University of Łódź
Faculty of Chemistry
Department of Organic & Applied Chemistry

Polish Chemical Society

VIIth International Mini-Symposium

Heteroatom containing compounds on the borderline of chemistry, biology, and medicine

21-22 May, 2013

Acknowledgement

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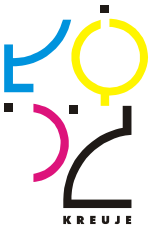

Organizing Committee thanks to WITKO company for support during Mini-Symposium

Program & Abstracts

Conference venue:

University of Łódź, Faculty of Chemistry, Tamka-Str. 12,

The Large Assembly Hall, A-1

Organizing committee:

Chairman:	Prof. dr. hab. Grzegorz Mlostoń
Secretary:	Prof. UŁ, dr. hab. Jarosław Romański
Members:	Dr. Katarzyna Urbaniak
	Małgorzta Celeda
	Zenona Frydrych

Program

Wednesday - May 21st, *The Faculty Council Hall (room 1-020)*

14:55 ***Opening and Welcome***

15:00 Filip Bures
L-1 University of Pardubice, Czech Republic

Thursday - May 22nd, *The Large Lecture Hall*

12:55 ***Opening and Welcome***

Keynote Lecture: *Introduced by Prof. Michał Pietrusiewicz (Maria Curie Skłodowska University, Lublin)*

13:00 – 13:45 Jean-Pierre Majoral
L-2 **CNRS Tolouse, France**

Session 1: ***Chairman:*** *Prof. Stafan Jankowski (Lodz University of Technology)*

13:45 – 14:15 Paweł Kafarski
L-3 Wroclaw University of Technology, Poland

14:15 – 14:45 Wiesław Szeja
L-4 Silesian University of Technology, Poland

14:45 – 15:15 Heinz Heimgartner
L-5 University of Zurich, Switzerland

15:15 – 15:45 Coffee break

Session 2 ***Chairman:*** *Prof. Piotr Kiełbasiński (Polish Academy of Science, Lodz)*

15:45 – 16:15 Christian Hackenberger
L-6 Leibnitz Institute Berlin, Germany

16:15 – 16:45 Grzegorz Bartosz
L-7 University of Lodz, Poland

16:45 – 17:15 Magdalena Markowicz
L-8 Medical University of Lodz, Poland

17:15 – 17:45 Damian Plażuk
L-9 University of Lodz, Poland

17:45 – 19:30 Garden Grill Party

L-1

Thiophene, pyridine and pyrimidine on duty in push-pull systems

Filip Bureš

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Nowadays, functionalized organic π-conjugated molecules are tremendously investigated due to their prospective applications as active materials in optoelectronic devices such as OLEDs, OPVCs, DSSCs or OFETs. A π-system end-capped with electron donors and acceptors constitutes a class of organic compounds called push-pull systems. Such molecules possess plenty of interesting and useful properties such as dipolar character, color, electrochemical activity, solvatochromic behavior, biological activity, nonlinear optical properties etc. Push-pull systems may adopt various arrangement, the most used are linear D-π-A, quadrupolar D-π-A-π-D or A-π-D-π-A (linear, X- and V-shaped) and octupolar $(D\text{-}\pi\text{-})_3A$ or $(A\text{-}\pi\text{-})_3D$ (T- and Y-shaped, tripodal). The property tuning of push-pull systems can mainly be achieved by attaching electron donors/acceptors of various nature, extension, planarization and composition of the π-system and also by the environment (solid, solution, polymer etc.). Recently, it has also been realized that incorporation of an heterocyclic moiety into the chromophore π-backbone renders molecules with pronounced properties such as intramolecular charge-transfer (ICT), (hyper)polarizability, (semi)conductivity and chemical and thermal stability. In this respect, various heteroaromates were utilized and used for the construction of push-pull molecules. Moreover, the heteroatom present in the heterocycle would represent a coordination site, basic center, electronegative and significantly polarizable molecule part and thus enhances the chromophore performance. In our group we have focused our recent synthetic efforts towards of five and six membered heteroaromates used for construction of push-pull molecules. Thiophene is one of the most versatile, tunable and polarizable five membered hetrocycle that feature also auxiliary donating character and can be effectively employed in push-pull chromophores **1**-**2** (Figure 1).[1,2] On the contrary, six membered (di)azines such as pyridine and pyrimidine represent electron deficient heterocycles that can be used as acceptor moieties in chromophore types **3** and **4**.[3,4] Synthesis, structure-property relationships and application of such molecules will be discussed.

Figure 1. General structures of thiophene, pyridine and pyrimidine derived push-pull chromophores.

