers for this rotation. The overall potential energy profile was obtained by QC calculations. Besides, in case of morpholine derivative (Figure, bottom structure) at the lowest accessible temperatures we have found spectroscopic indication of another dynamic process: morpholine ring pseudo-inversion (see Figure, bottom; cartoon schematically shows the side-view of the molecule: note, that the structure is not planar), which was further confirmed by QC calculations.



*AF thanks joint research project of JINR and Faculty of Chemistry of Wrocław University for financial support; PT thanks FRBR grant 14-03-00111 for partial financial support.*

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**Substituent effects in trans *p,p'*-disubstituted azobenzenes – X-ray at 100 K and DFT-calculated structures**

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The crystal and molecular structures of *para*-substituted azobenzenes with  $\pi$  – electron-donating  $-\text{N}(\text{Et})_2$  and  $-\text{COOEt}$  groups along with substituent effects of benzene rings aromaticity were described. In 4,4'-(diazenediyl)dibenzamine,  $\text{C}_{20}\text{H}_{28}\text{N}_4$ , (I), deformation of aromatic ring around  $-\text{N}(\text{Et})_2$  group may be caused by steric hindrance and  $\pi$ -electron-donating effects of amine group. In the structure one of the amine atoms demonstrates clear  $sp^2$  hybridisation and another is slightly shifted from the plane of surrounding atoms. The molecule of 4,4'-(diazenediyl)dibenzoate,  $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_4$ , (II), in the crystal lies on an inversion centre. Its geometry is normal and comparable with homologous compounds. Density functional theory (DFT) calculations were performed to analyse the changes in the geometry of the studied compounds in the crystal state and for the isolated molecules. The most significant changes are observed in the values of the N-N-C-C torsion angles which for the isolated molecules is close to  $0.00^\circ$ . The HOMA (Harmonic Oscillator Model of Aromaticity) index, calculated for the benzene ring, demonstrates a slight decrease of the aromaticity in (I) and no substantial changes in (II).

## Synthesis and biological evaluation of colchicine C-ring derivatives

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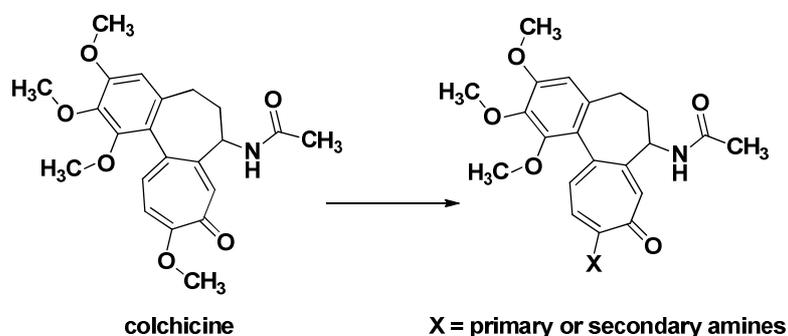
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Colchicine is a well documented pseudo-alkaloid obtained from *Colchicum autumnale*, widely used in therapy for the treatment of gout pain persisting for a very long time.

Colchicine is too toxic to be of value as an anti-tumour drug in its native form. Colchicine derivatives with improved therapeutic properties for anti-inflammatory and anti-tumour drugs are of commercial demand. These compounds are known to have clinical significance for the treatment of certain forms of leukemia and solid tumours.

Herein, we report that colchicine can be modified using relatively simple reactions to yield various functionalized derivatives, as shown in Scheme 1 with the aim of developing stronger potential anticancer activities.

The structures of the obtained compounds were studied using FT-IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and ESI MS.



Scheme 1

All the obtained compounds have shown potent antiproliferative activity against human cancer cell lines. Some of the synthesized compounds have shown good inhibitory activity against *Staphylococcus* strains and clinical isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus epidermidis* (MRSE).

## The effect of ethanol and trifluoroethanol on interdigitation of DPPC seen by excitation-emission fluorescence spectroscopy and PARAFAC

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It is now well established that saturated symmetrical phosphatidylcholines, like 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine (DPPC), can exist in an unusual gel phase in which acyl chains from opposing monolayers interdigitate. The inducer of interdigitation are typically small amphiphilic molecules with the ability to occupy the interfacial region of lipid bilayers, instead of water, and create a free volume area. Ethanol which has been extensively studied in a context of this phenomenon for a variety of lipids [1]. In this work, we have compared the potential of ethanol and trifluoroethanol, which is more hydrophobic compound, in forming the interdigitated phase. Trifluoroethanol (TFE) is known for stabilization of the  $\alpha$ -helical structure in proteins and can induce changes in membrane structure[2].

Since DPPC does not fluorescence on its own, Prodan was incorporated into the lipid bilayer and used to monitor the transition from the noninterdigitation state to fully interdigitation state. Prodan is an environmentally sensitive fluorescent probe, which locates in the region between the ester carbonyls at glycerol backbone and phosphate group[3]. Spectral changes are assigned to the probe relocation from less polar environment to more polar environment due to the lipid interdigitation. Hence, it seems to be a perfect dye to monitor structural changes of the membrane.

The use of chemometrics tool like parallel factor analysis (PARAFAC) allows us to monitor the membrane transition to interdigitation state. PARAFAC provides both a quantitative and qualitative model of this process.

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## In silico studies of carboplatin biotransformation hydrolytic and electron transfer mechanistic pathways

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The mechanism of carboplatin biological activity is still unclear and its explanation constitutes a very challenging task. In continuation of our study on mechanistic aspects of pharmacological action of platinum-based drugs [1], we present computational simulation of reaction courses that might unravel how the introduced carboplatin is turned into the shape of active drug able to interact effectively with target biomolecules.

The object of the study was the series of reaction paths initiated by impact of species present in biological milieu and able to trigger off the nucleophilic substitution (H<sub>2</sub>O) or dissociative electron attachment (e<sup>-</sup>-donors, free electrons, aquated electrons).

Consequently, the calculation of structural and energy parameters of the following reaction courses were carried out:

- (1) two stage carboplatin hydrolysis;  
the reactants were  $\{([Pt(NH_3)_2(OOC-C_4H_6-COO)] + H_2O) + H_2O\}$ ;
- (2) two stage electron impact on carboplatin;  
the reactants were  $\{([Pt(NH_3)_2(OOC-C_4H_6-COO)] + e^-) + e^-\}$ ;
- (3) electron and water gradual impact on carboplatin;  
the reactants were  $\{([Pt^{II}(NH_3)_2(OOC-C_4H_6-COO)] + e^-) + H_2O\} + H_2O$ .
- (4) water and electron gradual impact on carboplatin;  
the reactants were  $\{([Pt(NH_3)_2(OOC-C_4H_6-COO)] + H_2O) + e^-\}$ ;

Conclusions:

- The computational simulations of two alternative pathways, and their combinations, were investigated as hypothetical courses of carboplatin biotransformation.
- The comparison of calculated parameters allow to state that carboplatin biotransformation is not restricted to hydrolytic pathway as was commonly accepted;
- The most concurrent pathway represents the sequence of reactions initiated by electron attachment

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## Solvation of monatomic cations by polar solvents according to the mean spherical approximation

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The Mean Spherical Approximation describes electrolyte solutions using statistical mechanical methods for a mixture of hard spheres with a diameter  $d_s$  and a permanent dipole moment  $\mu$  representing solvent molecules and hard spheres with a charge  $z_i$  and a radius  $r_i$  representing ions. In the limit of infinite dilution the Gibbs free energy of ion solvation  $\Delta G_{\text{solv}}$  includes only the contribution from attractive ion-dipole interactions and dipole-dipole repulsive interactions. Fawcett showed [1,2] that the resulted solution can be simplified to Eq. 1 which is the well known Born equation with two additional corrections different for cations and anions but depending only on a solvent:  $f_{\text{dd}}$  depending on dipole-dipole interactions and  $\delta_s$  the correction to ionic radius:

$$\Delta G_{\text{solv}}(\text{MSA}) = \Delta G_{\text{solv}}(\text{Born}) (1-f_{\text{dd}}) [1/(1+\delta_s/r_i)] \quad (1)$$

It follows that for simple ions the plot of  $-z_i^2/\Delta G_{\text{solv}}$  against  $r_i$  should be linear giving  $f_{\text{dd}}$  and  $\delta_s$  from slope and intercept, respectively. The both parameters were found by Fawcett for monatomic ions in aqueous solutions and he suggested [1,2] that  $f_{\text{dd}}$  is important only in determining the solvation of anions but  $\delta_s$  only for cations.

