XXIV International Symposium "Advances in the Chemistry of Heteroorganic Compounds"

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Centre of Molecular and Macromolecular Studies
Polish Academy of Sciences

Section of Heteroorganic Chemistry
of the Polish Chemical Society

Jan Dlugosz University in Czestochowa

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is dedicated to

Professor

Piotr Kiełbasiński

on the occasion of his 75th birthday

and

to honor his 53 years of scientific activity
at the Centre of Molecular and Macromolecular Studies
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XXIV International Symposium

"Advances in the Chemistry of Heteroorganic Compounds"

Łódź, November 24, 2023 (Friday)

9:00 – 9:30	**OPENING**	
SESSION I – chairman: Radomir Jasiński		
9:30 – 10:15	PL-1	**Mar Ríos-Gutiérrez** University of Valencia, Spain *A modern rationalization of [3+2] cycloaddition reactions based on the Molecular Electron Density Theory*
10:15 – 11:00	PL-2	**Tsukasa Nakahodo** Kindai University, Japan *Synthesis and Properties of Polymer-nanotubes Hybrid Materials*
11:00 – 11:30	**COFFEE BREAK**	
11:30 – 12:30	**POSTER SESSION I (P001-P065)**	
SESSION II – chairman: Michał Pietrusiewicz		
12:30 – 13:15	PL-3	**György Keglevich** Budapest University of Technology and Economics, Hungary *The Application of Microwaves in the Synthesis of Organophosphorus Compounds as Intermediates and Biologically Active Species*
13:15 – 14:00	PL-4	**Claudio Santi** University of Perugia, Italy *Santi's Reagent 15 years of research on PhSeZnCl and its derivatives: from Green Chemistry to the Redox Paradox*
14:00 – 15:00	**LUNCH**	
15:00 – 16:00	**POSTER SESSION II (P066-P130)**	
SESSION III – chairman: Grzegorz Mlostoń		
16:00 – 16:45	PL-5	**Axel Schulz** University of Rostock, Germany *Rational design of phosphorus centered biradicals*
16:45 – 17:30	PL-6	**Cecilia Scimmi** University of Perugia, Italy *Selenium reagent for the treatment of biomasses: detoxification of olive mill wastewater and production of derived lignin-biomaterials*
17:30 – 17:45	**CLOSING**	

Lectures

PL-1
A modern rationalization of [3+2] cycloaddition reactions based on the Molecular Electron Density Theory

Mar Ríos-Gutiérrez[1] and Luis R. Domingo[1]

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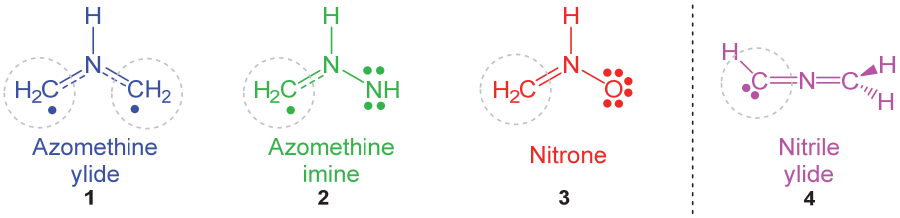
In 2016, Domingo proposed the Molecular Electron Density Theory (MEDT) [1] as a new theory, opposed to the widespread Frontier Molecular Orbital (FMO) theory,[2] to explain organic chemical reactivity. According to MEDT, it is the changes in electron density, and not molecular orbital interactions, that determine any chemical event.

MEDT has already challenged many traditional concepts such as the concerted [3] and pericyclic mechanisms,[4] making evident that a modern reinterpretation of organic chemical reactivity is needed. In the field of [3+2] cycloaddition (32CA) reactions, MEDT has allowed establishing a general classification into four different types depending on a novel structure/reactivity relationship found for the three-atom-components (TACs) involved (see Figure 1).[5]

In the present talk, I will show the application of MEDT to the study 32CA reactions. Besides exploring the practical application of some of the quantum chemical tools most frequently used in MEDT studies, the new rationalization [5] of these relevant organic reactions built upon MEDT, and how it compares to the still current textbook description, will be emphasized.



Structure			
pseudodiradical	*pseudoradical*	zwitterionic	carbenoid
Reactivity			
pdr-type	*pmr-type*	*zw-type*	*cb-type*
1.0 kcal/mol	7.7 kcal/mol	13.4 kcal/mol	7.8 kcal/mol

Figure 1. Electronic structure of simplest TACs and proposed reactivity types in 32CA reactions. MPWB1K/6-311G(d) gas phase activation energies of the non-polar 32CA reactions between the four simplest TACs **1** – **4** and ethylene **5**, relative to the corresponding molecular complexes, are given in kcal·mol^{-1}.

Acknowledgement

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PL-2
Synthesis and Properties of Polymer-nanotubes Hybrid Materials

Tsukasa Nakahodo[1,2]

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[2]*Faculty of Science and Engineering; Kindai University*
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In recent years, research on various types of nanotubes, including carbon nanotubes, organic nanotubes, and metal nanotubes, has been active. Polymer nanotubes are a type of nanotube that can be easily obtained by polymerizing monomers with electropolymerization capabilities (such as thiophene and pyrrole derivatives) in template pores. Additionally, the size of polymer nanotubes can be controlled by changing the size of the template used.[1,2] Various functionalities can be added to polymer nanotubes by introducing functional moieties into the monomers and polymerizing them.[3-7] For instance, optically active polymer nanotubes can be created by employing chiral monomers. These polymer nanotubes are anticipated to serve as chiral filters for sorting out optical isomers by letting racemic compounds pass through as well as for asymmetric synthesis applications that utilize the internal chiral environment. When polymer nanotubes act as hosts, substances of various sizes can be incorporated into their interiors, resulting in the emergence of new properties.[8] In this presentation, the results of our laboratory's investigation into synthesizing and characterizing polymer nanotubes, as well as incorporating materials into their interiors, will be discussed.

1. Synthesis of Polymer-nanotubes and Encapsulation in Its Nano-Cavities

Ethylenedioxythiophene (EDOT) or cyclohexyldioxythiophene (CDOT), were electropolymerized within the nanopores of a porous alumina template, resulting in the formation of polymer-nanotubes derived from EDOT (EDOT-PNTs) and CDOT (CDOT-PNTs). Using these PNTs, retained within the porous alumina, and using the principle of vacuum filtration, a dispersion solution of magnetite nanoparticles was introduced into the intrinsic inclusion spaces of the PNTs. Consequently, the peapod structures of PNTs were established with PNTs as the host and magnetite nanoparticles as the guest (Fig. 1).

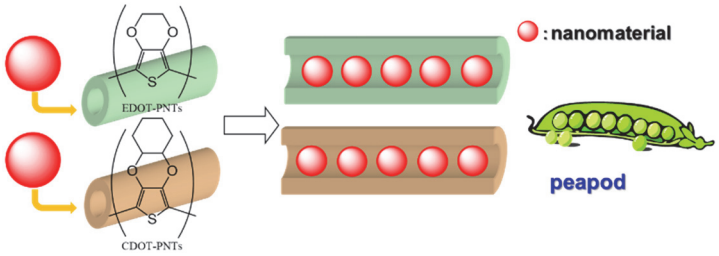


Fig. 1 Syntheses of EDOT-, CDOT-PNTs

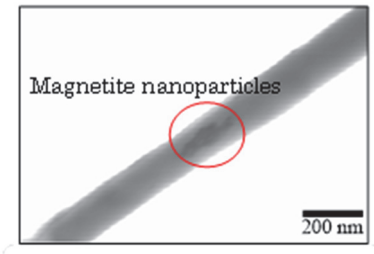
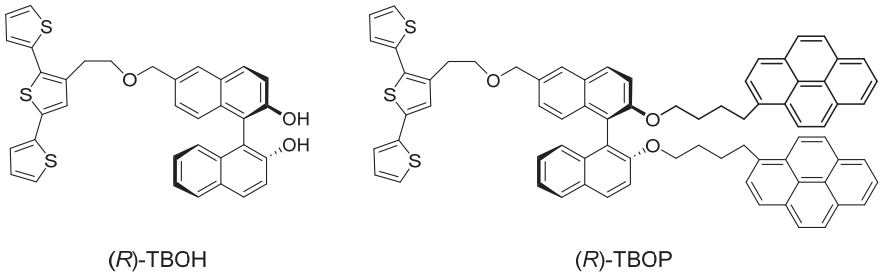


Fig. 2 STEM image of magnetite nanoparticles encapsulated in CDOT-PNTs.peapods.

Transmission electron microscopy (TEM) observations of these PNTs peapods validated the encapsulation of magnetite nanoparticles within the PNTs (Fig. 2). Given the magnetic attraction exhibited by the PNTs peapods infused with magnetite nanoparticles, it was confirmed that the magnetic properties of the internalized magnetite nanoparticles were preserved within the PNTs. Furthermore, (*R*)-BINOL and pyrene moieties were incorporated to synthesize (*R*)-TBOP (Fig. 3). Electropolymerization of these compounds successfully yielded (*R*)-TBOP-PNTs, which possess nanoscale chiral spaces internally. By introducing a toluene solution of C_{60} into the prepared (*R*)-TBOP-PNTs, C_{60} was incorporated into the hollow space of the PNTs. To investigate changes in fluorescence properties between (*R*)-TBOP-PNTs and C_{60}@(*R*)-TBOP-PNTs, each dispersed solution was exposed to UV light at 365 nm. It was discerned that fluorescence quenching occurred in C_{60}@(*R*)-TBOP-PNTs (Fig. 4). This phenomenon is postulated to be attributed to electron transfer from the pyrene moiety to the encapsulated C_{60}.

PL-2



(*R*)-TBOH (*R*)-TBOP

Fig. 3

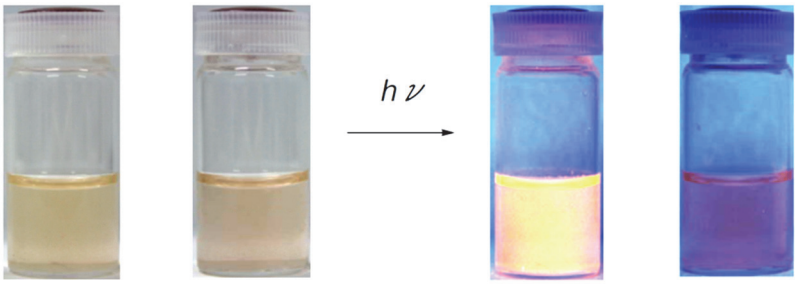
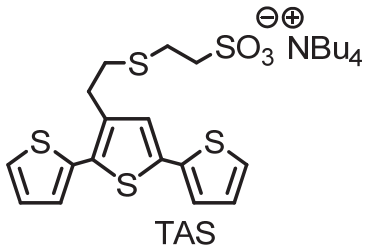


Fig. 4 Fluorescence of (*R*)-TBOP-PNTs and C_{60}@(*R*)-TBOP-PNTs.

2. Functionalization of Polymer-nanotubes and Capturing of Materials using Electrostatic Interactions

A tetrathiophene derivative bearing sulfonic acid groups (TAS) was synthesized. Using a porous alumina membrane with a pore diameter of approximately 200 nm as a template, electropolymerization was performed, culminating in the synthesis of water-soluble polymer-nanotubes (TAS-PNTs). Subsequently, the porous alumina membrane was dissolved in a NaOH*aq* solution and the resultant sample was observed by scanning electron microscopy (SEM) and transmission electron microscopy (TEM). These examinations confirmed the generation of TAS-PNTs with a narrow size distribution, possessing an external diameter of approximately 200 nm and an internal diameter of approximately 120 nm (Fig. 5, 6). In continuation, with the objective of probing the interfacial recognition capabilities of TAS-PNTs, the synthesis of cationic gold nanoparticles (Au-oxy-VL) was conducted (Fig.7).



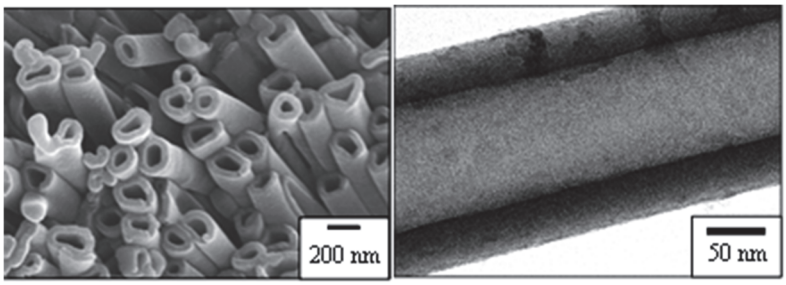
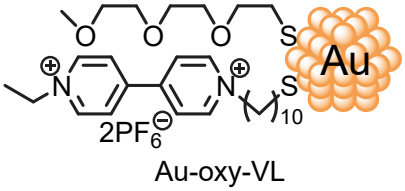


Fig. 5 SEM image of TAS-PNTs. **Fig. 6** TEM image of TAS-PNTs.



Au-oxy-VL

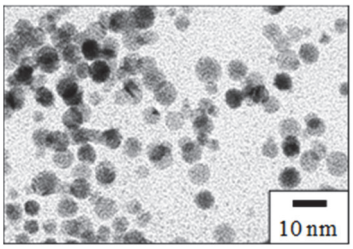


Fig. 7 TEM image of Au-oxy-VL.

Within the aqueous solution of synthesized Au-oxy-VL, an alumina membrane modified with TAS-PNTs was immersed, leading to the formation of an Au-oxy-VL-TAS-PNTs composite. Observations of the derived sample through SEM, STEM, TEM, and energy-dispersive X-ray spectroscopy (EDX) revealed that the cationic gold nanoparticles (Au-oxy-VL) were uniformly encapsulated within the internal space of the TAS-PNTs, without any evident aggregation (Fig. 8, 9).

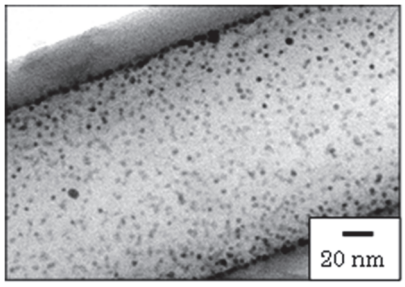


Fig. 8 TEM image of Au-oxy-VL@TAS-PNTs.

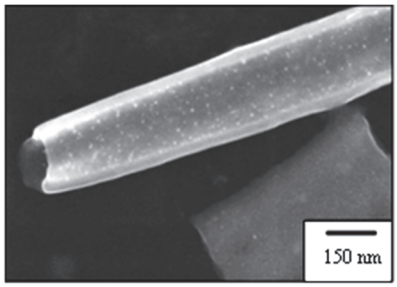


Fig. 9 Dark-field STEM image of Au-oxy-VL@TAS-PNTs.

3. Direct Preparation of Metallic Nanoparticles within the Confines of Polymer-nanotubes

(*S*)-TBOH containing chiral BINOL as a functional group was synthesized and electropolymerized using a porous alumina template to synthesize (*S*)-TBOH-PNTs. Subsequently, HCl*aq* solutions of $SnCl_2$ and $HAuCl_4$, respectively, were prepared. The $SnCl_2$ / HCl*aq* solution was then injected into the (*S*)-TBOH-PNTs still supported on the porous alumina template to form complex ions with the hydroxyl groups of the (*S*)-TBOH-PNTs. Then, after washing with deionized water, $HAuCl_4$ HCl solution was introduced into the (*S*)-TBOH-PNTs, and Au^0 was successfully loaded into the (*S*)-TBOH-PNTs by reductive deposition of Au^0 using the difference in standard electrode potentials between Sn^{2+} and Au^{3+} (Fig. 10).

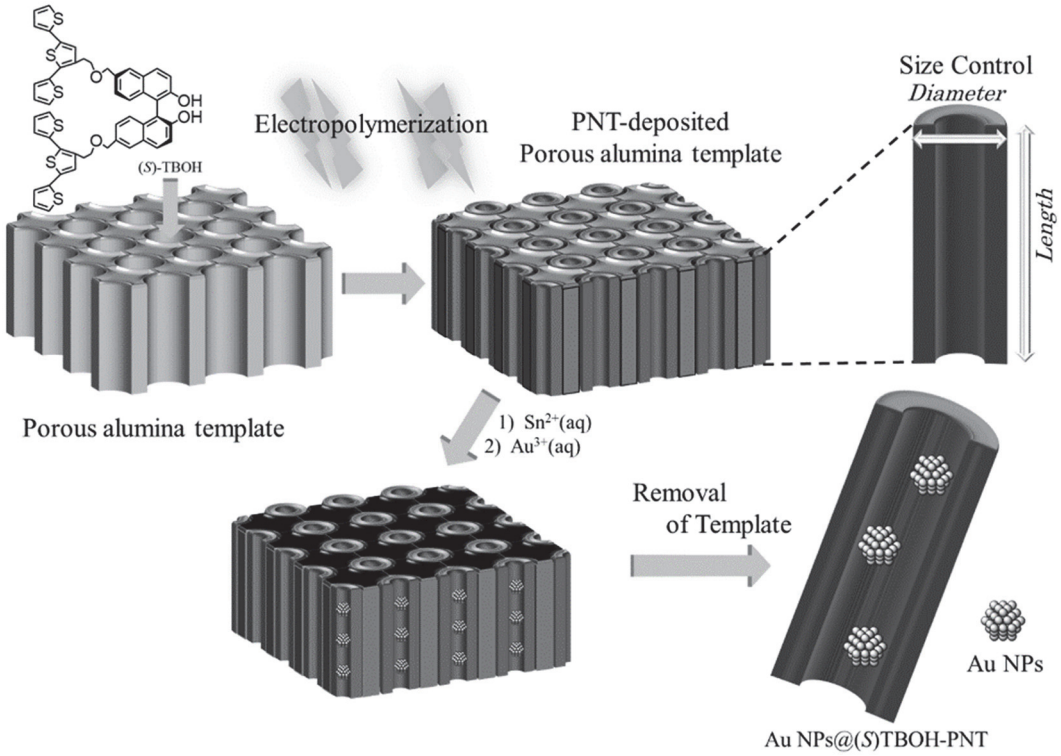
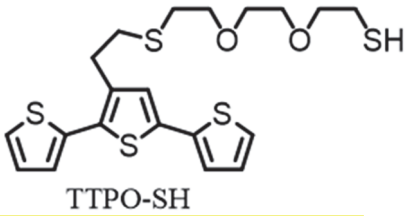


Fig. 10 Synthesis of Polythiophene Nanotubes [(*S*)-TBOH-PNTs] and Au NPs@(*S*)-TBOH-PNTs.

Due to their extremely high surface activity and instability, metal nanoclusters are usually prepared and isolated with various organic molecules as protecting groups.[9] Thus, an example of direct preparation and stable isolation of gold nanoparticles using the inner space of polymer nanotubes is considered to be very rare.[10,11] Moreover, in contrast to conventionally protected gold nanoparticles, those generated and encapsulated within polymer-nanotubes may possess numerous unshielded active sites, suggesting potential utility in catalytic reactions. Furthermore, this methodology confirmed the potential for the direct generation and loading of other metallic nanoparticles such as Ag and Pd within polymer-nanotubes. These results are expected to be applied to the study of the unique surface plasmon resonance phenomena observed at the metal-nanoparticle interface[12] and to the catalysis of various catalytic reactions involving asymmetric reaction fields.[13]

4. Synthesis of Metal Nanoparticle-Polymer-nanotubes Composites

In the presence of tert-thiophene oligoethylene oxide thiol (TTPO-SH), Au^{3+} ions and Pd^{2+} ions were reduced by $NaBH_4$, culminating in the preparation of gold nanoparticles with TTPO-SH as protective group (TTPO-Au, with a particle diameter of approximately 2.3 nm) and palladium nanoparticles (TTPO-Pd, with a particle diameter of approximately 2.7 nm) as depicted in Fig. 11.[13] Subsequently, employing nano porous alumina as a template, electropolymerization of each metallic nanoparticle was undertaken, successfully yielding gold and palladium nanoparticle-polymer-nanotubes composites (TTPO-Au-NTs, TTPO-Pd-NTs) as illustrated in Fig. 12.



TTPO-SH

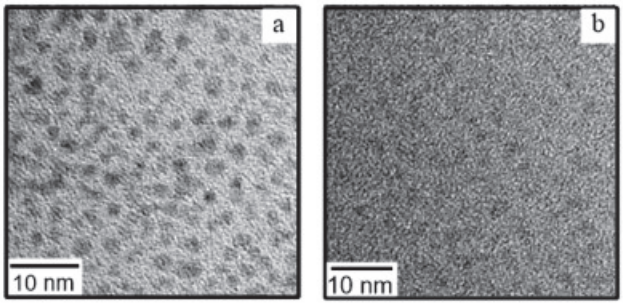


Fig. 11 TEM images of (a) TTPO-Au and (b) TTPO-Pd.

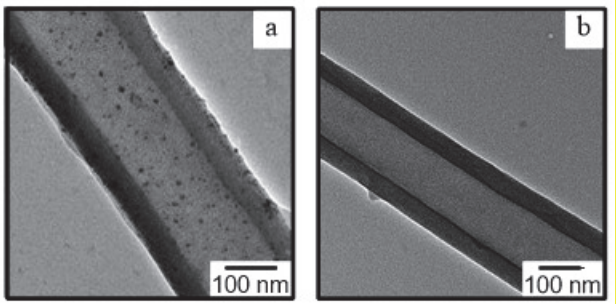
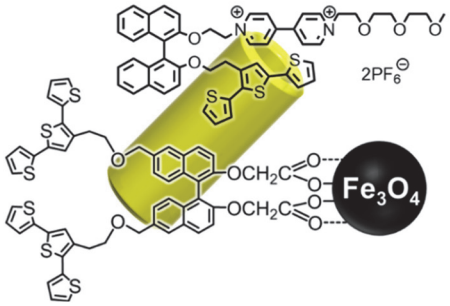


Fig. 12 TEM images of (a) TTPO-Au-PNTs and (b) TTPO-Pd-PNTs.

5. Creation of Polymer-nanotubes Possessing Redox Activity and Magnetism, and their Extension to Interphase Mass Transfer

Magnetite is an oxidized mineral manifesting profound magnetism, and upon reducing its size to an approximate diameter of 20 nm, it exhibits a unique characteristic known as superparamagnetism. Magnetite nanoparticles (MP) with such traits are anticipated for potential use in magnetically-induced drug delivery systems by adorning their surfaces with pharmaceuticals, antibodies, or metals possessing catalytic activities. Utilizing an electrolytic copolymerization method, we successfully synthesized polymer-nanotubes (PNTs) designated as (*S*)-VMP, which inherently combined both redox activity and magnetism. When (*S*)-VMP in water and introducing a magnet was introduced proximally, there was a perceptible attraction of the (*S*)-VMP toward the magnet (Fig. 13). Subsequently, capitalizing on the electrostatic interactions rendered by the viologen present in (*S*)-VMP, we endeavored to encapsulate Pyranine, a water-soluble fluorescent molecule. Observations from the PL spectrum denoted a temporal decline in Pyranine's fluorescence, confirming its successful incorporation within the PNTs (Fig. 14). Further investigations revealed that using a magnet the transportation of Pyranine, encapsulated within PNTs, between aqueous and organic phases. Additionally, through reductive reactions employing reducing agents on the viologen moieties, the entrapped Pyranine was successfully liberated and extracted.



(*S*) or (*R*)-VMP

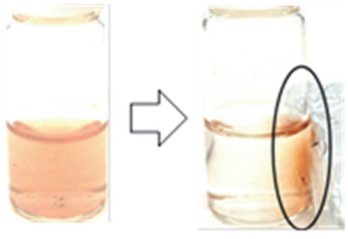


Fig. 13 Magnetic behavior of (S)-VMP.

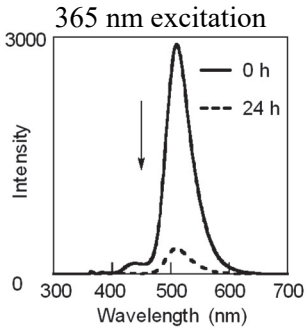


Fig. 14 PL spectra of pyranine in the presence of (S)-VMP in water.

Acknowledgement

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PL-3

The Application of Microwaves in the Synthesis of Organophosphorus Compounds as Intermediates and Biologically Active Species

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The microwave (MW) technique has become an important tool in organophosphorus chemistry. In this lecture, the advantages of MWs in different reactions are surveyed allowing green chemical accomplishments. The first case is the MW-assisted direct esterification of phosphinic-[1] and phosphonic acids,[2] along with phosphoric ester-acids[3] that all became more efficient in the presence of an ionic liquid catalyst. The O-alkylation of phosphonic acids and phosphoric ester-acid derivatives under MW irradiation is also a useful technique. A new field is the aminolysis of phosphinates and the alcoholysis of phosphinic amides.[4] Alcoholyses and hydrolyses of P-esters were also investigated and optimized.[5–7] MWs may substitute catalysts, in certain reactions, such as in the Kabachnik–Fields condensations of amines, aldehydes and >P(O)H reagents. The tandem phospha-Mannich reaction is a new protocol. A series of new α-aminophosphonate derivatives including acylated species were prepared that displayed significant anticancer activity on certain cell cultures.[8–10] Another valuable finding of ours is that in the Hirao P–C coupling of >P(O)H reagents and bromoarenes applying $Pd(OAc)_2$ as the catalyst, the slight excess of the >P(O)H species may substitute the usual P-ligands in the tautomeric >POH form.[11,12] Ni-catalyzed cases were also investigated involving an unexpected mechanism assuming a Ni(II) → Ni(IV) transition.[13] A halogene-free P-C coupling was also developed.[14] The synthesis of α-hydroxyphosphonates and derivatives,[15] as well as hydroxy-methylenebisphosphonates[16,17] as biologically active substrates or drugs in the treatment of bone diseases will also be discussed. Flow chemical accomplishments of a few reactions mentioned above, *e.g.* esterifications, alcoholyses and hydrolyses are also presented. It is also the purpose of this paper to elucidate the scope and limitations of the MW tool.

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PL-4

Santi's Reagent
15 years of research on PhSeZnCl and its derivatives: from Green Chemistry to the *Redox Paradox*

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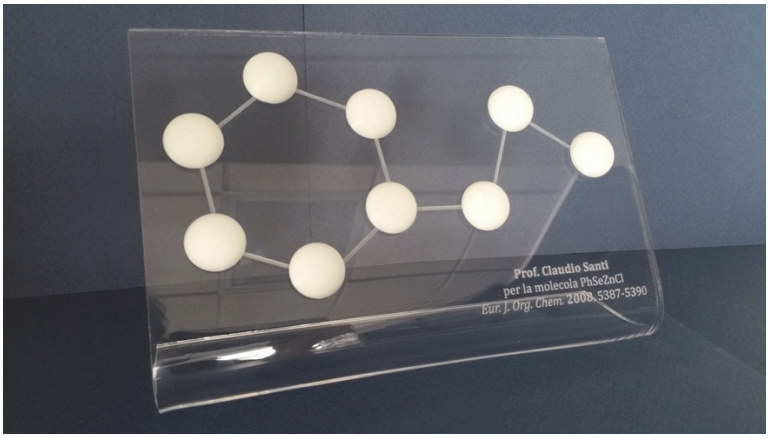
15 years ago, quite fortuitously, through the oxidative insertion of zinc into the Se-Cl bond of PhSeCl, I achieved the formation of the first stable form of selenate in non-inert ambient conditions. Interest in this new chemical species immediately focused on two fronts: the synthetic and the biological. The latter was mainly motivated by the fact that no stable selenorganic molecule is currently capable of reproducing the oxidation state that the selenium atom has in the native form of the glutathione peroxidase. From a synthetic point of view, these new zinc selenates have shown unexpected reactivity in on-water conditions, offering the opportunity to develop numerous synthetic processes responding to the dictates of Green Chemistry. As regards the biological activity, the initial enthusiasm linked to a marked GPx-mimetic activity has opened a new vision through what we named the "Redox Paradox", the first evidence of the need to address the biological redox of selenorganic compounds as a Complex System.



plaque commemorating the discovery of PhSeZnCl

Acknowledgement
I want to thank all my students, my coworkers and all the scientists that using and studing PhSeZnCl contributed to develop its novel and useful chemistry, profiling its toxicological and biological properties opening a new vision for the biological application of the organoselenium compounds.

PL-5
Rational design of phosphorus centered biradicals

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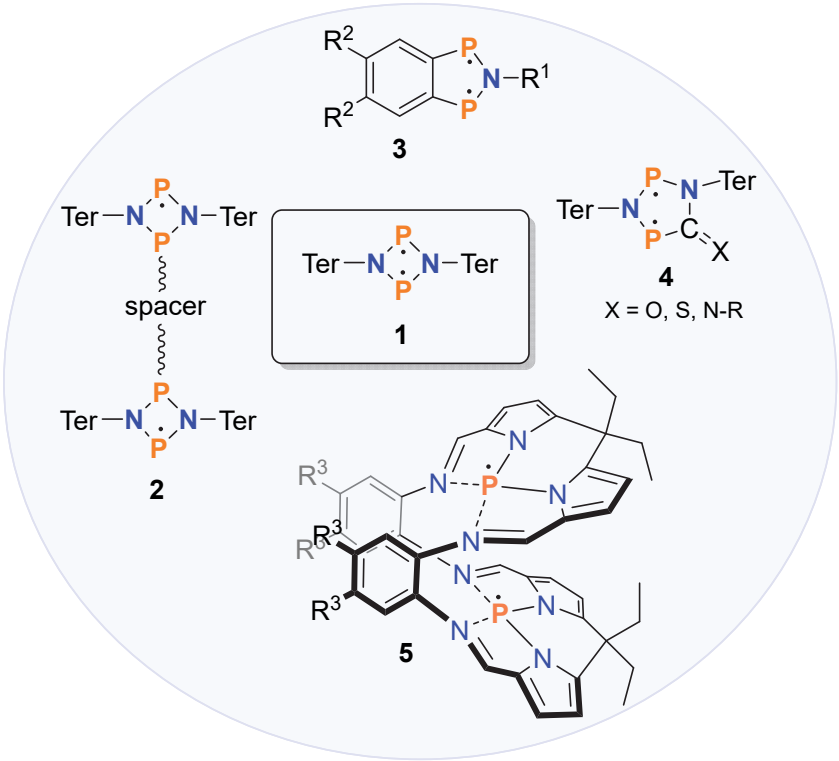
The diphosphadiazanediyl, [(μ-NR)P·]$_2$ (R = Ter = 2,6-dimesityl-phenyl, **1**),[1] is a four-membered heterocycle with a significant open shell singlet biradical character (25%) and is known to readily activate small molecules with single and multiple bonds.[2] Starting from the chemistry of biradical **1**, this talk covers the synthesis of new P-centered biradical systems such as the linkage of two monoradical species (**2**) using suitable spacers,[3] new five-membered biradicals (**3**, **4**),[1,2,4] and the embedding of radical centers in macrocycles (**5**).[5] The synthesis, structure, and properties are discussed, particularly with respect to the activation of small molecules and the use of these species as molecular switches.



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PL-6

Selenium reagent for the treatment of biomasses: detoxification of olive mill wastewater and production of derived lignin-biomaterials

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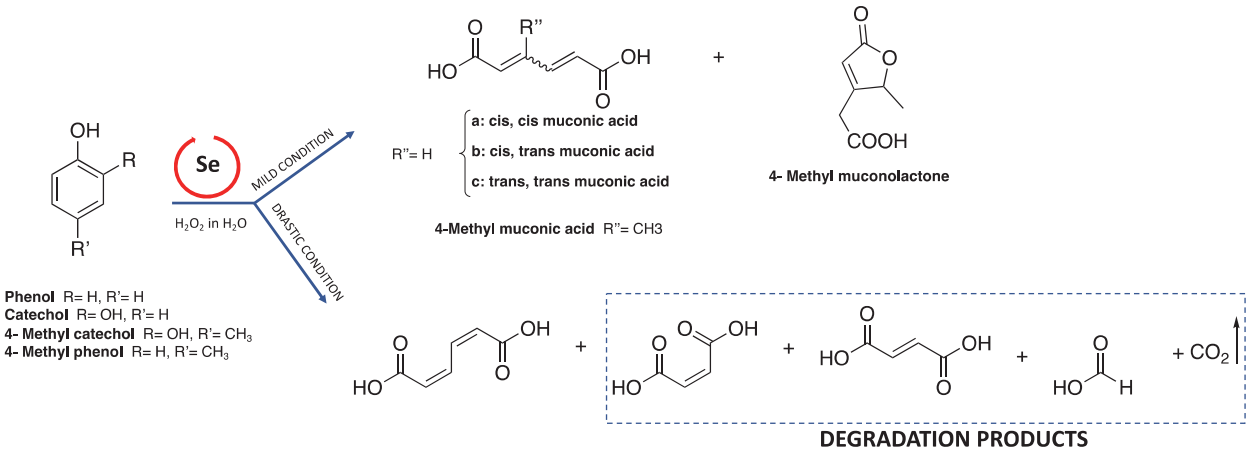
Nowadays, the traditional concept of the linear economy where the waste is considered just as something to throw away, is replacing by the circular economy, where the product has not an end of life but can reused after treatment. In this new vision, biomasses represent the waste that can be reintroduced in the society after opportune processing [1]. Two types of biomasses widely distributed in Italy are lignin (LI) and olive mill wastewater (OWM). While the first derives by the paper and bleaching industries, OMW is due by the production of olive oil. LI is known as the most abundant renewable source of aromatic compounds (50 million of tons/year) and for this reason several treatments were attempted to depolymerize LI and obtain fine chemicals, value added products that can be reused by the pharmaceutical and food industries [2]. On the other hands, OMW is a very toxic waste because of the presence of polyphenolic compounds that confer phytotoxicity and resistance to biodegradation. As before, different methods are used to eliminate and, in some cases, recover the polyphenols with the goal to reduce the toxicity of this waste [3]. In this context, we tested the possibility to use selenocompounds as catalyst in the oxidative treatment of both biomasses to detoxify OMW and depolymerize LI. The preliminary analysis was performed on model compounds (catechol, phenol and their derivatives) able to mimic synthons that are common for OMW and LI and depending on the conditions applied in term of amount of selenium catalyst and oxidant, time and source of irradiation we were able to reach the corresponding muconic acid and muconolactones or to obtain the degradation of the substrates (scheme 1). After proved the effectiveness of this new oxidative method, the protocol was successfully applied on the raw OMW, reaching a decrease in the amount of polyphenols and in the toxicity of the waste. To the best of our knowledge this is the first time selenium compounds are applied in the treatment of biomasses.



Scheme 1. Oxidative protocol.

Acknowledgement

CS thanks PON "Ricerca e Innovazione 2014-2020" for the PhD fellowship. "This work has been funded by the European Union – NextGenerationEU under the Italian Ministry of University and Research (MUR) National Innovation Ecosystem grant ECS00000041 - VITALITY - CUP J97G22000170005"

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Poster presentations

P-001

Investigating the therapeutic potential of morpholine-modified 1,3,5-triazines against colorectal cancer cell lines

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Colorectal cancer (CRC) ranks as the second leading cause of cancer-related deaths in the United States. As of 2023, an estimated 153,020 individuals will receive a diagnosis of CRC, with 52,550 succumbing to this ailment. Alarmingly, this figure includes 19,550 cases and 3,750 fatalities among individuals under the age of 50 [1]. Chemotherapy, the primary treatment modality, typically involves a limited selection of drugs, including 5-fluorouracil (5-FU), folinic acid, oxaliplatin, and capecitabine. Regrettably, these cytostatic agents often come with severe side effects, and some studies question their overall effectiveness. The future of cancer treatment now hinges on personalized therapy, wherein targeted drugs promise to be both safer and more efficacious [2]. In 2020, Wróbel A. and a team of scientists unveiled their research findings regarding 1,3,5-aminotriazine derivatives. These derivatives were subjected to rigorous testing against colorectal cancer cell lines, with promising results. Notably, the most potent among these ligands exhibited double the activity of 5-FU. These findings underscore the potential of these compounds as a novel class of agents for combatting cancer [3].

Given the high mortality rate, limited effectiveness of cytostatic drugs, and the absence of small-molecule targeted therapies, our research initiative aimed to create a new library of compounds with potent cytotoxic effects on cancer cell lines (specifically, SW480 and SW620) while preserving the integrity of healthy cells (CCD841). Our investigations yielded compounds characterized by remarkable cytotoxicity, with IC_{50} values below 10 μM for SW480 and SW620, surpassing the performance of the benchmark cytostatic, 5-fluorouracil. These novel compounds were synthesized using an innovative solvent-free method, enhanced by microwave irradiation and requiring only a few drops of water or DMF as a solvent. This groundbreaking approach enabled us to generate a substantial library of compounds within an astonishingly short timeframe, as brief as 2.5 minutes.

Acknowledgement

This work was supported by National Center for Research and Development (project No.LIDER/41/0206/L-12/20/NCBR/2021).

The project "Programming Excellence - PK XXI 2.0. Development Program of the Cracow University of Technology for 2018-22" co-financed by the European Social Fund Agreement No. POWR.03.05.00-00-z224/17. The project "WAY TO EXCELLENCE - a comprehensive university support program" implemented under the Operational Program Knowledge Education Development 2014-2020 co-financed by the European Social Fund Agreement No. POWR.03.05.00-00-Z214/18

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P-002

A Sustainable Method for Using Biosorbents for removal of organic dyes

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Water contamination is a serious concern that requires finding a solution for effective water treatment. Natural or modified biomaterials (synthetic ones) known as biosorbents have recently attracted attention due to cost-free and environmentally friendly materials. An overview of the possibilities of different biosorbents in water remediation is given in this abstract.

To find the most effective material for removing undesirable items from the water, we have selected various materials, including peels and waste of different agricultural products. We used oranges and lemon peels, potatoes, apples, coffee and tea residues, sunflower seeds, peanut husk, and so on.

For this project, we used dye solutions from different organic substances, such as bromocresol green, methylene blue, etc., and treated them with biosorbents to see the amount of color adsorption. The solutions were measured before and after adsorption using UV VIS Spectroscopy. To achieve the best working conditions, we have worked at different pH, concentrations, different amounts of absorbent, acid, and base modifications, etc.