1. Kulhánek J., Bureš F., Opršal J., Kuznik W., Mikysek T., Růžička A. *Asian J. Org. Chem.* **2013**, *2*, 422-431.
2. Wojciechowski A., Raposo M. M. M., Castro M. C. R., Kuznik W., Fuks-Janczrek I., Bureš F., Kityk I. V. *submitted.*
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L-2

Functional phosphorus dendrimers .
From chemistry and biology to medicine… and more!

Jean Pierre Majoral

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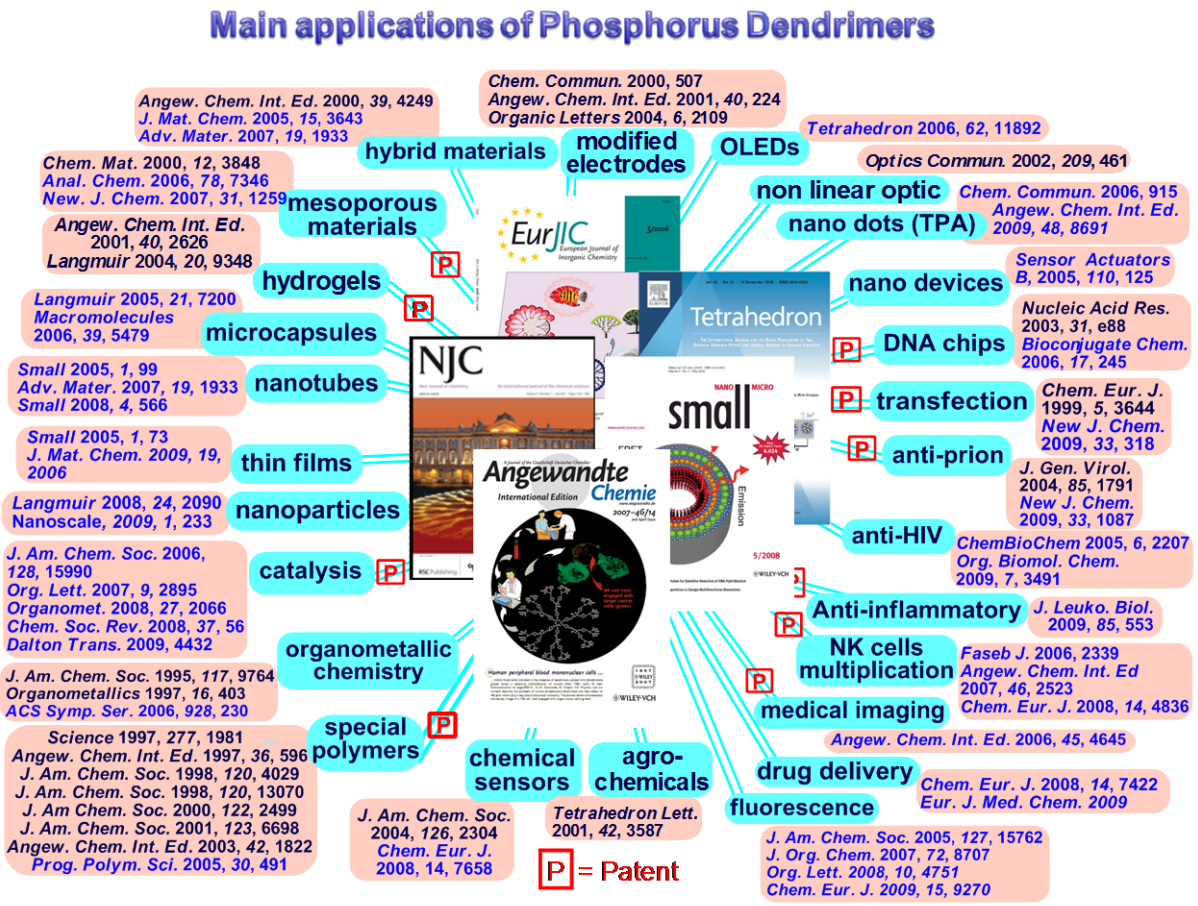
More and more applications of dendrimers are appearing in the literature covering many topics from biology, biomedicine, material sciences,catalysis. As a consequence such an appealing field of research implies to diversify the nature and the composition of existing types of dendrimers but also to propose the preparation of tailored new types of dendrimers which might be able to open new areas of investigations. Selected properties and applications of some of the phosphorus containing dendrimers we are currently working with will be presented and discussed.