In this work a similar analysis is made for monatomic cations of 1<sup>st</sup> and 2<sup>nd</sup> groups of Periodic Table in non-aqueous solutions. Excellent correlations (with determination coefficients  $R^2 > 0.99$ ) were found for 6 protic and 10 aprotic dipolar solvents with the electric permittivity  $> 20$ . It was shown that  $f_{\text{dd}}$  increases with the dimensionless parameter  $-\mu^2/4\pi\epsilon_0 d_s^3 kT$  describing in the theory of electric polarization the attraction between two dipoles in parallel arrangement ( $\uparrow\downarrow$ ). The obtained  $f_{\text{dd}}$  values do not support the suggestion of Fawcett [1,2] but indicate that repulsive dipole-dipole interactions reduce the cation-dipole attractive energy by significant values ranging from 16% for propylene carbonate to 34% for 1-propanol. On the other hand,  $\delta_s$  values found in the range from  $35\pm 18$  pm for 1-propanol to  $71\pm 23$  pm for nitromethane indicate substantial disruptive effects on solvent structures in accordance with Fawcett's results reported for aqueous solutions. Moreover,  $\delta_s$  values clearly decrease with the increase in the empirical solvent parameter  $\beta$  describing the hydrogen-bond acceptor basicity [3] in a solvation of cations.

Similar analysis could not be performed for monatomic anions because of the lack of a proper number of experimental  $\Delta G_{\text{solv}}$  in non-aqueous solutions.

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## Influence of intermolecular interactions on the properties of carbon materials

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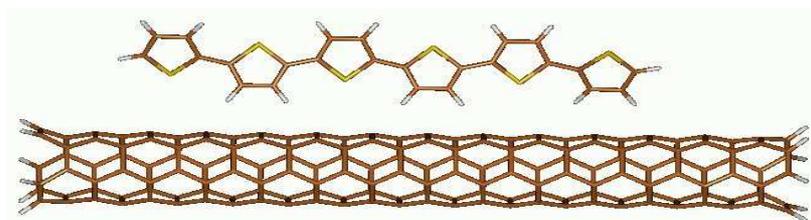
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Encapsulation of organic molecules in nanomaterials can be applied for tuning the properties of carbon materials such as graphene oxide, nanotubes or fullerenes. It is particularly interesting in the case of the nanotubes, since unlike the modification of the outer surface of the tubule, it does not cause the loss of the one-dimensionality and may not cause the surface defects [1-2].

Conjugated oligomers and polymers based on heterocyclic oligothiophenes have attracted strong interest in recent years due to their potential applications in organic electronic devices. Conjugated oligomers embedded on CNTs can form the basic components of new materials [3].

In the present study an introductory computational investigation was performed for small oligothiophenes containing from one up to six thiophene units. The oligomers interacting with various types of materials such as graphene and nanotubes were analyzed within the DFT formalism with inclusion of dispersion corrections.

Further on, the experimental examination of hybrid materials containing oligothiophenes was carried out. After the deposition of the oligothiophenes on different types of carbon materials (single and multiwall carbon nanotubes, carbon films and carbonized willow wood) the modern analytical techniques were applied for their characteristic: SEM, TEM, BET surface area, XPS and confocal microscopy.



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### 3-Hydroxypyridine dimers with pentamethylene spencer. Structural, spectroscopic and theoretical studies.

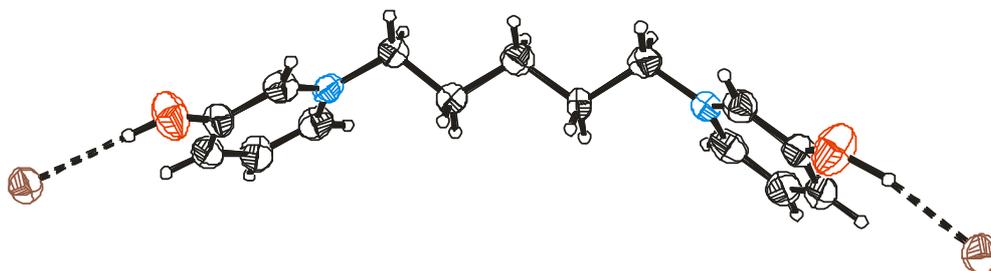
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3-Hydroxypyridine and its N-substituted 3-oxypyridyl betaines have received a lot of consideration because of its similarity to the pyridoxine (vitamin B<sub>6</sub>). In solution 3-hydroxypyridine occurs in the tautomeric equilibrium, as a neutral form or zwitterion [1]. Furthermore, at different pH values, it can give either the cationic or anionic form. The reactions of 3-hydroxypyridine with alkyl halides in organic solvents yield quaternary salts [2,3].

1,5-di(3-hydroxypyridinium)pentane dibromide was synthesized in reaction of 3-hydroxypyridine with 1,5-dibromopentane in ethanol. The product under a threefold excess of propylene oxide has been transformed to 1,5-di(3-hydroxypyridinium)pentane monobromide.

These compounds were characterized by FT-IR, Raman and <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy and a crystal structure of 1,5-di(3-hydroxypyridinium)pentane dibromide (Scheme 1) was determined.



Scheme 1. Crystallographic structure of 1,5-di(3-hydroxypyridinium)pentane dibromide.

Quantum-chemical calculations were performed at B3LYP/6-311++G(d,p) level of theory. After geometry optimization theoretical NMR and IR spectra were computed. The <sup>1</sup>H and <sup>13</sup>C magnetic isotropic shielding constants ( $\sigma_{\text{calc}}$ ) were obtained by GIAO approach. The linear relationships  $\delta_{\text{exp}} = a + b \sigma_{\text{calc}}$  between experimental chemical shifts ( $\delta_{\text{exp}}$ ) and the  $\sigma_{\text{calc}}$  were obtained. In the FTIR spectrum the most intensive bands were assigned to theoretically predicted vibrational frequencies and modes.

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## Molecular Dynamics Simulations of Proton Transverse Relaxation Times in Suspensions of Magnetic Nanoparticles

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Superparamagnetic iron oxide nanoparticles (Spion) are widely used as  $R_2$  contrast agents in magnetic resonance imaging (MRI) [1,2]. Their performance depends on many factors like: magnetic properties of the nanoparticles, structural factors and aggregation of nanoparticles into clusters. In our studies we have focused on the influence of intermolecular interactions, external magnetic field strength and aggregation of the nanoparticles. We proposed an original computational scheme, based on molecular dynamics, for determination of  $T_2$  relaxation times of water protons surrounding the nanoparticles. Our model accounts for magnetic dipole-dipole interactions, magnetic anisotropy effects, dispersion interaction between magnetic nanoparticles and water molecules and electrostatic interactions. Thus, it provides a complete description of the force field associated with the suspension of magnetic nanoparticles in aqueous media.

The obtained results provide a notion about the role of water adsorption on the nanoparticles surfaces, role of nanomagnetic protection layer on their surfaces and effects of agglomeration of the nanoparticles in bigger clusters.

We found that the optimal value of  $T_2$  is reached for clusters composed of 30-40 magnetic nanoparticles having diameters about 10-12 nm. By comparing our results with literature data concerning chitosan covered iron oxide nanoparticles, [2] we can conclude that their performance as contrast agents can still be improved by reducing the size of clusters. We also found that in typical conditions of high and low-field MRI, that is at 0.5 – 7 Tesla, the magnetizations of nanoparticles are tightly fixed along the field direction, however, for ultra-low-field MRI (~0.1T) thermal fluctuations strongly affect the  $T_2$  relaxation times.

### Acknowledgement

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## Tautomerisation of thymine acts against the Hückel 4N+2 rule

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Stability and aromaticity of the thirteen thymine tautomers were studied in the gas phase at the B3LYP/6-311++G(2d,2p) computational level. It was found that from energetic viewpoint the tautomeric preference of thymine contradicts to the Hückel 4N+2 rule. As a result, the most stable tautomer is not the most aromatic, as estimated by HOMA and NICS indices.

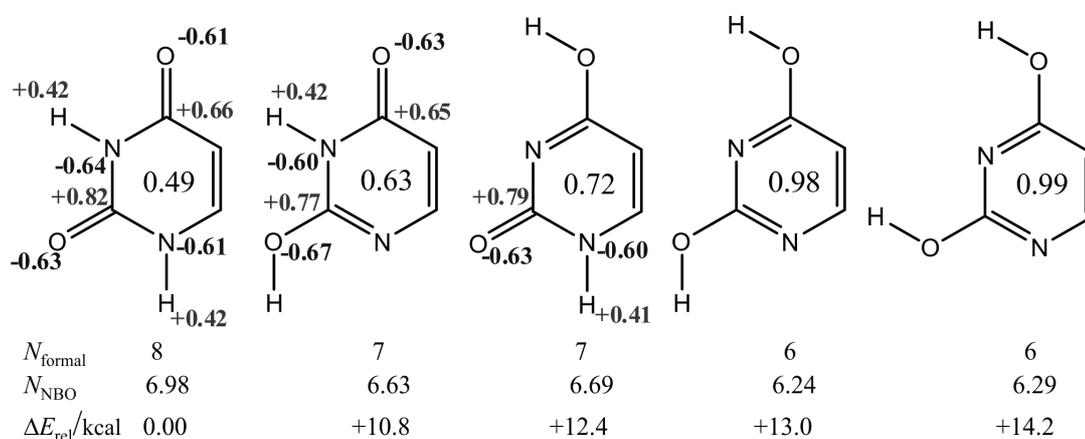


Fig. 1. Structures and selected NBO charges of five most stable thymine tautomers. Numbers in the ring center – aromaticity estimated by HOMA index.  $N$  – number of  $2p_z$  electrons in the ring.