According to the results, we have extraordinary outcomes, finding that these materials derived from agricultural waste can be applied daily to remove dye from wastewater. Additionally, biosorbents have several benefits over conventional water treatment techniques, including low cost, high selectivity, and biodegradability.

Furthermore, the effects of environmentally friendly materials of these products reduce concerns about contaminants in the environment, compared to traditional treatment approaches.

P-003

Examining the Fatty Acid Profile of the Calf Meat: Investigating the Relationship with Pasture and Food Farming Systems

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This study's primary objective was to examine the relationships between fatty acids and the predominant pattern that distinguishes two distinct agricultural systems based on the presence or absence of graze practices. In particular, the study assessed the effect of grazing on the fatty acid composition of meat samples collected from two farms during the 2022 season. It is essential to note that these farms were meticulously chosen to ensure that their non-grazing season locations and management practices were identical. The concentrations of fatty acids were determined using gas chromatography, a reliable analytical technique. The obtained results demonstrated significant differences in the fatty acid compositions of meat samples from grazing and non-grazing agricultural systems. These results suggest that the presence or absence of grazing practices has a discernible effect on the fatty acid composition of calf meat. By expanding the scope of this study and examining the differences in fatty acid content between the two agricultural systems, we can obtain valuable insights into the potential impact of grazing practices on the nutritional characteristics of meat. These results may have significant ramifications for producers, consumers, and the agricultural industry as a whole. Further analysis and investigation of this subject could contribute to the development of environmentally responsible and sustainable agricultural practices that maximize the nutritional value of livestock products.

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[6] GC-MS quantification of fatty acid profile including trans FA in the locally manufactured margarines.

P-004

Oxidative halogenation of a thiol/disulfide containing a 1,2,4-triazine ring

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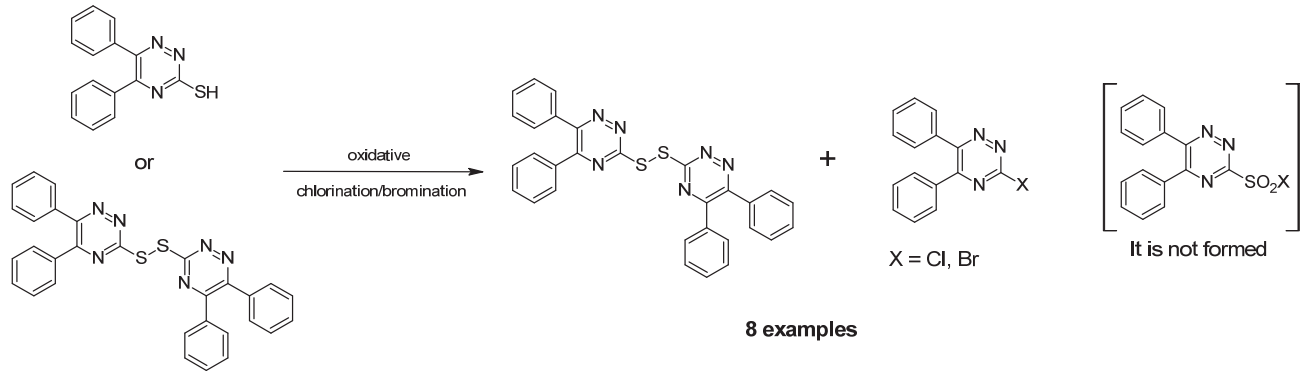
Sulfonyl halides are one of the most important reactive substrates in the reactions of synthesis with sulfonamides - compounds commonly used as drugs: antibacterial, analgesic, erectile dysfunction treatment, antidiabetic, diuretic, etc. Sulfonyl halides are obtained, inter alia, from thiols/disulfide by chlorination/bromination oxidation reactions. In publications to date, there have been methods described for the synthesis of aromatic, aliphatic sulfonyl halides, and those containing azaheteroaromatic rings with 1 or 2 nitrogen atoms (pyridines and pyrimidines). This publication aims to report the results of our works in the area of chlorinating and brominating oxidation reactions of 5,6-diphenyl-1,2,4-triazine-3-thiol. Instead of the expected sulfonyl-1,2,4-triazine chloride, the reaction yielded a disulfide and a chloro- or bromo-derivative. This may indicate increased electronegativity of the 1,2,4-triazine ring compared to the benzene, pyridine or pyrimidine ring. The results of quantum mechanical molecular modelling calculations which explain the differences in reactivity and durability of sulfonyl chlorides containing the pyridine, pyrimidine and 1,2,4-triazine rings will also be presented. The calculations were performed using the semi-empirical PM3 method with the ArgusLab computer program.



Scheme 1. Oxidative halogenation of 1,2,4-triazine thiol and 1,2,4-triazine disulfide.

Acknowledgement
This work was supported by the Ministry of Science and Higher Education project no. 19/20/B.

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P-005

X-ray studies of three 3,6-bis(pyridin-2-yl)-1,2,4,5-tetrazine cocrystals: an unexpected molecular conformation stabilized by hydrogen bonds

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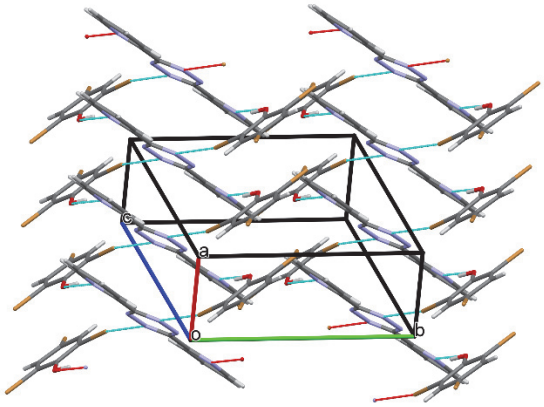
The 1,2,4,5-tetrazines belong to the class of nitrogen heterocyclic compounds.[1] Substitution with four N atoms (–N) of the methenyl groups (–CH) of the six-membered benzene ring results in a strong electron deficiency, i.e. there are four acceptor atoms in the aromatic ring. Moreover, the properties of s-tetrazine moieties can be modified by substitution at the 3- and 6-positions of the ring.[2] Nowadays, the 1,2,4,5-tetrazine derivatives often exhibit biological activity [3], being used as anticancer, antiviral, antimalarial, anti-inflammatory or antitubercular drugs.[4-5]

The results of the X-ray structure analysis of three novel 3,6-bis(pyridin-2-yl)-1,2,4,5-tetrazine cocrystals will be presented. Special attention is paid to a conformational analysis of the title tetrazine molecule in known crystal structures. Quantum chemistry methods are used to compare the energetic parameters of the investigated conformations. A structural analysis of the hydrogen and halogen bonds with acceptor aromatic tetrazine and pyrazine rings is conducted in order to elucidate factors responsible for conformational stability.[6]



Scheme 1. The layered arrangement of tetrazine molecules in cocrystal 3,6-bis(pyridin-2-yl)-1,2,4,5-tetrazine–2,4,6-tribromophenol.

Acknowledgement
Calculations were carried out using resources provided by the Wroclaw Centre for Networking and Supercomputing (grant No. 118).

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P-006

Application of enantiomerically pure NH-aziridine in the synthesis of atenolol derivatives

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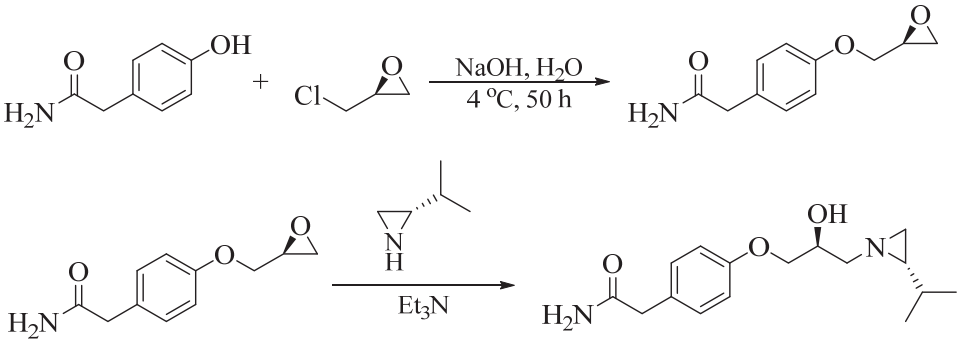
Chirality is a characteristic of optically active compounds whose two enantiomers are mirror images of each other, unable to overlap [1]. Moreover, it represents an extremely interesting area of organic chemistry and plays an important role in pharmacology and the synthesis of many pharmaceuticals, since compounds having a different configuration of the stereogenic center exhibit different properties. Some drugs are sold as single enantiomers, while others are sold as racemic mixtures. Enantiomers are characterized by a variety of pharmacodynamic and pharmacokinetic properties. It is very common that one of the enantiomers has a therapeutic effect, while the other enantiomer may have an adverse effect or even endanger human life [2,3].

The aim of my research was to obtain atenolol derivatives having an aziridine substituent in place of the amino group of the original drug. An extremely important aspect was the use of chiral, optically pure NH-aziridine, which should lead to a target compound in the form of a single diastereoisomer. Performing the synthesis in a controlled manner made it possible to obtain a product with a well-defined configuration, which is extremely important for studying the biological activity of optically pure compounds.



Scheme 1. Synthesis of the aziridine analogue of atenolol.

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P-007

Synthesis of pyrazole derivatives using mechanochemical technologies and film-forming properties study

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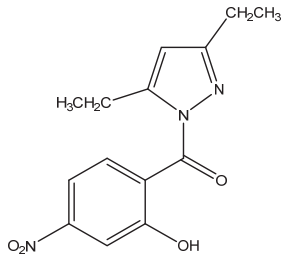
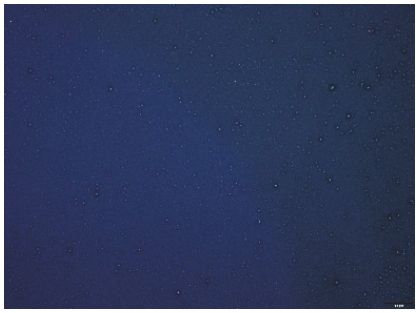
The aim of the presented work was to synthesize *N*-acylpyrazole derivatives using modern synthetic methods that fit into the principles of "green chemistry" [1]. These methods include mechanochemistry, sonochemical technologies and the use of microwave catalysis [2,3]. The obtained pyrazole derivatives containing an extended aromatic *N*-acyl substituent can possess luminescent properties, which can be used in the construction of, for example, organic OLED light-emitting diodes. On the other hand, the introduction of alkyl chains into the pyrazole ring should affect physicochemical properties such as solubility and the ability to form thin solid films. These properties are also very important when trying to use organic compounds in organic electronics components.

A series of *N*-acylpyrazole derivatives have been synthesized using the modern methods mentioned above, and the best, most reproducible method is the synthesis using a ball mill. While studying film-forming properties, I checked the effect of substrate, solvent and compound structure on the formation of thin solid films. The most promising compounds are 2-hydroxy-4-nitrobenzoic acid derivatives. They showed the best continuity of the film produced by the spin-coatig method, which is commonly used in the production of emission thin films in organic light-emitting diodes.





Scheme 1. Structure and thin film made for the presented compound.

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P-008

Novel *N*-cyclopentyl derivatives of pseudothiohydantoin with potential anticancer and 11β-HSD inhibitory activities

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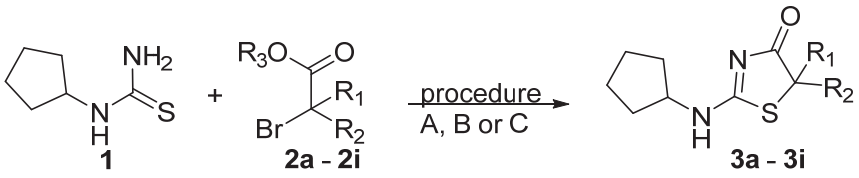
Pseudothiohydanoin derivatives have a number of biological activities, including antibacterial, antifungal, antiviral and anticancer effect. They are also a promising class of compounds in research on the search for selective 11β-HSD inhibitors (11β-hydroxysteroid dehydrogenase). 11β-HSD is an enzyme that occurs in the form of two isoforms: 11β-HSD1 and 11β-HSD2, which play an important role in the peripheral cortisol production mechanism. 11β-HSD1 mainly catalyzes conversion of cortisone to physiologically active cortisol, while 11β-HSD2 catalyzes reverse reaction. Inhibition of 11β-HSD1 activity causes a reduction in cortisol levels, and thus insulin resistance, central obesity and of total cholesterol level. Therefore, 11β-HSD1 inhibitors have significant potential in the treatment of type 2 diabetes, obesity and cardiovascular disease.

Cyclopentyl derivatives of pseudothiohydantoin were obtained in the reaction of a cyclopetyl-thiourea with 2 bromo esters. Depending on the type of bromo ester used, the reactions were conducted in different conditions (Scheme 1). As a result of the reactions, 9 new derivatives were obtained with the yield of up to 85%.



A: $CHCl_3$, RT; B: MeOH, MeONa, reflux; C: EtOH, DIPEA, reflux

Scheme 1. Synthesis of *N*-cyclopentyl derivatives of pseudotiohydantoin.

All synthesized compounds at a concentration of 10 μM inhibit the activity of 11β-HSD1 in the range of 19-90%, while 11β-HSD2 in a lesser extent - up to 46%. The derivative containing the spiro system of thiazole and cyclohexane rings showed the strongest 11β-HSD1 inhibitory effect (IC_{50} = 0.07 μM) and was more selective than carbenoxolone. In turn, in the studies of anticancer activity on selected cell lines, a slight decrease in cell life was observed for most compounds.

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P-009

Regio- and stereoselectivity of the [3+2] cycloaddition reactions between (Z)-C-(3-pyridyl)-N-methylnitrone with (E)-2-R-nitroethenes

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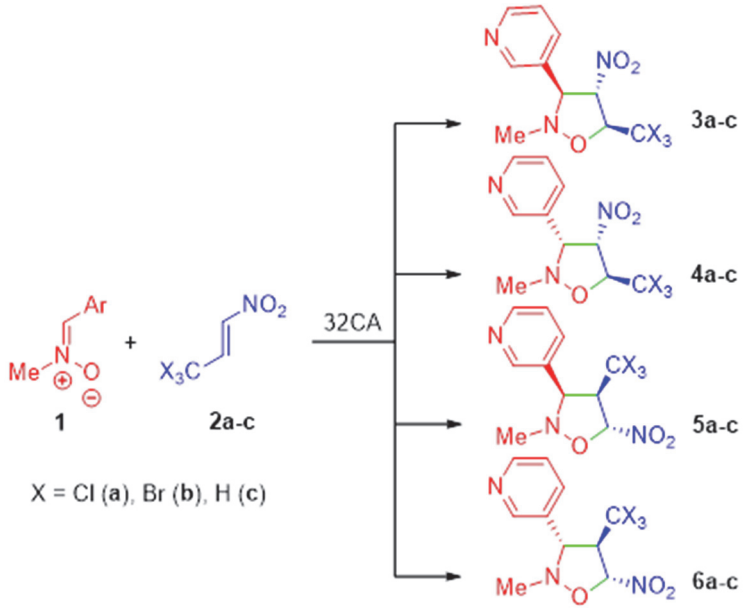
[3+2] Cycloaddition reactions with the participation of Z-C-(3-pyridyl)-N-methylnitrone and series of E-2-R-nitroethenes were explored both experimentally and theoretically in the framework of Molecular Electron Density Theory. It was found that all considered processes are realized under mild conditions and in full regio- and stereocontrol. In all cases, respective 3,4-cis-4,5-trans-4-nitroisoxazolidine analogs were isolated as single product. The observed selectivity can be explained on the basis of characteristic of electronic structures of reagents. The ELF analysis additionally shows that the studied reaction proceeds by a "non-concerted", two-stage, one-step mechanism.



Scheme 1. Theoretically possible channels of 32CAs of (Z)-C-(3-pyridyl)-N-methylnitrone (1) with (E)-2-R-nitroethenes (2a-c).

Acknowledgement

This research was supported in part by PL-Grid Infrastructure. All calculations reported in this paper were performed on the "Prometheus" supercomputer cluster in the CYFRONET computational center in Cracow.

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P-010

Reaction between (2E,4E)-2,5-dinitro-2,4-hexadiene and diazomethane in the light of MEDT computational study

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One of the possible methods to obtaine bipyrazole analogues is the reaction of nitrodienes with diazocompounds. The synthesis involves a double cycloaddition, sigmatropic rearrangement of the hydrogen atom and the elimination of the HNO_2 molecule.[1,2]

In the presented research, the quantum-chemical studies of the reaction of (2E,4E)-2,5-dinitro-2,4-hexadiene with diazomethane were carried out (Figure 1). For this purpose, the Molecular Electron Density Theory (MEDT) was used. The research includes the analysis of electronic structures and the assessment of the reactivity of the used reagents as well as the analysis of energy profiles and critical structures occurring on the paths of the reactions.

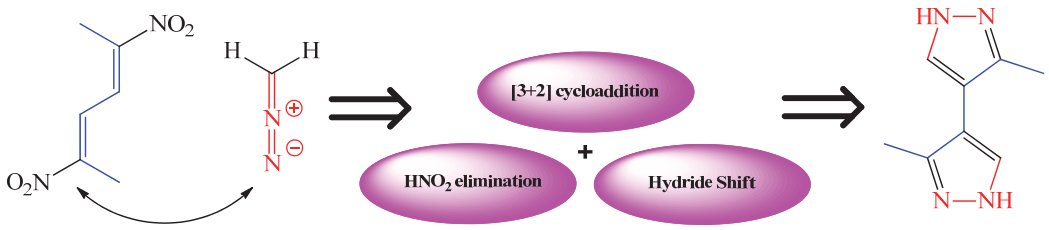

Figure 1. Scheme of studied reaction.

Acknowledgement

The presented research was supported by the PLGrid Infrastructure. All presented calculations were performed on the "Ares" supercomputer located at the CYFRONET Academic Computer Center in Cracow. We would like to thank Infrastructure PLGrid and ACK CYFRONET for providing computer equipment and support.

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P-011

Reaction between diarylnitrilimine and 3,3,3-trichloro-1-nitroprop-1-ene – en experimental and a computational study

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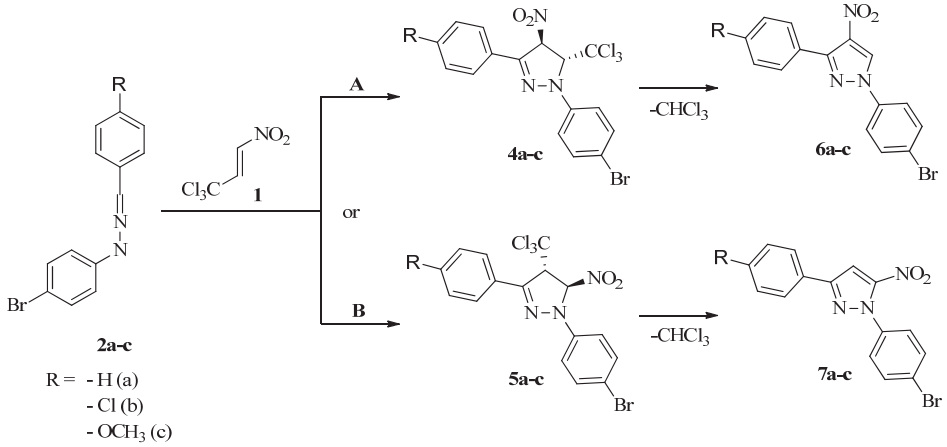
Pyrazolines are five-membered heterocyclic compounds with two nitrogen atoms in their structure. [1] They have many applications, especially in medicines. [2] The following work presents the experimental and theoretical studies on the reaction between 3,3,3-trichloro-1-nitroprop-1-ene (TNP) **1** and N-(4-bromophenyl)-C-arylnitrylimine (NIs) **2a-c**.

The experimental results of this 32CA, showed that this reaction occurred with full regioselectivity and the obtained products are extremely unstable, spontaneously getting converted through $CHCl_3$-elimination to pyrazole systems. From the experimental point of view, this reaction lead to one of the two possible 1-(4-bromophenyl)-3-phenyl-5-nitropyrazole (**6a-c** or **7a-c**) instead of the expected Δ^2-pyrazoline molecular system (**4a-c** or **5a-c**). [3] The observed mechanism was described in the framework of the Molecular Electron Density Theory (MEDT). The theoretical results showed that both of the possible channels of [3+2] cycloaddition were favorable, but obtainment of 1-(4-bromophenyl)-3-aryl-4-tricholomethyl-5-nitro-Δ^2-pyrazoline **5a-c**, and next was more probable. This was confirmed by the results of MEDT study, where the determination of the reaction path is mainly described by the interactions between the Cβ atom of electrophilic TNP **1** and the carbon atom of the –N=N=C- fragment of nucleophilic NIs **2a-c** [3].



Scheme 1. Theoretically possible reaction paths of 32CA between TNP **1** and NIs **2a–c**.

Acknowledgement

This research was supported in part by PL-Grid Infrastructure. All calculations reported in this paper were performed on the "Prometheus" supercomputer cluster in the CYFRONET computational center in Cracow.

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P-012

Unique examples of non-catalysed Hetero Diels-Alder reactions with the participation of conjugated nitroalkenes

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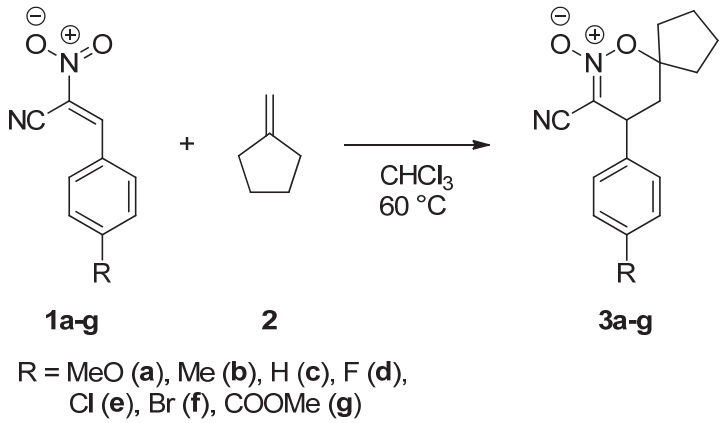
Hetero Diels-Alder (HDA) reactions with the participation of E-2-aryl-1-cyano-1-nitroethenes (**1a-g**) and methylenecyclopentane (**2**) were evaluated on the basis of experimental as well as quantumchemical data [1]. It was found that contrary to most known HDA reactions, title processes are realised under non-catalytic conditions and with full regiocontrol. The DFT study shows, without any doubt, the polar but single-step reaction mechanism. Deeper exploration using Bonding Evolution Theory (BET) techniques gives a clear image of the sequences of electron density reorganisation along the reaction coordinate. The first C4-C5 bond is created in phase VII by merging two monosynaptic basins, while the second O1-C6 bond is created in the last phase by a donation of the nonbonding electron density of O1 to C6. Based on the research, we can conclude that the analysed reaction proceeds according to a two-stage one-step mechanism.



Scheme 1. Thermal [4+2] cycloaddition of (*E*)-2-aryl-1-cyano-1-nitroethenes (**1a-g**) with methylenecyclopentane (**2**).

Acknowledgement

We gratefully acknowledge Poland's high-performance computing infrastructure PLGrid (HPC Centers: ACK Cyfronet AGH) for providing computer facilities and support within computational grant no. PLG/2022/015777.

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P-013

Influence of the LA catalyst on the molecular mechanism of the [4+2] cycloaddition between cyclopantadiene and selected nitropropenates

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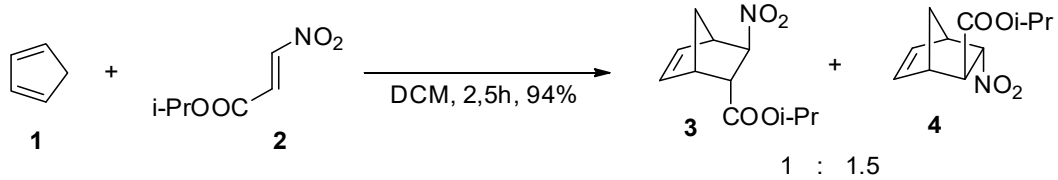
The molecular mechanism of the Diels-Alder reaction with the participation of cyclopentadiene and isopropyl 3-nitroprop-2-enate was examined based on wb97xd/6-311+G(d) (PCM) quantum chemical calculations. It was found that the type of the mechanism of conversion of addends de-pends significantly on the reaction conditions. In the less-polar environment, the one-step polar mechanism is realized. In the more polar solvents, the formation of "extended"-type zwitterionic intermediates is possible. In contrast, in the presence of an LA-type catalyst, the one-step mecha-nisms are replaced to respective stepwise mechanisms with zwitterionic or heterocyclic inter-mediates.



Scheme 1. Stereoselectivity of the thermal [4+2] cycloaddition between cyclopentadiene and iso-propyl nitropropenate.

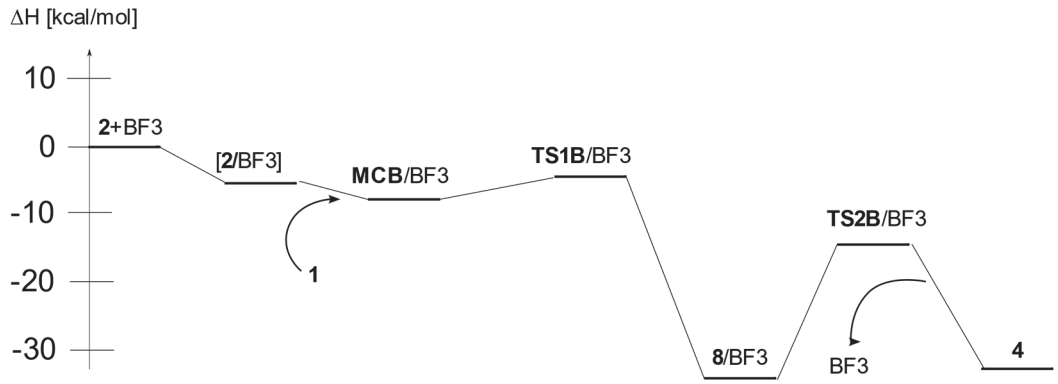


Figure 1. Enthalpy profiles for the BF_3-catalysed **1**+**2**→**4** reaction in the DCM environment

P-014

The new photosensitive cellulosic materials based on phenosafranin-modified silsesquioxane analog for bactericidal applications

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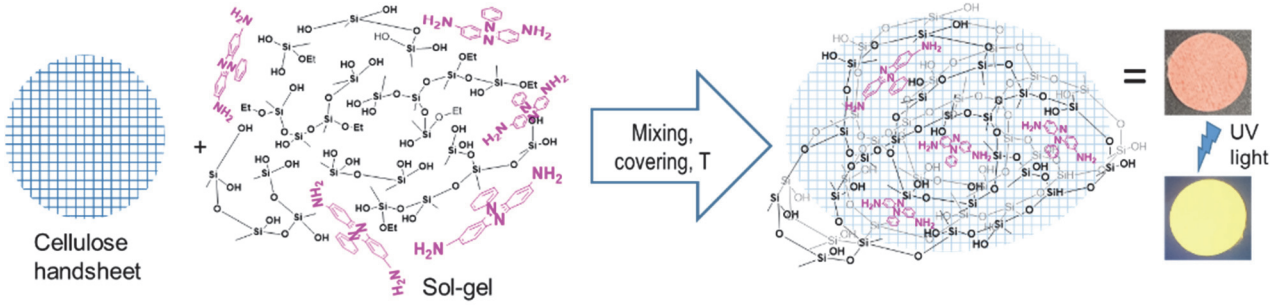
The presence of various infections caused by harmful microorganisms in the area of human health is becoming a big problem particularly since the resistant bacteria development and the transmission of COVID-19. Every day, materials employed in healthcare systems can accumulate infectious agents such as the coronavirus, vancomycin-resistant enterococci, and methicillin-resistant Staphylococcus aureus (MRSA). The shortcomings of antimicrobial medicines can be overcome by the integration of bactericidal materials, photodynamic inactivation and personal protective equipment (PPE) against infections to control the spread of diseases. The conventional PPE can passively adsorb or physically block pathogens from entering the body but without the ability of their neutralization and biological or chemical deactivation. Consequently, the presence of living bacteria or viruses could potentially lead to cross-contamination, that is a great challeng in terms of PPE recycling, disinfection, and disposal. Nowadays, we propose the bacterial photodynamic inactivation (PDI) system involves photosensitizers grafted to silsesquioxane network on the surface of cellulose fibers to generate reactive oxygen species (ROS) under light irradiation. These agents exhibit capability to eliminate pathogens with a high degree of efficiency. ROS, including singlet oxygen ($^1O_2$), play a pivotal role in inducing oxidative stress, which in term leads to damage in both Gram-positive and Gram-negative bacteria. [1], [2]



Scheme 1. Schematic structure highlighting the role of phenosafranin in a sol-gel process to produce a photosensitive coating for cellulose sheets.

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P-015

Yeast vehicles as templates for hybrid bioinspired poly(dopamine/phenosafranin) microparticles with immobilized Myoglobin retaining compromise activity

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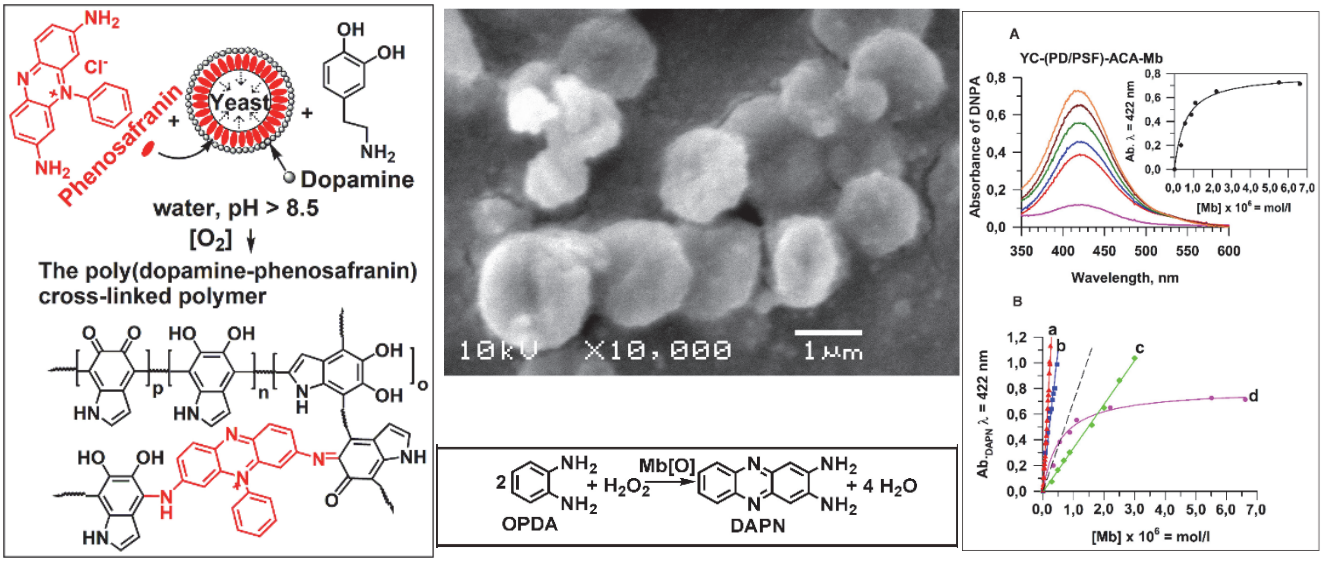
Yeast capsules (YCs) were effectively loaded with a photosensitive phenosafranin dye by electrostatic force-driven spontaneous deposition and served as bioinspired vehicles acting as colloidal templates for the synthesis of disc-shaped biocompatible microparticles of poly(dopamine/phenosafranin) or YC(PD/PSF). Oppositely charged compounds, i.e. dopamine and phenosafranin, used as monomers, were encapsulated and deposited onto the yeast polysaccharide scaffold through ionic complexation. Subsequently, in situ, self-oxidative polymerization was carried out resulting in the formation of microparticles. The obtained YC(PD/PSF) rigid microparticles had a distinct flat spherical shape resembling micro discs. The new eco-friendly biomaterial was used for the immobilization of myoglobin (Mb).



Scheme 1. Subsequently, on the left side is the illustration of the synthesis route of YC(PD/PSF) microparticles, then their SEM micrograph**.** The panel on the right side depicts A) the catalytic activity of [YC(PD/PSF)-ACA-Mb] determined using OPDA, and B) The comparison of the catalytic activity of Mb for (a) the native Mb in water solutions for 10 min (y = -0.0182 + 4331846x, R^2 = 0.995), (b) the encapsulated YC-Mb in water suspensions for 60 min (y = 0.045 + 2134554x, R^2 = 0.992), (c) the encapsulated YC-Mb in water suspensions for 10 min (y = -0.005 + 341794x, R^2 = 0.999), and (d) the immobilized [YC(PD/PSF)-ACA-Mb] in water suspensions for 60 min (y = 696075 x, R^2 = 0,999).

Acknowledgement
The authors wish to thank for financial support from the Centre Molecular and Macromolecular Studies Polish Academy of Science, project 854-02, it is gratefully acknowledged.

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[1] The publication is in evaluation in Colloids and Surface B: Biointerfaces.

P-016

New steroid conjugates connected with a 1,2,3-triazole ring

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New steroid conjugates linked by a 1,2,3-triazole ring have been obtained. A Cu(I)-catalyzed Huisgen reaction was employed between steroid derivatives containing terminal multiple bonds or azide groups [1]. The reaction mentioned earlier can be seen in Figure 1. This reaction is an example of applying "Click" chemistry for synthesizing complex chemical compounds. "Click" chemistry reactions are characterized by high yields, simple reaction conditions, and stability under physiological conditions [2-5].

The structures of all conjugates were confirmed using spectral techniques (^{1}H and ^{13}C-NMR, FT-IR), mass spectrometry (ESI-MS), and semiempirical PM5 methods. The pharmacotherapeutic potential of the synthesized compounds was initially assessed using the PASS method (Prediction of Activity Spectra for Substances). The cytotoxicity of the compounds was evaluated *in vitro* in a hemolytic test using human erythrocytes as a cellular model. Results indicate that selected compounds exhibit interesting biological activity. Additionally, molecular docking was conducted for selected products.

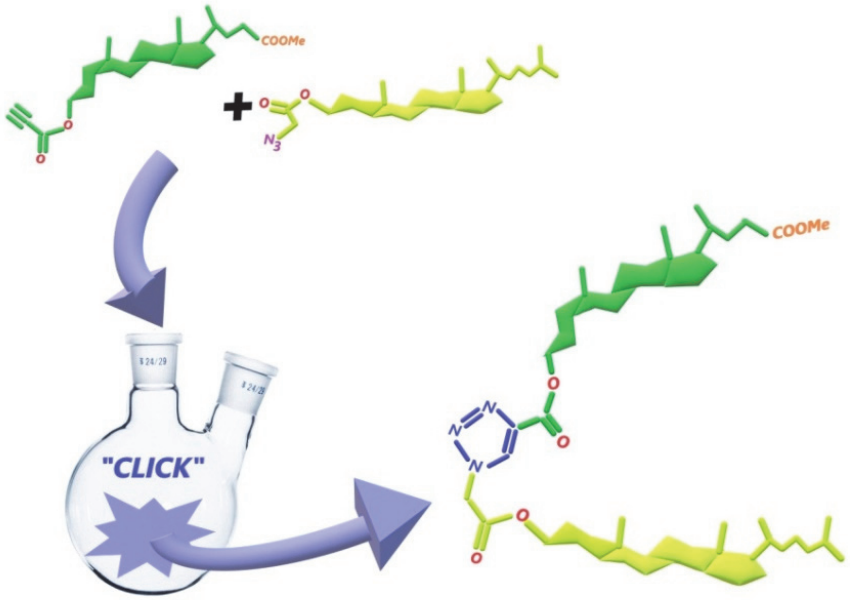

Figure 1. Model representation of the reaction for obtaining steroid dimers using "Click" chemistry.

Acknowledgement
Times New Roman, 11pt, Normal.