L-3

Aminophosphonate inhibitors of enzymes – chemists point of view

Paweł Kafarski

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Aminophosphonic acids are broadly defined as analogues of amino acids, in which the carboxylic group is replaced by a phosphonic acid or related group (usually phosphonous or phosphinic acids). This results in the presence of the characteristic N-C-P scaffold. Quite often, they are considered as simple analogues of their natural counterparts. Although carboxylic and phosphonic acid groups differ in shape (tetrahedral at phosphorus versus planar at carbon), acidity (with phosphonic acid being significantly more acidic), and steric bulk (the phosphorus atom has a much larger atomic radius than carbon), they frequently exhibit similar properties, with the phosphonic acid being recognized by enzymes or receptors as false substrates or inhibitors. However, such simple analogues quite rarely have found commercial applications in medicine and agriculture. More often, strong inhitory activity have been found for those, in which the tetrahedral geometry of substituents around the phosphorus moiety causes it to resemble the high-energy transition state (TS) of ester and amide bond hydrolyses.

Research on the design, synthesis and evaluation of phosphonic acid inhibitors of key enzymes of socially important diseases is a hallmark of our department. It was initiated as log ago as in 1959 by Prof. Przemysław Mastalerz, who discovered potent phosphonic inhibitors of glutamine synthetase. Today, these studies are considering such enzymes as: aminopeptidases (as anticancer, antibacterial and antimalarial agents), urease (as potential drugs against stomach ulcer and bacteria forming stones in urinary tract), cathepsins (as possible anticancer drugs), glutamine synthetase (agents against tuberculosis) and δ1-pyrroline-5-carboxylate reductase (antibacterials). Additionally over 200 bisphosphonates have been synthesized and tested as potential antiosteoporetic agents.

L-4

Sugar moiety structure as a proncipal determinant of isoflavone biological activity

Wiesław Szeja[a], Tadeusz Bieg[a], , Anna Kasprzycka[a], Gabriela Pastuch-Gawołek[a], Ilona Wandzik[a], Katarzyna Komor[a], Roman Komor[a], Przemysław Hahn[a], Agata Ptaszek-Budniok[a], Piotr Świerk[a], A.Byczek[a], A.Rusin[b], G.Grynkiewicz[c]

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Approximately half of the existing drugs are derived from (or inspied by) natural products, while recently obtained large synthetic combinatorial libraries fail to deliver experimentally validated new drug candidates. Secondary metabolites, successfully exploited in medicinal chemistry as pharmacological models or drug leads, frequently contain in their structure a glycosidic element, seemingly indispensable for their biological activity. [1] At a dawn of glycobiology and glycomic era we learn to appreciate molecular recognition mechanisms of carbohydrates on a biopolimer level (which govern majority of the vital cell sociology phenomena) [2], but we are still mystified by functions performed by a single monosaccharide moiety in a low molecular weight ligand. Chemical glycosylation is a useful tool applied in medical chemistry in modification of complex compounds isolated from natural sources [3]. In our experience, addition of a glycosyl residues to pharmacophoric scaffold can be very useful for creating diversity of structure and function in many classes of medicinally useful compounds, but efficient and stereoselective glycosylation of complex aglycones remains difficult, particularly in scale up. Screening of several methods of regioselective substitution [4] and stereoselective chemical glycosylation on genistein derivatives will be discussed, with focus on application of hex-1-enitols (glycals) as glycosyl donors [5]. Results of a research program, consisting of chemical derivatization of genistein, molecular modeling and biological activity studies of new derivatives aimed at proposing new potential anticancer compounds will be discussed. Biological screening *in vitro* of new glycoconjugate derivatives of 2,3-unsaturated mono- and disaccharides derivatives using cancer cell lines (Hct 116 +/+p53, Hct 116 -/-p53, Ht 29, AGS, LNCaP, PC3, DU 145, A549) indicated a number of compounds of increased potency, actually more effectively inhibiting cancer cell growth in comparison to the parent compound, genistein [5]. The assumed biomolecular mechanism was partially based on the genistein molecular targets, i.e. tyrosine kinases, however, for some derivatives also a new mechanism associated with microtubules, was found [4]. The described group of compounds are important objects for the structure - activity relationship studies because of at least two reasons: formerly none of the genistein derivatives with the spacious group added at C7 of genistein was reported to inhibit tyrosine kinases more efficiently than genistein, microtubules appeared to be new promising target for isoflavonoid derivatives.

References

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L-5

L-6

When Staudinger Meets Huisgen – New avenues for chemoselective P(III)-reagents

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The Hackenberger laboratory aims to develop new chemoselective organic transformations for studying the biological and functional aspects of protein modifications.[1] In this, we have recently employed Staudinger reactions with different P(III)-reagents including phosphites and phosphonites to deliver functional peptide and protein-conjugates. Applications of these reactions, which will be presented in this talk include a PEGylation strategy for the intracellular stabilization of peptides,[2] a novel concept for the formal coupling of two azido-containing molecules and the generation of protein-based scaffolds for the presentation of multivalent ligands.[3]

References

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