Stability and aromaticity of these tautomers depend on the number of C=O groups attached to the ring. The main factor responsible for stability of the tautomers is their stabilization due to the extra interactions between  $\text{N}^{\delta-}\text{H}^{\delta+}$  and  $\text{C}^{\delta+}\text{O}^{\delta-}$  dipoles. Higher number of such interactions in the tautomer leads to its higher stability. Aromaticity of the ring strongly depends on the number of C=O groups in the tautomer. The most aromatic systems are tautomers with two hydroxyl groups *i.e.* containing no carbonyl group.

As it is known, the Hückel rule was formulated for cyclic  $\pi$ -electron hydrocarbons, and an addition of any functional groups to the cycle may affect the effectiveness of this rule, as earlier observed in benzoquinones[1].

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## Synthesis of new BODIPY compounds

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Main goal of this research is to obtain new 4,4-Difluoro-4-bora-3a,4a-diaza-s-indacenes (so called BODIPY) dyes that fluoresce at relatively long wavelengths. These kinds of compounds are well-known thermal and photochemical stable fluorophores, with very high fluorescence quantum efficiency ( $\Phi_f$ ) and high molar extinction coefficient. What is more its structure can be easily modified to achieve desirable properties. We synthesized 1,3-Dimethyl-4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene, 1,3-Dimethyl-2-ethyl-4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene and new indole-based BODIPY (Fig.1) . Compounds were prepared through condensation of appropriate aldehydes with pyrrole derivatives in present of phosphorus oxychloride at low temperature. After a standard complexation with boron trifluoride etherate, the corresponding BODIPY dyes were isolated. Geometry, electronic structure and theoretical spectra of absorption and emission were studied by hybrid DFT/*ab initio* and TDDFT calculations. Obtained compounds should make great core for fluorescent sensors, which creation is our next goal. Such novel fluorescence probes should base on the intramolecular photoinduced electron transfer (PET) mechanism and they should have practical applications for biology and toxicology.

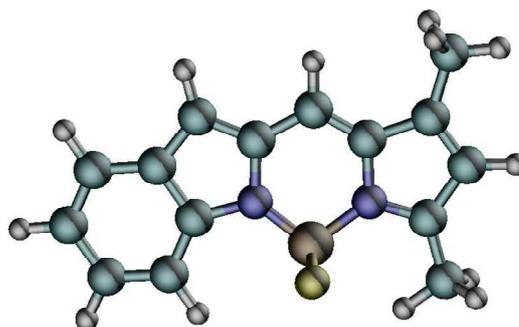


Fig. 1. New synthesized aromatic ring-fused BODIPY based on indole, with expected red-shifted absorption and emission spectra

## Near-infrared spectroscopy studies of enflurene influence on the chain-melting phase transition of DPPC liposomes

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Near-infrared spectroscopy studies (NIR) were applied to study phase transitions in water dispersions of dipalmitoylphosphatidylcholine (DPPC) liposomes in the presence of different enflurene concentration. This technique was used for the first time to try to identify the spectral changes centered at around 5660 and 5774  $\text{cm}^{-1}$  and assigned to the bands of the first overtones of the symmetric ( $2\nu_s(\text{CH}_2)$ ) and antisymmetric ( $2\nu_{as}(\text{CH}_2)$ ) stretching vibrations of  $\text{CH}_2$  groups of lipid aliphatic chains, respectively. The spectral parameters of  $2\nu_{s,as}(\text{CH}_2)$  bands such as a decrease in intensity, broadening and a high-frequency shift were correlated with the decrease in the ratio of the *trans* to *gauche* rotamers populations of lipid  $\text{CH}_2$  groups caused by the growth in the enflurene content and heating of mixed liposomes. The principal component analysis (PCA) carried out on the region of  $2\nu_{s,as}(\text{CH}_2)$  vibrations spectra of the enflurene-mixed DPPC liposomes, obtained in increased temperatures, gave the reduction of this multidimensional data set to one principal component. The dominant process in all studied systems associated with the first principal component was attributed to the main phase transition of enflurene/DPPC membranes. The temperature of the lipid chain-melting phase transition ( $T_m$ ), decreased with the rise in the anesthetic concentration and was accompanied by a similar character of the *trans-gauche* isomerization. Moreover, when the interdigitated lipid phase was dominated at higher enflurene concentrations,  $T_m$  was almost constant and independent on a further increase of the admixture amount. A good agreement with the literature data referred to the enflurene/DPPC membranes studied by many other techniques [1,2] showed that NIR could be applied to the studies in conditions where the MIR measurements cannot be done.

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**FTIR-ATR studies of membrane solubilization caused by the presence of hydrophilic analogs of fluphenazine with high anti-multidrug-resistance activity**

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Fluphenazine (FPh) belongs to a large group of phenothiazine compounds, which are known as effective inhibitors of multidrug resistance (MDR) of tumor cells to chemotherapeutic agents. An attenuated total reflectance Fourier transfer infrared spectroscopy (FTIR-ATR) was applied to study the effect of three hydrophilic analogs of fluphenazine with a high anti-MDR activity on the structure and physicochemical properties of sphingomyeline (SM) membranes of liposomes.

The analysis of the lipid  $\nu_{s,as}(\text{CH}_2)$  bands together with different vibrational bands of two pyrimidine analogs of FPh inserted into the SM membrane of liposomes allowed us to show a disturbance of a lipid bilayer structure and associated with this an analog release from a lipid to water phases. Non-bilayer assemblies were favored by the high concentration of two pyrimidine analogs of FPh and the increase in temperature. On the other hand, the third analog (*i.e.*, amino acid analog of FPh) did not do the membrane solubilization. The phase transition observed in SM liposomes mixed with all FPh analogs had a low cooperativity and a temperature of the chain-meting phase transition decreased with the increase in analog concentration. The transition of mixed bilayer from the *trans*-rich low-temperature gel phase to the *gauche*-rich high-temperature liquid crystal state of bilayer structure took place only in lower concentrations of all admixtures. Pyrimidine analogs of FPh in a lipid environment differed from these in a water solution by interactions of HCl molecules with amine moieties of the analog side chain and by the state of the aromatic ring core and connected with it the  $\text{CF}_3$  group.

## Degradation of synthetic polymers - computational aspect

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Synthetic polymers are widely used in many branches of industry mainly due to their processability and stability. However very long time of their decomposition may become disadvantageous, especially when the products become not required and cover dumping grounds. The pollution of our environment may be significantly decreased if we are able to design degradable polymers.

Presented poster reports work on theoretical methods of prediction of the degradability of polymers. This feature is correlated with the properties obtained from ab initio calculations, such as stability, binding energy, hydrophilicity, Mulliken charges and hydrolysis reaction rate constant. All calculations were performed using DFT formalism with B3LYP potential. Polymers were modelled by oligomers which consist of 1 to 10 mers.

Analysis of the results allows to arrange tested polymers according to their susceptibility for degradation. It can be helpful in the design of new materials of desired properties.

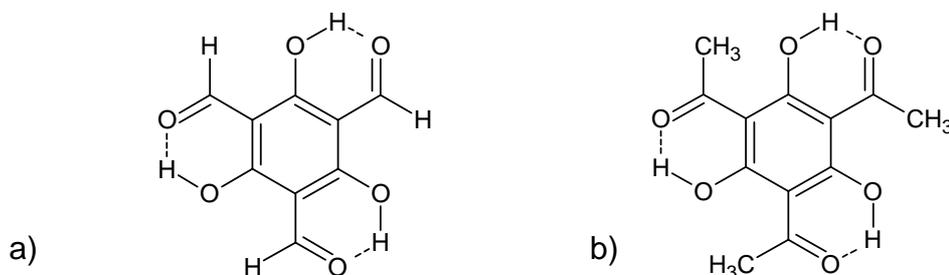
## Triple hydrogen bonding in a circular arrangement: synthesis and spectroscopy studies of *tris*-hydroxyaryl enamines

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The vicinity of a hydrogen donor (O-H) and a hydrogen acceptor (C=O or C=N-R) in ortho-Schiff base results in significant structural variations compared to the substituted derivatives that are reflected in the electronic structure and thus in the spectroscopic properties. This interplay between intramolecular hydrogen bonding and multicenter p-electron delocalization is the origin of the concept of *resonance-assisted hydrogen bonding (RAHB)*.

The objectives of investigations are compounds with three hydrogen bond donor-acceptor pairs.



Scheme 1. 2,4,6 – triformylglucinol (a) and 1,1',1''-(2,4,6-trihydroxybenzene-1,3,5-triyl)triethanone (b).