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P-017

The fluorescent properties of 3-arylbenzo[*b*]phosphole oxides

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Many of 2,3-benzo[*b*]phosphole oxides have already proven strong fluorescence in the solution.[1] Since the fluorescent properties of 2,3-benzo[*b*]phosphole oxides depend on the substitution pattern at the 2,3-positions, the influence of substituents at the 3-position is worth to recognize. Recently, the access to 3-arylbenzophosphole oxides was achieved.[2] We proposed the other route to 3-arylbenzo[*b*]phosphole oxides under Suzuki-Miyaura coupling.[3] In this poster we present theoretical, crystallographic and fluorescence studies of to get the insight into their photophysical properties.[3]

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P-018

The investigation of the reactivity of benzophosph-3-yl triflates

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Benzophosph-3-yl triflates can be readily converted into 2-ethynylphenyl(diaryl)phosphine oxides in the ring opening reaction.[1] Herein, we want to present the further investigation of the reactivity of benzophosph-3-yl triflates.[2]

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P-019

Synthesis and theoretical studies of new steroid bioconjugates containing 1,2,3–triazole rings

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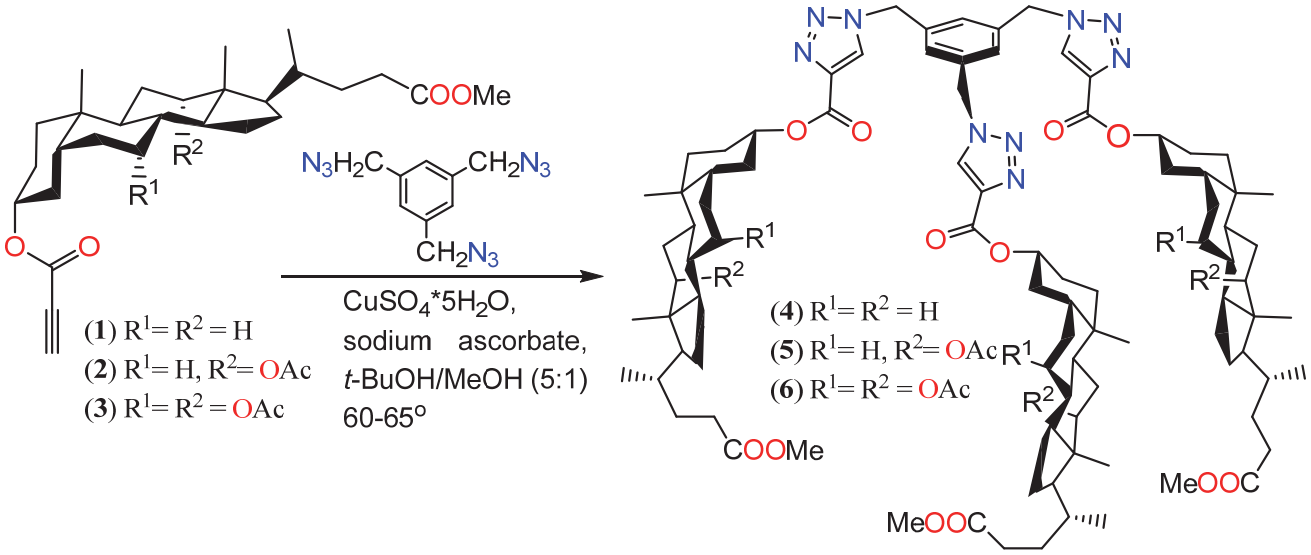
Using the extremely attractive „click" chemistry method, the synthesis of new steroid conjugates was carried out. As a result of 1,3–dipolar cycloaddition of propionyl derivatives of bile acid esters and 1,3,5-tris(azidomethyl)benzene, quasi-podands containing 1,2,3–triazole rings were obtained. Their structures were confirmed by spectroscopic analysis (^{1}H NMR, ^{13}C NMR and FT-IR), mass spectrometry, and theoretical calculations were made, obtaining their most optimal molecular geometry. The conducted *in silico* tests demonstrate the high biocidal activity of the new steroid compounds [1–7].



Scheme 1. Synthesis of steroid bioconjugates.

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P-020

Theoretical search for the most stable structure of a potential drug carrier containing cellobiose units

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One of the important problems in modern pharmacology is to find such drug transporters, which will cause better biodistribution of drugs and decrease their toxicity. The role of drug carrier may play cryptand named: 1,10-*N,N'*-bis-(β-D-ureidocellobiosyl)-4,7,13,16-tetraoxa-1,10-diazacyclooctadecane (T1) [1]. The latter has a specific structure that contains two cellobiose units linked to the diazacrown ether by urea bridges. The saccharides are able to recognize the target tissue [2], while the crown ethers are known for their very good complexation abilities toward ions and neutral molecules [3]. The experimental studies have shown that T1 is well soluble in water and is able to form a stable complex with the anticancer drug busulfan [1].

There is rather little knowledge about the compound T1, especially about its structural geometry, which, despite attempts, was not determined experimentally [1]. The structural description of T1 can be achieved using computational chemistry methods by performing a very extensive conformational analysis. In our study, the latter was divided into three steps, in which the accuracy of the computational methods is gradually increased: starting from very fast but very approximated molecular mechanics (step I), through semiempirical methods combined with computer simulations (step II), and finally using the density functional theory (DFT; step III).

On the poster, we present the results obtained with the DFT methods, in particular the most stable structures and the corresponding energy values. According to the M06-2X-D3/6-31G(d,p) calculations, the most stable structure of T1 has a compact shape resulting from the orientation of the two ureidocellobiosyl units on the same side of the diazacrown ring.

Acknowledgement

Part of calculations has been carried out using resources provided by Wroclaw Centre for Networking and Supercomputing (http://wcss.pl), grant No. 443.

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P-021

Amorphization of Ethenzamide and Ethenzamide Cocrystals - Study of Single and Binary Systems Forming Low-Melting Eutectic Phases Loaded on/in Silica Gel

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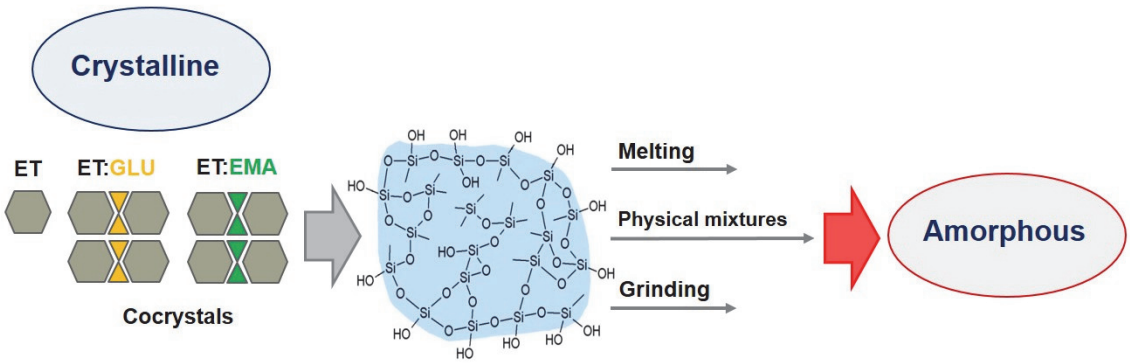
The applicability of different solvent-free approaches leading to the amorphization of active pharmaceutical ingredients (APIs) was tested. Ethenzamide (ET), an analgesic and anti-inflammatory drug, and two ethenzamide cocrystals with glutaric acid (GLU) and ethyl malonic acid (EMA) as coformers were used as pharmaceutical models. Calcinated and thermally untreated silica gel was applied as an amorphous reagent. Three methods were used to prepare the samples: manual physical mixing, melting, and grinding in a ball mill. The ET:GLU and ET:EMA cocrystals forming low-melting eutectic phases were selected as the best candidates for testing amorphization by thermal treatment. The progress and degree of amorphousness were determined using instrumental techniques: solid-state NMR spectroscopy, powder X-ray diffraction, and differential scanning calorimetry. In each case, the API amorphization was complete and the process was irreversible. A comparative analysis of the dissolution profiles showed that the dissolution kinetics for each sample are significantly different. The nature and mechanism of this distinction are discussed. [1]



Acknowledgement
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P-022

α-Amido sulphones as useful intermediates in the preparation of C-chiral α-aminophosphonates and α-aminophosphonic acids

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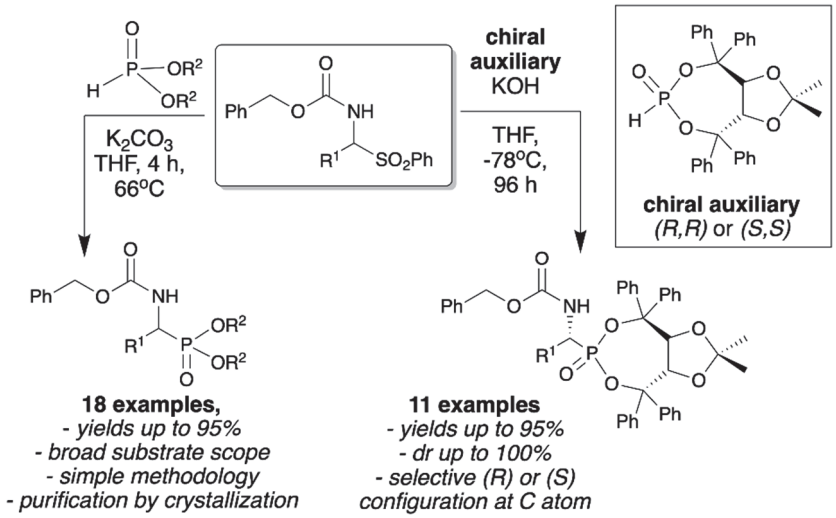
α-Amido sulphones[1] have been used as useful starting materials in the preparation of C-chiral α-aminophosphonates and α-aminophosphonic acids. The developed methodology is based on a one- pot, base-catalysed in situ generation of an imine intermediate followed by addition of a phosphorus nucleophile. The presented protocol is simple and effective and can be applied to a variety of structurally diverse α-amido sulphones and phosphorus nucleophiles, leading to the desired pure products after simple crystallization in very good yields. Importantly, the use of *H*-phosphonate bearing a chiral auxiliary allows the reaction to be performed with high diastereoselectivity (a single diastereoisomer is generated and isolated) and the possibility of precise control of the configuration at the newly generated C-chiral centre.[2]



Scheme 1. α-Amido sulphones as starting materials in the preparation of C-chiral α-aminophosphonates.

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P-023

Theoretical characterization of structural and NMR parameters of coptisine alkaloid from *Chelidonium majus* L.

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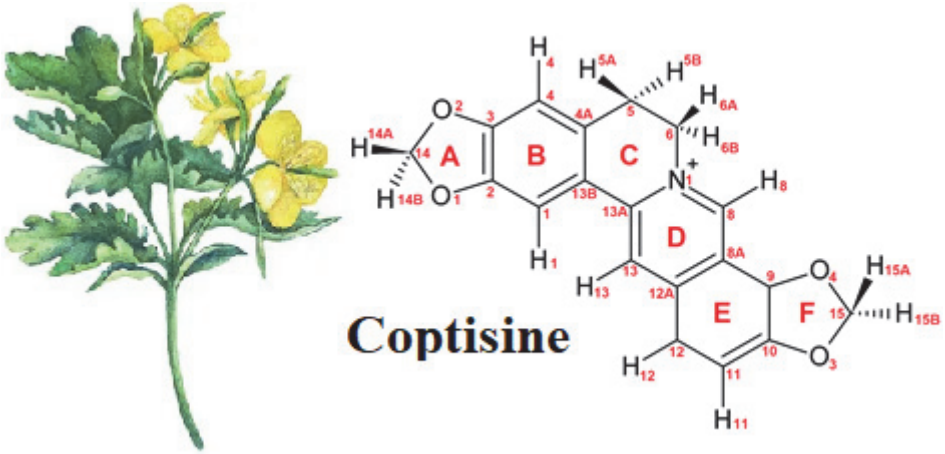
Coptisine is an organic heterocyclic compound. In the natural environment, it occurs as one of the most abundant *Chelidonium majus* L. alkaloids. This metabolite is known from its therapeutic activity.[1,2] The theoretical structure of isolated coptisine and in chloroform, methanol, DMSO and water solutions (using PCM model[3]) was predicted using density functional theory (DFT) with B3LYP, B971, B972, B98, M062X and PBE functionals. A large and flexible triple-zeta basis set (aug-cc-pVTZ) was selected for all calculations. Gauge-including atomic orbital (GIAO) NMR calculations with six selected density functionals enabled prediction of theoretical multinuclear isotropic shieldings and chemical shifts in the gas phase and solution. Individual spin-spin coupling constants for selected coupling constants were also calculated using the "mixed" version of basis set at the same level of theory. Aromaticity of individual rings of coptisine was analyzed by calculation of nucleus independent chemical shift (NICS) and harmonic oscillator model of aromaticity (HOMA) indexes.[4,5]

The presented work enables a more detailed theoretical characterization of the structure of coptisine and similar alkaloids using B98, B971 and B972 density functionals. On the other hand, the M062X functional, which successfully predicts energy, is not suitable for NMR parameter determination.



Acknowledgement

N. M. and T. K. were partly supported by the University of Opole. All calculations were performed using hardware and software provided by WCSS Wrocław.

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P-024

Synthesis of unsymmetric α-aminobisphosphoric analogs

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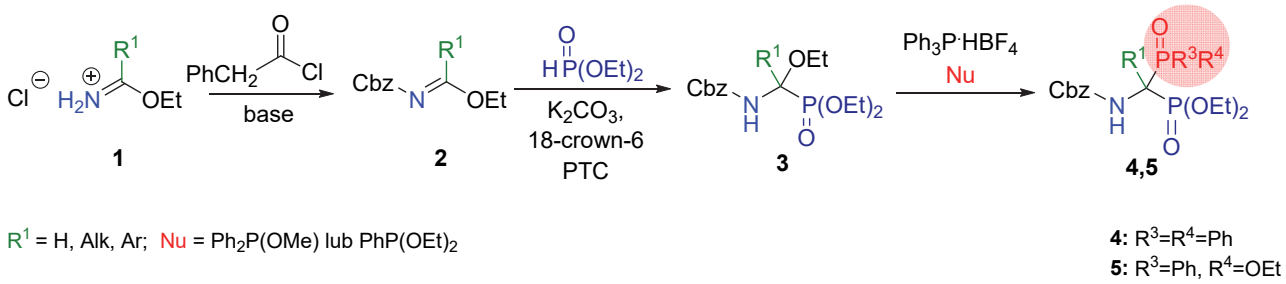
α-Aminobisphosphoric derivatives belong to a class of geminal 1 amino-1,1-bisphosphonates and due to their unique properties and multidirectional biological activity they are considered as very useful agents in the synthesis of biologically active compounds. Herein, we present our studies on development of first general method for the synthesis of potentially biologically active unsymmetric phosphonyl-phosphinyl and phosphonyl-phosphinoyl α-aminobisphosphoric analogs. The key step of the proposed strategy involves one-pot reaction of *N*-protected 1-ethoxyphosphonates **3** with triphenylphosphonium tetrafluoroborate and an appropriate phosphorus nucleophile (diethyl phenylphosphonite or methyl diphenylphosphinite).[1] The starting 1-ethoxyphosphonates **3** were synthesized according to a previously described two-step protocol which consists of acylation of the imidate hydrochloride **1** with an acyl chloride and the Michaelis–Becker-like addition of diethyl phosphite to ethyl *N*–acylimidate **2**.[2] The proposed strategy provides good to very good yields under mild catalyst-free conditions and allowed us to obtain 13 novel, structurally diverse bisphosphoric analogs **4,5**.



Scheme 1. Synthetic route for the preparation of unsymmetric bisphosphoric derivatives.

Acknowledgement
This work was supported by Silesian University of Technology (Poland) BKM Grant No. 04/020/BKM212/1056.

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P-025

Synthesis of *N*-heterocyclic carbene silver(I) complexes

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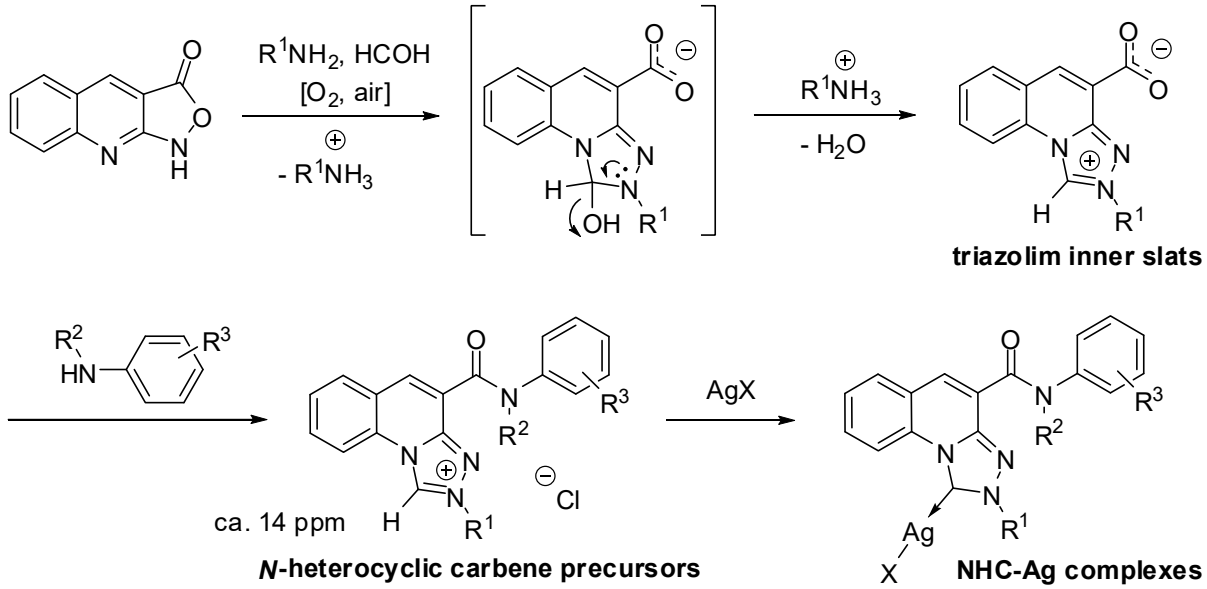
Carbenes are defined as neutral compounds incorporating a divalent carbon atom and six-electron valence shell. The incomplete electron octet and coordinative unsaturation of the carbon atom render them highly reactive and unstable species. *N*-heterocyclic carbenes (NHC) proved to be excellent ligands for transition metals, hence their complexes found a notable number of applications, including metallopharmaceuticals, homogeneous catalysis (cross-coupling, olefin metathesis, asymmetric catalysis), and coordination to surfaces. Metal-carbene complexes are potent anti-cancer and antibacterial agents and their biological activity is believed to be conditioned by lipophilicity and stability of the complexes.[1,2] Recently, we have developed a novel carben precursor platform based on 4-carboxy-2-alkyl-[1,2,4]triazolo[4,3-*a*]quinolin-2-ium inner salts, which upon transformation to the corresponding phenylcarbamoyl derivatives readily react with silver(I) salts to give the novel type of NHC-Ag complexes (Scheme 1). We have shown that R^1, R^2, R^3 substitution pattern conditions solubility and antibacterial activity of the obtained complexes.



Scheme 1. Synthesis of triazolim inner slats and their application to the formation of NHC-metal complexes.

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P-026

Synthesis and antiproliferative activity on new cyclohex-3-ene-1-carboxylic acid derivatives

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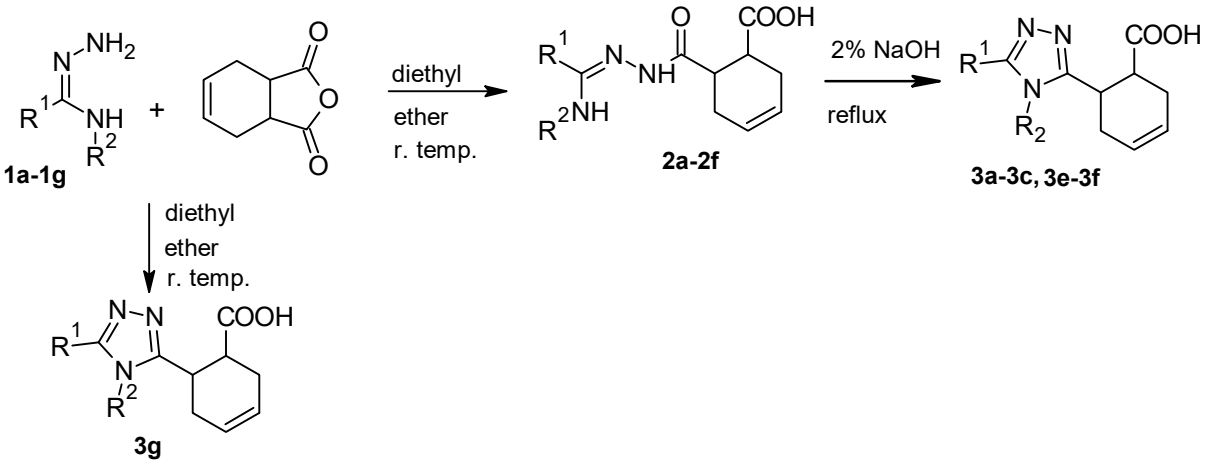
A series of new cyclohex-3-ene-1-carboxylic acid derivatives **2a-2f** were obtained in equimolar reaction of carbohydrazonamides **1a-1f** with *cis*-1,2,3,6-tetrahyrophthalic anhydride carried out in anhydrous diethyl ether (**Scheme 1**). The 1,2,4-triazole derivatives **3a-3c** and **3e-3f** were obtained by cyclization of compounds **2a-2f** in an alkaline solution followed by precipitation with dilute hydrochloric acid. The structures of obtained compounds **2a-2f, 3a-2c,** and **3e-3f** were determined by spectral (^{1}H NMR, ^{13}C NMR, MS) and elemental analyses. New compounds were tested for their toxicity and antiproliferative properties in freshly isolated peripheral blood mononuclear cell (PBMC) cultures and demonstrated no toxicity in used concentrations (10 µg/mL, 50 µg/mL and 100µg/mL) for unstimulated leukocytes. However, the some of studied derivatives significantly decreased the proliferation of human leucocytes stimulated with phytohemagglutinin (PHA) in 72 h cell cultures. The influence of the structure of the tested compounds on their biological activity will be discussed.



R^1 = 2-pyridyl, phenyl; R^2 = 2-pyridyl, 4-pyridyl, phenyl, 4-nitrophenyl, 4-methylphenyl

Scheme 1. The synthesis of compounds **2a-2f** and **3a-3c**, **3e-3g**.

P-027

Is acriflavine an efficient co-drug in chemotherapy?

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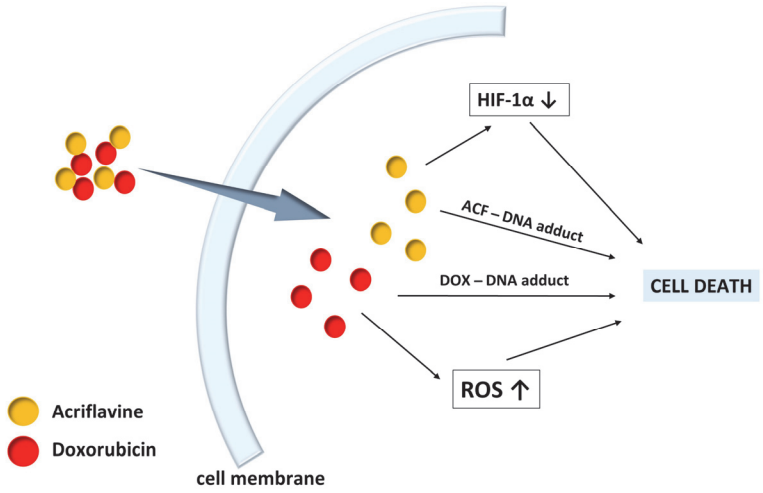
Acriflavine (ACF) is considered the most potent HIF-1 inhibitor in anticancer therapy among the 336 drugs approved by the FDA [1]. Acriflavine, like doxorubicin, is a DNA intercalator. The use of high doses of doxorubicin (DOX) can cause oxidative stress due to increased levels of reactive oxygen species (ROS), resulting in overexpression of HIF-1α in tumor cells, promoting drug resistance and tumor progression. To prevent this, it may be appropriate to use a potent HIF-1 inhibitor (ACF) in the therapy of doxorubicin (Scheme 1).

We present interaction (fluorescence and NMR analysis) and cytotoxicity of the anticancer drugs acriflavine and doxorubicin were studied as candidates for co-delivery of drugs in the treatment of cervical cancer (HeLa) [2]



Scheme 1. The proposed mechanism of action of the acriflavine (ACF) : doxorubicin (DOX) complex in the fight against cancer.

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P-028

2-(cyclohexylamino)thiazol-4(5H)-one derivatives as 11β-hydroxysteroid dehydrogenase type 1 inhibitors – synthesis and in vitro studies

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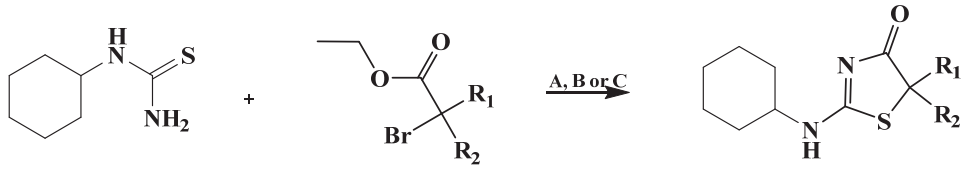
Glucocorticoids are important hormones responsible for metabolism, immune response, and the body's response to stress. The main representative of glucocorticosteroids is cortisol. Excess cortisol leads to diseases such as Cushing's syndrome, obesity and type 2 diabetes [1]. Moreover, increased cortisol levels in the tumor microenvironment cause local immunosuppression and thus encourage tumor cells to escape from the surveillance of the immune system [2]. The enzyme that regulates cortisol levels is 11β-hydroxysteroid dehydrogenase (11β-HSD). There are 2 isoforms of this enzyme: 11β-HSD1 and 11β-HSD2. 11β-HSD1 is an enzyme that catalyzes the conversion of inactive cortisone into active cortisol, while 11β-HSD2 dehydrogenase catalyzes the reverse reaction [1]. Inhibition of 11β-HSD1 reduces cortisol levels systemically and locally in tissues, therefore 11β-HSD1 inhibitors have great potential in the treatment of metabolic syndrome diseases or innovative treatment/prevention of cancer.

In order to search for new inhibitors of 11β-HSD1, nine new N-cyclohexyl derivatives of 2-aminotiazol-4(5H)-one with various substituents at the fifth carbon of the thiazole ring were synthesized. The reaction between cyclohexylthiourea and the appropriate α-bromo ester was carried out under different conditions depending on the α-bromo ester used.



A - $CHCl_3$; B - MeONa, MeOH, reflux; C - EtOH, DIPEA, MW (155°-160°C)

All obtained compounds were tested in vitro for inhibition of 11β-HSD1 dehydrogenase. The results of the conducted research showed that the synthesized compounds at a concentration of 10 μM inhibit the activity of 11β-HSD1 dehydrogenase in the range of 27.47 - 93.99% (including six compounds showing 11β-HSD1 inhibition percentage above 80%). The strongest compound turned out to be 2-(cyclohexylamino)-1-thia-3-azaspiro[4.5]dec-2-en-4-one (IC_{50} = 0.045 μM). The activity of this compound is higher than that of the known 11β-HSD1 inhibitor - carbenoxolone (IC_{50} = 0.08 μM), so it is worth subjecting this compound to further tests.

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P-029

Anticancer effect of 5-fluorouracyl and 4-isoselenocyanato-1-butyl 4′-fluorobenzyl sulfoxide combined treatment in in vivo model of triple negative breast cancer

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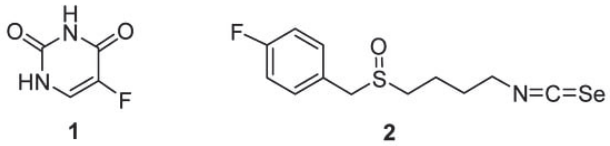
4-Isoselenocyanato-1-butyl 4’-fluorobenzyl sulfoxide (ISC) is an organofluorine isoselenocyanate analog of sulforaphane. It bears the 4-fluorobenzyl substituent bonded to the sulfinyl sulfur atom, which is linked with the isoselenocyanate moiety (in place of the isothiocyanate group present in the original sulforaphane), via an alkyl chain, consisting of four methylene groups [1]. Based on the promising anticancer activity of 5-fluorouracyl and ISC combined treatment in in vitro model of triple negative breast cancer, its combined effects were investigated in in vivo model [2].



Scheme 1. Structural formulas of 5-fluorouracyl 1 and 4-isoselenocyanato-1-butyl 4′-fluorobenzyl sulfoxide 2.

Female BALB/c mice were injected orthotopically with murine breast cancer cells. The mice were randomly divided into four groups: control group, 5-FU alone treatment group, ISC alone treatment group, and combined treatment group. 5-FU (100 mg/kg m.c.) was administered intravenously. ISC (50 mg/kg m.c.) was administered intraperitoneally. During autopsy, the heart, liver, lungs, and spleen were weighed. A blinded macroscopic count for metastatic foci on the surface of lung tissue and a blood morphological analysis was performed. Also, the type of interaction between ISC and 5-FUwas indicated.

An additive type of interaction between 5-FU and ISC was observed in the in vivo model. All tested treatments decreased the number of metastases in the lung in comparison to the control group. After the 5-FU alone treatment and after combined treatment, the number of metastases in the lung dropped significantly by 50% in comparison to the control. Importantly, this combination was shown to be non-toxic in animals.

The combined treatment can be regarded as a promising anticancer strategy for highly aggressive and invasive triple-negative breast cancer treatment.

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P-030

Antitumour and antimetastatic activity of dietary dose of sulforaphane in the model of triple-negative breast cancer

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Many phytochemicals, including a popular supplement – sulforaphane (SFN), are considered hormetic compounds, meaning they exert divergent effects at low and high concentrations [1]. SFN is an isothiocyanate, which precursor gluocoraphanin is found in the vegetables from brassicae family [2]. Numerous studies show SFN in high concentrations act as an anticancer agent in various cancer types, mainly in breast cancer. On the other hand at low concentrations SFN tends to promote proliferation which taking into account its low bioavailability in human plasma after consumption can have serious side effects for those who have transformed cells in the body. While in a healthy body this effects of SFN is beneficial, in a developing cancerous tumor action of SFN, especially in low concentrations, SFN can induce the opposite effect: it can increase tumor formation.

Our aim was to test dietary dose of SFN on the proliferation and migration of the triple negative breast cancer (TNBC) cells in the *in vivo* and *in vitro* model. TNBC is a subtype of breast cancer characterized by receptors deficiency, an heterogeneous and aggressive phenotype with limited treatment options.

The study was conducted on an *in vitro* model using MDA-MB-231 cell line and *in vivo* model using murine breast tumor model in female Balb/c mice with 4T1 cells implanted. The safety and antitumor effectiveness of small dose of SFN was evaluated *in vivo* and an *in vitro* studies on a human TNBC 2D and 3D model was conducted to determine SFN mechanism of action - whether trough the cytotoxic effect or the inhibition on metastasis (i.e. proliferation or migration).

The cytotoxicity on a 2D model shows that SFN at low concentrations shows a stimulating effect on cells proliferation in 2D culture, but it does not stimulate the 3D cells proliferation, which is relevant to the situation of developing tumors in the body. SFN shows an inhibition of cells migration already in low concentrations, but only from cells derived from spheroids and *in vivo*, but not from 2D *in vitro* culture. Results of the *in vivo* experiment showed a up to 31% tumor growth inhibition in mouse model with 0.026mg/kg SFN weekly dose. Histological analysis of tumor sections revealed that SFN treatment lowered proliferating potential of cancer cells, reduced areas of necrosis and immune cells infiltrations proving less malignant type in contrast to non-treated group. Also mean number of lung metastases and median were both lower after sulforaphane treatment.

In conclusion SFN at low concentrations showed anticancer and antimetastatic activity in the 3D *in vitro* and *in vivo* model, but not 2D *in vitro* model. The proposed mechanism of action of dietary dose of SFN on cancer is epithelial–mesenchymal transition inhibition and activation of the Nrf2 pathway, mobilization of neutrophils to primary tumor and elimination of tumor with reduction of lung metastases.

Acknowledgement
The study was partially funded by the National Science Center, Poland, 2021/41/N/NZ7/02530.

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P-031

Steroid-based imidazolium salts - synthesis and antimicrobial properties

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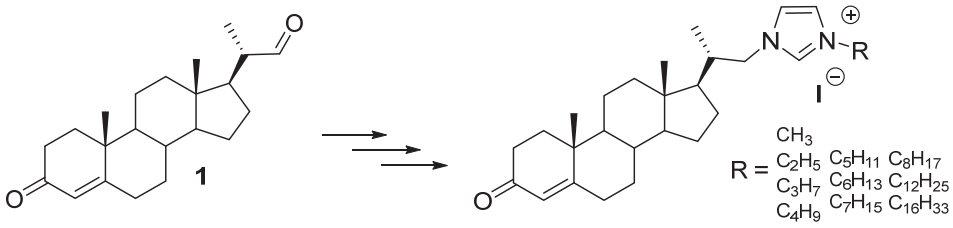
Steroids, among others, are components of cell membranes, signaling molecules, and physiological regulators. Imidazolium salts have a broad spectrum of biological activity: antineoplastic, antimicrobial, and antioxidant properties [1-3]. The imidazole ring is common in nature and plays a key role in many structures and functions of living organisms [4]. Combining these two systems within one molecule allows for synergistic biological action.

Here we present, a highly efficient synthesis of steroid–based imidazolium salts (Scheme 1) from 3-oxo-23,24-dinorchol-4-en-22-al (**1**). The obtained salts show significant biological activity: antibacterial activity, especially in the strains Gram (+), and antifungal activity [5-7].



Scheme 1. Imidazolium salts based on 3-oxo-23,24-dinorchol-4-en-22-al (**1**).

Acknowledgement

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P-032

Reactions of 3-hydroxy-2-phenylbenzo[*e*]isoindol-1-one: Synthesis of benzophthalazin-1(2*H*)-ones and benzoindan-1-ones

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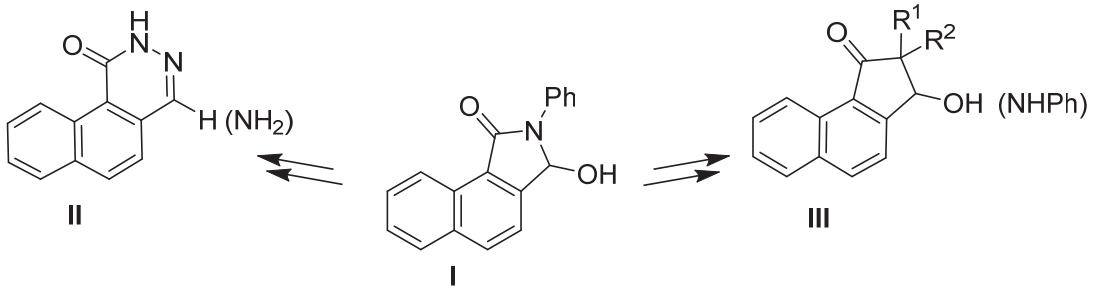
The isoindolinone framework is present as the core unit in many synthetic and naturally occurring derivatives with interesting biological properties.[1,2] For a long time, we have been interested in the synthesis and functionalization of substituted isoindolinones.[3]

Our recent work has focused on the synthesis of 3-hydroxybenzo[*e*]isoindol-1-one **I** and its conversion into hetero- (benzophthalazinones **II**) and carbocyclic (benzoindanones **III**) systems (Scheme 1).

The results of the aforementioned transformations will be presented.



Scheme 1. Reactions of 3-hydroxybenzo[*e*]isoindol-1-one (R^1, R^2 = H, Alkil)

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P-033

In vivo and in vitro studies of efficient mephedrone adsorption over zirconium-based metal-organic frameworks

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Mephedrone (4-MMC), known for its psychoactive effects similar to amphetamine and cocaine and affordability, has become one of the most abused drugs by adolescents. Its prevalence, coupled with its low price, makes it one of the stimulants leading to strong psychological and physical addiction, overdose risks, and severe withdrawal symptoms [1]. This work focuses on an investigation of zirconium-based metal-organic frameworks (MOFs) for efficient and gradual removal of 4-MMC. Several methods including FTIR, µRaman, 1H NMR, UV–Vis, and DFT were used to characterize the 4-MMC adsorption on MOFs. The results of 4-MMC adsorption tests indicated that the adsorption efficiency and kinetics are strongly influenced by the MOF's structural parameters. The highest 4-MMC adsorption, reaching approximately 45 wt% from 1000 µM aqueous solutions was achieved by NU-1000. Moreover, a modulated synthesis of UiO-66 with hydrochloric acid increased the 4-MMC adsorption efficiency from 24 wt% to 35 wt%. The in vitro and in vivo experiments have confirmed that the addition of MOF to the 4-MMC solutions decreases the 4-MMC concentration allowing proper Danio rerio embryo development. Furthermore, the in vivo experiments proved that MOFs are potentially safe for model organisms.

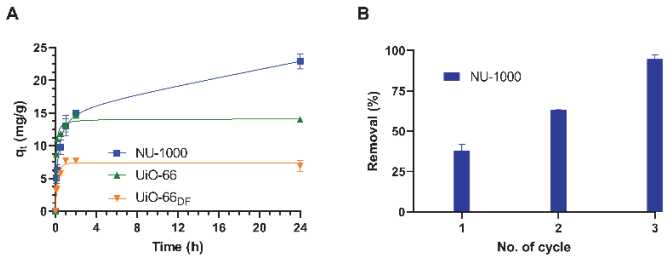

Figure 1. (A) 4-MMC removal efficiency on prepared Zr-MOFs, (B) 4-MMC cascade removal efficiency on NU-1000 sample

Acknowledgement

The work was supported by the National Science Centre, Poland, under the research project "MOF-antidote": Novel detoxification materials based on metal-organic frameworks for drugs of abuse removal – synthesis, chemical characterization, toxicity and efficacy in in vivo and in vitro studies", no. UMO-2021/43/B/NZ7/00827.

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P-034

Metal-organic frameworks for efficient mephedrone detoxification or supervised withdrawal – synthesis, characterization and *in vivo* studies

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Metal-organic frameworks (MOFs) are defined as a group of highly porous materials with high chemical stability, low cytotoxicity, and high biodegradability. They consist of inorganic metal ions and organic ligands. Biocompatibility and high degrees of drug packing in MOF structures provide opportunities for their use in modern drug delivery systems (DDS) [1].

Nowadays, one of the most widespread problems is the phenomenon of drug addiction. Among the many types of substances, it is the group of synthetic cathinones (SCs) that is the most broadly used. This may be due to the fact that their action resembles the pharmaceutical properties of amphetamines. The main representative of this group is mephedrone (4-methylmethcathinone, 4-MMC) [2].

Tachycardia or hypertension are typical symptoms of 4-MMC overdose. Substances in the β-blocker group have been shown to have antiarrhythmic effects and prevent palpitations. An example is propranolol (PRO), applied during 4-MMC overdose to reduce the side effects of the drug taken. Safe and effective delivery of the drug is a key aspect of addiction therapy. The use of MOFs as carriers of PRO used in 4-MMC overdose appears to be a sophisticated and rational approach. In addition, the metal-organic framework has a protective effect against drug-loaded molecules [3]. Our study included synthesis of MOF materials, loading of PRO, formation of PRO@MOF composites, and subsequent. PRO release profiles were determined from the composites into water and a solution simulating human body fluid. Moreover, *in vivo* cytotoxicity tests and theoretical methods were conducted.

Acknowledgement

The work was supported by the National Science Centre, Poland, under the research project "MOF-antidote: Novel detoxification materials based on metal-organic frameworks for drugs of abuse removal – synthesis, chemical characterisation, toxicity, and efficacy in *in vivo* and *in vitro* studies", no. UMO-2021/43/B/NZ7/00827. Thermal studies were performed within the framework of funding for statutory activities of AGH University of Science and Technology in Kraków, Faculty of Materials Science and Ceramics (16.16.160.557).