NMR spectroscopy provides valuable information on the structure and dynamics of the systems with hydrogen bonds. Formation of AH $\cdots$ B hydrogen bond leads to low-field shift of the proton signal. Signs and values of the signals of A and B nuclei are specific and depend on the interacting functional groups. Scalar spin-spin couplings between nuclei of proton donor and proton acceptor give valuable information about overlapping of electron clouds of partner groups upon formation of hydrogen bond.

The isotope effects in hydrogen bonded systems A-B were investigated through IR spectra and Raman spectra dates.

**Synthesis, physico-chemical and biological study  
of 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene  
(BODIPY) derivatives**

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A set of fluorescent dyes BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-s-indacene) was designed and synthesized (Figure 1). Physico-chemical properties of compounds were studied by UV-vis and NMR spectroscopy.

Theoretical structures were designed and optimized using Gaussian09 program suite. Influence of solvent effects on the absorption and emission spectra was examined. For that purpose, ground and excited state calculations were carried out with DFT and TD-DFT methods and different functionals (PBE0, M062X). Theoretical and experimental data were compared.

Biological properties were investigated using confocal microscope and *in vitro* method.

Obtained graphs, spectra and main conclusions will be presented.

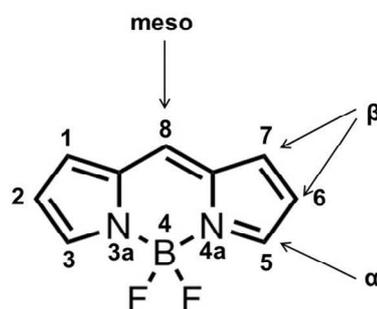


Figure 1. The core of 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) and its IUPAC numbering system.

## On the nature of N-oxo bond

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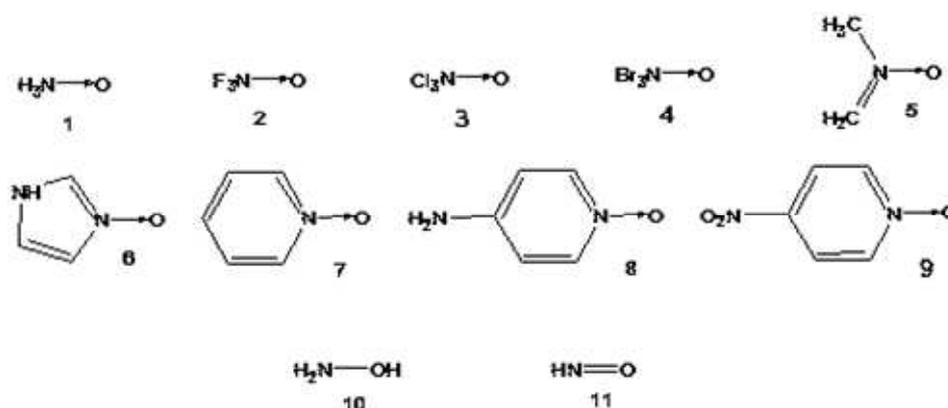
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The aim of the study was analysis of noncovalent interactions between pyridine *N*-oxides (Lewis bases) and Lewis acids. However, analysis of changes in electronic structure of oxygen atom in complex requires knowledge of the electronic structure of oxygen atom in isolated base molecule. Unfortunately there is not much information on this topic in the literature. Few papers on this subject do not provide complete information about the nature of *N*-oxo bond[1].

The analysis of the structures of number of model compounds containing N-O bond was carried out. Compounds with single or double bond between nitrogen and oxygen atoms were studied for comparison. The nature of N-O bond in *N*-oxides was determined on the base of quantum chemical calculations using DFT method, NBO analysis and on the base of analysis of the topology of the electron density consistent with QTAIM theory[2]. The results obtained from theoretical chemistry research were compared with experimental data obtained from search through CSD database[3].



*Scheme 1: Structures of analyzed compounds*

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[3] F.H.Allen, *Acta Cryst. B*, 58 (2002) 380-388

## A novel series of co-crystal structures with *N*-oxide group as a hydrogen bonding acceptor

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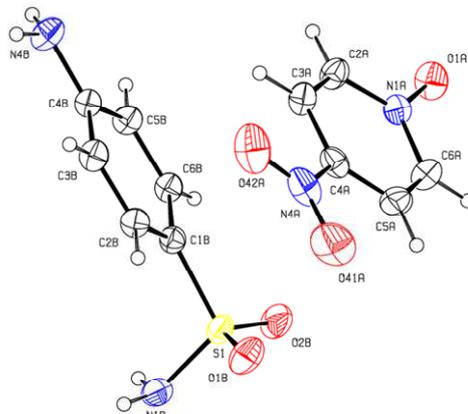
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Co-crystals are defined as homogenous crystalline materials consisting of two or more neutral components in a specific stoichiometric ratio. They may be obtained only from compounds which are in solid state in ambient conditions [1]. Co-crystals are intensively exploited in pharmaceutical industry, crystal engineering, textile industry, photography and electronics. Their popularity can be attributed to the fact that it is relatively easy to control the composition of the substance by the methods of molecular recognition, including the use of hydrogen bonds [2]. Thus it is possible to obtain co-crystals with certain physical and chemical properties. Synthesis of the various co-crystals of the same active ingredient is a way to obtain the optimal solid form of a drug [3]. Although the considerable practical application of co-crystals they still remain low explored, as evidenced by the small number of such structures in the Cambridge Structural Database (CSD) (less than 0.5% of all published structures) [2].

Pyridine *N*-oxide derivatives are compounds of great interests of pharmacists and chemists. Reason of this is fact that some of these compounds are already used in cancer or HIV treatment [4-5].

The main subject of the presented study were four new solid state complexes of 4-nitropyridine *N*-oxide and Lewis acids. Synthesized co-crystals were studied by X-ray diffraction in order to determine their crystal structure. In addition, Hirshfeld surfaces analysis was used to define the nature and main motifs of intermolecular interactions in obtained structures.



Scheme 1: Representative structure of 4-nitropyridine *N*-oxide with sulphonamide co-crystal

[1] Ch. B.Aakeröy, M. E. Fasulo, J. Desper, *Molecular Pharmaceutics*, 4 (2007) 317-322

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[5]: L. Medina – Gundrum, C. Cerna, L. Gomez, E. Izbicka, *Invest. New Drugs*, 23 (2005) 3 – 9

## New derivatives of colchicine - synthesis, structure and activity

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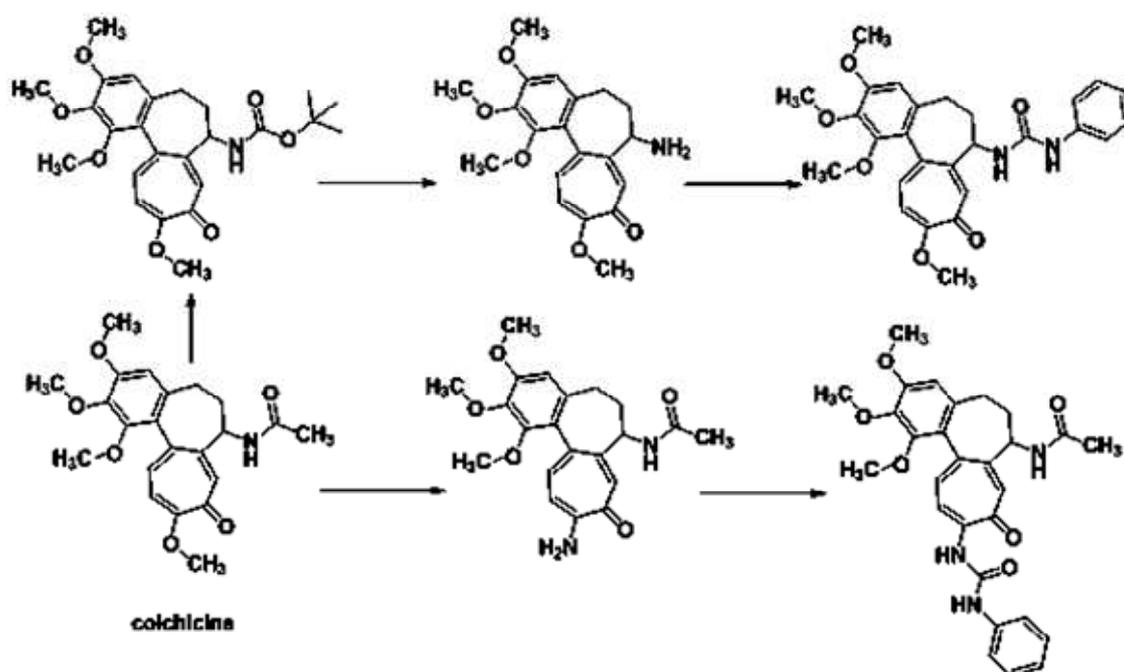
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New colchicine derivatives have been synthesized with the aim of developing stronger potential anticancer activities. We report that colchicine can be modified using relatively simple reactions to yield various functionalized derivatives as shown in Scheme 1.

The structures of the obtained compounds were studied by FT-IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, EI MS, ESI-MS and X-ray methods.



The compounds were evaluated for their antiproliferative effect on various cancer cell lines with IC<sub>50</sub> values in the submicromolar range.

## Experimental charge density study, the case of oxaphosphinin derivative

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A combined experimental and theoretical study of one oxaphosphinane derivative was made on the basis of a topological analysis of its electron density distributions. The electron density was determined from a high-resolution X-ray diffraction data set measured with synchrotron radiation at 100K, whereas theoretical calculations were performed using DFT methods at the B3LYP/6-311++G(3df,3pd) level of approximation. The charge density distribution and analysis of topological properties revealed that the P-O bond is of the transit closed shell type. The crystal structure possesses one intra- and several inter-molecular hydrogen bonds. They were characterized quantitatively by topological properties using Bader's Atoms in Molecules theory [1]. All hydrogen bonds were classified as weak. Further analysis of the experimental electron density by the Source Function [2] allowed the intra-molecular hydrogen bond to be characterized as an isolated hydrogen bond in contrast to the resonance-assisted hydrogen bond in related molecules, like chromone derivatives [3].

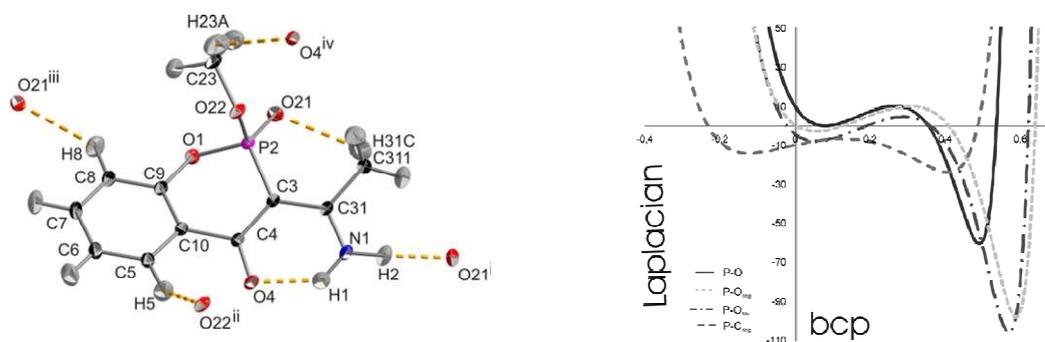


Fig. 1. a) View of molecular structure with atom numbering scheme and hydrogen bonds. The symmetry codes are: (i)  $1-x, -\frac{1}{2}+y, \frac{1}{2}-z$ ; (ii)  $\frac{1}{2}+x, \frac{1}{2}-y, -z$ ; (iii)  $\frac{1}{2}+x, \frac{3}{2}-y, -z$ ; (iv)  $-\frac{1}{2}+x, \frac{1}{2}-y, -z$ . b) Laplacians along the bond path of the P2-O22: P-O(Me); P2-O1: P-O(ring); P2-O21: P-O and P2-C3: P-C(ring) bonds. The horizontal axis measures the distance to the BCPs.

**Acknowledgements** The high-resolution measurement was carried out within the projects I-20090042EC and I-20110099EC at the light source DORIS III at HASYLAB/DESY, Hamburg, Germany.

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[2] C. Gatti, "The Source Function Descriptors as a Tool to Extract Chemical Information from Theoretical and Experimental Electron Densities", *Struct. & Bond.*, (2012). 1-93.

[3] M. Małecka, L. Chęcińska, C. Paulmann, *Struct. Chem.* 23, (2012), 801-807.

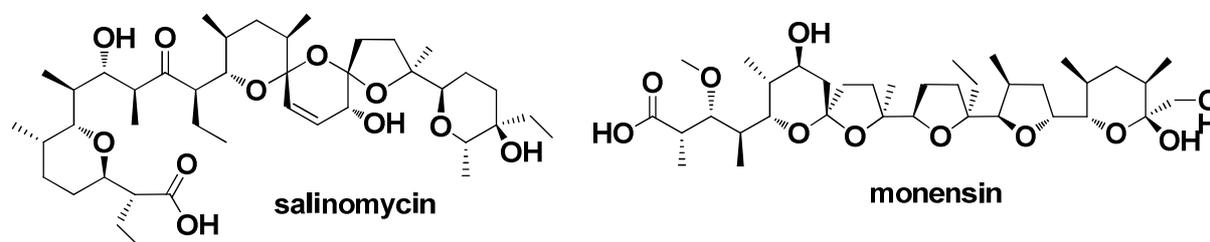
## Bioconjugates of the ionophore antibiotics

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The natural polyether ionophore antibiotics such as salinomycin and monensin might be important chemotherapeutic agents for the treatment of cancer. The polyether ionophores and their derivatives have shown potent activity against the proliferation of various cancer cells, including those that display multidrug resistance (MDR) and cancer stem cells (CSC).



The main purpose of our research was to design and synthesise derivatives of polyether ionophores showing considerable cytotoxic activity against human cancer cell lines.

Therefore, two series of novel derivatives of salinomycin and monensin have been obtained. The first group of compounds is their bioconjugates with **silibinin** – a hepatoprotective active flavonoid. These compounds have been obtained by the esterification between silibinin and respective ionophores. The other group of compounds is bioconjugates of ionophores with 3'-azido-3'-deoxythymidine (AZT) and 3'-azido-2'-deoxy-fluorouridine obtained by 'click' chemistry approach based on the copper(I) catalyzed Huisgen azide–alkyne.

The obtained bioconjugates have shown potent antiproliferative activity against human cancer cell lines. For this reason salinomycin and monensin bioconjugates are interesting scaffolds for the development of novel anticancer agents.

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*The author's participation in the conference is co-financed by the European Union from the European Social Funds The Human Capital Operational Programme, Sub-measure 4.1.2.*

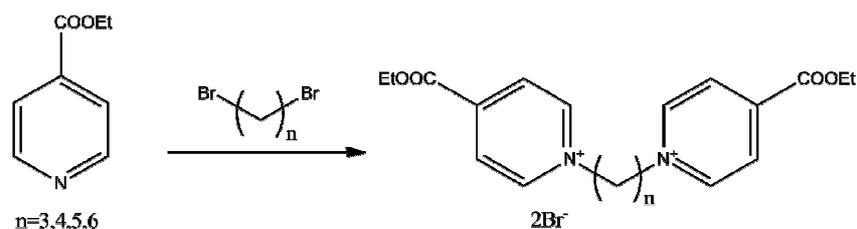
## Microwave-assisted synthesis of bis(4-ethoxycarbonylpyridinium) dibromide with polymethylene linker

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Microwave irradiation has become an increasingly valuable tool in organic chemistry, since it is a versatile and facile technique applicable to a large variety of syntheses. Thus, a large number of organic reactions can be carried out under microwave irradiation to give often higher yields than conventional methods after shorter reaction times and under milder conditions.

In order to obtain the desired bis-ethoxycarbonylpyridinium salts bearing polymethylene linker, the alkylation of ethyl isonicotinate with 1,ω-dibromoalkane, under both classical heating and microwave irradiation conditions were performed.



Scheme 1. Synthesis of bis(4-ethoxycarbonylpyridinium) dibromide with polymethylene linker.

A comparative study of microwave vs. classical conditions has been done (Table 1). Under classical heating conditions, these reactions have some major disadvantages including long reaction times (5-10 days), low yields and in some cases, only monomer was formed.

Table 1. Yield and time comparison of reaction heated in microwaves and under classical conditions.

Compound	Microwaves		Comments	Classical		Comments
	Time [min]	Yields [%]		Time [days]	Yields [%]	
(INeT) <sub>2</sub> Pr	60	82	Dimer	10	40	Dimer
(INeT) <sub>2</sub> But	30	95	Dimer	8	25	Monomer
(INeT) <sub>2</sub> Pen	60	85	Dimer	7	19	Monomer
(INeT) <sub>2</sub> Hex	30	67	Dimer	5	25	Monomer

The microwaves irradiation remarkably accelerated these N-alkylations, the reaction times decreased dramatically and the yields are much higher. Four new bis-ethoxycarbonylpyridinium salts of potential practical interest were obtained, and they were characterized by spectroscopic methods (<sup>1</sup>H, <sup>13</sup>C NMR and FT-IR).

## Synthesis and antimicrobial properties of novel ruthenium(III) complexes with pyrazine derivatives

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The medical properties of platinum metals are being recognized. Among them, ruthenium complexes are showing promising biological activity. The activity of ruthenium compounds depends on both: the oxidation state and the type of ligand. By manipulating these attributes, ruthenium-centered complexes could be used as more effective, less toxic and safer drugs [1,2].

The novel complexes of ruthenium(III) ion with pyrazine derivatives: 2,3-bis(2-pyridyl)pyrazine (2,3-dpp), pyrazine-2-amidoxime (paox), 2-amino-5-bromo-3-(methylamino)pyrazine (abmap) and pyrazine-2-tiocarboxamide (ptca) were synthesized [3]. The prepared compounds were assayed structurally by spectroscopy techniques (<sup>1</sup>H NMR, IR, UV-Vis). The electronic spectral data of the obtained complexes suggests octahedral nature of these compounds. For complexes of Ru(III) ion with N, N-donor chelate ligands, the influence of chemical structure of these compounds on the potential antimicrobial properties were discussed.