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P-035

Synthesis and anticonvulsant activity of 3-aminopyrrolidine-2,5-dione derivatives

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Epilepsy is one of the most common neurological disorders, affecting approximately 0.5–1 % of people worldwide. It is a chronic and progressive in nature, characterized by recurring seizures of various manifestations. The basic method of treatment of epilepsy is pharmacotherapy. In most cases, pharmacological treatment gives positive results, but there are many drug-resistant people for whom the only hope is new antiepileptic drugs [1,2].

The main goal of the presented research was to develop procedures for the synthesis of new functionalized succinimide derivatives and to test them for anticonvulsant activity. Succinimide derivatives were obtained from a simple solvent-based reaction and a mechanochemical aza-Michael reaction of maleimide or its N-substituted derivatives with selected amines. The structure of the compounds was confirmed by spectroscopic methods (NMR, FT-IR, HPLC, ESI-MS, EA and XRD). The cytotoxic activity of the succinimide derivatives was evaluated using HepG2 cells for hepatocytotoxicity and SH-SY5Y cells for neurocytotoxicity. The anticonvulsant activity of each compound was tested using the psychomotor seizure test (6 Hz, 32 mA) in mice. The most active compounds were also tested in the MES test and three of the N-unsubstituted succinimide derivatives were active with ED50 values between 128.53 and 157.51 mg/kg. Furthermore, the selected succinimide derivatives were evaluated for their activity in the scPTZ test. The most active compound 3-((4-chlorophenyl)amino)pyrrolidine-2,5-dione revealed antiseizure activity in all seizure models and showed better median effective doses (ED50) and protective index values than the reference compound, ethosuximide [3].

Acknowledgement

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P-036

Biotransformation of pyrimidine derivatives

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In medicinal chemistry, naturally occurring five- and six-membered heterocyclic compounds containing from one to three heteroatoms in the ring are of particular interest due to the wide spectrum of biological activity. Their synthetic analogues are successfully used as agrochemicals and pharmaceuticals. Currently, it is estimated that over 85% of drugs have a heterocyclic scaffold. Among heterocyclic compounds, pyrimidines and their derivatives have a number of biological properties, e.g.: 2-sulfanilamidopyrimidines have antibacterial properties, structural analogues of barbituric acid are antiemetics, analgesics and diuretics, while condensed triazolopyrimidine derivatives have antifungal, anti-inflammatory, anticonvulsant, antiallergic and anticancer properties [1].

This work presents the microbiological modification of pyrimidine derivatives in the asymmetric desymmetrization reaction of the prochiral carbonyl moiety. The biotransformation was carried out in the presence of the microbiological preparation Blossom Protect and selected strains of *Aureobasidium pullulans*. The efficiency and stereoselectivity of the process depended on the structure of the prochiral substrate and the chirality of the dehydrogenases with which the bioreagent is equipped.

In microbiological bioreduction catalyzed by the microorganism *Aureobasiudium pullulans*, contained in the antifungal preparation Blossom Protect, as well as selected strains of *A. pullulans* with a moderate degree of conversion and excellent selectivity (>99% ee), 3*N*-phenacyl derivatives of pyrimidine bases are reduced. An excess of the *R*-configuration enantiomer was obtained, which indicates the selective transfer of one of the prochiral hydride ions of the cofactor to the *si* side of the carbonyl bond.

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P-037

Stable and Catalytically Active Chiral NHC-Au-Cl_3 Complexes; Unexpected Influence of Metal Tosylate on Enantioselectivity

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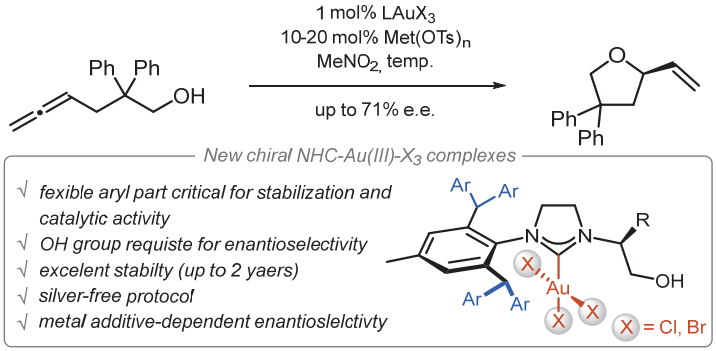
Enantioselectivity in gold catalysis is quite difficult to achieve by linear NHC – Au(I) – X catalysts. However, NHC – Au(III) – X_3 catalysts can provide better enantioselectivity due to its square planner spatial arrangements which usually induces better control of enantioselectivity. But the main drawback of Au(III) catalysis is that control of enantioselectivity in the product, and also maintaining the stability and reactivity of the catalyst. In this project our main focus was to devise a new method to prepare chiral, stable and catalytically active NHC – Au(III) – Cl_3 complexes. The main advantage of the NHC – Au(III) – Cl_3 catalyst is the presence of aromatic ring in the NHC scaffold which provides better selectivity and catalytic activity. Also better enantioinduction is achieved via the interaction of the chiral amino alcohol side chain with the reactant. In addition to that it was found that enantioselectivity for the cyclization of allenic alcohols to the corresponding vinyl tetrahydrofuran is very much dependent on different types of transition metal based tosylates such as Cu, Fe, Ru, Zn, Bi, Ga, In and Sn under Ag free conditions. Further it was found that very high degree of enatioselectivity was also achieved when $In(OTs)_3$ and $Sn(OTs)_2$ were used as activators for NHC – Au(III) – X_3 catalyzed cyclization of allenic alcohols to the corresponding vinyl tetrahydrofurane derivative in comparison to Ag mediated protocol.



Scheme 1. Application of NHC – Au(III) – Cl_3 in enantioselective cyclization.

Acknowledgement
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P-038

Synthesis of Conducting Polymers for High Energy Efficiency

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Polyaniline and polythiophene are prominent conductive polymers with remarkable properties that make them ideal candidates for various energy applications.[1] This study focuses on synthesizing polyaniline and polythiophene and explores their potential for excellent energy-related uses, including energy storage and conversion. These materials are synthesized via various methods, such as chemical oxidative polymerization, electrochemical deposition, and solution-based techniques, particularly optimizing their electrical conductivity, morphological characteristics, and environmental sustainability.[2]

These polymers' electrical conductivity and charge storage capacity are critical factors in their effectiveness for energy storage applications, including supercapacitors and solar cells. Furthermore, their compatibility with various substrates and the ability to be incorporated into flexible and lightweight devices make them promising candidates for next-generation energy storage solutions.

In addition, the versatility of polyaniline and polythiophene extends to energy conversion applications, including photovoltaic devices and energy harvesting technologies. Their unique optical and electrochemical properties can be harnessed to enhance the efficiency of solar cells and create novel approaches for converting environmental energy sources into electricity.

This study examines the recent advances in synthesizing polyaniline and polythiophene, their structural modifications, and their integration into practical energy applications. By exploring the synthesis and characterization of these conductive polymers, this research contributes to the growing knowledge surrounding innovative materials for sustainable energy solutions, offering promising avenues for developing efficient, eco-friendly, and high-performance energy devices.

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P-039

Molecular modeling of meconic acid from *Chelidonium majus* L.

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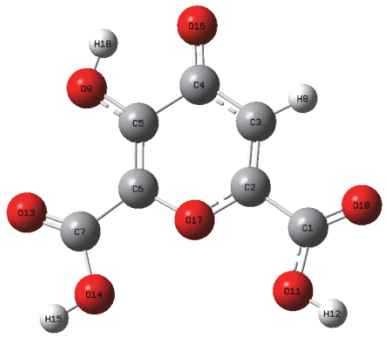
Numerous plants contain natural bioactive metabolites. *Chelidonium maius* L. grows in Europe and Asia and in folk medicineis commonly used for treatment of many diseases. The entire plant, containing and orange colored juice, is a source of many bioactive compounds, including two simple heterocyclic acids – chelidonic and meconic acids. Their properties are of interest in contemporary medicine, too. However, the use and distribution of many plant metabolites is controlled by law restrictions against psychoactive substances. [1] For example, Polish legislation allows for collecting poppy milk and opium from poppies and the herb or resin of non-fiber hemp solely to conduct scientific research, subject to prior approval from the Chief Pharmaceutical Inspector. [3] On the over hand, the European Commission has only issued recommendations regarding the prevention of the presence of opium alkaloids and their reduction in poppy seeds and products derived from poppy seeds. [4] Interestingly, the presence of meconic acid was observed and studied in the assay of opium by the U. S. P. 1890 process. [2]

For better insight into biological activity of this metabolite, as continuation of our recent investigation [1], in the current paper we report on our theoretical modeling of meconic acid structure, energy, vibrational and NMR properties. Both isolated molecules and in solution were studied using density functional theory (DFT) and gauge included atomic orbital (GIAO) NMR approach. [1]

The presented work reports on a more detailed theoretical DFT characterization, combined with large basis sets, of the structure and magnetic properties of meconic acid (its molecular structure is shown below).



Acknowledgement

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P-040

Asymmetric epoxidation of enones promoted by dinuclear magnesium catalyst

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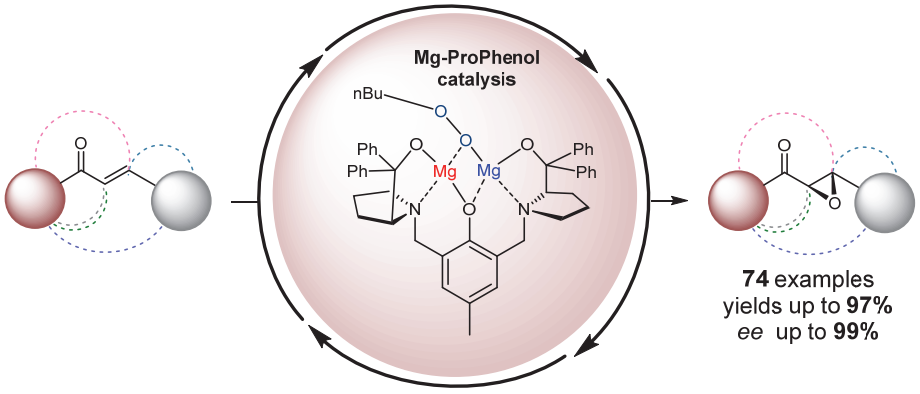
Asymmetric synthesis with cheaper and non-toxic alkaline earth metal catalysts is becoming an important and sustainable alternative to conventional catalytic methodologies mostly relying on precious metals. In spite of some sustainable methods for enantioselective epoxidation of enones, the development of a well-defined and efficient catalyst based on magnesium complexes for these reactions is still a challenging task. In this perspective, we present the application of chiral dinuclear magnesium complexes for asymmetric epoxidation of a broad range of electron-deficient enones.

We demonstrate that the *in situ* generated magnesium-ProPhenol complex affords enantioenriched oxiranes in high yields and with excellent enantioselectivities (up to 99% *ee*). Our extensive study verifies the literature data in this area and provides a step forward to better understand the factors controlling the oxygenation process. Elaborated catalyst offers mild reaction conditions and a truly wide substrate scope.



- Readily available or easily to synthesis ProPhenol ligands
- Mild reaction condition
- wide substrate scope
- The use of environmentally friendly non-toxic Mg metal

Acknowledgement

Financial support from the Polish National Science Centre: OPUS Grant No. NCN 2017/27/B/ST5/01111

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P-041

O,P-acetals – an effective building blocks

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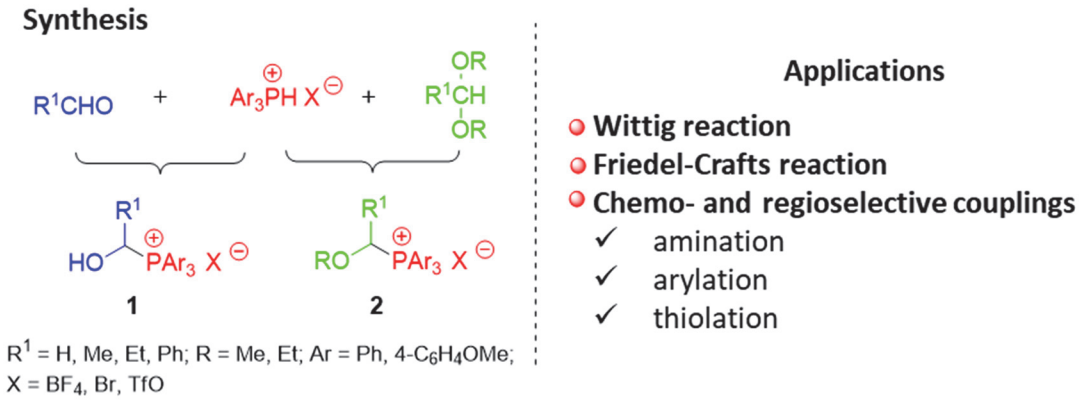
O,P-acetals can be defined as phosphorus compounds containing a P-C-O moiety. The general method for their synthesis is based on the reaction of carbonyl compounds (e.g. aldehydes or ketones) with phosphorus reagents. The 1-hydroxyalkylphosphonium salts **1** and 1-alkoxyalkylphosphonium salts **2** are specific examples of *O,P*-acetals. They are widely used as substrates in many reactions, such as Wittig reactions, Friedel-Crafts reactions, or chemo- and regioselective couplings (amination, thiolation, or arylation).[1]

Recently, we have developed new, efficient protocols for their synthesis using aldehydes or acetals and phosphonium salts (HAr_3P^+ X^-). Next, we confirmed their synthetic suitability in reactions with amide-type compounds and (hetero)arenes to obtain 1-(*N*-acylamino)alkylphosphonium salts and 1-arylalkylphoshonium salts, respectively.[2]



Scheme 1. Synthesis and applications of *O,P*$^+$-acetals **1** and **2**.

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P-042

Theoretical study of interaction of flavonoids inhibitors with NBD of GRP78

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Glucose-Regulated Protein 78 (GRP78), also known as BiP (Binding Immunoglobulin Protein) belongs to the family of Heat Shock Protein. It is a highly conserved protein that belongs to the major endoplasmic reticulum (ER) chaperone, which is responsible for protein folding and maturation, protein quality control, Ca^{2+} binding and activates the unfolded protein response pathway (UPR) during stress conditions [1-3]. In normal conditions, GRP78 binds to the ER stress sensors like ATF-6, PERK, and IRE1 and suppresses them [4]. GRP78 or BiP has the function of a co-receptor for cell surface signaling and also is potent anti-apoptotic protein and has a significant role in tumor cell survival, tumor progression, metastasis, and resistance to therapy by altering the glucose metabolism of cancer cells [5, 6]. Therefore, GRP78 can be considered a relevant target for cancer therapy [4]. Chaperone GRP78 protein consists of a total of 633 residues and has two domains: a nucleotide-binding domain (NBD), which binds to ATP and a substrate-binding domain (SBD) for substrate binding. Some natural compounds that can inhibit GRP78 are flavonoids, which are plant-derived and can bind to the ATPase domain of GRP78 and inhibit its catalytic activity, inducing ER stress and cell death in various cancer cells. GRP78 is often overexpressed in cancer cells and plays an important role in their survival and growth. Here, we analyzed some natural inhibitors like; Epigallocatechin Gallate, Kaempferol, Naringin, Poncirin, and Prunin. To investigate the binding efficiency of those compounds to the active site of GRP78, we performed the series of theoretical analysis including molecular docking, and protein-ligand binding analysis. Results indicate that some of natural inhibitors have higher binding energy towards this protein than native ATP.

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P-043

Synthesis of 1,1-dialkylpiperazinium derivatives of 6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid with potential antibacterial and antibiofilm activity

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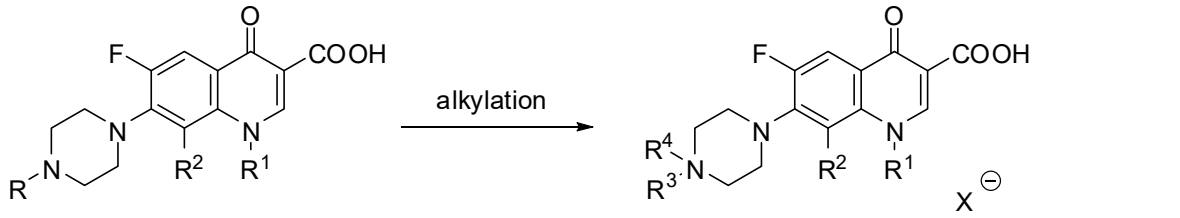
Antibiotics comprise a specific group of compounds crucial in combatting infections caused by pathogens. Their misuse and overuse in recent years has led to the emergence of drug-resistant strains of bacteria, consequently resulting in increased treatment costs, complications, and mortality rates among infected patients. To counter this issue, researchers are focusing on the development of new compounds with unique antibacterial mechanisms. In an attempt to control microbial growth effectively, the fusion of two active molecules with different targets have been explored. This has led to the synthesis of hybrid compounds that integrate a fluoroquinolone core with a quaternary ammonium salt group [1-4], *i.e.* 1,1-dialkylpiperazinium. These compounds are anticipated to exhibit a dual antibacterial mechanism, targeting the inhibition of bacterial DNA gyrase and topoisomerase IV *via* the fluoroquinolone component, and the destabilization of phospholipid membranes in bacterial cells through the 1,1-dialkylpiperazinium group's quaternary nitrogen atom. Following extensive synthetic work, a set of novel compounds was successfully obtained, with their structures confirmed by IR, ^{1}H-NMR, and MS spectra analysis. Subsequent research will involve evaluating the expected antibacterial and antibiofilm properties of these derivatives through studies using both Gram-positive and Gram-negative bacterial strains, along with additional biochemical tests.



R = H, Me, Et

$R^3 = R^4$ = Me, Et, Bn
R^3 = Me, Et; R^4= Bn, 4-*t*BuBn, 2-PhBn, 3-PhBn

Scheme 1. Synthesis of novel 1,1-dialkylpiperazinium derivatives of 6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid.

Acknowledgement

This work was supported by the Polish National Agency for Academic Exchange [grant number PPN/BEK/2019/1/00217]; and Medical University of Gdańsk (Poland) subsidies.

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P-044

On How Substitution and Intramolecular Hydrogen Bonding Influence the Integral NICS Aromaticity of the Chloro- 8-Hydroxyquinoline Molecule

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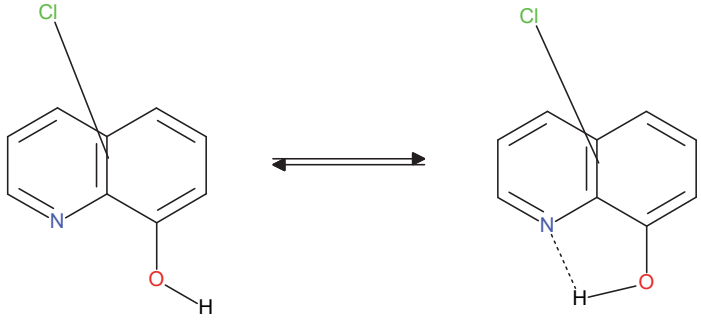
Recently Stanger proposed the integral NICS aromaticity index, [1] and Berger et al. demonstrated [2] that the index is physically justified through its relation to the ring current via Ampère-Maxwell's law. In 2022, we demonstrated that the integral, INICS, index [3] calculated using the ARONICS program written by Dudek [4] is the most robust and indicative in evaluating the aromaticity of the aromatic amino acids. Quite recently, we studied ring's aromaticity in the pyridine[m,n]diazepines based on the integral INICS index [5] and found that the six-membered pyrido rings have negative $INICS_{ZZ}$ values and can be aromatic only if not protonated at the N-atom. In contrast all protonated pyrido rings exhibit meaningful positive $INICS_{ZZ}$ values and can be assigned as antiaromatic.



Scheme 1. Intramolecular hydrogen bond formation in mono-chloro-8-hydroxyquinolines.

The 8-hydroxyquinoline is interesting as many of its derivatives can play the role of ligands in metallodrugs. In this study, we examine the influence of different substitutions and intramolecular hydrogen-bond formation on the aromaticity of the pyridine and hydroxy-substituted benzene rings in the chloro-8-hydroxyquinoline system (Scheme 1) using the INICS index. We hope to find correlations helpful in modeling metallodrugs composed of 8-hydroxyquinoline ligands.

Acknowledgement
This work was financed by the Polish National Science Centre Grant 2022/47/B/NZ7/02765. The statutory funds from the Institute of Chemistry and Nuclear Technology and the computational grant from the Świerk Computing Centre (CIŚ) for the J.Cz.D. group are gratefully acknowledged.

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P-045

On Integral INICS Aromaticity of Pyridodiazepine Constitutional Isomers and Tautomers

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Pyridodiazepines are benzodiazepine analogs with an extra N-atom incorporated into the benzene ring, i.e., they are bicyclic systems in which the six-membered pyridine ring is fused with a non-planar seven-membered diazepine one.

The aim of this study was to gather knowledge about the relationship between pyridodiazepines' structure, tautomerism, stability, and aromaticity and to test our new integral NICS (INICS) index and the ARONICS program written in our group [1-3].

The structure, energetics, and aromaticity of c.a. 100 constitutional isomers and tautomers of pyrido[m,n]diazepines (m = 1, 2; n = 2, 3, 4, 5; m 6= n) were studied at the B3LYP/cc-pVTZ level. The pyrido[1,3]diazepines appear the most, while pyrido[2,4]diazepines are the least stable (ca. 26 kcal/mol). In the pyrido[1,n]diazepine group (n = 2–5), the [1,5] isomers are higher in energy by ca. 4.5 kcal/mol and the [1,4] ones by ca. 7 kcal/mol, and the pyrido[1,2]diazepines are the least stable (ca. 20 kcal/mol). All the most stable pyrido[1,n]diazepines have N-atoms near the ring's junction bond but on opposite sites. The most stable [2,n]-forms are also those with the pyridine ring N6-atom near the junction bond.

The ring's aromaticity in the pyridine[m,n]diazepines was established based on the integral INICS index resulting from the $NICS_{ZZ}$-scan curves' integration. The six-membered pyrido rings have negative $INICS_{ZZ}$ indices and can be aromatic only if they are not protonated at the N-atom. All protonated pyrido and seven-membered rings exhibit meaningful positive $INICS_{ZZ}$ values and can be assigned as antiaromatic. However, some non-protonated pyrido rings also have substantial positive $INICS_{ZZ}$ indices and are antiaromatic. A weak linear correlation (R^2 = 0.72) between the $INICS_{ZZ}$ values of the pyridine I(6) and diazepine I(7) rings exists and is a consequence of the communication between the -electron systems of the two rings.

Acknowledgement

This work was financed by statutory funds from the National Medicines Institute (DS8/2023). The Polish National Science Centre Grant 2020/39/B/ST4/01670 financially supported the integral aromaticity index study.

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P-046

Ambident Reactivity of Enolizable 5-Mercaptotetrazoles Towards in situ Generated Thiocarbonyl *S*-Methanides

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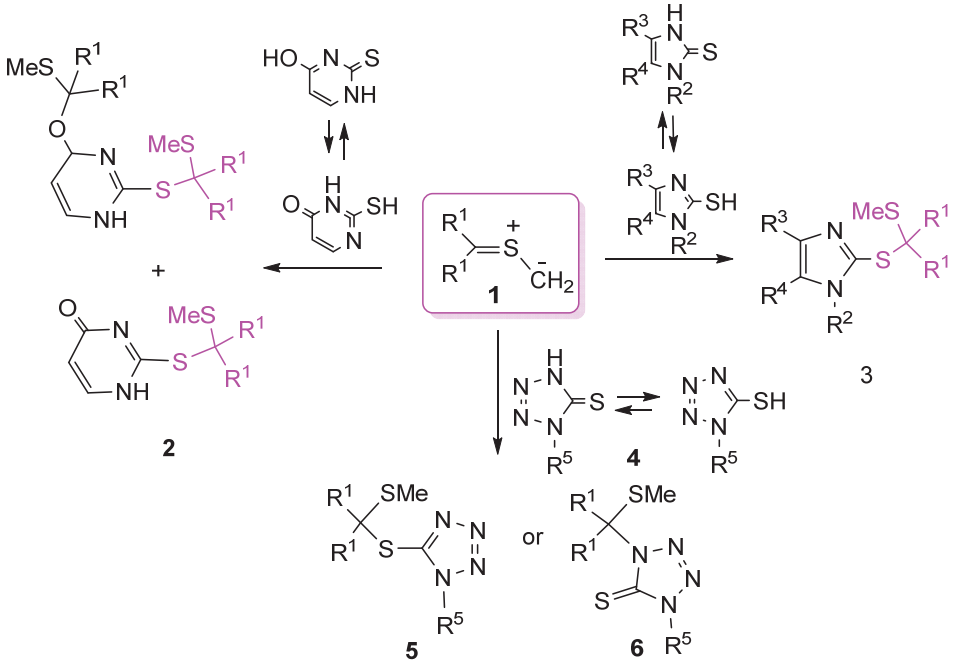
The in situ generated thiocarbonyl *S*-methanides **1** derived from cycloaliphatic thioketones are known to react as superior, electron-rich 1,3-dipoles which easily undergo (3+2)-cycloadditions with thiocarbonyl dipolarophiles (e.g. thioketones, dithioesters, etc.) yielding 1,3-dithiolanes in a regioselectivite manner [1]. They react also with enolizable, azaheterocyclic thiones but in this case insertions into the S-H bonds of the mercapto-form, and not cycloadditions with the C=S bonds, are observed. For example, thiouracyl and imidazole-2-thiones react with cycloaliphatic **1** to give dithioacetales of type **2**, and **3** as sole products, respectively (Scheme 1) [2].



Scheme 1. Insertion reactions of 1,3-dipoles **1** into S-H and N-H bonds.

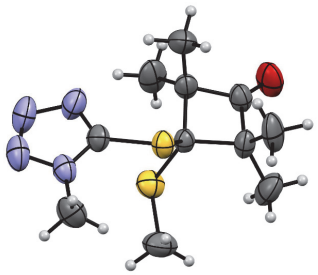


Figure 1. X-Ray structure of dithioacetale of type **5** obtained from 1-methyl-5-meracpto 1,2,3,4-tetrazole and 3-thioxo-2,2,4,4-tetra-methyl-cycloabutanone *S*-methanide.

In the present study we report on the newest results obtained in reactions of selected thiocarbonyl S-methanides **1** with 1-substituted 5-mercaptotetrazoles **4**. Unexpectedly, in this series, ambident reactivity of enolizable **4** was observed and products of the insertion into both, S-H as (products **5**) well as N-H (products **6**), respectively, were obtained. Structures of products were established based on spectroscopic data and in some instances, they were confirmed by single crystal X-Ray diffraction analysis, e.g. structure of a product of type **4** (R^5 = Me) is presented in Figure 1.

Acknowledgement

Authors thank Prof. Marcin Palusiak (University of Łódź) for X-ray analyses of a selected insertion products derived from 1-methyl-5-mercapto 1,2,3,4-tetrazole.

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P-047

Synthesis of biogenic amine derivatives with 2-halogen-pyridines

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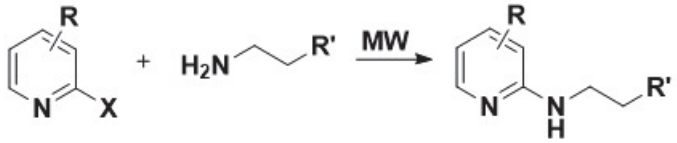
Biogenic amines (BAs) commonly exist in beverages and foods and indicate freshness and quality due to their formation in protein-rich matrices. Their high concentrations in food can cause adverse effects, resulting in foodborne illnesses and intoxication.

Currently, researchers primarily focus on expanding our knowledge of the presence of BAs in food and developing suitable procedures for routine analyses. High-performance liquid chromatography, known for its high selectivity, sensitivity, and simple sample treatment, is the preferred technique for determining BAs after derivatisation. However, the structural similarities among BAs, their high polarity, low analyte concentration in the sample matrix, and the lack of sufficient chromophores make it mandatory to derivatise BAs before conducting analyses.

The presented research concerns the selection of conditions for the synthesis of biogenic amine derivatives (BA) from 2-halogen-pyridines using a microwave reactor. Pyridine derivatives were obtained with 3-nitro, 5-nitro, 5-cyano, and 5-trifluoromethyl groups. The reactions carried out take place according to the mechanism of nucleophilic substitution in the aromatic ring. The influence of the substituent in the pyridine system and the leaving group on the efficiency of the synthesis and the possibility of using it in the analysis of food products was also checked. All obtained derivatives with a cyano substituent were tested for their fluorescent properties.



Scheme 1. General reaction of BAs derivatives synthesis.

Acknowledgement

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P-048

Synthesis of amino acids derivatives with halogenobenzene

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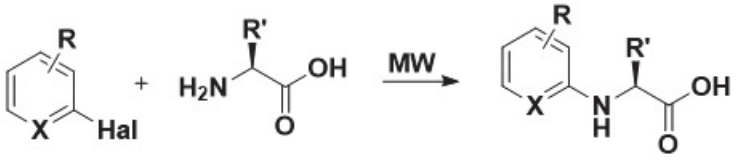
Over the last few years, the determination of free amino acids has increased significantly for the comprehensive analysis of nutritional issues. These compounds create sweetness, sourness, bitterness, and umami taste in foods. Moreover, they are precursors of bioactive amines, which have a significant role as neurotransmitters and are involved in biological functions.

The identification and separation of amino acids is difficult due to their high polarity, low volatility and absence of strong chromophoric groups. For this reason, all determination methods require the derivatization stage of amino acids using appropriate derivatizing reagents.

As part of the research on derivatives of selected amino acids (AAs), their reaction with halogenoaromatic systems was carried out. AAs derivatives with 1-fluro-2-nitro-4-trifluoromethylbenzene (FNBT), 1-halogeno-4-nitro-2-trifluoromethylbenzene, 4-chloro-3,5-dinitrotrifluorobenzene (CNBF), p-toluenesulfonic chloride and nitropyridines were obtained. The reactions were carried out in a microwave reactor using "green chemistry" methods. The derivatives were obtained according to the mechanism of nucleophilic substitution in the aromatic ring. The obtained compounds constituted standards for the analysis of food samples and cosmetic raw materials.



Scheme 1. Scheme of AAs derivatives synthesis.

Acknowledgement
This research was financially supported by National Science Centre, Poland holding the decision number UMO-2020/39/B/NZ9/01694 [grant number 2020/39/B/NZ9/01694].

P-049

An unexpected method of synthesis of derivatives 2-oxo-4-(1*H*-pyrrol-3-yl)but-3-enoic acid based on Ugi bisamides

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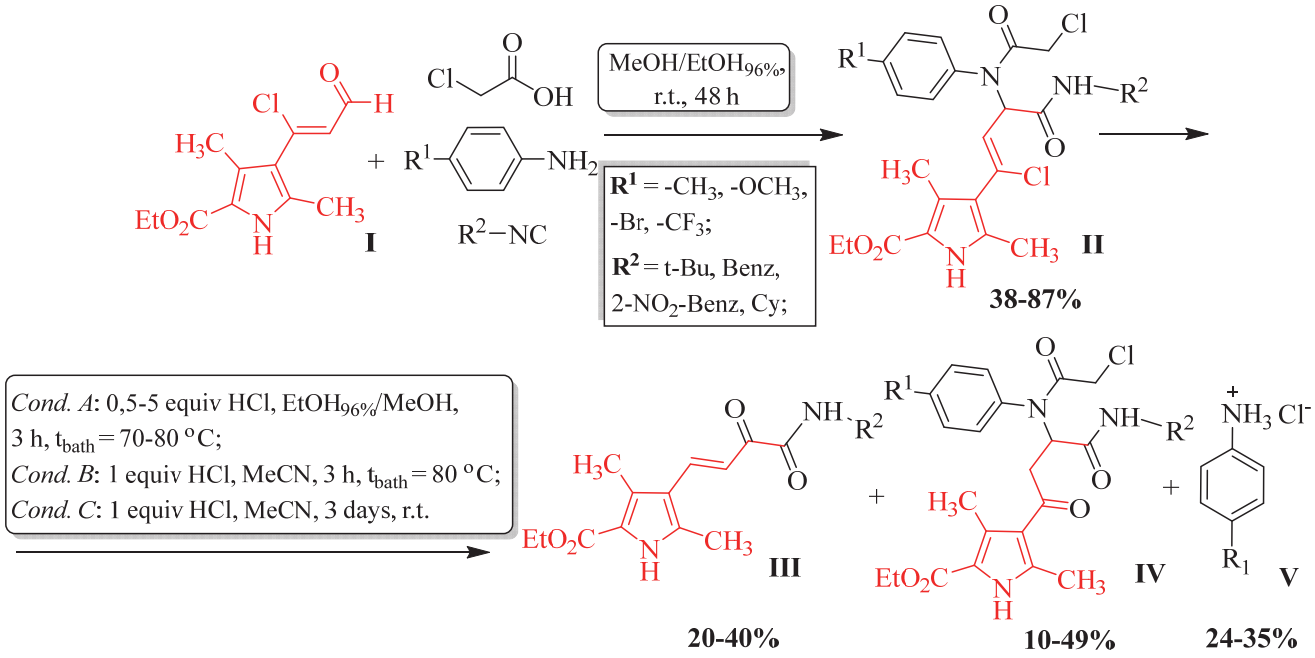
The multicomponent Ugi reaction is a powerful tool for creating libraries of organic substances, which may include new biologically active compounds and new components of functional materials. A special role is played by so-called post-Ugi reactions, which can include various post-cyclizations or subsequent modifications of functional groups and amide bonds in Ugi products.

On the basis of pyrrolyl-*β*-chlorovinylaldehyde **I**, chloroacetic acid, *para*-substituted anilines and corresponding isocyanides, we synthesized Ugi bisamides **II** with acceptable to good yields, which under acid hydrolysis give three main products, one of which is a derivative of vinyl-(3-pyrrolyl)pyruvic acid **III**.



Scheme 1. Synthesis of Ugi bisamides **II** and their further transformation under acid hydrolysis conditions.

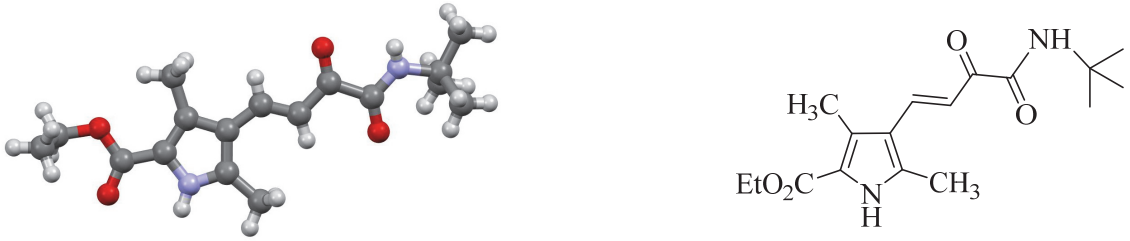


Figure 1. X-ray crystalography analisis of 2-oxo-4-(1*H*-pyrrol-3-yl)but-3-enoic acid amide **III**

Acknowledgement

The authors thank the National Academy of Sciences of Ukraine for financial support in the frame of the project "Directed synthesis, chemical transformations and properties of new nitrogen-containing heterocyclic compounds" (0122U001857).

P-050

5-Methylbenzotriazole: A Comprehensive Study on Structure, Vibrational Spectra, and Microbiological Properties

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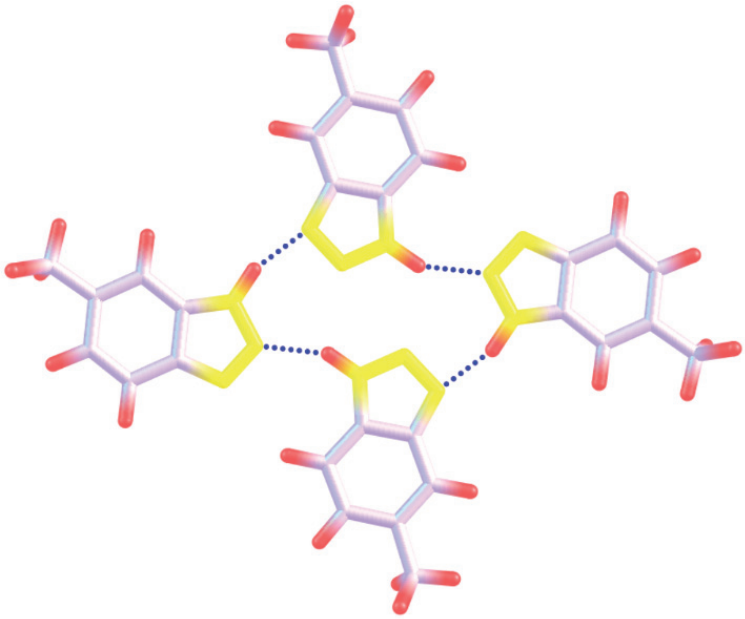
Three tautomeric forms of 5-methylbenzotriazole (5MeBTA), namely 1*H*-, 2*H*-, and 3*H*-5MeBTA, were investigated, along with a tetramer that includes the 1*H*-5MeBTA and 3*H*-5MeBTA tautomers connected by N3···N3 and N1···N2 intermolecular hydrogen bonds. Density functional theory (DFT) calculations were carried out using B3LYP, B3LYP-D3, and ωB97XD methods with a 6-31++G(d,p) basis set. The computed intermolecular distances in the tetramer closely matched those reported for the crystal structure of 5MeBTA [1]. The theoretical Raman and infrared spectra of the tetramer agreed well with experimental FT-Raman and FT-IR spectra of 5MeBTA in the solid state. Microbiological *in vitro* studies conducted on 5MeBTA and benzotriazole (BTA) revealed that introducing a methyl group at position 5 of BTA increased its activity against the tested strains. For more detailed information, please refer to reference [2].



Scheme 1. Theoretical model.