The compounds under studies exhibit the antibacterial activity against both: gram-negative and gram-positive bacteria. The derivatives of pyrazine under investigation do not possess activity against bacteria and fungus. The ruthenium(III) complexes with pyrazine derivatives exhibit reasonable inhibitory action on bacterial and fungus multiplication. The values of *MIC* (*Minimal Inhibitory Concentration*) and the *MBC* (*Minimal Bactericidal Concentration*) are in the range 0,5-8 mg/ml.

This work was financially supported by BMN 538-8232-B345-14.

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## Shift of the critical mixing temperature in strong electric fields. Theory and experiment.

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We studied the shift in the critical temperature  $T_c$  in binary mixtures in strong electric fields. In experiments we have measured the nonlinear dielectric effect (NDE) in a mixture of nitrobenzene and n-octane and we find that the critical anomaly of Piekara's factor is a function of an electric field strength.

We propose to explain this observation as a result of a downward shift of  $T_c$ . We amend Landau and Lifshitz's formula and show that the downward shift of  $T_c$  can be estimated from a simple mean-field theory taking into account the linear and quadratic terms in an expansion of the constitutive relation between the electric constant  $\epsilon$  and mixture composition  $x$

$$\epsilon = \epsilon_c + \epsilon_1(x - x_c) + \frac{1}{2} \epsilon_2(x - x_c)^2$$

where  $x$  is volume fraction of polar component,  $x_c$  is critical volume fraction. The theory invented by the authors offer two solutions of the question of electric field effect on  $T_c$ . When concentration fluctuations are spatially symmetric the  $T_c$  shift is given by an equation:

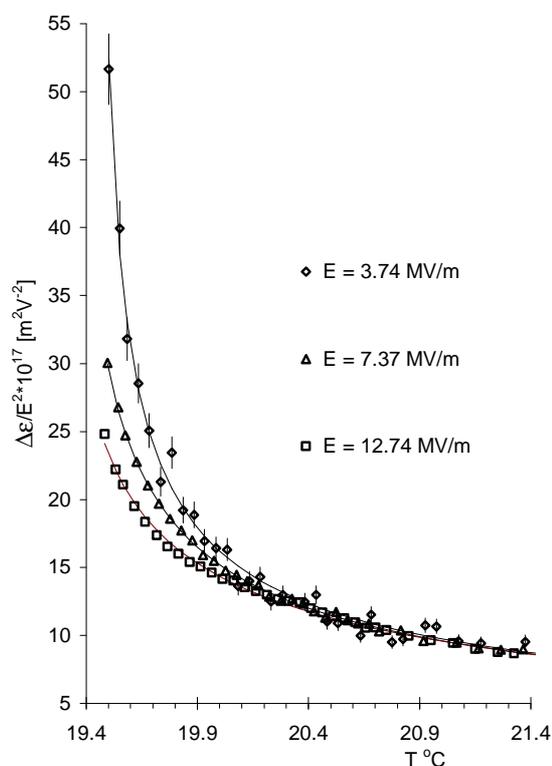
$$\Delta T_c = \frac{v_0}{4k_B} \epsilon_0 \left( \frac{1}{2} \epsilon_2 - \frac{1}{3} \frac{\epsilon_1^2}{\epsilon_c} \right) E_0^2$$

where  $v_0$  is the volume of a molecule of polar component,  $E_0$  is an electric field strength. Using the parameters of  $\epsilon(x)$  relation the derivative  $(\partial T_c / \partial E^2)$  was calculated to be  $(-2.8 \pm 0.4) \cdot 10^{-16} \text{ Km}^2/\text{V}^2$ . This is very close to the experimental value obtained previously from the analysis of the  $\epsilon(T)$  dependence measured at low intensity electric field<sup>1</sup>.

For high fields when composition fluctuations are elongated in the direction parallel to the  $E$  field the theory predict a different  $T_c$  shift:

$$\Delta T_c = \frac{v_0}{4k_B} \epsilon_0 \left( \frac{1}{2} \epsilon_2 - \frac{\epsilon_1^2}{\epsilon_c} \right) E_0^2$$

Using experimental  $\epsilon_i$  parameters the  $(\partial T_c / \partial E^2) = (-22 \pm 4) \cdot 10^{-16} \text{ Km}^2/\text{V}^2$  was calculated, that is very close to  $(\partial T_c / \partial E^2) = (-22 \pm 10) \cdot 10^{-16} \text{ Km}^2/\text{V}^2$  obtained from the direct measurement using the NDE method.



<sup>1</sup> Orzechowski K., Kosmowska M.; Adamczyk M.; J. Phys. Chem. B. 2012, 116, 2492.

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**Synthesis of novel peptidomimetics which can restrain the process of osteoclastogenesis.**

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Osteoporosis is a disease which affects more than 200 million people all over the world. Most of the patients are postmenopausal women, but according to the newest research the disease also concerns men and premenopausal women. As the number of patients grows and the treatments which are being applied aren't sufficient enough, there is a need to produce a new drug or apply a new treatment.

In my research I would like to design and synthesize new compounds and investigate the connection between the type and size of aromatic rings from these compounds, which appear to have great importance in the restraining of the osteoclastogenesis process. Moreover, if the peptidomimetics that I will synthesize show an anti-osteoclastogenesis activity, which will lead to reducing the osteoclasts activity or their amount, they could be used in further research which will determine their use as potential therapeutics.

All of the substances are being designed and synthesized at Department of Biomedical Chemistry at Faculty of Chemistry of the University of Gdansk.

The biological assay of designed and synthesized compounds will allow to determine the connection between the type and size of aromatic rings used and their influence on the process of osteoclastogenesis. The presence of heterocyclic rings, which can be observed for example in a UV diagnosis, may also create the opportunity to recognize the path of action of the peptide derivatives or its cellular target(s). That will lead to an improvement in designing new therapeutics and will probably create a new path in therapy. Moreover, if the new compounds show anti osteoclastogenesis activity, they can be tested as potential drugs.

## Equilibrium studies in the formation of lasalocid acid complexes with amines and metal cations

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Lasalocid acid (LAS) is natural occurring carboxylic polyether ionophore isolated from *Streptomyces lasaliensis*. It is able to form complexes with mono- and divalent metal cations and transport them across lipid bilayers. It is also able to form complexes with amines [1].

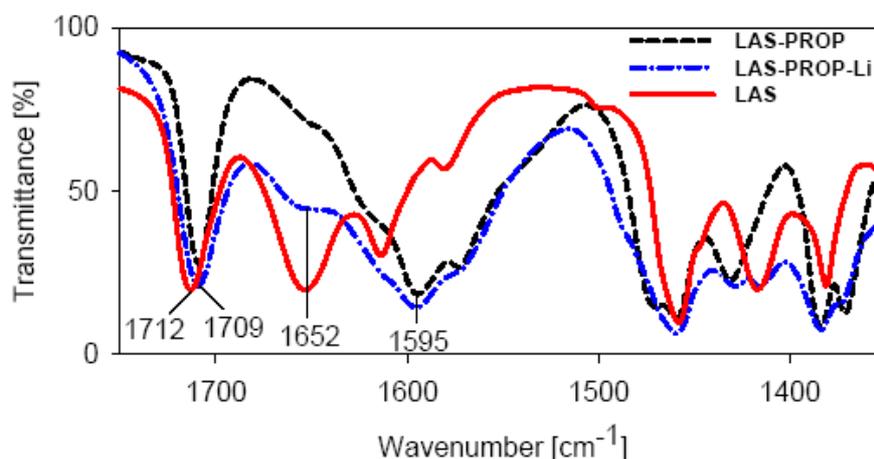


Fig. 1 FT-IR spectra of chloroform solutions of: lasalocid acid (solid line), LAS-PROP complex (dashed line) and LAS-PROP complex with addition of lithium cation (dashed-dotted line) in range 1750 - 1350  $\text{cm}^{-1}$

A new complex of lasalocid acid with propargylamine (LAS-PROP) has been obtained and studied by X-ray, and spectroscopic methods. The structure of obtained complex is stabilized by intra- and intermolecular hydrogen bonds formed between protonated amine molecule and deprotonated LAS anion. The spectroscopic studies have shown that the structure of the complex present in the solid state is generally comparable with the structure in the solution. Affinity of lasalocid acid to form complexes with the metal cations in presence of amine, or to form the complexes with amines in presence of the metal cation, was studied by using spectroscopic methods and discussed in detail. After addition of the cation to the complex of lasalocid with propargylamine, changes on FT-IR spectrum has been observed, indicating existence of equilibrium in formation of the complexes of lasalocid acid with amines and the metal cation.

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## The temperature-dependent polymorphism of an imidazole-N-oxide

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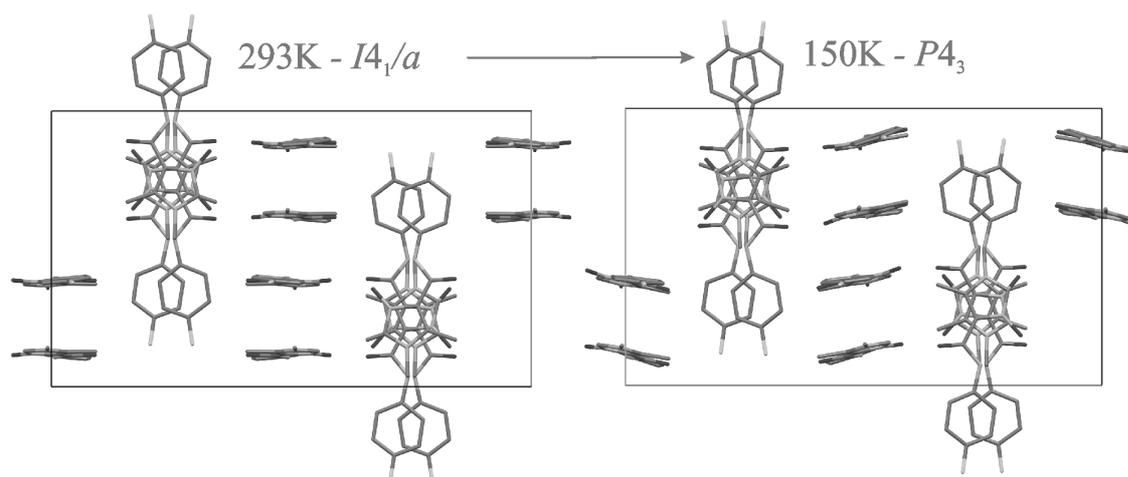
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Research on new imidazole and benzimidazole *N*-oxides and their applications in biology has focused particular interest in recent years as some of them exhibit biological activity, e.g. as insecticides, plant growth regulators, antiinflammatory and antiprotozoal agents [1,2]. There are also published some reports on imidazole derivatives containing amide or hydrazide groups as potential pharmaceuticals [3].

Herein we present results of X-ray studies on *N*-(4-fluorophenyl)-1,5-dimethyl-1*H*-imidazole-4-carboxamide 3-oxide, a compound which reveals the temperature-dependent polymorphism associated with the crystallographic symmetry conversion [4]. The observed crystal structure transformation corresponds to a symmetry reduction from  $I4_1/a$  (I) to  $P4_3$  (II) space groups. The phase transition mainly concerns the subtle but clearly noticeable reorganization of molecules in the crystal space, with the structure of individual molecules left almost unchanged.

The Hirshfeld surface analysis shows that various intermolecular contacts play an important role in the crystal packing, revealing graphically the differences in spatial arrangements of the molecules in both polymorphs. The *N*-oxide oxygen atom acts as a formally negatively charged hydrogen bonding acceptor in intramolecular hydrogen bond of N-H...O<sup>-</sup> type. The combined crystallographic and theoretical DFT methods demonstrate that the observed intramolecular *N*-oxide N-H...O hydrogen bond should be classified as a charge-assisted, closed-shell very strong non-covalent interaction.



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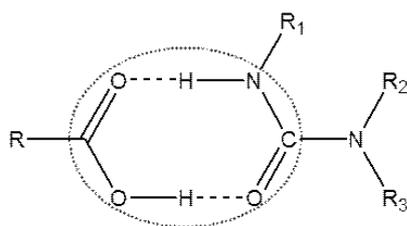
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## O-H...O and N-H...O double hydrogen bonds motif in supramolecular synthon of carbamide and carboxylate groups

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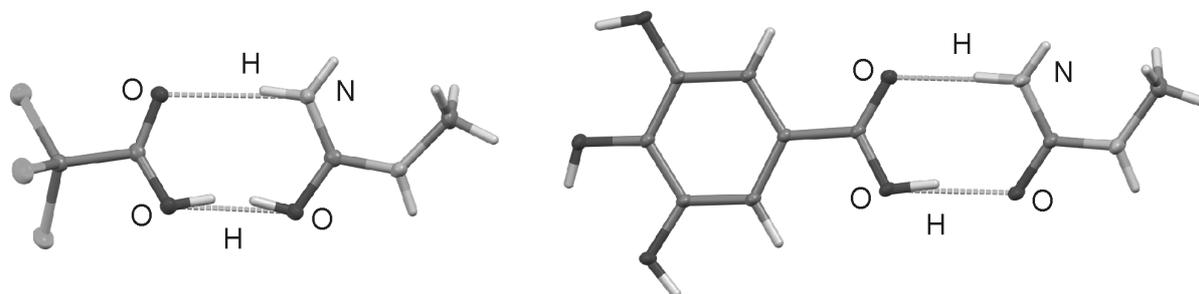
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Recent growth of scientific interests in co-crystallization is caused by its possible applications in pharmacy as a method of changing physical properties of active pharmaceutical ingredients [1-3]. Co-crystallization of various molecular components may be also understood as a supramolecular heterogeneous synthesis which utilizes versatile intermolecular interactions. Due to these reasons we have focused our attention to a co-crystallization of simple molecular blocks: urea and carboxylic acid derivatives. Special interests in urea are caused by its special properties in formation of intermolecular interactions - it can act as both hydrogen-bond donor through NH protons and acceptor with lone pairs of carbonyl group [4].



Our recent studies on N-methylurea co-crystals let identify carbonyl-urea double homo-heteroatomic O-H...O / N-H...O hydrogen bonding motif [5]. It has turned our attention also due to a potential double proton transfer *via* O-H...O and N-H...O hydrogen bonds and an assumption that these interactions could be classified as Low Barrier Hydrogen Bonds.

The presented studies are focused on analysis of O-H...O and N-H...O hydrogen bonds in urea-carboxylic acid complexes by means of experimental X-ray diffraction methods and theoretical quantum chemistry calculations. The analysis of the title synthon were performed in order to characterize the nature of intermolecular interactions in terms of their geometry, energetic and topological electron density properties.



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## Predicting the electron affinity of superhalogens by the quantitative structure property relationship method

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Superhalogens are inorganic compounds exhibiting enormously large electron affinities (significantly exceeding that of the Cl atom). The existence of these systems was postulated in 1981 by Gutsev and Boldyrev [1] who employed various theoretical chemistry tools to support their hypothesis. In fact, this prediction not only allowed for introducing novel class of molecular anions (formed by an excess electron binding to superhalogen molecules) but also greatly extended the range of the electronic stability the negatively charged systems might be characterized with [2].

In the absence of experimental data, a range of computational methods can be applied to fill those data gaps. One of the widely used techniques is Quantitative Structure–Property Relationships (QSPR) approach. This approach is based on defining and exploiting mathematical dependencies between the variance in molecular structures, encoded by so-called molecular descriptors, and the variance in a given physicochemical property within a set of compounds.

In this study, we have developed a QSPR model to predict the electron binding energy of superhalogens. New developed QSPR model defines which structural properties of superhalogens affect their electron binding energies and allow to verify the electron affinity of these compounds at the early stage of the design new superhalogens.

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## Synthesis and properties of polyether antibiotic - Cinchona alkaloid conjugates via click chemistry

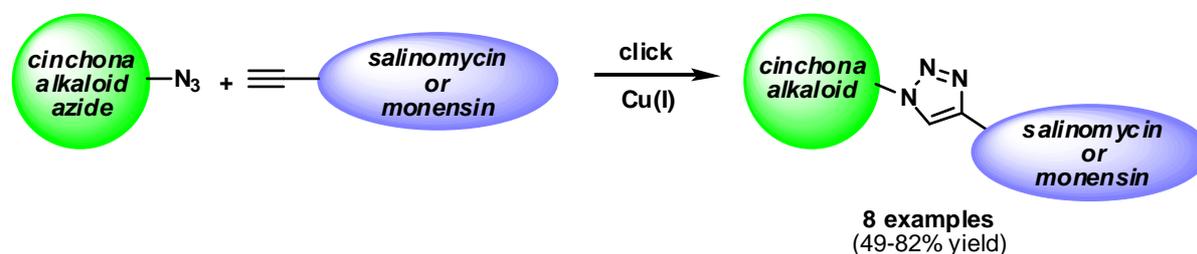
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The natural polyether ionophore antibiotics such as salinomycin and monensin as well as some of their derivatives exhibit significant cytotoxic properties thus are considered as novel chemotherapeutic agents for the treatment of some cancer types [1-4].

The main purpose of presented research was to design, synthesis and spectroscopic characterisation of new conjugates of polyether ionophores (salinomycin and monensin) with series of Cinchona alkaloids. These conjugates were easily accessible by 'click' chemistry approach based on the copper(I) catalyzed Huisgen azide-alkyne cycloaddition involving *N*-propargyl amides of salinomycin and monensin with four diverse Cinchona alkaloid azides. Based on high biological activity of counterparts, broad screening of conjugates in particular their *in vitro* cytotoxicity is currently underway.