Acknowledgement

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P-051

Analysis of interactions in biologically important systems - co-crystallization of dipicolinic and quinolinic acids with amino acids

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A co-crystallization of dipicolinic and quinolinic acids with selected amino acids was conducted to discover and characterize interactions in biologically important systems. In the first step, preliminary statistical analysis of data collected from the CSD (Cambridge Structural Database) was performed. After careful verification, optimal conditions for crystallization were determined, and the initial crystallizations were carried out.

As is well known, amino acids serve as the fundamental building blocks of all living organisms. Dipicolinic acid enhances the heat resistance of endospores (spore forms) in conditions of elevated environmental humidity, in comparison to vegetative cells. Quinolinic acid, a structural isomer of dipicolinic acid, is one of the end products in the tryptophan metabolism within the kynurenine pathway and exhibits a strong neurotoxic effect. [1] The pursuit of multicomponent crystals composed of mixtures of these chemical species is of significance in the context of structural analysis and, furthermore, in biological studies.

The overarching objective of this research is to examine the structural, chemical, and biological behaviors of the molecules under investigation, contingent on the positioning of functional groups and their environment in the (co-)crystal state. Particularly, we are focused on discerning the structural relationships within the studied molecular systems that directly result from intermolecular interactions. [2]

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P-052

Preparation of P-diastereomerically pure morpholino units for synthesis of P-stereodefined phosphorothioate of morpholino analogs

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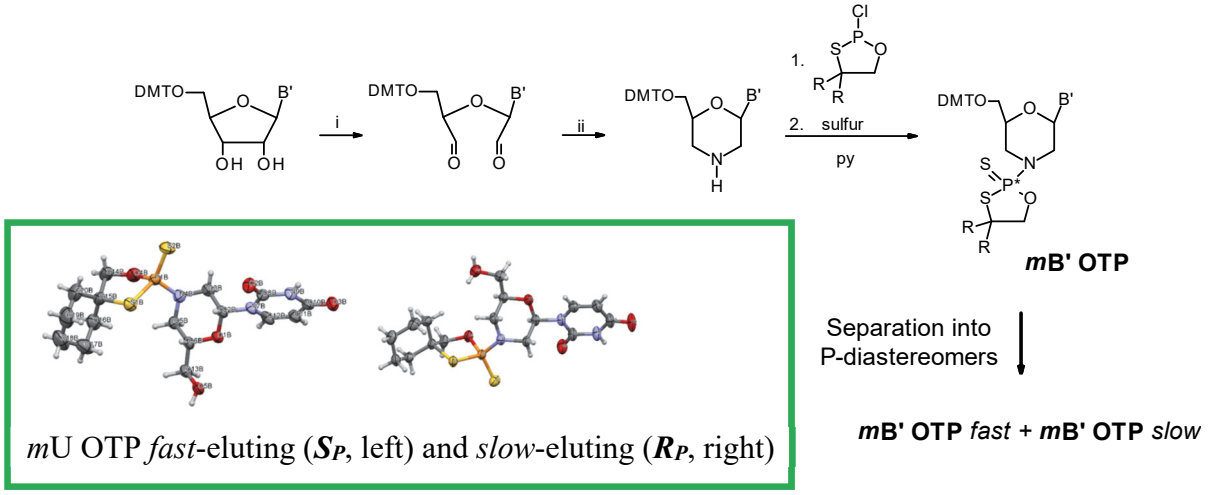
Herein, we present the preparation of P-diastereomerically pure morpholino units for synthesis of **novel P-stereodefined phosphorothioate of morpholino analogs** (*mB'* OTPs, 1; see Scheme 1). Synthesis of morpholino nucleosides were performed according to the published protocols[1]. Briefly, 5'-*O*-dimethoxytrityl uridine was oxidatively converted in the acyclic dialdehyde derivative, followed by reductive cyclization upon treatment with $NaCNBH_3$. Morpholino nucleosides were transformed into corresponding N-(2-Thio-4,4-pentamethylene-1,3,2-oxathiaphospholane) derivatives of morpholino-type nucleosides (*m*B' OTPs, **1**) according to a general procedure published for the synthesis of the standard OTP monomers[2]. *m*B' OTPs (**1**) were isolated as a mixture of P-diastereomers and were characterized by FAB MS and ^{31}P NMR. OTP monomers were separated into P-diastereomers (*fast*-eluting and *slow*-eluting) by preparative HPLC using silica gel column and their diastereomeric purity was confirmed by ^{31}P NMR, ^{1}H NMR, ^{13}C NMR.



Scheme 1. i. $NaIO_4$ (1.2 equiv), anhydrous methanol; $(NH_4)_2B_2O_7$ (1.2 equiv), 6 h; **ii**. $NaCNBH_3$ (2.0 equiv); CH_3COOH (2.0 equiv), 16 h

X-ray analysis showed that *fast*-eluting *m*U OTP has the P-atom of the S_P absolute configuration and *slow*-eluting *m*U OTP - R_P (according to the Cahn–Ingold–Prelog rules the endocyclic sulfur atom has higher priority than the exocyclic one). It should be noted that we have presented the first determination of the stereochemistry at stereogenic phosphorus atom in morpholino analogs. Pure P-diastereomers of *mB'* OTPs were used in manual synthesis of novel P-stereodefined phosphorothioate of morpholino analogs (see Katarzyna Jastrzębska's poster).

Acknowledgement
This project was supported by NCS **2021/43/D/ST4/02433**.

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P-053

Manual Solid-Phase and Solution-Phase Syntheses of P-stereodefined of morpholino dinucleoside 3',6'-thiophosphoramidates

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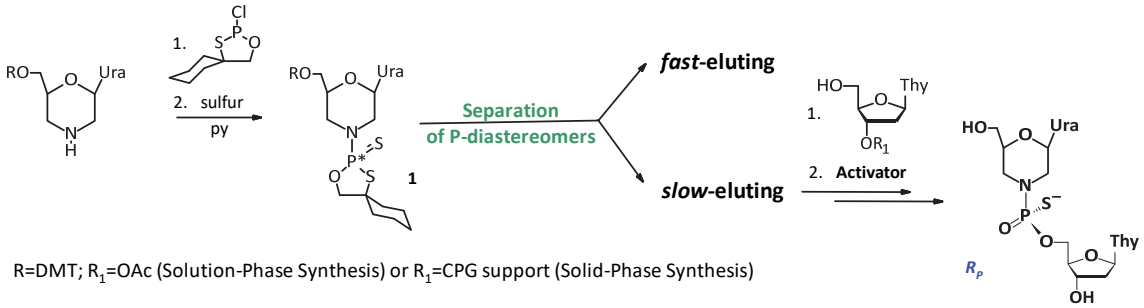
Several stereopure PS-DNA oligomers are currently in clinical development, e.g. at Wave Life Sciences, where they are being tested against diseases of the central nervous system, liver and eye.[1] To date, only a few methods have been developed to synthesize the PS-Oligos in a **stereocontrolled manner**, namely the oxathiaphospholane method developed by Stec et al.[2], (OTP, see Figure 2), the method using nucleoside 3'-*O*-(3-*N*-acyl)oxazaphospholidine derivatives[3], and the method based on the stereoselective synthesis of nucleoside 3'-O-oxazaphospholidine monomers[4]. Recently, Baran's team described a fast citrus route to chiral phosphorus.[5] We present **modified OTP method** to the synthesis of novel **P-stereodefined phosphorothioate analogs of "morpholino" nucleic acids (sTMO)** in the presence of **unexpected activators** and provide valuable structural insights into their stereochemistry. The P-diastereomerically pure monomers **1** ***fast*** and **1** ***slow*** (see Patrycja Antończyk's poster) were used for the synthesis of P-stereodefined dinucleotides **2** (Scheme 1). X-ray analysis allowed for assignment of the R_P absolute configuration of the phosphorus atom in the detritylated *m*U$_{PS}$T dinucleotide obtained from slow-eluting diastereomer.



Scheme 1. P-stereodefined dinucleotide **2** obtained from *slow*-eluting P-diastereomer.

Further experiments using the developed oxathiaphospholane method for solid-phase synthesis of **s**tereodefined **T**hiophosphoramidate **M**orpholino **O**ligomers (**sTMO**) are in progress. Recently, P-stereorandom TMO were synthesized using the phosphoramidite approach[6]. Dumbović et al. and Le et al. described these P-stereorandom TMO constructs which exhibit interesting biological properties and considerable therapeutic potential[7]. Therefore we are curious whether those biological activities might be elicited by oligomer(s) with proper absolute configuration of the phosphorus atoms. Successful completion of this project may allow for the identification of the most biologically active stereoisomers of TMO-based drugs or the use of sTMO as molecular probes in biochemical studies.

Acknowledgement
This project was supported by NCS **2021/43/D/ST4/02433**.

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P-054

Study of the cytotoxic and antimicrobial activity of new rhenium complexes

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Many metal complexes have therapeutic and diagnostic utility in treating cancer, diabetes, inflammation, cardiovascular, neurodegenerative, and infectious diseases. Still, only a few platinum (Pt)-metallodrugs have been approved for use in oncology. This is because of the systemic toxicity of the Pt-based drugs and inherent or acquired resistance of cancer cells to platinum drugs.

Our preliminary research has recognized a group of Rhenium (Re) and Rhodium (Rh) metal complexes with promising anticancer activity against selected model cell lines and antibacterial activity on reference and clinical strains. Thus, the new Re/Rh complexes are attractive starting structures to search for new potent nonplatinum (non-Pt) anticancer agents and simultaneously search for new metalloantibiotics to fight against antimicrobial resistance (AMR) problem.

In this study we present several new Re complexes and their cytotoxicity on cell lines and antimicrobial effects on bacterial strains.

Acknowledgement
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P-055

A convenient synthesis of ω -hydrazinoalkylphosphonic acids

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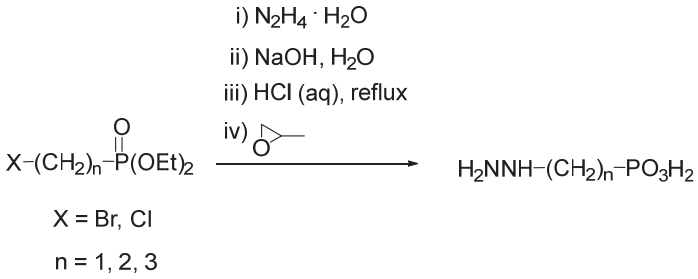
The hydrazinoalkylphosphonate moiety constitutes an important building block for azaheterocyclic phosphonates [1] which are of synthetic and biological significance.[2] For example, they have been demonstrated to protect cultivated plants from the phytotoxic action of herbicides. [3] Recently, we have demonstrated hydrazinoethylphosphonic acid as a useful synthon for the synthesis of five- and six-membered heterocycles.[4]

Some synthetic approaches to hydrazinoalkylphosphonic acids have already been reported.[5]

Herein we present a simple, efficient, and cost effective method that has been developed for the synthesis of ω-hydrazinoalkylphosphonic acids via the nucleophilic substitution reaction of diethyl ω-haloalkylphosphonates and hydrazine using mild reaction conditions, followed by hydrolysis with hydrochloric acid.



Acknowledgement
The authors thank the University of Lodz for financial support.

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P-056

Reactivity of the tRNA wobble 5-methylaminomethyl-2-selenouridine under oxidative and reducing stress conditions

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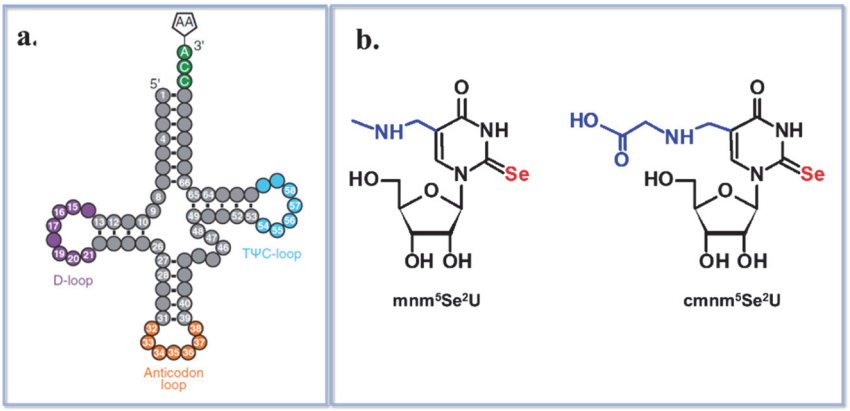
5-Metylaminomethyl-2-selenouridine (mnm5Se2U) is a hypermodified nucleoside found in the wobble position of transfer RNA (tRNA) in bacteria. There are some data suggesting that mnm5Se2U, as a modification in the anticodon region of tRNA, plays a crucial role in the precise and efficient decoding of mRNA codons during translation. It may contribute to the accuracy of protein synthesis by ensuring that the correct amino acids are added to the growing polypeptide chain.

It is worth noting that the dynamic regulation of tRNA modifications in response to environmental changes, including various types of stress, is a critical mechanism by which cells can adapt and regulate the synthesis of the proteins most needed at a given time. The reasons for the incorporation of selenium into the wobble nucleosides of tRNAs are not fully understood. One of the hypotheses and possible benefits associated with this modification suggest that 2-selenouridines may contribute to the protection of cells from oxidative damage.

Recently, we presented a detailed study on the oxidation of 2-selenouracil (Se2Ura) and 2-selenouridine (Se2U) [1,2]. Continuing our research on the biological function of selenium-containing tRNA components, we conducted the studies with the aim of elucidating in detail the process of oxidation of 5-metylaminomethyl-2-selenouridine under various conditions that mimic oxidative stress in the cell. We present the detailed analysis of the oxidation products of mnm5Se2U by liquid chromatography-mass spectrometry (LC-MS).



Scheme 1. a) Cloverleaf structure of transfer RNA; b) Chemical structures of 5-substituted-2-selenouridines identified in position 34 of bacterial tRNA.

Acknowledgement

This work was supported by The National Science Centre of Poland grant no. UMO-2018/29/B/ST5/02509 to B.N.

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P-057

Novel Furopyrimidine Nucleosides with 5-Alkynyl Substituent and their Antiviral Activity

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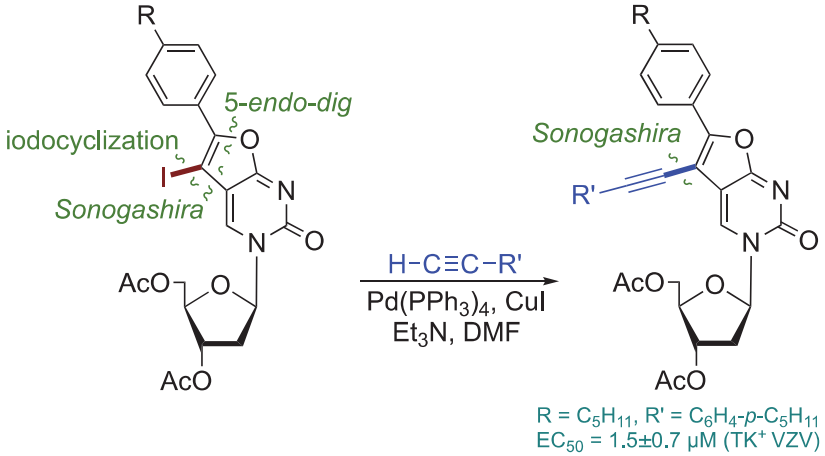
A novel methodology to access alkynyl nucleoside analogs was elaborated. Highly fluorescent 5-alkynylfuropyrimidines were synthesized (97-46%) and their antiviral properties investigated *in vitro*. Specific side of appending alkynyl group was achieved by installing an iodine via 5-*endo-dig* electrophilic halocyclization of acetyl 5-*p*-tolyl- or 5-*p*-pentylphenylethynyl-2'-deoxyuridine. Structure of one of the resulting nucleosides, 6-*p*-tolyl-5-iodo-2'-deoxyribofuranosyl-furo[2,3-*d*]pyrimidin-2-one, was confirmed by X-ray crystallography. Diverse alkynyl substituents were introduced at the heterobicyclic base C-5 position via Sonogashira coupling of 5-iodo-2'-deoxyribofuranosyl-furo[2,3-*d*]pyrimidin-2-ones.[1] The resulting compounds had fluorescence emissions of 452 to 481 nm. High quantum yields of 0.53-0.60 were observed for 9-ethynyl-9-fluorenol and propargyl alcohol/methyl ether-modified furopyrimidines. These modified nucleosides, designed in the form of ribose acetyl esters, represent potential tools for fluorescent tagging, studying nucleoside metabolism, 2′-deoxyribonucleoside kinase activity, and antiviral activity. Antiviral assays against a broad spectrum of DNA and RNA viruses showed that in human embryonic lung (HEL) cell cultures some of the compounds showed antiviral activity (EC_{50} 1.3-13.2 μM) against varicella-zoster virus (VZV). The alkynyl furopyrimidine with two *p*-pentylphenyl substituents emerged as the best compound with reasonable and selective anti-VZV activity, confirming *p*-pentylphenyl potency as a pharmacophore. The 5-alkynylfuropyrimidines can also be converted into their corresponding dicobalt hexacarbonyl derivatives.[2]



Scheme 1. Synthesis of 5-alkynylfuropyrimidines.

Acknowledgement

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P-058

Arylcyanomethylenequinone oximes the potent antifungal agents

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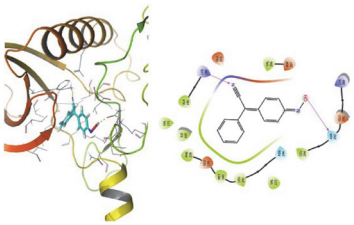
Fungal infections are continually associated with high mortality rates, especially in immunocompromised patients. Candida species are responsible for the majority of fungal infections in humans. The overuse, prolonged treatment, and environmental exposure to contemporary antifungal drugs have led to the emergence and widening of drug resistance. The shortcomings of currently used antifungal drugs dictate the urgent and growing need to discover new classes of antifungal medicines. Nevertheless, since the beginning of the 21st century, only five new antifungal agents have been authorized: caspofungin, micafungin, anidulafungin, isavuconazole, and ibrexafungerp. Herein, we present the design and synthesis of new antifungal agents bearing quinone methide oxime framework.

As we have already reported, phenylcyanomethylenequinone oxime (4-AN) [1] exhibits potent fungistatic and fungicidal activity against Candida species (MIC/MFC = 4 μg/mL) [2]. The series of new drug candidates was obtained by direct functionalization of readily available 4-AN at the oxygen atom.

Biological studies carried out on 9 Candida species indicate that proper selection of functional groups may increase the antifungal activity of new 4-AN derivatives to a level comparable to that of reference antibiotics such as caspofungin, ketoconazole, and amphotericin B (MIC < 2 μg/mL). Moreover, at a concentration of MIC/16, our new compounds prevent hyphae formation, and at a concentration of MIC/4, they effectively disaggregate mature biofilms. The influence of new drug candidates on 100 clinical isolates of C. albicans indicates that some of the compounds were also active against drug-resistant strains. On the other hand, no toxic effects of 4-AN derivatives on either human erythrocytes or zebrafish embryos were observed.

The explanation of the biological activity of 4-AN derivatives was proposed based on a study of their interaction with a set of 20 protein kinases.



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P-059

The (3+2)-Cycloadditions of Levoglucosenone (LGO) with Fluorinated Nitrile Imines Derived from Trifluoroacetonitrile [1]

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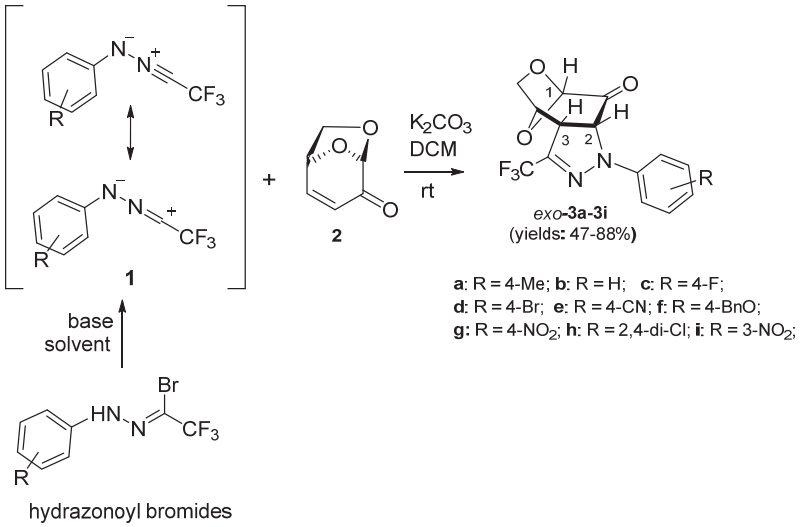
The (3+2)-cycloaddition reactions developed by R. Huisgen in 1960's are recognized as one of the most general methods widely applied for the preparation of five-membered heterocyclic rings, which in many cases are of great importance for manufacturing of drugs, agrochemicals and many useful organic materials [2].

In the present study, we report, that the *in situ* generated, from hydrazonoyl bromide, *N*-aryl nitrile imines **1** smoothly undergo (3+2)-cycloadditions onto the enone fragment of the levoglucosenone (**2**) molecule yielding the corresponding, five-membered cycloadducts **3**. These reactions lead to stable pyrazolines in chemo- and stereoselective manner. Based on the result of X-ray single crystal diffraction analysis for **3a**, these adducts were established as *exo*-cycloadducts with the location of the *N*-Ar terminus of the 1,3-dipole at the α-position of the enone moiety.



Scheme 1. Highly selective (3+2)-cycloadditions of fluorinated nitrile imines **2**, with levoglucosenone **1** leading to trifluoromethyl substituted, fused pyrazolines **3a**–**3i**.

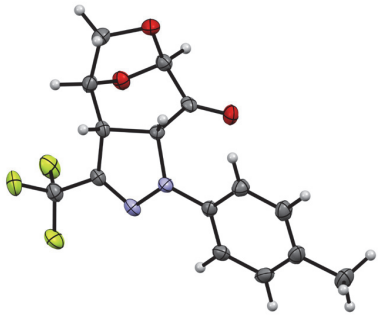


Figure 1. X-Ray structure of cycloaduct **3a**

Acknowledgement

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P-060

A Comparison of Reactivity of Enolizable Tetrazole-5-thiones and other Mercapto Azoles in Reactions with D-A cyclopropanes

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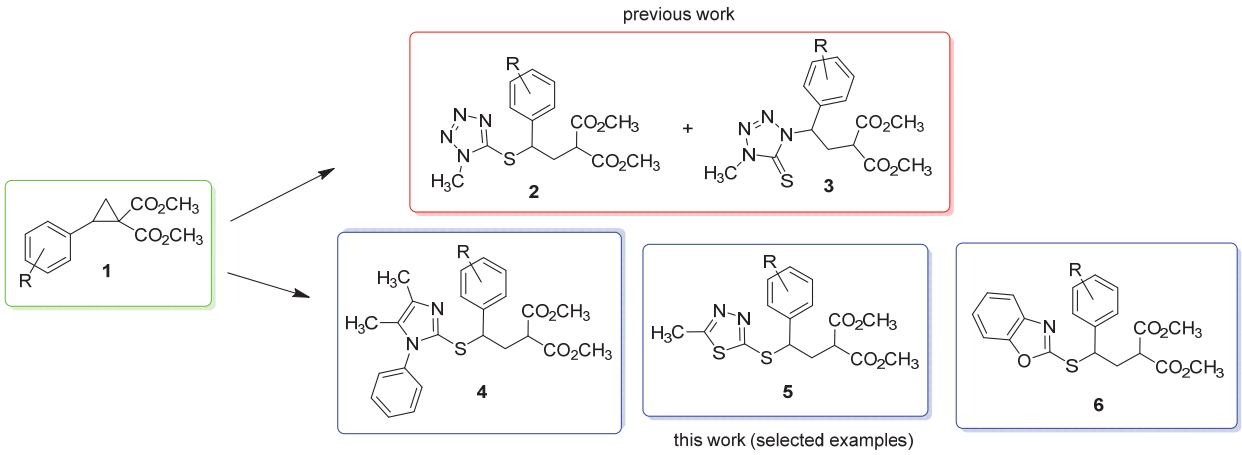
In recent years, easily available Donor-Acceptor (D-A) cyclopropanes have become an useful class of building blocks for the synthesis of *S*-, and *N*-heterocyclic compounds with variable ring size [1]. In recent years, reactivity of D-A cyclopropanes was tested in our group, using diverse nucleophilic thiocarbonyl compounds, i.e. thioketones [2], thioketenes [3] and recently, also tropothione. In all these reactions single products of cycloaddition reactions were obtained. In our communication of the last year, ambident reactions of tetrazole-5-thiones/5-mercaptotetrazoles with D-A cyclopropanes leading to both *S*- and *N*-adducts **2** and **3**, respectively. were presented.

In this communication, analogous reactions of D-A cyclopropanes **1** with imidazole-2-thiones/ 2-mercaptoimidazoles, as well as with other mercapto azoles, e.g. 2-mercapto-1,3,4-thiadiazoles and 2-mercaptobenz[*d*]oxazoles, catalyzed by $Sc(OTf)_3$ as a Lewis acid, will be presented (**Scheme 1**). In comparison to tetrazol-5-thiones/5-mercaptotetrazoles, the ^1H NMR analysis of crude mixtures demonstrated formation of corresponding *S*-adducts **4-6** as single products. In the poster a plausible mechanism of the insertion reaction into the C-C bond of D-A cyclopropanes, will be discussed.



Scheme 1. Comparison of reactivity of various types of nucleophilic thiocarbonyl compounds with D-A cyclopropanes **1**.

Acknowledgement
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P-061

New methods for the preparation of ring-fused π-delocalized stable radicals

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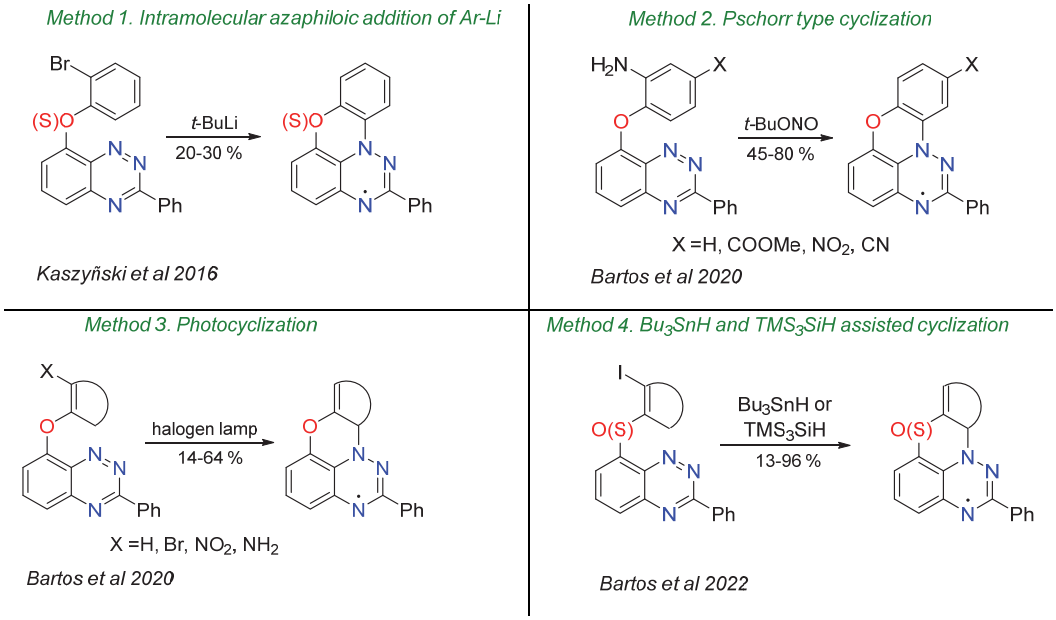
Open shell organic molecules are becoming important structural elements of advanced functional materials, used in organic electronics and spintronics. In recent years exceptionally stable 1,4-dihydrobenzo[*e*][1,2,4]triazin-4-yl radicals are gaining much interest due their high spin delocalization, narrow electrochemical window and low excitation energies. Therefore, development of synthetic methods leading to these class of radicals is of particular importance.

In recent years, our team has developed four synthetic methods to access planar Blatter radicals [1-4]. This discovery gave access to several dozen new derivatives and opened the possibility of further exploration of functionalized benzo[*e*][1,2,4]triazin-4-yls, especially their magnetic properties in the context of information storage and processing. New achievements in the synthesis of planar Blatter radicals and the utility of the methods in the preparation of paramagnetic liquid crystals and nanographenes will be presented.



Scheme 1. New methods for the preparation of stable ring-fused benzo[*e*][1,2,4]triazin-4-yls.

Acknowledgement

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P-062

Synthesis of 6-(isothiocyanatohexyl)phosphonates conjugated with Altretamine as a novel class of potential anticancer compounds

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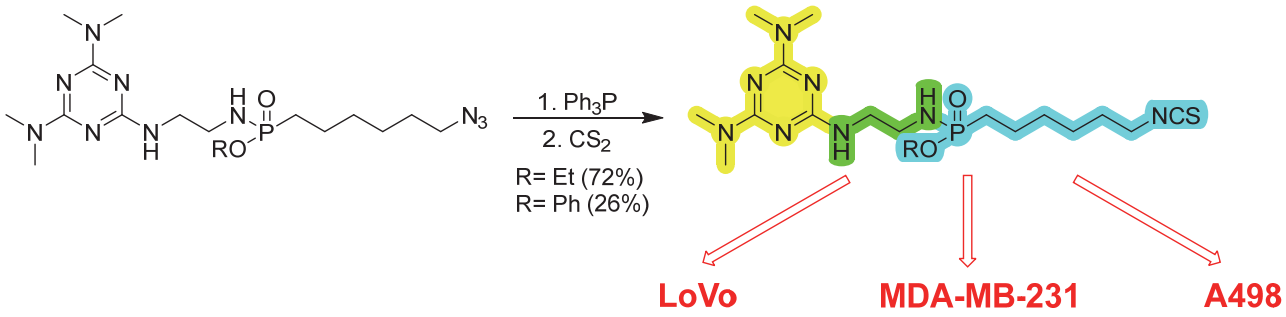
Isothiocyanates (ITCs) are an actively biological class of organic compounds found in cruciferous vegetables such as Brussels sprouts, broccoli, wasabi and horseradish. Natural ITCs, which include sulforaphane (SFN), inhibit the growth of cancer cells or induce apoptosis [1]. In addition to natural ITCs, we also distinguish synthetic analogs of SFN, in which the methylsulfonyl group was replaced by a phosphonate group containing aliphatic or aromatic substituents. This change resulted in increased biological activity compared to natural SFN [2].



The aim of this project was the synthesis of ethyl and phenyl 6-(isothiocyanatohexyl)phosphonates conjugated with an ethylenediamine linker with the triazine ring of Altretamine. Final compounds were synthesized from mixed 6-(azidohexyl)phosphonates in tandem Staudinger/aza-Wittig reaction using triphenylphosphine and carbon disulfide with low and high yield. In addition, obtained products were evaluated *in vitro* on human colon adenocarcinoma LoVo, breast cancer MDA-MB-231 and kidney cancer A498.

Acknowledgement

The project was funded by the Young Researchers Fund of the Faculty of Chemistry of the Lodz University of Technology (W-3D/FMN/5G/2022).

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P-063

Synthesis and study of hemostatic and antibacterial activity of novel compounds containing ciprofloxacin and lysine analogues with hemostatic activity

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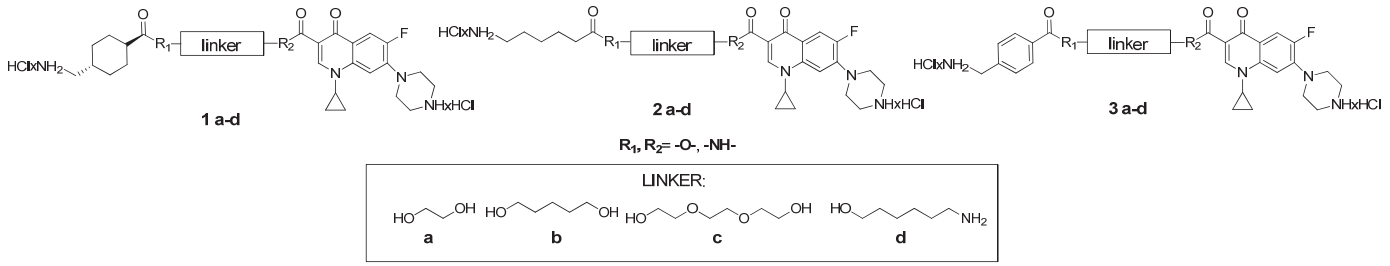
Hemostasis involves a complex network of interactions between blood components and the vascular wall, which is responsible for inhibiting bleeding after vascular disruption and maintaining the fluidity of the circulating blood. It is crucial to maintain a balance between the coagulation cascade that leads to fibrin clot formation and the fibrinolytic system that breaks down fibrin clots [1]. To most popular antifibrinolytic agents that control the bleeding process include synthetic lysine analogues like: tranexamic acid (TA), aminocaproic acid (EACA) and (4-aminomethyl)benzoic acid (PAMBA). Ciprofloxacin is a fluoroquinolone antibiotic used to treat bacterial infections such as urinary tract infections and pneumonia. It inhibits DNA replication by inhibiting bacterial DNA topoisomerase and DNA gyrase [2]. Of the fluoroquinolone class, ciprofloxacin has the strongest activity against Gram-negative bacteria.

The aim of the project was to synthesize of a library of new, biologically active and structurally diverse compounds consisting of ciprofloxacin (an antibacterial drug) and lysine analogues with hemostatic activity linked by an aliphatic linker. The synthesis of compounds containing two pharmacophores seemed to be justified, because breaking the continuity of blood vessels (necessary is than to use hemostatics) is usually accompanied by a bacterial infection (need to use antibacterial compounds). The project is a continuation of research carried out at the Institute of Organic Chemistry PŁ, where eight dipeptides with hemostatic properties were obtained [3].



Scheme 1. Scope of synthesized compounds **1-3**a-d.

The novel compounds were obtained in a four-step synthesis as hydrochlorides with total yields between 33-40%. All synthesized compounds will be tested for antibacterial activity and hemostatic activity (coagulation times, clot formation rates and CFF fibrinolysis).

Acknowledgement
The research was founded from "Young Scientists Fund" nr W-3D/FMN/7G/2022.

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P-064

New chlorinated *N*-(1,4-dihydroquinazolin-2-yl)naphthalene-1-sulfonamide as a new, low-basic 5-HT$_6$R ligands

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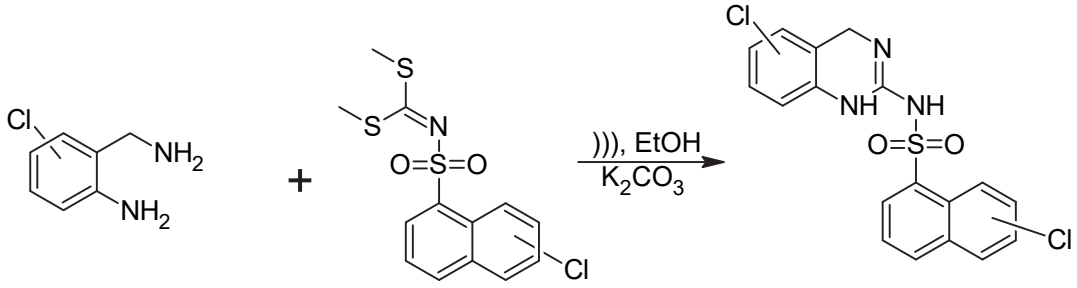
5-hydroxytryptamine 6 receptor (5-HT^{6}R) antagonists may be used in the treatment of neurodegenerative diseases, depression and obesity [1]. Recent reports indicate the role of this receptor in brain metastases in triple-negative breast cancer (TNBC) [2-3]. Clinical interest in this target indicates the need to search for its new ligands.

In our research, we obtained a set of low-base ligands from the group of halogenated derivatives of *N*-(1,4-dihydroquinazolin-2-yl)naphthalene-1-sulfonamide. We have developed a fast, ecological sonochemical synthesis method that allowed us to obtain compounds with an efficiency of over 60% in 45 minutes. The molecules were obtained by reacting the appropriate diamine with dimethylnaphthylsulfonyl)-carbonedithioimidate in the presence of K_2CO_3 and tetra-*n*-butylammonium bromide (TBAB) in ethanol. The ligands showed moderately strong affinity for 5-HT6R. We elucidated biological activity using molecular modeling methods, including ligand-protein docking and hybrid QM/MM methods.



Scheme 1. Method of obtaining designed ligands.

Acknowledgement

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P-065

The unexpected effect of Biginelli's reaction

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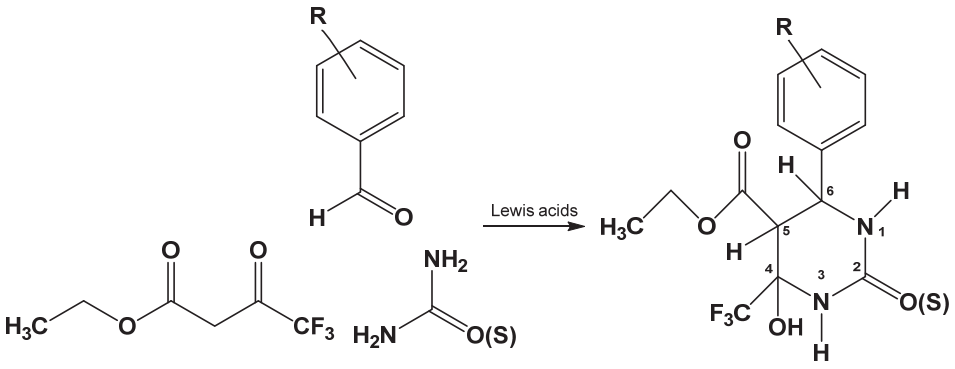
The three-component Biginelli reaction has been known for over a hundred years and allows the preparation of 3,4-dihydropyrimidin-2-(*1H*)-ones or 3,4-dihydropyrimidin-2-(*1H*)-thiones derivatives. [1] The obtained compounds show, among others, anti-inflammatory, antifungal, antibacterial and anticancer activity. [2] Taking into account the wide range of biological activity of compounds obtained as a result of the Biginelli reaction, we planned to synthesize two series of derivatives containing an oxygen or a sulfur atom at the C-2 position. To carry out the first series of syntheses, we used ethyl 4,4,4-trifluoroacetoacetate, substituted benzaldehydes and urea. In the second series, thiourea was used instead of urea. As a result, we obtained ethyl 4-hydroxy-6-aryl-2-thioxo-4-(trifluoromethyl)hexahydropyrimidine-5-carboxylate and ethyl 4-hydroxy-6-aryl-2-oxo-4-(trifluoromethyl)hexahydropyrimidine-5-carboxylate instead of the expected derivatives containing the core 3,4-dihydropyrimidin-2-(*1H*)-one or core 3,4-dihydropyrimidin-2-(*1H*)-thione. The structures of the obtained products have been clearly confirmed by X-ray crystal structure analysis.