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## Determination of interaction energies between pairs of O-phosphorylated and charged amino acids in water

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Phosphorylation is a post-translational modification. The transfer of phosphate group from ATP compounds (or ATP derivatives) to polar side chains of serine (Ser), threonine (Thr) or tyrosine (Tyr) is regulated by protein kinases. The binding the phosphate group, which is negatively charged, to a polar side chain causes changes in local protein conformations. Moreover, if changes take place in their secondary structures, their biological activities are different. Reversible protein phosphorylation is one of the most widespread cellular mechanisms regulating their functions. Experimental studies are very often not sufficient tool to study mentioned-above interactions. In this case theoretical studies are very helpful. One of the advantages to use them is a lower cost of the experiment.

In this presentation we show results of our work on determination of interaction energies between pairs of O-phosphorylated and charged amino acids in water. We performed a series of umbrella-sampling molecular dynamic (MD) simulations using by AMBER force field for pairs of O-phosphorylated serine, threonine and tyrosine and oppositely charged (as lysine and arginine) or the same charged (as glutamic and aspartic acids) amino acids with the use of TIP3P water model as a solvent at 298K. The interaction of pairs is represented as the potential of mean force (PMF), which is in our case a function of distance and orientation. The shape of PMF curves is characteristic with contact and solvent-separated minima, and desolvation maxima. For pairs of oppositely charged side chains contact minima corresponding to salt-bridge between charged pairs of interacting particles. Therefore, the minima corresponding to head-to-head and side-to-side orientations are in most cases deeper and with double or more minima than to those corresponding to the head-to-side and side-to-head orientations. For like-charged pairs the minima of head-to-head orientation is more deeper (about 0.5 kcal/mol) and shifted to larger distance than those of side-to-side orientation. In each cases, the minima corresponding to side-to-side are observed at a shorter distance.

## Synthesis and biological evaluation of colchicine C-ring analogues containing halogenated benzyl amine substituents

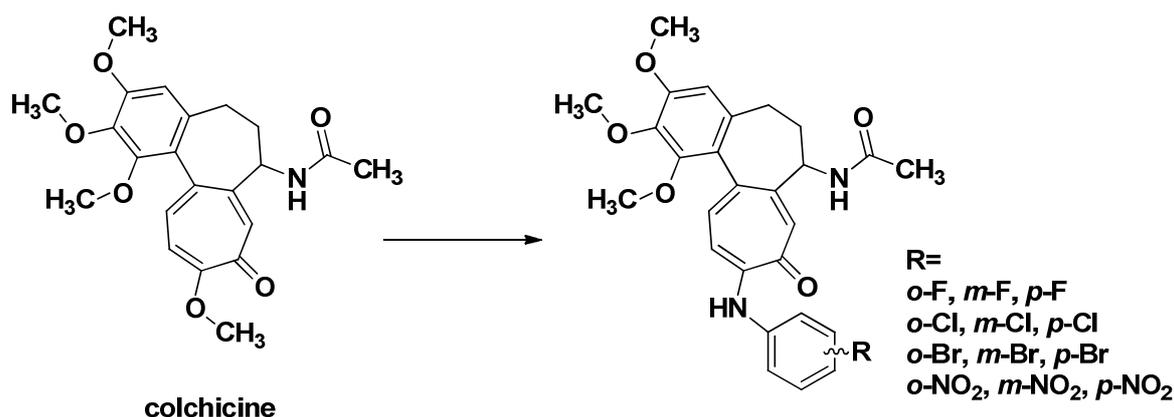
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Colchicine is a plant alkaloid that shows antimitotic effects on a number of cancer cell lines. Colchicine binds to tubulin, inhibiting the formation of microtubuli and, thus, blocks mitosis and reduces cell motility in certain cell types. Unfortunately, colchicine is too toxic to be useful as an antitumor agent. Several hundred colchicine derivatives have been synthesized in the search for analogs with lowered toxicity, and their structure/activity relationship (SAR) is, therefore, well characterized [1-2].

Herein, we report that colchicine can be functionalized at C-ring by a simple reaction with benzyl amines to yield various derivatives (Scheme 1).



We report also the structural elucidation of novel colchicine derivatives using spectroscopic methods.

The *in vitro* antiproliferative effect on various cell lines of colchicine derivatives is currently underway.

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## Differentiating between healthy and malignant lymph nodes at dielectric spectroscopy

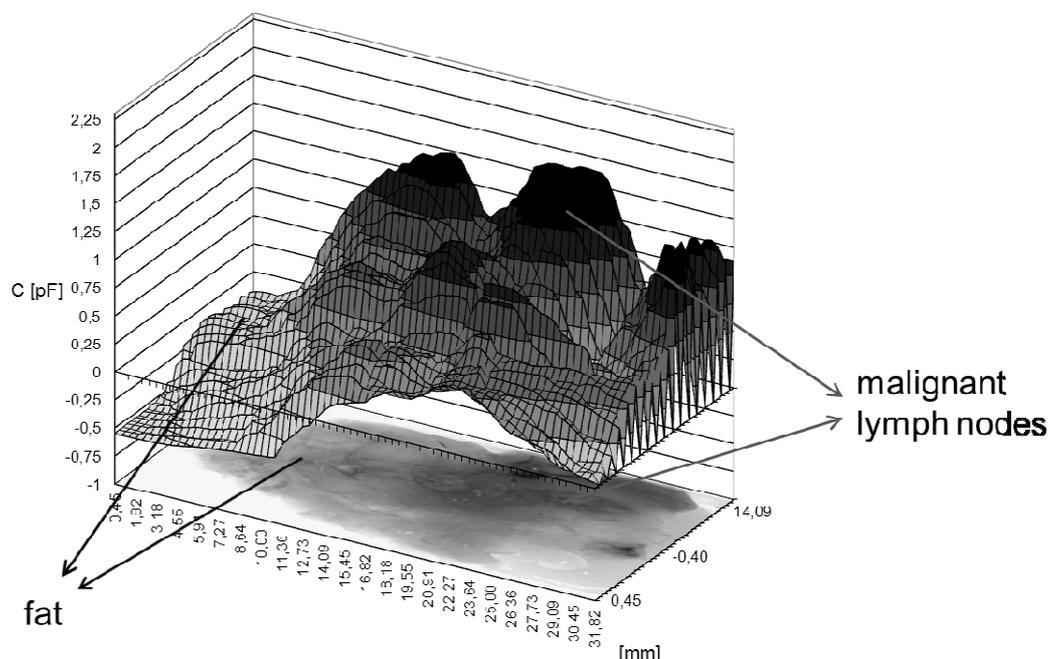
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It is well known that electric permittivity and conductivity of neoplasm tissue are usually higher than those of healthy tissue. Fat has the lowest electric permittivity and conductivity among different types of soft tissue. It is probably the main reason for the dielectric differences between normal and cancer breast tissue.

We have shown that dielectric spectroscopy could be a potential method in lymph node analysis. The figure shows a dielectric map and the photo of the sample (at the bottom). The sample consists of fat and embedded in the metastatic lymph nodes. High value of capacity (proportional to the  $\epsilon'$ ) reflects malignant lymph nodes. The similarities between the photo, and the dielectric map are evident.

We intend to construct an intraoperative probe which allows to estimate condition of lymph nodes.



## Molecular dynamics simulations of interactions of congo red with single-walled carbon nanotubes

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Congo red (CR) is a diazo dye revealing the ability of forming ordered amyloid-like organization of protein aggregates and is used in testing amyloid proteins, including Alzheimer plaque proteins and prions. It is also well-known that CR forms rigid ribbon-like micelles in water solutions. The rigidity depends on pH of solution, the lower pH the stronger interactions due to reduction of repulsive electrostatic interactions<sup>1</sup>.

Studies of interaction of CR with carbon nanotubes (CNT) have not been reported in literature so far. Thus, we anticipate that, depending on pH, the CR-CNT conjugates may change their stability and structure. Therefore we prepared a molecular dynamics simulation code for the purpose of determination of binding energy of CR to CNT at various pH values. We assumed that at neutral pH the CR exists in deprotonated form and at acidic pH the amine groups of CR become additionally protonated.

The molecular dynamics simulations were based on the generalized AMBER force field (GAFF)<sup>2</sup> and were performed using the open source lammps code<sup>3</sup>. We consider several cases that is: starting system, for testing purposes, containing 20 CR molecules, 2300 water molecules and Na<sup>+</sup> ions in the amounts of two ions per each CR molecule and systems containing single walled carbon nanotubes with chiralities (10,0) and (30,0) and 20-40 CR molecules..

We will show how structural parameters CR micelles change with pH, that is the parameter representing the planarity of a single CR molecule and the parameter representing spatial structure of the ensemble of CR molecules (distribution of angles between individual CR molecules). We will also discuss how binding energy between CR molecules and CNT varies with pH and how the free energy of binding is affected by the CR density, CNT parameters and pH values.

### Acknowledgement

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