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P-066

Molecular modeling of ibotenic acid from *Amanita muscaria*

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The presence of forest mushrooms containing natural psychoactive metabolites is well known. It poses a serious danger to inexperienced mushroom pickers. On the other hand, *Amanita muscaria L.* is a toxic mushroom which is well known and easily recognized. For centuries, it was collected by Siberian tribes for its psychoactive properties and used in shamanistic rituals[1]. Its psychotoxicity arises from the psychoactive properties are of interest in contemporary medicine, too[3, 4]. Ibotenic acid and muscimol are structural analogs of glutamic acid[5], and γ-aminobutiric[6] acid (GABA), respectively.

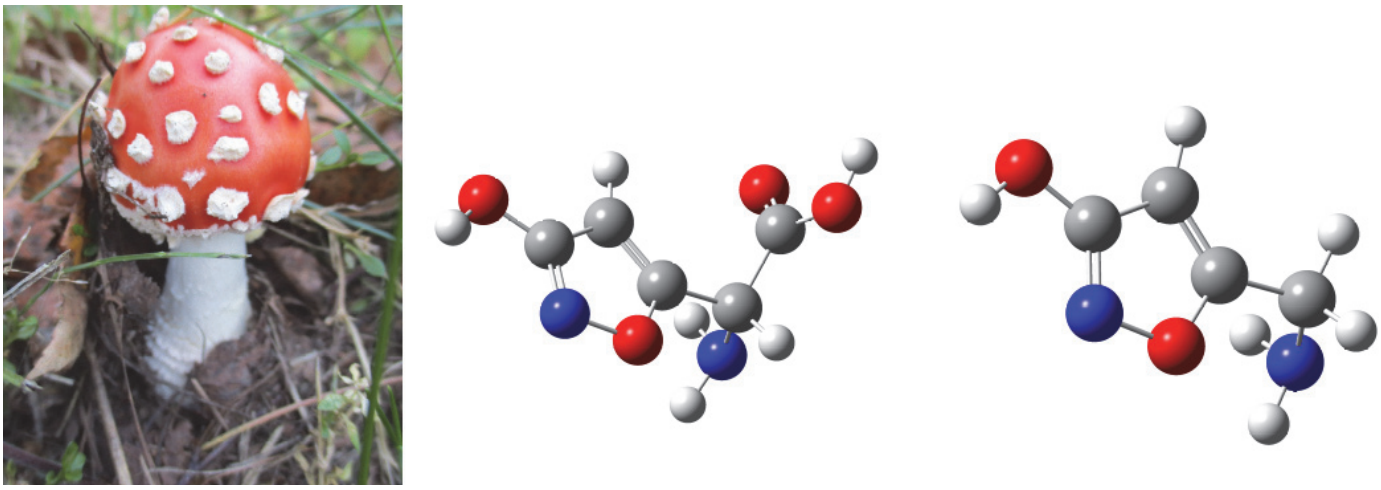

Figure 1. From left: Fly agaric mushroom (*Amanita muscaria*), ibotenic acid and muscimol.

As a continuation of research on mushroom toxins[7-9], we report on our theoretical modeling of ibotenic acid structure, energy, vibrational and NMR properties. Both isolated and soluted (in water, chloroform and methanol) systems were studied using subsequent GFN2/GBSA and DFT/PCM calculations.

Acknowledgement
Calculations have been carried out using resources provided by Wroclaw Centre for Networking and Supercomputing (https://wcss.pl).

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P-067

Synthesis of new pyrene fluorophores by modification in the K region

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The interest in pyrene derivatives due to their photophysical properties means that new methods of functionalization of this system are constantly being sought. The most reactive are positions 1, 3, 6, 8 of the pyrene system. Most literature reports concern modifications in this area. The chemistry of the K region is much less known.

In recent years, we have proposed a regioselective method for the synthesis of thioamides and amides derived from pyrene and 2,7-di-*tert*-butylpyrene.[1] We have also shown that secondary *N*-*tert*-butyl and *N*-benzyl amides undergo *ortho*-lithiation, forming substitution products in the K region.[2,3]

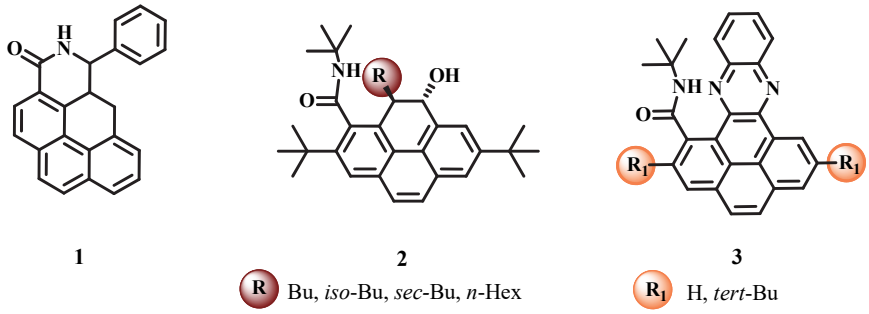

Figure 1. Examples of modifications in the K region of pyrene derivatives.

Moreover, the above-mentioned amides undergo oxidation in the K region, which allows for further expansion of the chromophore system, leading to azaacenes **3**. The fluorophores we obtained (**Figure 1)** are characterized by strong fluorescence both in solutions and in the solid state.

Acknowledgement

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P-068

Cascade synthesis of benzoxazole anticancer ansamycins

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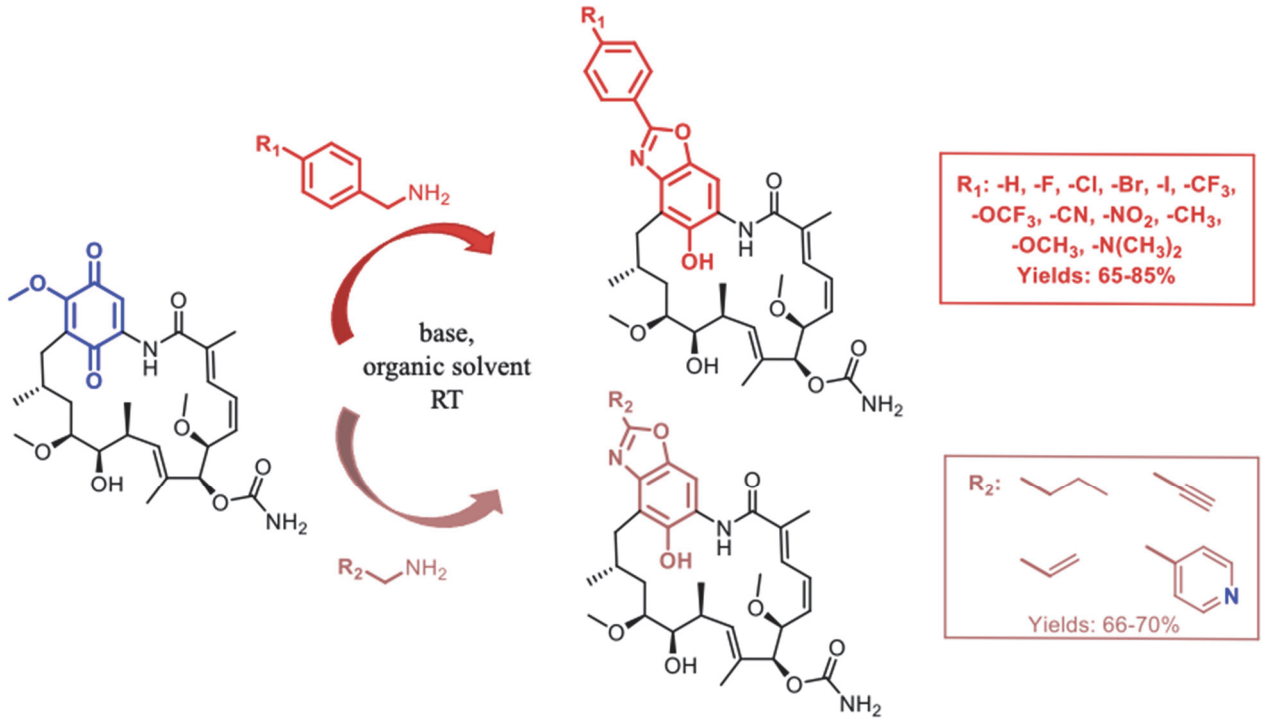
Geldanamycin **GDM** is a benzoquinone antibiotic classified as a member of ansamycin family. Due to high toxicity **GDM** cannot be used in cancer treatment. Transformation of benzoquinone core performed by our group resulted in minimalization of unwanted cytotoxic effect and synthesis of 16 new compounds with reduced benz[*d*]oxazole core [1]. New derivatives turned out to be even more effective inhibitors to chaperone protein *Hsp90* then **GDM**. New compounds showed decreased cytotoxicity in human dermal fibroblast cell line (HDF) and attractive anticancer activity.

Synthetic procedure includes conjugated addition-elimination reaction of amines in C(17) position of **GDM** and subsequent cascade heterocyclization. We examined the influence of amine structure (EDG/EWG character of substituent) on reaction progress and yield of heterocyclization process. We have proposed a new metal-free synthetic method of **GDM** benzoquinone core heterocyclization compatible with green chemistry concepts. The reaction can be used in synthesis of new *Hsp90* inhibitors. Confrontation of structural data, biological activity and physicochemical properties allowed us for SAR discussion.



Scheme 1. Heterocyclization of **GDM** benzoquinone core into benzoxazole [1].

Acknowledgement

Research was co-financed by NCN project Opus 13 no. UMO-2017/25/B/ST5/00291 and project Preludium 20 no. UMO-2021/41/N/ST4/02137..

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P-069

Novel Pyrrolidine Derivatives of Spiramycin in the Heck Reaction

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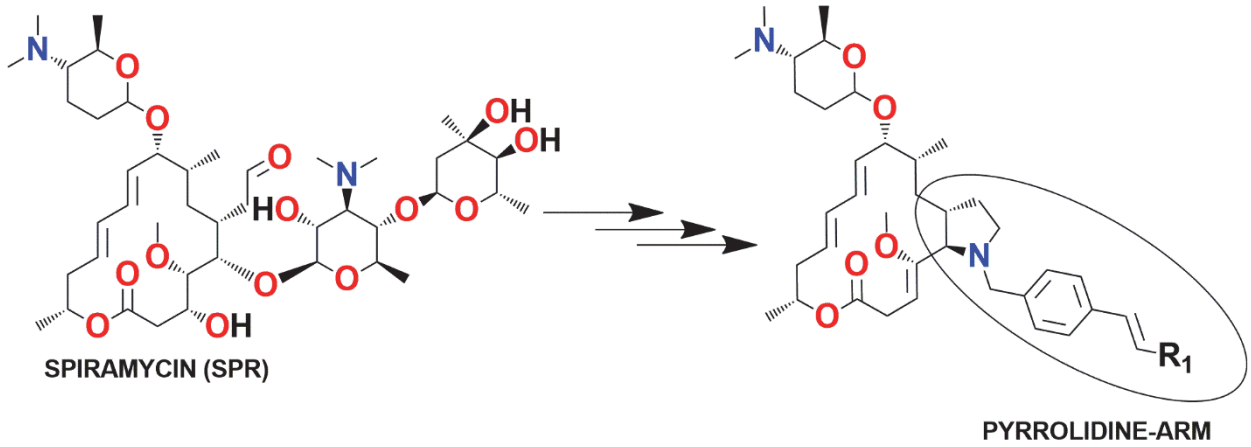
Spiramycin (**SPR**) is one of the representatives of macrolide antibiotics naturally produced by *Streptomyces Ambafaciens* bacteria. A characteristic feature is the presence of a 16-membered lactone ring in the structure.[1] **SPR** has bacteriostatic and bactericidal effects, which it has found application in the treatment of many diseases of the respiratory system and toxoplasmosis.[1][2] Its mechanism of action is to inhibit the synthesis of proteins in bacterial cells. Spiramycin binds in a ribosomal tunnel, near where the newly formed peptide leaves the ribosome, between the peptide transferase center, and narrowing the tunnel. The previously reports showed furan derivatives of spiramycin that were characterized by an altered profile of activity from antibacterial to anticancer one.[1][3][4]

The synthesis of new spiramycin derivatives led to obtain compounds characterized by more effective antibacterial activity and physicochemical properties in relation to the parent antibiotic- SPR. I've synthesized new bicyclic derivatives of **SPR** containing the bicyclic group with pyrrolidine which were then used for Heck reaction. The new derivatives were synthesized by multistep approach via number of reactions aimed at, among others, protecting functional groups or removing saccharides moieties. The structure of a new pyrrolidine derivatives of spiramycin antibiotic was confirmed using a number of spectroscopic and spectrometric methods (FT-IR, 1D and 2D NMR, ESI-MS)



Scheme 1. Synthesis of new pyrrolidine derivatives of Spiramycin.

Acknowledgement
The work was financed partially within the framework of the project "ID-UB" No. 049/34/UAM/0009.

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P-070

Synthesis of novel heterocyclic geldanamycin derivatives containing triazole-saccharide arms

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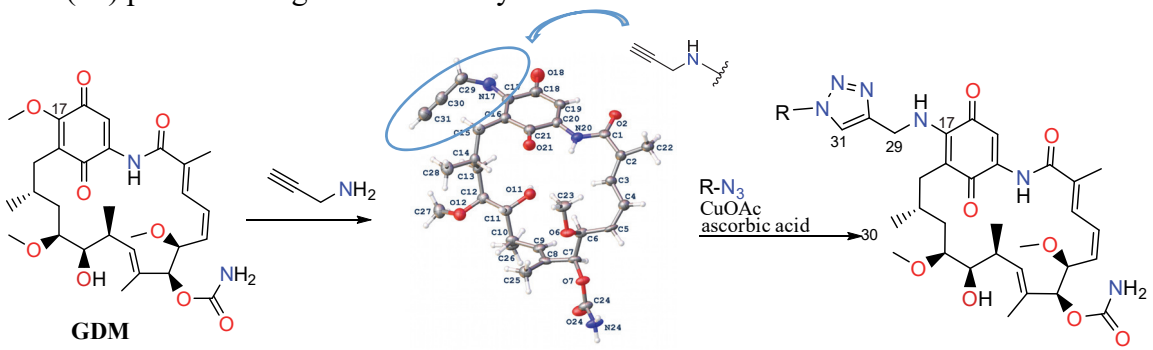
According to the World Health Organization (WHO), cancer is the leading cause of death worldwide. The progressive increase in mortality resulting from cancer patients was the reason for the intensified search for effective anticancer agents. These investigations are largely based on natural products and their structural modifications, which, due to their complex structure, are linked to a molecular target[1].

Geldanamycin (**GDM**) is a naturally occurring antibiotic from the benzoquinone ansamycin family. The antitumor effect of **GDM** is the inhibition of Hsp90, which promotes the development of cancer cells, by stabilizing the structure of abnormal proteins. **GDM** was not classified as a drug due to poor water solubility, hepatotoxicity, and metabolic instability.[2] One of the reasons for **GDM** toxicity is the unstable nature of the benzoquinone moiety containing the C(17) methoxyl group, which we decided to modify by introducing the 1,2,3-triazole ring as a stable linker between the core and the saccharide cap. Compounds containing the 1,4-disubstituted 1,2,3-triazole ring are characterized by high chemical stability and the ability to form hydrogen bonds with Hsp90, which makes them highly suitable for drug design[3].

The aim of my research was to synthesize new **GDM** derivatives containing a functionalized triazole-sugar arm at the C(17) position using click chemistry.



Scheme 1. Synthesis of novel heterocyclic derivatives of Geldanamycin. The crystal structure of the intermediate product is shown in the middle.

Acknowledgement

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P-071

Synthesis of novel N-alkyl analogues of rifamycin based on an amine derivative of rifamycin

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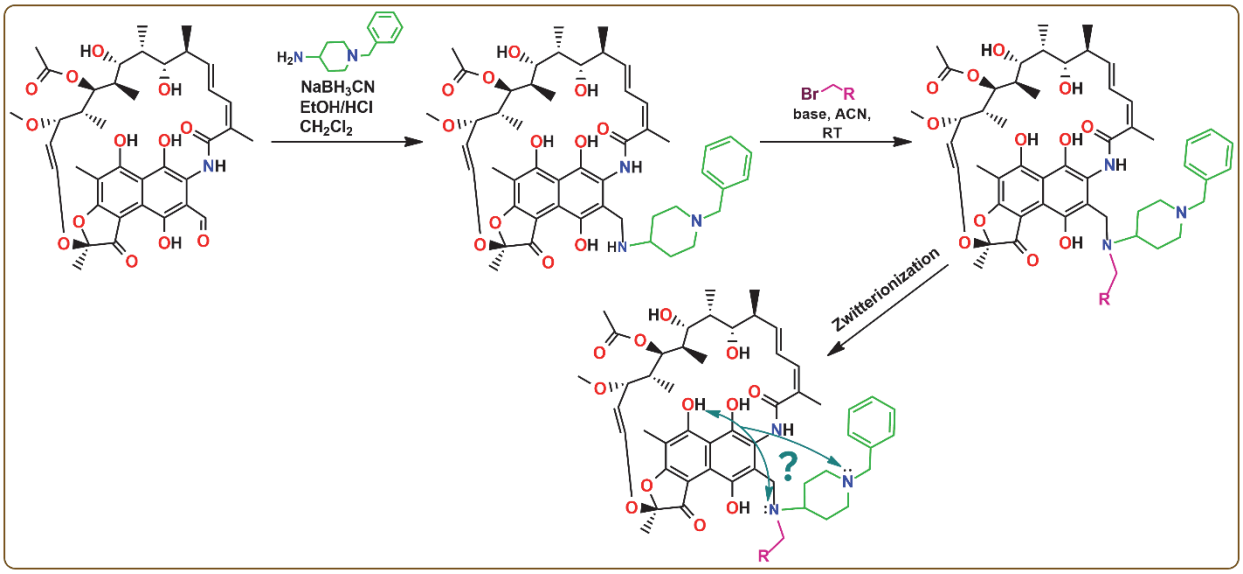
Rifamycins are an ansamacrolide type antibiotic, with a characteristic structure, consisting of an ansa handle and an aromatic core, such a system is referred to as a 'basket'. This structure is responsible for inhibiting the transcription process in bacteria. [1] The key phenomenon responsible for the antibacterial activity of these antibiotics is zwitterionization in protic solvents. The C(3) protonated basic substituent of this macrolide is involved in intermolecular hydrogen bonds with amino acids (N448 and E445) of bacterial RNA polymerase. [2]

N-alkylation reactions on a known rifamycin amine derivative (**Scheme 1**) were performed to investigate the effect of arm structure on the C(3) arm of rifamycin and to continue the initiated studies on structure-activity relationships (SAR). The amine analogue of rifamycin revealed antibacterial activity, particularly against *M. tuberculosis strain H37Rv* MIC= 0.005 μg/ml (Minimum Inhibitory Concentration). [3] However, nitrogen atom substitution provides a chance of better stabilization of the antibiotic in bacterial polymerases (with the σ finger of RNAPs) and contributes to improved antibacterial activity when compared to rifampicin.



Scheme 1. A reaction sequence leading to novel N-alkyl derivatives of rifamycin.

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P-072

2-[Perfluoro(hetero)arylo]benzothienobenzothiophene derivatives - synthesis, optical properties, and theoretical calculations

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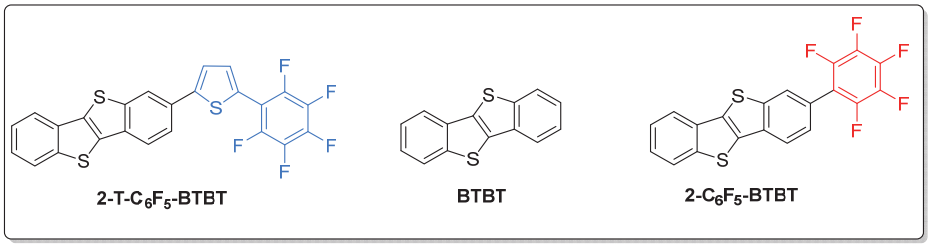
The development of π-conjugated small molecule semiconducting materials is an emerging and continuously growing research area in organic electronics.[1] Since the initial report of small molecule-based OFETs, the search for this type of semiconductors has primarily focused on fused (hetero)acene structures including [1]benzothieno[3,2-*b*][1]benzothiophene (BTBT) derivatives.[2]



Scheme 1. Structure of BTBT, 2-C_6F_5-BTBT and 2-T-C_6F_5-BTBT.

In the last few years fluorinated BTBT derivatives have gained attention in the field of organic electronics due to their tunable properties and the potential for creating high-performance devices. Fluorinated compounds may play a primary role as active materials in OLEDs and OFETs because they can behave as ambipolar or n-type semiconductors, contrary to the p-type nature of the corresponding non-fluorinated compounds.[3]

We present herein the synthesis and characterization of two BTBT derivatives bearing perfluorophenyl (C_6F_5) and (perfluorophenyl)thienyl (T-C_6F_5) substituent (Scheme 1). The introduction of electron-withdrawing substituents into a BTBT core results in lowering the energy of frontier orbitals and the energy band gap, which is important for transistor efficiency. Moreover, such functionalizations extend π-conjugation and facilitate electron injection/delocalization on the molecular π-backbone. We expect that the presence of these functional groups will result in a change in character from p to n-type semiconductor.

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P-073

Click organometallic-erlotinib conjugates active against lung cancer cells

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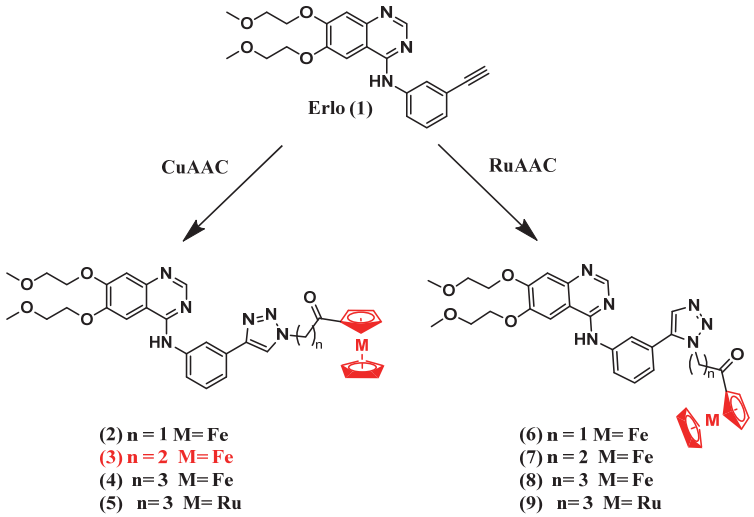
According to National Cancer Institute in 2023 we have over than 1 500 000 new cases of different types of cancer, where about 15% of them are cases of lung cancer [1].

Erlotinib (Tarceva™) **1** is an anticancer drug whose mechanism of action relates to the inhibition of epidermal growth factor receptor (EGFR). Specific mutations in EGFR cause lung cancer cells resistant to **1**. Thus new drugs to overcome resistance are required.

The major goal of my work was to obtain new organometallic derivatives of erlotinib and examine their anticancer activity against lung cancer cells (A549, H1395, H1650, H1975). Conjugates were obtained with CuAAC and RuAAC reactions [2,3].



Scheme 1. Structures of erlotinib **(1)** and metallorganic-erlotinib conjugates **(2-9)**.

Some of the synthesized conjugates were more active than parental drug against assayed cancer cells. In particular, it was found that the ferrocenyl isomer **3** with –C(O)CH_2CH_2– linker was the most active compound against H1650 cells (IC_{50} = 12μM *vs* erlotinib IC_{50} = 40μM). On the other hand, conjugate **2** showed high activity against erlotinib resistant A549 cells (IC_{50} = 3,4μM) [3]. Mechanism of action of **3** involve ROS generation, mitochondrial transmembrane potential imbalance and apoptosis [2].

Acknowledgement
P.B. thanks the National Science Center in Cracow, Poland (grant PRELUDIUM 20 UMO-2021/41/N/ST4/00059) for financial support.

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P-074

Aromaticity of Biaryl Monophosphines

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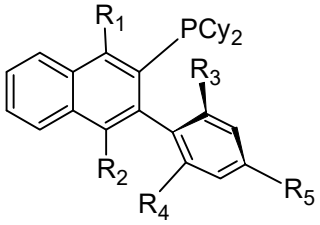
Biaryl monophosphines are important ligands in Pd-catalyzed cross-coupling reactions. Their use in catalysis, in particular to form C–N bonds under mild synthesis conditions, has been widely studied over recent years [1-2]. Our goal was to investigate the aromaticity in the group of selected biaryl monophosphine derivatives (*Scheme 1*). The molecules were chosen to study the subtle differences in their steric and electronic properties due to various substitution with electron-rich substituents such as -OCH_3 or -OH groups. We present their crystal structure and Hirshfeld surface analysis. Selected aromaticity indices were compared. The results may help in better understanding the electronic properties of biaryl monophosphines.



Acknowledgement

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P-075

In-silico study of Novichoks' non-covalent binding affinity to human acetylcholinesterase

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Despite the potential medical use of organophosphorous inhibitors of acetylcholinesterase (AChE) [1] most of applications of these class of compounds is related to life termination - the ability to irreversible impair the enzymatic operational stability makes them ideal candidates for lethal warfare agents [2].

AChE, known for its high turnover number, rapidly hydrolyzes the cholinergic neurotransmitter, acetylcholine (ACh). Thus, any permanent inhibition of the enzyme would lead to an excess of ACh in the cholinergic system, causing severe damage of nerve cells, leading in consequence to swift death.

The artificial organophosphorus nerve agents (OPNAs) are believed to be able to precisely inhibit AChE by binding with one of the amino acids (serine) in the AChE catalytic triad, especially the newest, A-generation of OPNAs, so-called "Novichoks" [3], the structure and properties of which remain to a certain degree unknown and the literature reports on them are relatively scarce.

The in-silico studies were performed to assess the binding affinity towards the AChE of acetylcholine (the natural agonist of the enzyme) and its synthetic, neurotoxic counterparts – selected Novichoks compounds as well as molecules from the G- and V-series of warfare agents (Fig. 1). Quantum mechanical calculations, molecular docking and molecular dynamics (MD) with molecular mechanics Generalized-Born surface area (MM/GBSA) were applied to quantitatively assess differences between their binding energies to AChE.

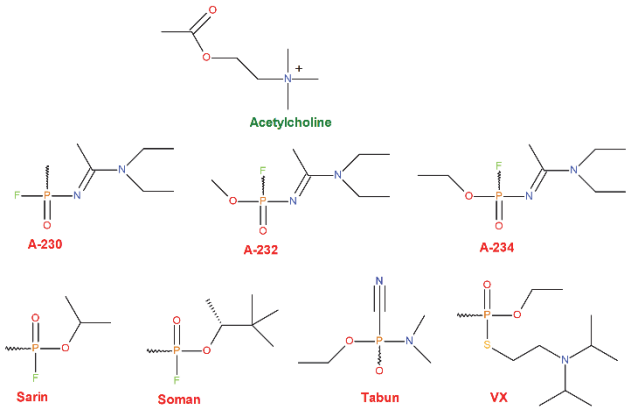

Figure 1. Structures of investigated compounds.

Acknowledgement
This research was supported in part by PLGrid Infrastructure.

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P-076

Computer-designed up-cycling of chemical waste

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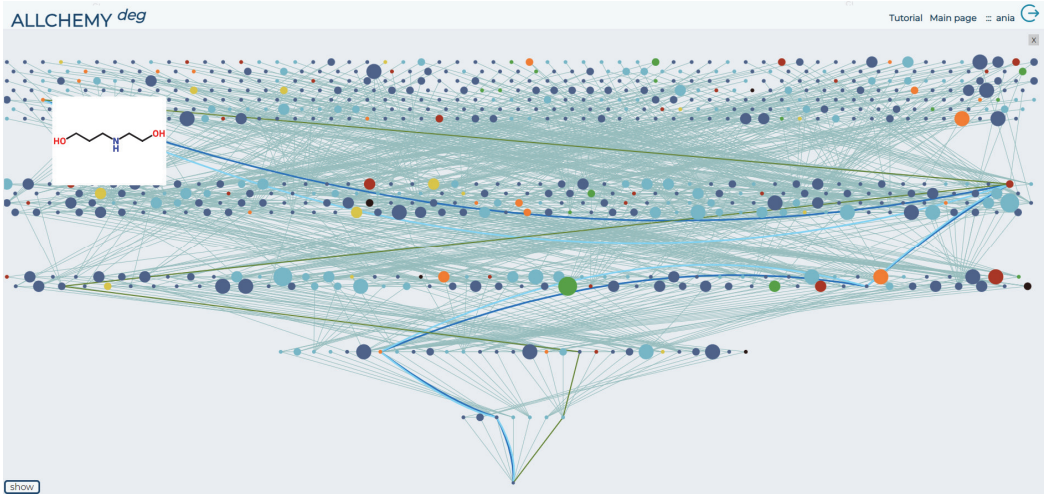
The controlled degradation of biomass and industrial waste shows potential in supporting the global objective of achieving a petrochemical-independent and waste-free civilization. These feedstocks encompass a diverse array of platform organic compounds that can be transformed into valuable chemicals and energy fuels in just a few synthetic steps. The focus of this work is on the planning of degradation pathways – that is, syntheses that fragment larger, either harmful or renewable molecules into smaller, defined, isolable yet useful building blocks.

Our analyses rely on Allchemy software, which is comprised of roughly 1600 generalized expert-coded reaction transforms that reflect the underlying reaction mechanism, scope of permissible substituents, groups incompatible with a given reaction, typical conditions (reagents, solvents, temperature) and illustrative references. The reaction transforms are iteratively applied to the substrate of interest with user-specified number of steps, called generations. Although, reaction networks created by this method expand very rapidly with the number of generations, program allows for *in silico* testing of very large number of synthetic options which may be quickly categorized using different filters (e.g. mass, structure, log P, polar surface area, price *etc.*). By experimental validation, we confirmed that computer software Allchemy effectively facilitates the planning of such transformations.[1]



Scheme 1. Screenshot from Allchemy showing a network of degradative reactions originating from inexpensive (< 1 $/g) biomass, citric acid feed.

Acknowledgement
Allchemy, Inc; Polish National Science Centre, Poland (SONATA 2020/39/D/ST4/01890).

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P-077

Development and implementation of new technology of obtaining of non-opioid analgesic active substance

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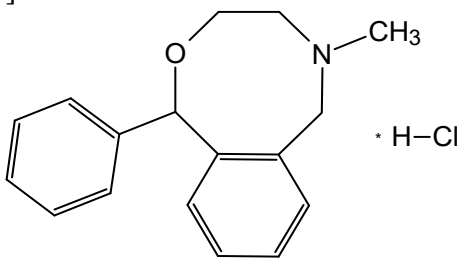
Nefopam hydrochloride is a non-opioid, non-steroidal, centrally acting analgesic active pharmaceutical ingredient with anti-inflammatory potency. It is used for the prevention of postoperative pain, severe hiccups, chronic pain and has relaxant, anticholinergic and antihistamine activity. It is only indicated in the treatment of acute painful conditions. [1] [2] [3]



Scheme 1. Nefopam hydrochloride

Warszawskie Zakłady Farmaceutyczne Polfa S.A., Ipochem Branch are one of global manufacturers of Nefopam hydrochloride, which is produced in four countries around the world only. That is why maintenance of continuity of production and national export of Nefopam is highly anticipated. As the current route of synthesis involves the use of genotoxic solvent, which is supposed to be forbidden, the development of completely new technology of obtaining of Nefopam with use of more safety and environment-friendly organic solvents, reagents and raw materials is a matter of concern.

The aim of this project is the development and optimization of route of synthesis in laboratory scale, determination of impurity profile of active pharmaceutical ingredient and full spectral and chromatographic analysis of new intermediates and impurities which will extend the knowledge on chemistry of heterocyclic compounds. Moreover, performance and development of all analytical methods either of in-process control or quality control is supposed to be done. As soon as the laboratory part is completed the technology transfer to the production scale is set, followed by process validation batches and the final implementation of new technology of obtaining of Nefopam hydrochloride.

Acknowledgement
This research was financed by PIW Ipochem Sp. z o.o.

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P-078

Synthesis of co-amorphous solid dispersions of valsartan with ascorbic acid (vitamin C)

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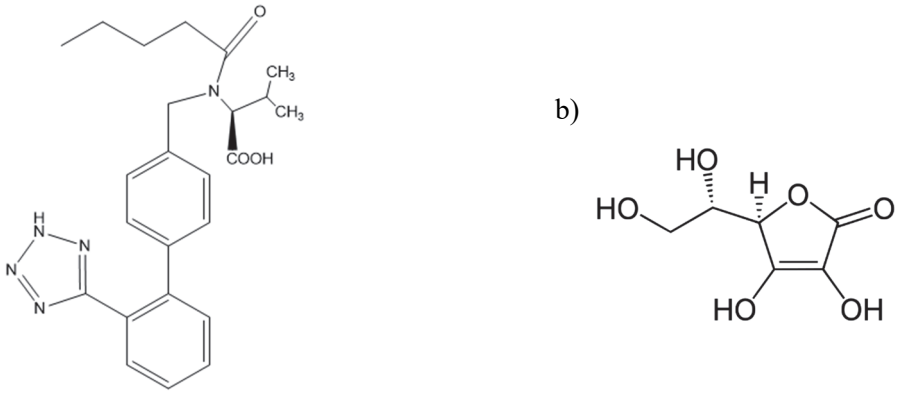
The main objective of the experimental work was the synthesis of co-amorphous solid dispersion of valsartan with ascorbic acid (vitamin C) as a bifunctional drug with increased solubility and additional supplementary effects associated with the presence of vitamin C, which has beneficial effects on the cardiovascular system (Scheme 1). The synthesis was carried out by using solvent evaporation method (methanol). Various ratios of valsartan and vitamin C were used to obtain co-amorphous solid dispersions in 1:1, 2:1 and 3:1 molar ratios. The obtained compounds were characterized by X-ray powder diffractometry (XRPD), infrared spectroscopy (FT-IR) and differential scanning calorimetry (DSC). Finally, the equilibrium solubility of the obtained products was determined. On the basis of results obtained, it can be concluded that co-amorphous VAL/VitC products with bifunctional action were obtained. Based on the analyses, it can be deduced that the hydroxyl group of vitamin C and the amide carbonyl group of valsartan are involved in the formation of intermolecular interactions between the components of the solid dispersions

a) b)



Scheme 1. Chemical structure of valsartan (a) and vitamin C (b).

Acknowledgement

The work was financed by the National Science Centre (NCN), Poland based on the decision number UMO-2019/33/N/ST5/01602.

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P-079

Fluorinated ω-(pyrazol-4-yl)alkanoic acids through deacylative aromatization of bicyclic pyrazoline derivatives

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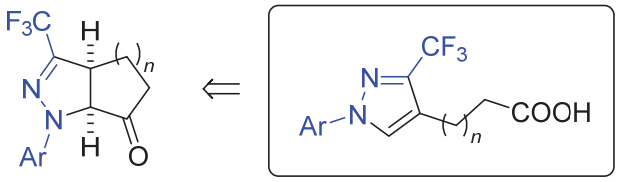
There is increasing interest in pyrazole-functionalized alkanoic acids recognized as promising non-steroidal anti-inflammatory drugs and antifungals.[1] However, the general synthetic methods towards fluorinated analogues suffer limitations such as low availability of appropriate fluorine-containing building blocks and multi-step character of the reported protocols, among the others. In this context, here we report on novel approach for preparation of trifluoromethylated alkanoic acids of type **A** via fully regioselective (3+2)-cycloaddition of nitrile imines with cyclic enones followed by key MnO_2-mediated deacylative aromatization of the first formed bicyclic pyrazoline derivatives **B**.[2,3]



B **A**

Scheme 1. Structures of target carboxylic acids **A** and pyrazoline intermediates **B**.

Acknowledgement
Financial support by the University of Lodz (IDUB grant no. 9/DGB/2022) is acknowledged.

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P-080

Benzothienobenzothiophene oxides: synthesis, structural, optical and electronic properties

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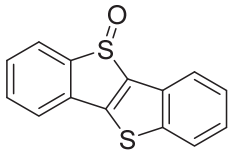
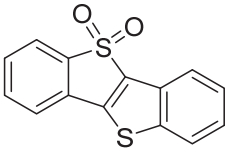
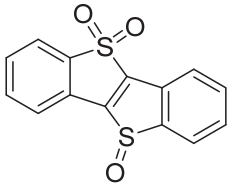
Benzothieno[3,2-*b*]benzothiophene (**BTBT**) is an excellent core for creating new compounds for use as materials for organic field-effect transistors (OFET), OLEDs, and thin-film transistors [1,2,3]. The compound in its structure contains two phenyl groups and two thiophene groups connected by a common ethylene bridge. **BTBT** is fully aromatic and exhibits donor properties. The presence of two sulfur atoms allows this moiety to be further modified through selective oxidation, producing a series of new compounds exhibiting new physical and chemical properties. As a result of the selective oxidation of **BTBT** under various conditions, we obtained monosulfoxide **BTBTMO**, dioxide **BTBTDO**, trioxide **BTBTTriO** and tetraoxide **BTBTTO** in moderate and very good yields.



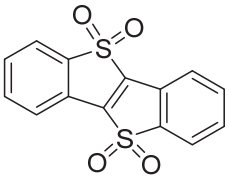
BTBTMO



BTBTDO



BTBTTriO



BTBTTO

Scheme 1. Times New Roman, 11pt, Normal. Recommended style - ACS 1996.

X-ray analyses and optical and electronic properties of these compounds will be presented.

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P-081

Highly oriented thin films based on new BTBT tetraoxides derivatives

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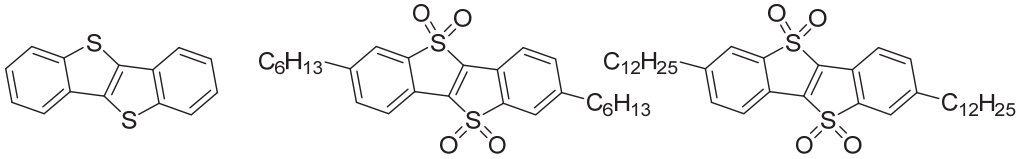
Compounds containing [1]benzothieno[3,2-b][1]benzothiophene (**BTBT**) moiety exhibit interesting optical and electronic properties and therefore might be applied as fluorescent markers or material for organic electronic.[1][2][3] In the course of our studies, we have turned our attention to oxidated **BTBT** derivatives. After calculation, we have found that they may have improved properties in comparison with non-oxidized counterparts. Herein we present a route for obtaining two new representative [1]benzothieno[3,2-b][1]benzothiophene tetraoxides (BTBTTO) derivatives containing alkyl chains at 2 and 7 positions. The structures of both compounds were confirmed by X-ray analysis. Their thermal and optical properties in the solution and solid state, were also investigated.



Acknowledgement
Authors thank for financial support from the Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences.

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P-082

Synthesis of dihydrobenzo[1,4]oxaselenines as a new approach for the selenocyclization reaction

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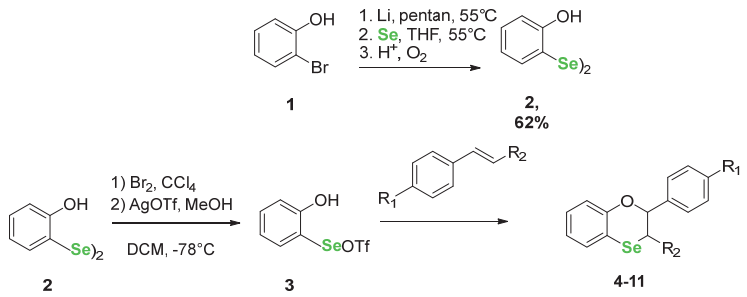
Selenium-containing heterocycles continuously attract the attention of organic chemists due to their broad applicability in modern organic synthesis and medicinal chemistry.[1,2] This research aimed to develop an efficient methodology for the synthesis of dihydrobenzo[1,4]oxaselenines **4**-**11**. The first stage of the procedure included the preparation of bis(2-hydroxyphenyl)diselenide **2** utilizing the acidification and oxidation method of an intermediate organometallic product, resulting from the reaction of 2-bromophenol **1** with metallic lithium and selenium. Then, bis(2-hydroxyphenyl)diselenide **2** was transformed into selenium triflate **3**, which, as an electrophilic reagent, took part in addition to the appropriate aromatic alkenes, forming eight dihydrobenzo[1,4]oxaselenines **4**-**11**, unknown in the literature.



4 R_1=H, R_2=H, **87%**
5 R_1=OCH_3, R_2=H, **95%**
6 R_1=OCH_3, R_2=CH_3, **83%**
7 R_1=CH_3, R_2=H, **20%**
8 R_1=Cl, R_2=H, **75%**
9 R_1=CH_2Cl, R_2=H, **78%**
10 R_1=H, R_2=*trans*-Ph, **75%**
11 R_1=H, R_2=*cis*-Ph, **70%**

Scheme 1. Methodology for synthesis of dihydrobenzo[1,4]oxaselenines.

The reaction will be further investigated in the near future to synthesize a broad group of diversified products.

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P-083

Antioxidant and anticancer properties of *N*-substituted with long carbon chain benzisoselenazolones and diselenides

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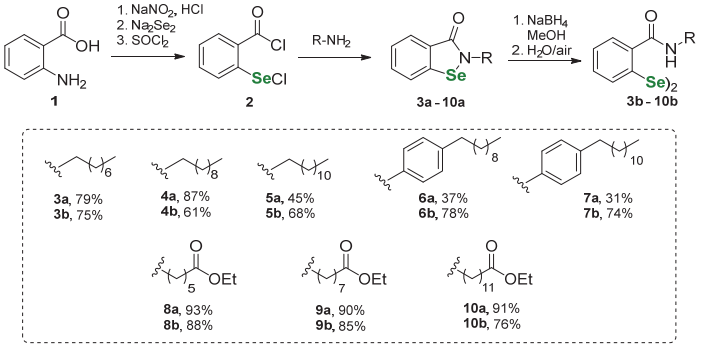
The unique properties of the selenium atom and the possibility of constructing heterorganic molecules that can mimic the activity of selenoenzymes, result in that organoselenium compounds are well-known for their numerous biological activities. The first stage of the research involved the synthesis of *N*-functionalized benzisoselenazol-3(2*H*)-ones **3a-10a** and corresponding diselenides **3b-10b** possessing lipophilic long carbon chains, solely or with additional polar insets: phenyl linkers and ester groups. First, compounds **3a-10a** were obtained in the reaction of 2-(chloroseleno)benzoyl chloride **2**, synthesized from anthranilic acid **1** according to our previously reported method [1], with appropriate primary amines. In the case of products **8a-10a** and **8b-10b,** the substrate ester amines had to be synthesized from corresponding carboxylic acids by the treatment with thionyl chloride and ethyl iodide. Next, the obtained benzisoselenazolones **3a-10a** were transformed to diselenides **3b-10b** by a sodium borohydride reduction and air oxidation method. All compounds were obtained in good yields (45-93%) [2] (Scheme 1).



Scheme 1. Synthesis of *N*-functionalized benzisoselenazol-3(2*H*)-ones **3a-10a** and diselenides **3b-10b**.

Benzisoselenazolones **3a-10a** and diselenides **3b-10b** were evaluated for antioxidant (DTT-assay [3] and ABTS method [4]) and antiproliferative (MTT viability assay [5]) activity.

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P-084

Organometallic markers for imaging biomolecules

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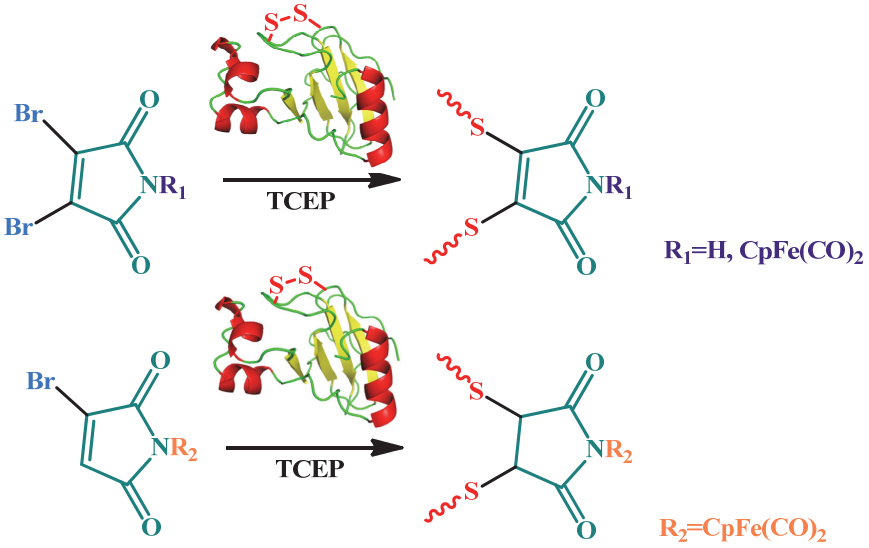
Advances in protein modification by chemical means have led to the development of a range of protein bioconjugation methodologies which have been successfully applied to the number of fields like fluorescent tagging of proteins, the development of therapeutic protein conjugates for treating malaria, cancer, HIV or even as diagnostic tools. The new approach to peptide modification focuses on amino-acids such as lysine and cysteine, which contain the -SH group in their structure. This group participates in the formation of disulfide bridges which affect the structure of proteins, stabilize the conformation of proteins and allow various peptide chains connections. [1,2]

Among the methods of modification and labeling of peptides, a special attention should be paid to the "artificial stapling" (stapling or rebridging) of peptide chains by small molecules which the main task is to "replace" various types of bonds in proteins. Maleimide chemistry stands out in the bioconjugation toolbox by virtue of its synthetic accessibility, excellent reactivity, and practicability. [3]

In this communication, we want to present the use of metallocarbonyl complexes bearing bromomaleimide moiety as rebridging agents. We react them with thiol groups from reduced disulfide bridges of protein and obtain bioconjugates easy to detect by IR spectroscopy (Scheme 1).



Scheme 1. Protein labeling with rebridging agents.

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P-085

Anisotropy of Diastereotopic Methylene Protons in New Ethyl Esters of *tert*-Butyl(aryl)phosphinic Acids

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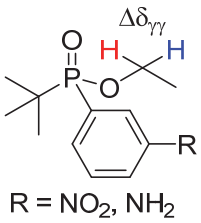
Two unknown ethyl esters of phosphinic acids bearing *tert*-butyl and aryl substituents bonded to the phosphorous atom were synthesized and characterized. Due to the chirality center located on the phosphorous atom the new compounds expressed anisotropy of diastereotopic methylene protons within the ethoxy moiety, similarily to several cathinones described in our earlier work.[1]. The effect was studied by means of multinuclear NMR spectroscopy.



Scheme 1. Diastereotopic methylene protons in ethyl esters of tert-butyl(aryl)phosphinic acid.

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P-086

Piano-stool organometallic carbonyl Fe^{II} and Ru^{II} complexes bearing maleimidato, phosphine or phosphite ligands: Synthesis, anticancer activity and molecular docking study

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In recent times, organometallic complexes containing transition metals like Fe, Ru etc. are being extensively investigated for their versatile physico-chemical applications.[1-4] As an example, (η^1-*N*-maleimidato) metallocarbonyl compounds have been found to be efficient biomarkers due to their specific absorption bands in the mid-IR spectral range resulting from the stretching vibrations of carbonyl ligands. Maleimide derivatives are commonly used in bioconjugation processes due to their reactivity towards bio-thiols.[5] The search for an appropriate ligand that effectively controls the stability and reactivity of metal complexes plays an essential role in organometallic chemistry.[6]

Herein, we report a series of (η^5-cyclopentadienyl) $M^{II}(CO)(L)(\eta^1$-maleimidato) complexes bearing iron(II) and ruthenium (II) metal with alkyl/aryl phosphine or phosphite ligands (L), their synthesis, characterization, X-ray diffraction analysis followed by their influences in peripheral blood mononuclear (PBM) cells as normal cells and different cancer cell lines like human leukemic, HL-60 and non-small-cell lung cancer cells, A549. Each of reported complexes were synthesized by photolysis, using visible or UV light with a satisfactory yield and purity. NMR (^{1}H, ^{31}P, ^{13}C), FT-IR and ESI-MS spectral study were utilized for their characterization. X-ray diffraction analysis further confirmed the structures of many of them. To study the genotoxic potential of complexes in cancer cells, we selected those complexes that were the most cytotoxic for these cells and were less cytotoxic for normal PBM cells, comparing IC_{50} doses. We also used the plasmid relaxation assay to determine the potential of these complexes to directly damage DNA. Molecular docking studies were performed to observe the DNA binding properties of some selected complexes. In the search for new anticancer drugs, selective activity of these complexes towards cancer cells and lack of effect on normal cells are of key importance. For this reason, iron(II) and ruthenium(II) complexes described here are expected to open new ways for anticancer research.

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P-087

New chiral benzofuryl *β*-amino alcohols - synthesis, properties and application

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Chiral amino alcohols represent the rich resources in organic and medicinal chemistry. *β*-Amino alcohols are found in the structural units of many building blocks, chiral auxiliaries, and ligands. Moreover, optically active *β*-amino alcohols containing heteroaryl moieties are of great importance as a key intermediates for the synthesis of physiologically active compounds. Among a wide variety of heterocyclic compounds, benzofuran is considered as an important structure due to its diverse biological profile. There have been many reports on the synthesis of benzofuran derivatives because of its clinical importance.[1]

An attractive method for the *β*-amino alcohols synthesis is the asymmetric transfer hydrogenation of *α*-functionalized ketones. Asymmetric transfer hydrogenation (ATH) is established as an excellent reduction method due to its versatility, operational simplicity, avoiding the use of explosive hydrogen gas, catalysts resistant to moisture and air oxidation, and high stereoselectivity. In our previous asymmetric syntheses of benzofuryl *β*-amino alcohols, the transfer hydrogenation of *α*-halo ketones, *α*-imino ketones, and *α*-dialkylamino ketones was a key step.[2] Hereby, the corresponding *β*-amino alcohols possessing secondary and tertiary amine groups were obtained. Applying the above-mentioned method, *β*-amino alcohols with primary and secondary amine groups were also obtained from the *α*-sulfonyloxy, *N*-Cbz protected *α*-amino ketones, *α*-succinimide, and *α*-phthalimide ketones.[3] *β*-Amino alcohols containing azole rings have been also obtained with high enantioselectivity.[4] Continuing these studies, the synthesis of chiral benzofuryl *β*-amino alcohols containing a thiazole moiety was developed. For this purpose the benzofuryl *α*-amino ketones were synthesized by the reactions of the corresponding *α*-bromo ketones with 2-aminothiazole. Iminothiazole derivatives required (before reduction) protection by acetyl group (Ac) on the nitrogen atom because the imine double bond was also reduced. The asymmetric reduction was carried out with formic acid as a hydrogen source, catalyzed by both, RhCl[(*R*,*R*)-TsDPEN](C_5Me_5) and RhCl[(*S*,*S*)-TsDPEN](C_5Me_5), in dichloromethane at reflux for 24h. All new benzofuryl *β*-amino alcohols were formed in high yields and excellent enantioselectivities. The absolute configuration of products was confirmed by means of ECD spectroscopy supported by theoretical calculations. All racemic and optically active amino alcohols were tested against four bacterial and two fungal species. In addition, *β*-amino alcohols with a thiazole substituent can be easily converted into analogues of Levamisole (a drug used to treat parasitic infections). Upon treatment with tionyl chloride, amino alcohols furnished (benzofuran-2-yl)-5,6-dihydroimidazo[2,1-b]thiazoles in good yields. On the other hand, benzofuryl *α*-bromo ketones (by reaction with 2-aminopyridine in ethanol) can be converted into (benzofuran-2-yl)imidazo[1,2-a]pyridines.

Acknowledgement
Heartfelt thanks to Prof. Marcin Kwit for determining the configuration of chiral products and Prof. Patrycja Golińska for performing biological test.

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P-088

New application of Photochemical Fries Rearrangement

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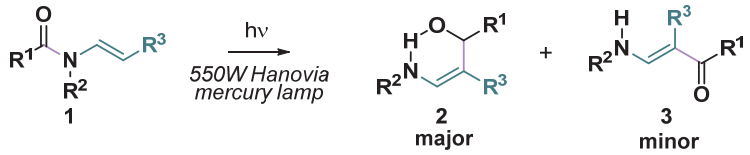
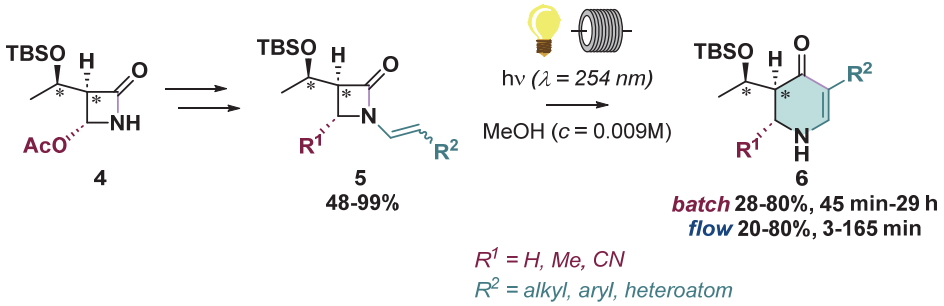
The process of photochemical rearrangement allows for the conversion of various compound classes into molecules with diverse structural arrangements and interesting applications. This technique generates molecular complexity that may not be achievable through conventional methods. In the late 1960s, Lenz and Hoffmann first observed the products **2** and **3** of the [1,3]-acyl shift photochemical reaction upon irradiation of acyclic *N*-vinylacetamides **1** (**Scheme 1**).[1]



Scheme 1. Photochemical rearrangement of acyclic *N*-vinylacetamides.

Based on the presented methodology, we have discovered the appropriate *N*-vinylazetidinones **4** undergo an analogous photochemical reaction leading to optically pure 2,3-dihydro-4-pyridinones (enaminones) **5** (**Scheme 2**).[2] Cyclic 6-membered enaminones **5** are versatile intermediates for the synthesis of bioactive natural products such as indolizidines and quinolizidines.[3] The developed method opens a flexible pathway for the synthesis of high-value 2,3-dihydro-4-pyridones **5** bearing complex substitution patterns with marked operational facility. Furthermore, in addition to using classical reaction conditions in batch, we have performed photochemical reactions in a continuous flow system which enabled convenient remote real-time control of the reaction course via UV-Vis spectroscopy (**Scheme 2**).



Scheme 2. Photochemical rearrangement of *N*-vinylazetidinones.

Acknowledgement

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P-089

Towards alkynyl-substituted anthracenes

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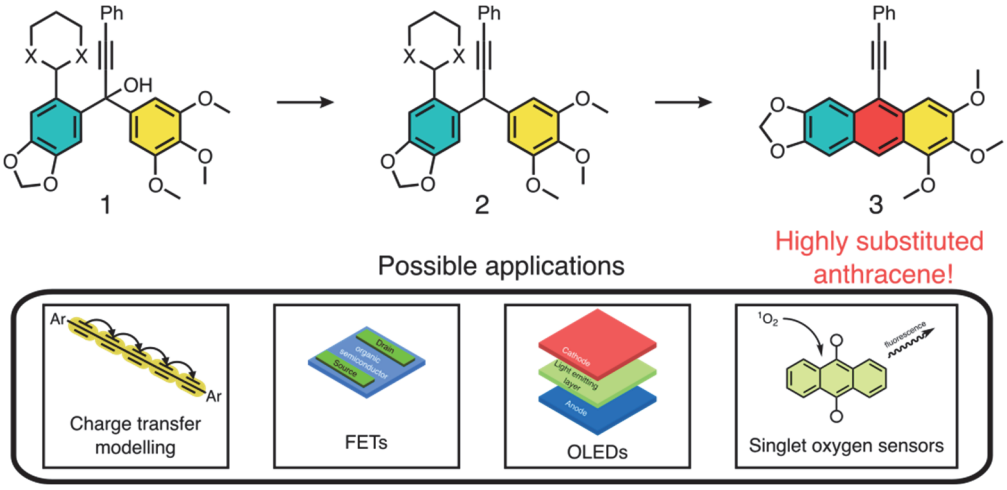
Substituted anthracenes have been of great scientific interest since the first report of their electroluminescent properties by the Pope group in 1963.[1] Ever since, substituted anthracenes – or, more generally, acenes – have been used as Organic Light Emitting Diodes (OLEDs) and Field Effect Transistors (FETs), as well as singlet oxygen sensors, pushing the limits of electronic device design. [2,3]

The addition of an alkynyl group to the anthracene backbone can modify the blue shift of anthracene molecules, as well as many other photophysical properties. [4] Such systems are essential for developing charge transfer models in molecular junctions, thus broadening the extent of OLEDs and FETs in the industry. [4]



Scheme 1. The synthesis of alkynyl-substitued anthracene **3**.

In this study, we show possible pathways for synthesizing alkynyl-substituted anthracenes **3**, using the Friedel-Crafts/Bradsher reaction.[5] To date, the synthesis has been developed up to the compound **1**. The synthesis is quite challenging due to the instability of the systems containing *ortho*-arylacetal substituted aryl propargyl alcohols. The most promising pathways for the synthesis of precursor **2** include the radical Barton-McCombie deoxygenation or blocking the π bond in alkynyl moiety by the Nicholas reaction.

Acknowledgement
This research work was funded by the National Science Center, grant number UMO-2019/33/B/ST4/02843.

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P-090

Search for new selective drug delivery systems for lung cancer treatment - designing and synthesis of *s*-triazine - peptide conjugates

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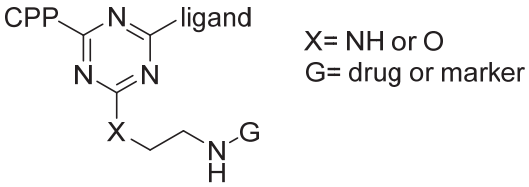
The search for and designing new and more effective medicinal active substances is one of the goals that have been pursued for many years. One of the targeted diseases are cancers considered as civilizational diseases and among them one of the most prominent is lung cancer. The lung cancer is responsible for approximately 20% deaths caused by cancers worldwide [1]. The main reason for such high mortality is lack of early detection and preventional medical examination, but also low selectivity of available treatment methods. The aim of our study is to develop *s*-triazine - peptide conjugates that exhibit increased affinity to cancer cells and contain fragment responsible for anti-cancer activity. We assumed that the central part of the designed molecules would be an *s*-triazine derivative. The structure of *s*-triazine allows the attachment of three different substituents to the 1,3,5-triazine ring [2] (Scheme 1). As substituents we intend to use two types of peptides: 1) fragments that have affinity toward non-small cell lung cancer (NSCLC) being homing peptide, and 2) hexaproline fragment that exhibit increased permeability through cell membranes to increase bioavailability due to its cell-penetrating properties. Proline derivatives constitute a group of cell penetrating peptides (CPP) without a positive charges [3]. The third substituent is intended to be ethylenediamine or ethanolamine linker with far end accessible for further modifications, which would allow to use this molecule as a drug carrier or attach fluorescent marker for in-cells distribution studies.



Scheme 1. *S*-triazine based peptide conjugate.

Preliminary results of biological tests indicate that peptide derivatives of Tretamine or Altretamine have activity against NSCLC cells.

It is also planned to synthesize pool of compounds with fluorescent marker (carboxyfluorescein) attached to the linker and test their distribution in cancer cells and conjugates with anticancer drugs.

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P-091

Triphenylphosphonium derivatives of betulin - synthesis and properties

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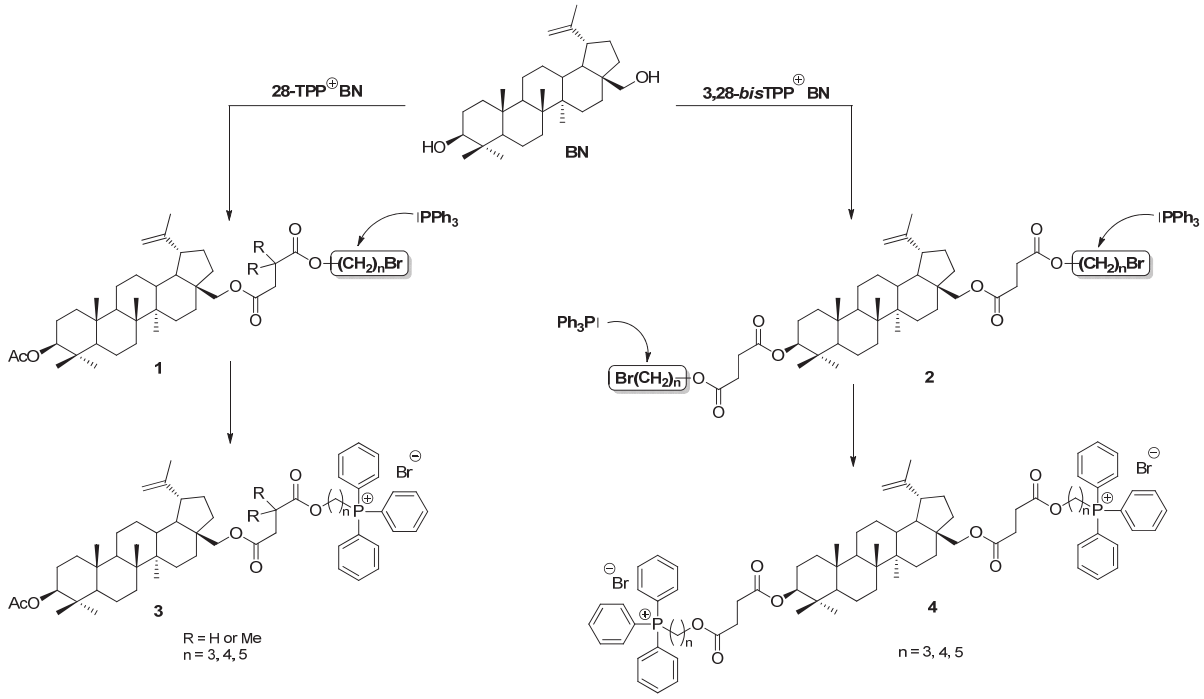
Betulin (BN, 3-lup-20(29)-ene-3,28-diol) is an interesting example of a biologically attractive natural parent molecule with high safety profile and the possibility of making a variety of structural modifications [1].

Recently we developed few-stage methodology that enable the preparation of both mono- and *bis*(TPP$^{\oplus}$) derivatives from easily available, cheap, natural BN by simple transformations in high yields. We synthesized nine new molecular hybrids of BN by covalent linkage of alkyltriphenylphosphonium moiety to the parent skeleton *via* linker O(CO)CH_2CR_2COO (Scheme 1). As expected, triphenylphosphonium derivatives of BN (**3** and **4**) showed greater cytotoxicity than natural BN towards cell lines tested (HCT 116 and MCF-7) [2].



Scheme 1. Synthetic route for the preparation of 28-TPP$^{\oplus}$ BN (**3**) and 3,28-bisTPP$^{\oplus}$ BN (**4**).

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P-092

ITC calorimetric study of L-α-tryptophan complexation with Q7 cucurbituril

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From among 20 coded amino acids commonly occurring in protein polypeptide chains three neutral amino acids: L-α-tryptophan, L-α-tyrosine and L-α-phenylalanine belong to aromatic amino acids. The aromatic rings of tryptophan and tyrosine as amino acids with ambivalent side substituents, whose amino acid side chains occur both on the globular protein surface and inside them, are chromophores. The absorption of electromagnetic radiation by the side substituents of these amino acids is widely used in the biochemical studies on proteins and their interactions with ligand molecules [1].

Cucurbiturils are a relatively new class of nano-carriers which show low toxicity and make it easier for ligand molecules to cross through the cellular membrane. These macrocyclic compounds can bind cationic centers of ligand molecules with high affinity [2].. Macrocycles of cucurbiturils may be used as nano-transporters of toxic drugs to reduce their toxicity and to prolong their circulation time. It is important to determine cucurbituril binding affinity not only for the drug but also for other components naturally occurring in body fluids. Therefore the aim of our study was to determine thermodynamics of binding of L-α-tryptophan (as model amino acid) with Q7 cucurbituril in aqueous 20 mM HCl solution.

Isothermal titration calorimetry results show that cucurbituril molecule (Q7) binds to tryptophane (Trp) cation forming thermodynamically stable supramolecular complexes in an aqueous 20 mM acidic solution of hydrochloric acid pH = 1.7. Thermodynamic binding parameters such as the equilibrium constant of the bound tryptophan and enthalpy and entropy of the formed complex were calculated, using the model of independent sites (1:1 stoichiometry). Calculated binding parameters confirm the quite strong interactions between tryptophan cation and the Q7 macrocycle. Complexation of the tryptophan by Q7 cucurbituril is endothermic ($\Delta H<0$) and is accompanied by a decrease in the disorder of the reactants ($\Delta S<0$).

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P-093

Enhancement of Enzymatic Kinetic Resolution by a New Chemoenzymatic Cascade Strategy

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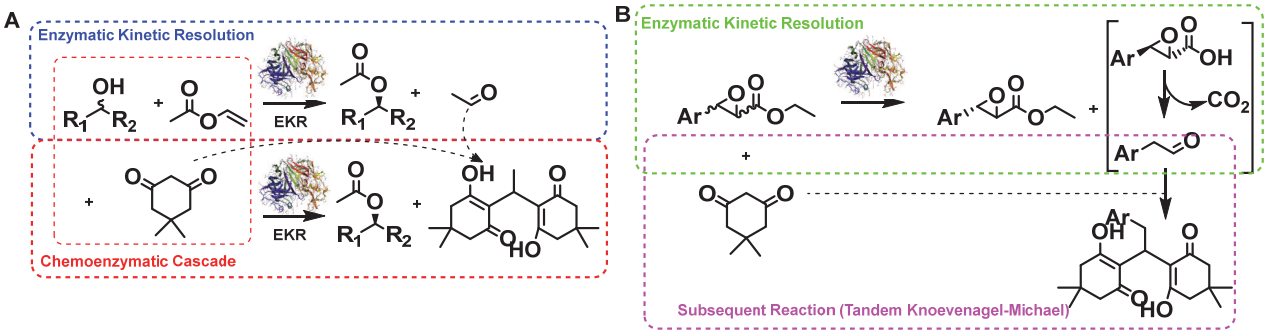
Chiral enantiomerically pure compounds are key intermediates for pharmacy and medicial chemistry. Despite the huge progress in the development of asymmetric catalysis [1, 2], the resolution of racemate is still one of the most convenient method for the synthesis of optically pure compounds.[3] Aldehydes are common by-products in enzy,atic kinetic resolution (EKR) and enzymatic dynamic kinetic resolution reactions (EDKR) [4]. Due to their high reactivity, physical properties and explosive character they are hardly tolerated in organic laboratories especially in large scale experiments. The most volatile acetaldehyde is a main by-product in enzymatic esterification of alcohols, amines or thiols when vinyl acetate is used as an acyl group donor. The hydrolysis of epoxyesters also led to the formation of aryl and alkyl aldehydes which are often effective enzyme inhibitors. To overcome this limitations we propose a new strategy based on the combination of enzyme-catalyzed reaction with simultaneous removal of formed aldehyde. It can be achieved by the introduction of the subsequent reaction engaging the formed aldehyde (Scheme 1). This lead to cascade of chemical reaction in which the by-product (aldehyde) immediately reacts with dimedone forming respective xanthedione derivatives, compounds of importance for pharmacy, medicinal chemistry and material sciences. [5] The utilization of formed aldehydes makes the process environmentally friendly, and greatly eliminates the enzyme inhibitors what is crucial for successful experiments.



Scheme 1. Chemoenzymatic cascades with dimedone.

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P-094

New colchicine derivatives: synthesis, cytotoxic activities, semi empirical and molecular modeling studies

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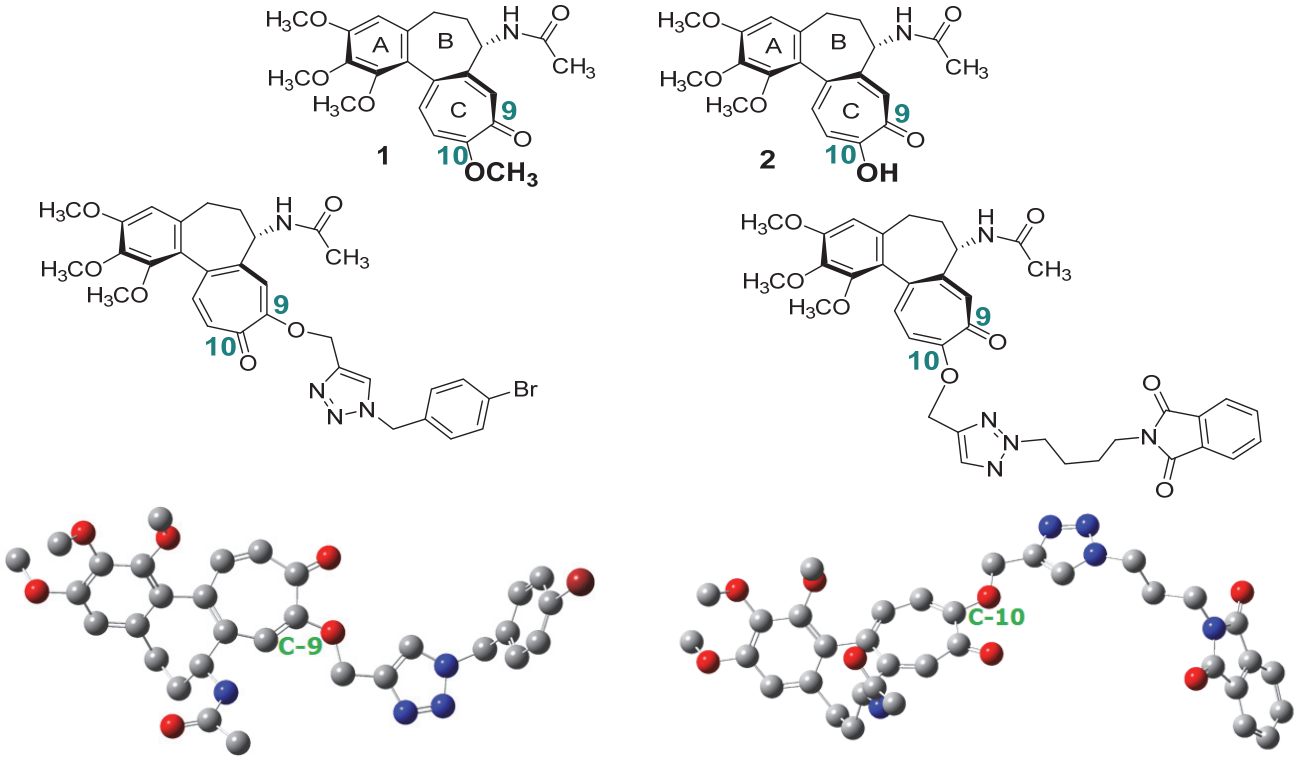
Colchicine **1** is a tropolone alkaloid naturally occurring in plants of the *Liliaceae* family, especially in meadow saffron (*Colchicum autumnale*). It possesses antimitotic, antifibrotic, anti-inflammatory activity and can efficiently relieve the symptoms of gout attacks. Moreover, colchicine is a potent anti-mitotic agent and shows carcinogenic activity [1]. Synthesis of colchicine derivative has been made to reduced its toxicity and enhance its therapeutic properties [2-4].



Scheme 1. Colchicine **1**, colchiceine **2,** example of C- 9and C-10 derivatives.

A series of colchicine **1** derivatives, converted to colchiceine **2** in first synthesis step, substituted at C-9 and C-10 positions have been synthesized. Their cytotoxic activity was tested against cancer cell lines SKOV-3, MFC-7, A-549 and normal cell line CCD39Lu. Moreover, structures of new derivatives were calculated by DFT and semiempirical methods.

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P-095

New colchicine chloride complexes - their biological activities, semi empirical and molecular modeling studies

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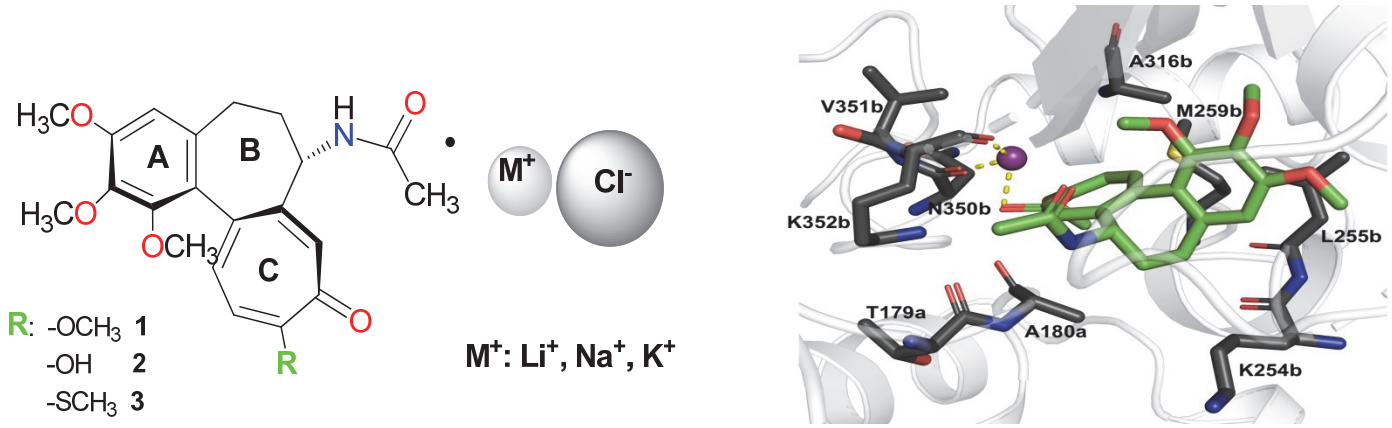
Colchicine **1** is a well known traditional bio-active alkaloid, naturally occurring in plants of the *Liliaceae* family especially in meadow saffron (*Colchicum autumnale*), whose antimitotic activity has been mainly applied for acute gout therapy [1]. Synthesis of colchicine derivative has been made to decrease its toxicity and increase its therapeutic properties [2-4].



Scheme 1. Colchicine **1**, colchiceine **2, 10**-methylthiocolchicine **3** and complexes (on the left) and molecular modeling of complex **3-Li**$^+$(on the right).

Colchicine **1**, colchiceine **2** and 10-methylthiocolchicine **3**, complexes with Li^+, Na^+, K^+ cations as chlorides (Scheme 1.) have been synthesized and studied by spectral analysis, DFT theoretical studies and molecular modeling. The compounds have also been screened against their fungicidal, herbicidal, insecticidal and cytotoxic activities.

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P-096

Regioselective photochemical deoxyalkylation of carbohydrate-based lactones: Convenient way to the synthesis of 2-deoxysugars

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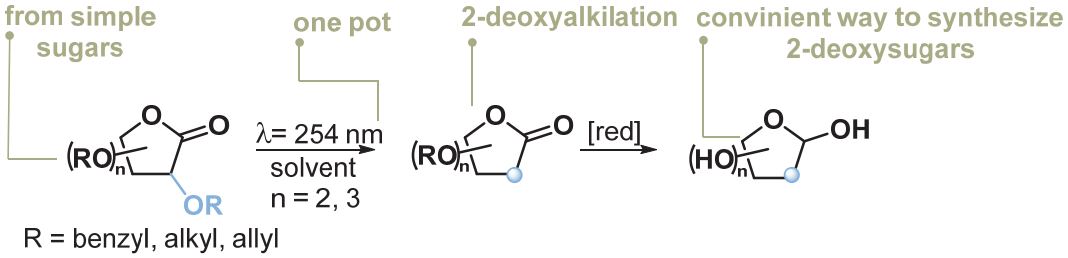
Glycosides, in which the C-2 hydroxyl group is replaced by a hydrogen atom, are important motifs in many bioactive natural products and pharmaceutical molecules.[1] The chemical synthesis of these complex molecules requires the large-scale availability of different 2-deoxysugars. Unfortunately, although we know many methods for the synthesis of 2-deoxysugars, most of them have one fundamental drawback: they are multi-step processes with low atom economy.[2] Our work is a step towards overcoming these drawbacks. Herewith, we report an environmentally benign and sustainable method for the photon-promoted deoxyalkylation of carbohydrate-based lactones to 2-deoxysugars. This operationally simple and environmentally friendly method works under pure light irradiation without any catalysts or additives, with high atom economy and good functional group compatibility. The scope of the developed method and its mechanisms will be discussed during the presentation.



Scheme 1. Regioselective photochemical deoxyalkylation of carbohydrate-based lactones.

Acknowledgement
Financial support from the National Science Center, Poland (grant OPUS 2019/35/B/ST4/02794 for B. Furman) is gratefully acknowledged.

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P-097

Polycyclic fluorinated pyrazoles via (3+2)-cycloadditions of nitrile imines with nitrocoumarins

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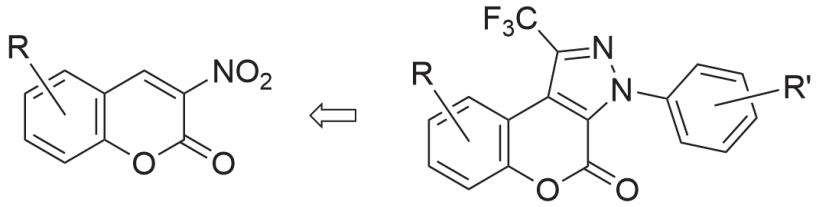
Coumarin and its analogues belong to an important class of natural lactones (essential oils of legumes and orchids) with a wide range of practical applications.[1] Notably, physiochemical and biochemical behaviour of coumarin derivatives can easily be tuned e.g. by introduction of functional groups and/or by extending the π-system through additional (hetero)cyclic rings, and hence, they are recognized as highly useful substrates for organic synthesis.

In continuation of our studies aimed at application of nitrile imines in the synthesis of fluorinated heterocycles,[2] we turned our attention to coumarin analogues considered as potentially attractive reaction partners for (3+2)-cycloaddition reactions. Here we report on successful application of nitrocoumarins as suitable dipolarophile for preparation of hitherto unknown polycyclic CF_3-functionalized pyrazole derivatives. The dual role of the NO_2 substituent, both as directing and leaving group, assured excellent regioselectivity of the cycloaddition step and smooth aromatization of the first formed adducts under the applied reaction conditions. The scope and limitations of the devised protocol will be discussed.



Scheme 1. Structures of key building blocks and the target fused pyrazoles.

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P-098

Organometallic analogues of transcription associated cyclin-dependent kinases inhibitors

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In 1970s and 1980s, a family of approximately 20 serine-threonine kinases were discovered. Those proteins – cyclin-dependent kinases (CDKs) can be divided into two major subclasses – cell cycle associated (e.g. CDK1, CDK2, CDK4 and CDK6) and transcription associated (e.g CDK7, CDK8, CDK9 and CDK12). In tumors, CDKs are often dysregulated, overexpressed and play a crucial role in cancer cell growth and survival, which makes them interesting and promising therapeutic targets.[1] Over the past few years, many inhibitors of CDKs were discovered and studied in clinical trials as potential anticancer chemotherapeutics. Cell cycle associated inhibitors (e.g. Ribociclib, Abemacyclib and Palbociclib) have proven clinical activity in some types of cancer such as mantle cell lymphoma (MCL) and hormone receptor positive breast cancer and were implemented for treatment.[2] On the other hand, transcription associated CDKs inhibitors are still under clinical studies (phase I and phase II) and have not entered clinical usage.

In cancer cells , transcription associated CDKs are highly overactive due to a mechanism called transcriptional addiction. For example, in T leukemia cells, overexpression of certain genes leads to overactivity of CDK7. Furthermore, it has been discovered that besides well-known resistance mechanisms such as mutations in the estrogen receptor alpha, Erα, overexpression of ABC proteins (e.g. ABCB1, ABCG2), other cell cycle-related mechanisms of acquired resistance such as CDK2, CDK4 and CDK6 amplification and CDK7 overexpression are taking place.[3]

The conjugation of an organic molecule with metallocenes (ferrocene and less ruthenocene) may lead to increasing of bioactivity of the resulting molecule. It allows to tune the activity of resulting molecules such as hydrophilicity, reactive oxygen species (ROS) generation or cause interactions with proteins which are not present for “normal” organic molecules. Over past 35 years many organometallic conjugates has been developed. In many cases, the presence of organometallic moiety was increasing the activity of the molecule in comparison to parenting, “purely organic” compound. (e.g. ferrocifene [4], taxol derivatives [5]). Additionally, for some conjugates, a new mechanism of action has been discovered. For example, replacing the phenyl group with a ferocenyl substituent in plinabulin caused the resulting compound to inhibit the activity of ABCB1 and ABCG1 proteins, while plinabulin did not show such activity [6].

Herein, the synthesis of organometallic conjugates of selected, known inhibitors of transcription-associated CDKs will be presented.

Acknowledgement
This work was financially supported by University of Lodz based on the Excellence Initiative - Research University (IDUB) grant for young researchers, decision no. 42/2021.

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P-099

Selective sorption of organic dyes with polymeric network based on β-cyclodextrin and biphenyl anhydride

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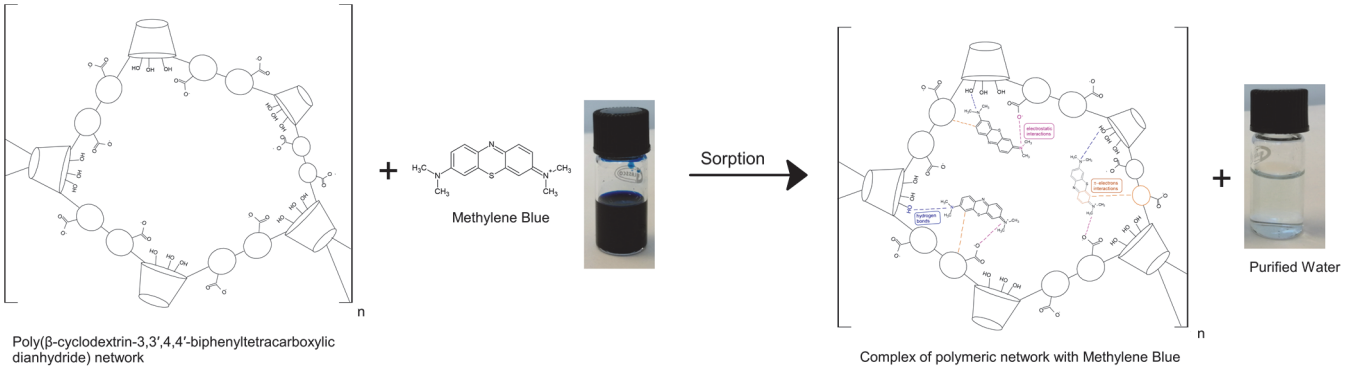
Recently, an increase in the concentration of various chemicals such as dyes, pharmaceuticals, detergents, pesticides in water and sewage has been observed. This is caused by the increased demand for the production of clothing and improving the quality of health, which also leads to the discharge of this type of substances with industrial or municipal wastewater as a result of washing dyed fabrics [1]. The polymeric network based on β-cyclodextrin (β-CD) and biphenyl anhydride [2] was evaluated towards removal of different kind of pollutants during sorption processes. The studied pollutants were methylene blue (MB), crystal violet (CV), malachite green (MG), acid orange 7 (AO7), nickel/zinc/copper ions. The most effective removal was observed for MB with 96.15 mg/g of sorption capacity. The performed studies indicated selective removal of cationic dyes like MB, CV and MG, but not attraction to anionic dye like AO7 or metal cations like Ni^{2+}, Zn^{2+} or Cu^{2+}. The analysis of results indicated favourisation of cationic dyes, especially MB, for sorption process with polymeric network. The selective character was presumably induced by presence of carboxyl group, through electrostatic interaction. To sum up, the presented polymeric material based on CD is efficient and selective sorbent towards cationic dyes like MB.



Scheme 1. Sorption of MB via polymeric network based on β-cyclodextrin and biphenyl anhydride.

Acknowledgement

The authors gratefully acknowledge Jan Dlugosz University in Czestochowa for the support in presented research.

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P-100

Synthesis of 2*H*,10*H*-pyrano[2,3-*f*]chromen-2,10-diones and coumarin-pyrazole or coumarin-pyrimidine hybrids based on them

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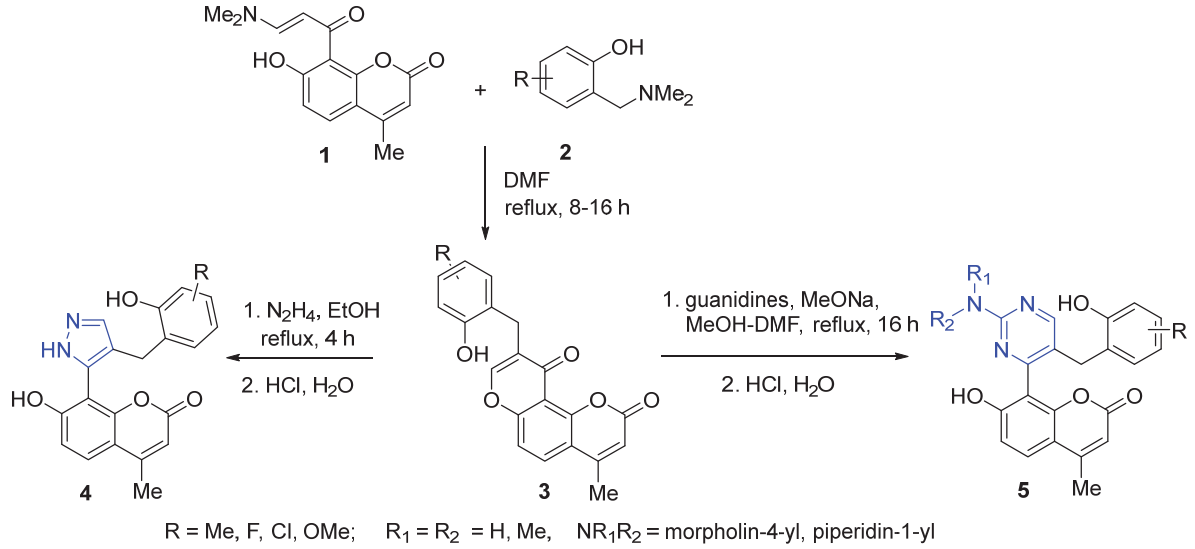
Previously we reported an efficient one-pot method of the synthesis of B-ring hydroxylated homoisoflavonoids that does not require the protection of the phenolic groups [1]. In this research in the *oxa*-Diels–Alder reaction of 8-[(2E)-3-(dimethylamino)prop-2-enoyl]-7-hydroxy-2H-chromen-2-one **1** with thermally generated *ortho*-quinone methides from 2-(*N,N*-dimethylaminomethyl)phenols **2** and the subsequent cascade of reactions were obtained 2*H*,10*H*-pyrano[2,3-*f*]chromen-2,10-diones **3**.

The application of flavonoids for the construction of bioactive molecules consists of a great deal of research work because the flavonoid scaffold is inspired to play the mutual role with other functional moieties and flavonoid becomes a scaffold for various modifications including ANRORC (Addition of the Nucleophile, Ring Opening, and Ring Closure) with various nucleophiles.



Scheme 1. Synthesis of 2*H*,10*H*-pyrano[2,3-*f*]chromen-2,10-diones and coumarin-pyrazole or coumarin-pyrimidine hybrids based on them.

In this framework, synthesis of pyrazole–7-hydroxycoumarin hybrids **4** was performed by recyclization of pyranochromone core of compounds **3** under hydrazine actions. Reaction of 2*H*,10*H*-pyrano[2,3-*f*]chromen-2,10-diones **3** with guanidine hydrochloride or related *N,N*-disubstituted derivatives as 1,3-bidentate nucleophiles in MeOH-DMF mixture at presence of NaOMe affords amino-, dimethylamino-, 1-piperidino-, and 4-morpholino substituted pyrimidine-coumarin hybrids **5**.

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P-101

Reaction of *ortho*-Quinone Methides with Amphiphilic Nucleophiles

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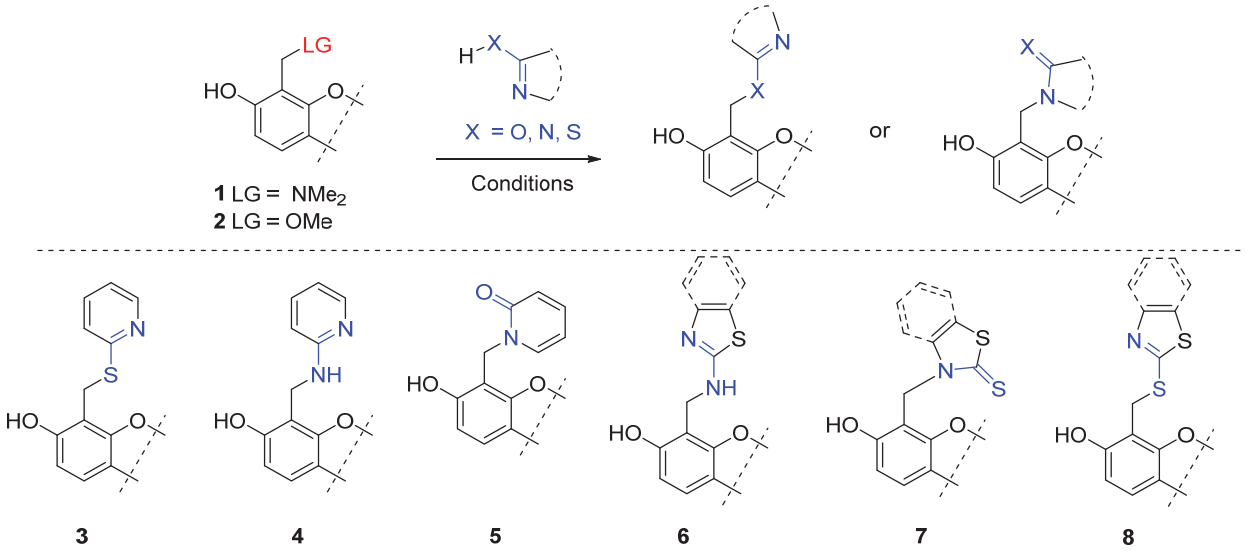
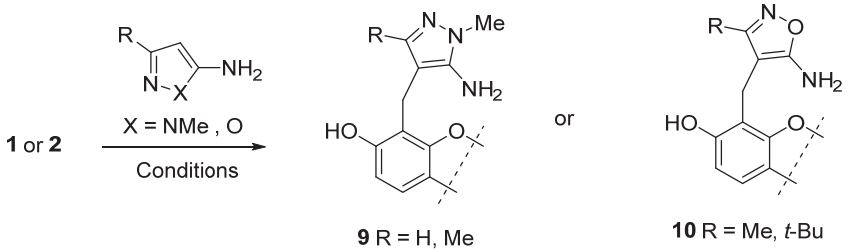
Nitrogen-based heterocyclic compounds have received a lot of attention in the last two decades, and they have contributed to the discovery of a lot of organic synthesis techniques and several applications in the biological/chemical sciences. Because of the ability of the N-atom to form hydrogen bonds with biological targets, nitrogen heterocycles comprising the pyrazole, imidazole, piperidine, etc. backbone are used as key components in many drugs [1]. In continuing our studies on flavonoid-like scaffolds as privileged structures in medicinal chemistry, we studied the reaction of isoflavonoid derivatives with amphiphilic nucleophiles with heterocyclic cores.



The direction of the reaction significantly depends on starting phenols **1** and **2**, nucleophiles, and reaction conditions. Thus, applying phenolic Mannich bases **1** led to the preferable formation of compounds **4-7** *via* thermal formation of *ortho*-quinone methides in aprotic solvents and subsequent Michael addition; only traces of compounds **1** and **8** were observed. However, these compounds were synthesized in the case of using methoxymethyl derivatives **2** in ethanol at reflux. Formation of compounds **5** did not depend on starting compounds **1** or **2**, in all cases applying aprotic solvents was required for the thermal generation of *ortho*-quinone methides.



In the case of the reaction of compounds **1** or **2** with 5-amino-1-methylpyrazoles or 5-aminoisoxazoles, only C-alkylation of these amines was observed. It should be mentioned that this reaction was successfully applied for the synthesis of chromone, coumarin, and aurone derivatives.

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P-102

Synthesis of the [1,2,4]triazino[5,6-b]indole derivatives as UPF1 ATP mimetics in NMD pathway

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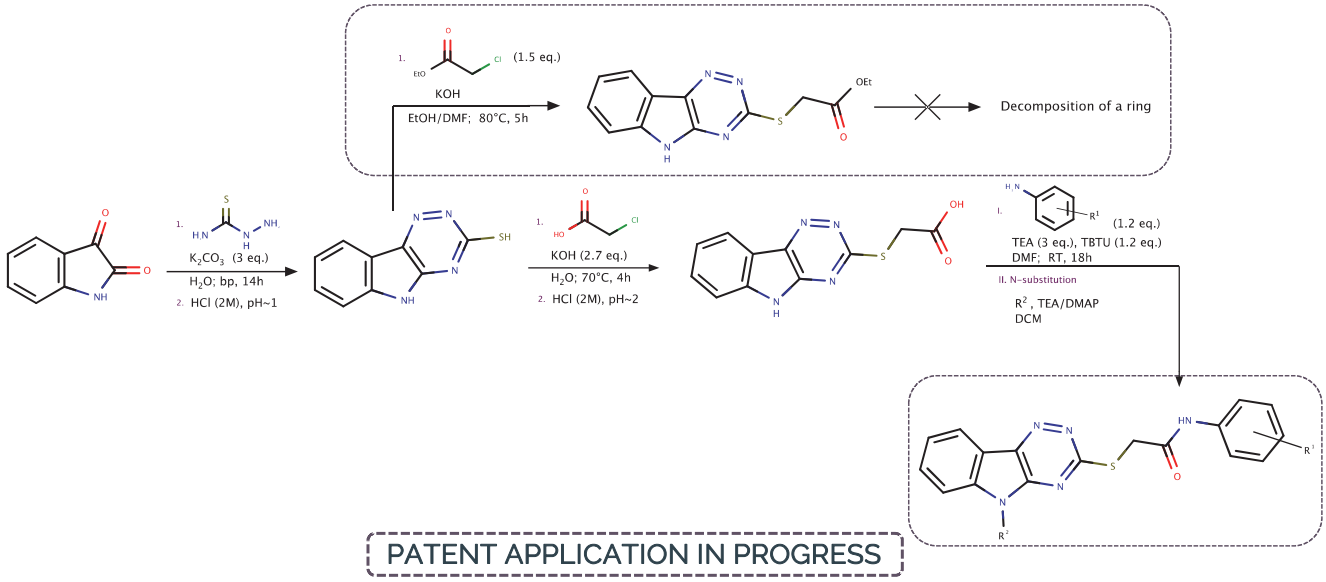
We directed our efforts towards the investigation of the Nonsense-mediated mRNA Decay (NMD) and its primary regulator, the UPF1 protein. Previous research has indicated that disrupting the NMD machinery in cells can lead to various consequences. [1,2] On that point, the regulation of the NMD mechanism and, in particular, the inhibition of the UPF1 protein, contributes to a better understanding of the interactions within the UPF proteins system. In conjunction with the regulation of the pathway, the UPF1 protein has shown promising potential as a cancer drug therapy target. [3,4] Based on the *in silico* screening and molecular dynamics simulations of the small-molecule inhibitors, functionalized derivatives containing a [1,2,4]triazino[5,6-b]indoles moiety, as potential UPF1 ATP mimetics, have been identified and selected. Several methods and optimization procedures for the organic synthesis of the selected chemical structures have been performed. Our synthesis procedure includes 4 steps. Starting from the condensation reaction of isatin with thiosemicarbazide – it successfully results in the obtaining of a key substrate with the [1,2,4]triazino[5,6-b]indole-3-thiol scaffold. One of the possible pathways involves the following reactions between 2-((5H-[1,2,4]triazino[5,6-b]indole-3-yl)thio)acetic acid and various aniline derivatives, which have proceeded in moderate yields. The final step included N-substitution reactions of the obtained structures. Synthesized compounds represent novel ligands expected to possess biological and anticancer activity. The inhibition potential of the products will be evaluated by sandwich ELISA, TSA, and CETSA assays.



Scheme 1. One of the synthetic pathways towards obtaining the selected compounds.

Acknowledgement

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P-103

Preliminary studies on PROTAC-mediated degradation of Rab geranylgeranyl transferase

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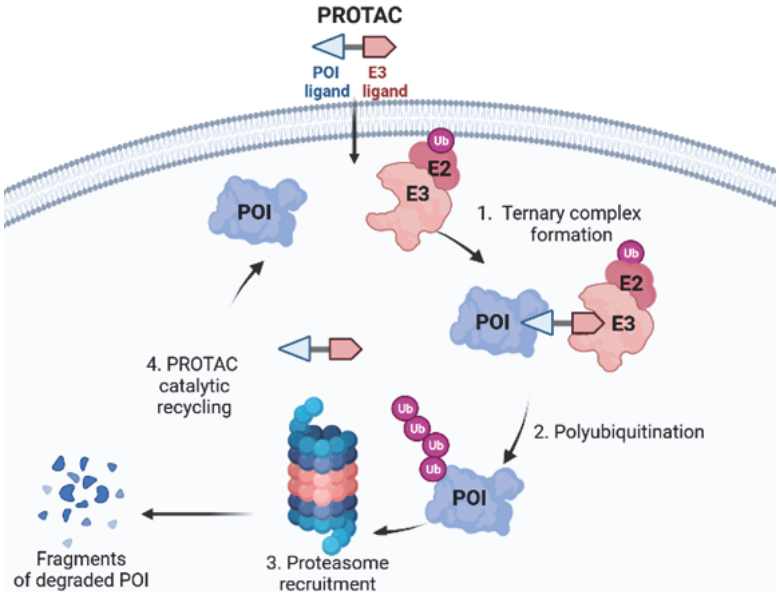
Rab geranylgeranyl transferase (RGGT) is an enzyme that catalyzes protein prenylation, one of the crucial post-translational modifications. Prenylation involves the attachment of a 15-carbon farnesyl or 20-carbon geranylgeranyl group to a protein. Prenylated proteins manifest increased hydrophobicity that targets them to the cell membrane.[1] Abnormal prenylation of Rab GTPases is associated with various human pathologies, including cancer, neurodegenerative disorders, and diabetes.[2] Therefore, we aimed to develop an innovative strategy to directly stimulate the degradation of RGGT. To achieve this, PROteolysis TArgeting Chimaeras (PROTACs) approach based on the ubiquitin-proteasome system (Figure) was employed.

A series of PROTACs and their ester precursors was synthesized. They were built from three elements: a VHL ligand for E3 ligase, alkyl and PEG linkers, and the targeted enzyme's inhibitor, phosphonocarboxylate. All new compounds were tested for their RGGT protein degradation properties in the mammalian breast cancer cell system - MCF-7 cell line. Western blot testing allowed for the identification of compounds with degenerative potential. The effect of PROTACs on the level of prenylated proteins such as Rab GTPases will be determined in the future.



Scheme 1. Targeted degradation via the PROTAC-induced ubiquitin-proteasome system.[3]

Acknowledgement
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P-104

Theoretical insight into different types of complexation with pyridine

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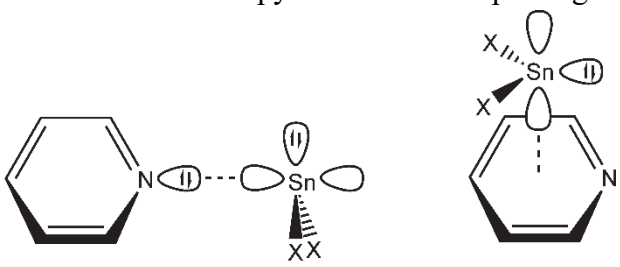
Pyridine serves as a common σ-donor ligand. A single lone pair at its nitrogen atom is capable of complexing a diverse range of metal centers. In addition to the σ-donor ability of pyridine, its aromatic π-electron cloud can potentially act as a Lewis base toward acidic metal centers.

In this work, the σ- and π-complexation interactions between simple tin(II) molecules SnX_2 (X = H, F, Cl, Br, I) and pyridine in a series of their model complexes SnX_2·pyridine (Scheme 1) were characterized using a variety of quantum chemical methods.[1] Both these separate interactions and their coexistence in a single complex were studied. The interplay between the two types of SnX_2 complexation with pyridine was established in terms of structural changes, interaction energies, interaction energy components and topological electron density parameters.

It was established that the π-complexation interaction in the model SnX_2·pyridine complexes was relatively weak, almost three times weaker than the σ-complexation interaction leading to the Sn←N coordination bond between SnX_2 and pyridine. Although dispersion was the dominant contribution to the π-complexation interaction between SnX_2 and pyridine, the structure of such π-complexes could be elucidated in terms of the locations of molecular electrostatic potential extrema for SnX_2 and pyridine. The π-complexation interaction was weakened by the σ-complexation of another SnX_2 molecule. The coexistence of the two types of complexation in the resulting binuclear SnX_2·pyridine·SnX_2 model complexes actually decreased the strengths of both π- and σ-complexation interactions yet the former was weakened to a much greater extent. This interplay was associated with the py→SnX_2 charge transfer that affected the magnitude of molecular electrostatic potential minima for the pyridine sites complexing the subsequent SnX_2 molecule.



(a) (b)

Scheme 1. Schematic representation of (a) σ- and (b) π-complexation interactions between SnX_2 and pyridine.

Acknowledgement

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P-105

New resorcinol[4]arenes with high dipole moments: synthesis and anion binding

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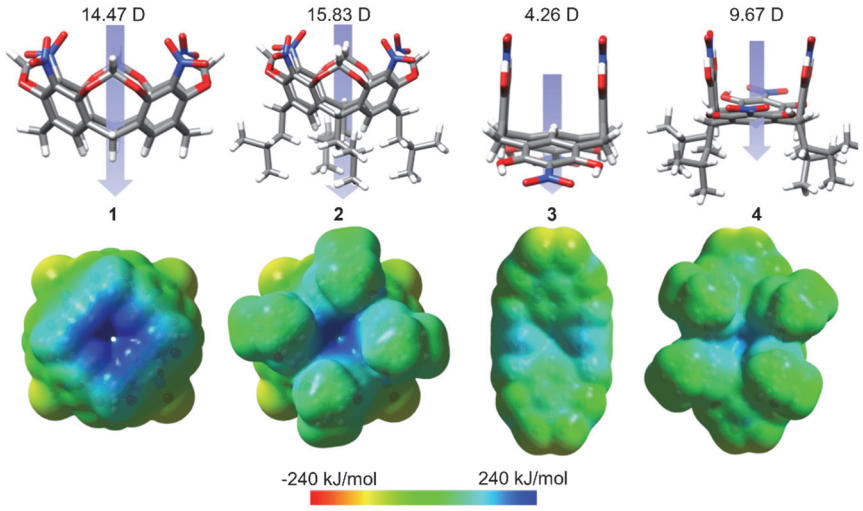
The dipole moment (DM) is a quantity that characterizes many key properties related to their relative position in the condensed phase and to phenomena related to electron transport and interaction with light. Non-ionic organic molecules with high DM find applications as ferroelectrics, in non-linear optics (NLO), and as elements of solar cells promoting charge separation at the interface. Inducing a high DM usually involves placing electron-donating and electron-withdrawing groups (the negative and positive poles of the dipole, respectively) at opposite ends of an aromatic backbone or another conjugated multiple-bond system. Aminobenzonitriles, used in NLO, have DM in the range of 5.0–5.6D, and the highest DM obtained so far for substituted benzene is 14.5D.

Resorcinarenes are macrocyclic polyphenolic compounds, which, due to the shape of the vase and the gap, are used in the construction of receptors and as building blocks of molecular capsules. Due to unique geometry, the vertical components of the dipole moments add up, while the horizontal ones are cancelled. We have recently synthesized tetranitroresorcinarene **1**, which, shows unique binding properties. The results of DFT calculations suggest that this molecule has a very large dipole moment. Macrocyclic compounds with such large dipole moments are not known. These theoretical findings, together with unusual recognition properties detected experimentally open new directions in the construction of supramolecular receptors.



Scheme 1. The results of DFT calculations of the geometry, dipole moments (μ), and electrostatic surface potential (ESP) for designed receptors **1**-**4**; All calculations at DFT B3LYP/dgdzvp level in THF (PCM model), ESP mapped onto isosurfaces at $\rho = 0.005$ e/au^3, H_a atoms marked with green circles (if possible).

Acknowledgement

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P-106

Axially Chiral Stable Radicals: A Promising Class of Functional Materials for Potential Applications

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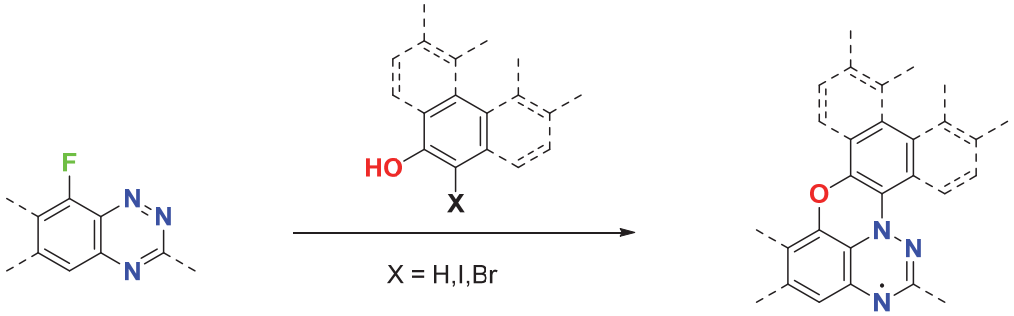
Benzo[e][1,2,4]triazinyls, or Blatter radicals, are stable free radicals, first reported by Blatter in 1968.[1] Blatter-type radicals have many interesting physical properties, such as antiferromagnetic or ferromagnetic interactions, spin π-delocalization, narrow electrochemical window and low excitation energy, which attract attention from scientists. More importantly, Blatter radicals have excellent stability to air and water, and are stable for up to 30 years.[2] In contrast to their nitroxide counterparts, their properties can be modified more easily through simple variation of substitutents.[3] Recently three procedures, Pschorr-type cyclization, photocyclization (halogen lamp irradiation) and Bu_3SnH- and TMS_3SiH-assisted cyclizations were reported to synthesize the planar Blatter radicals.[4-6] The goal of our project is to use planar Blatter radical as the central paramagnetic structural element of axially chiral paramagnetic derivatives and investigate their chiro-optical and chiro-magnetic properties in solutions, organized media and on metal surfaces as monolayers.



Scheme 1. Preparation of π-extended benzo[*e*][1,2,4]triazin-4-yls.

Acknowledgement
This work was supported by the National Science Centre (2020/38/A/ST4/00597).

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P-107

Biocatalytic Characterization of an Alcohol Dehydrogenase Variant Deduced from *Lactobacillus kefir* in Asymmetric Hydrogen Transfer

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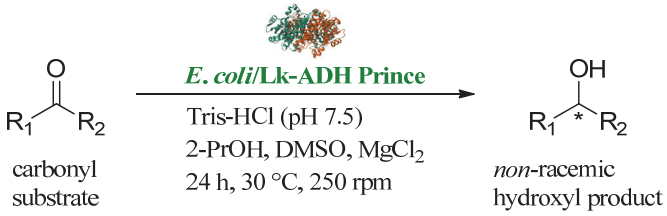
Chiral alcohols are key building blocks supporting the synthesis of high-value-added products, so it is essential to develop practical, selective, scalable, and environmentally friendly methods to obtain them. Unfortunately, most methods for preparing optically active alcohols have significant limitations related mainly to low reaction yields and the high cost of isolation and purification of the products. Therefore, desymmetrization of prochiral substrates is considered one of the most valuable transformations. At the same time, the vast majority of efficient and selective biocatalysts capable of reducing carbonyl compounds are alcohol dehydrogenases (E. C. 1.1.1) (ADHs). Hence, hydrogen-transfer biocatalysts for preparing optically pure chiral secondary alcohols are of great interest, especially for stereodiscrimination of sterically demanding 'bulky-bulky' ketones.

In this study, we describe the biocatalytic potential of an anti-Prelog (*R*)-specific ADH variant from *Lactobacillus kefir* (Lk-ADH-E145F-F147L-Y190C named Lk-ADH Prince) [1] used as an *E. coli*/ADH whole-cell biocatalyst and its characterization for the stereoselective reduction of prochiral carbonyl substrates. Crucial parameters of the enzymatic reaction were determined, including reaction medium, cofactor dependence assessment, tolerance to organic co-solvent, and substrate loading. Next, we investigated 34 carbonyl derivatives to explore the range of Lk-ADH Prince substrates in hydrogen transfer reactions. The products are either important precursors of pharmaceutical compounds or are APIs themselves. Our results show that *E. coli*/Lk-ADH Prince exhibits catalytic activity against structurally diverse ketones, providing optically active alcohols with excellent anti-Prelog (*R*)-stereoselectivity (up to >99% ee) with high yields (up to 91%) without requiring the addition of costly exogenous nicotinamide NAD(P)H cofactors [2].



Scheme 1. Asymmetric reduction of prochiral ketones using *E. coli*/Lk-ADH Prince.

Acknowledgement

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P-108

One-Pot Photo-Biocatalytic Deracemization of *sec*-Alcohols Combining Photocatalytic Oxidation and Bioreduction

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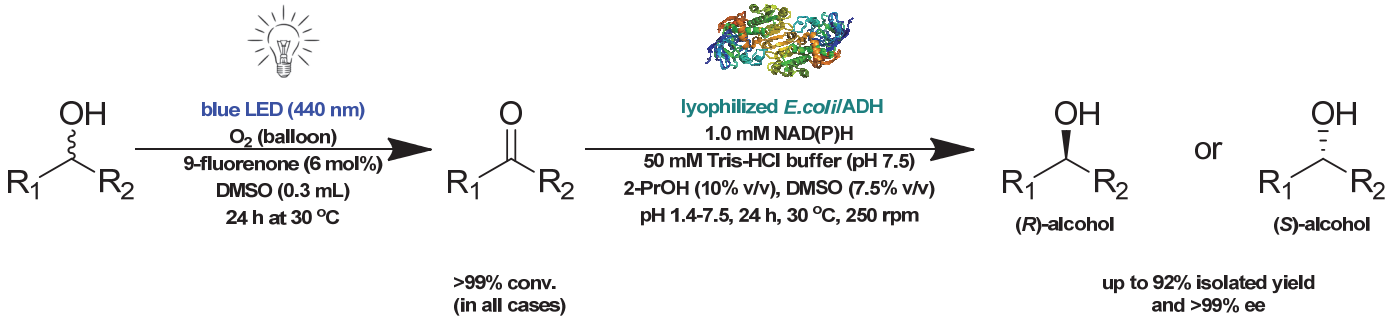
Developing new, more efficient, and environmentally friendly chemoenzymatic strategies for synthesizing optically active alcohols is essential for chemists involved in stereocontrolled organic synthesis. This is mainly because chiral, non-racemic synthons are used in the production of high-value-added compounds, including pharmaceuticals.

One of the newest trends in asymmetric organic synthesis is the use of light as an unlimited and sustainable energy source for enhancing chemical reactions. Photocatalytic reactions can also be used in combination with highly stereo-, chemo- and regioselective enzymes, offering new opportunities for more efficient preparation of chiral derivatives. In addition to generating unique reactivity, photo-biocatalytic reactions enable process intensification and thus shorten process times, further improving the cost-effectiveness of such methods in the industry [1].

In this study, we report a novel one-pot, two-step photo-biocatalytic procedure for the deracemization of secondary alcohols, leading to optically active alcohols obtained with very high chemical and enantiomeric purity. The photo-biocatalytic reactions were carried out in a cascade manner without separating intermediates. In this case, 9-fluorenone was used as a metal-free photocatalyst promoting photooxidation of racemic alcohols. At the same time, the subsequent bioreduction step was catalyzed by stereocomplementary recombinant alcohol dehydrogenases (EC 1.1.1.1) (ADH) overexpressed in the competent *Escherichia coli* cells.

Photo-biocatalytic deracemization of racemic alcohols using a 9-fluorenone-O_2-blue LED-DMSO-*E.coli*/ADH system carried out on a semi-preparative scale (0.25 mmol; 63mM final conc. in 4 mL) at room temperature yielded non-racemic aryl alcohols with conversion from 82% to >99%, in up to 92% isolated yields and excellent optical purity from 97% to >99% ee and complementary chirality.



Scheme 1. Photo-biocatalytic deracemization of racemic alcohols using 9-fluorenone-O_2-blue LED-*E.coli*/ADH system.

Acknowledgement

This research was funded by the National Science Center (NCN) of Poland grant "OPUS 24" (Grant No. 2022/47/B/ST4/0139). Statutory support by the Department of Chemistry, Warsaw University of Technology (WUT) is also acknowledged. N.A. and A.R. acknowledge financial support from the IDUB project ("Scholarship Plus" program for Ph.D. students). The University of Graz and the Field of Excellence BioHealth are acknowledged for financial support.

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P-109

Chemoenzymatic Synthesis of Tenofovir

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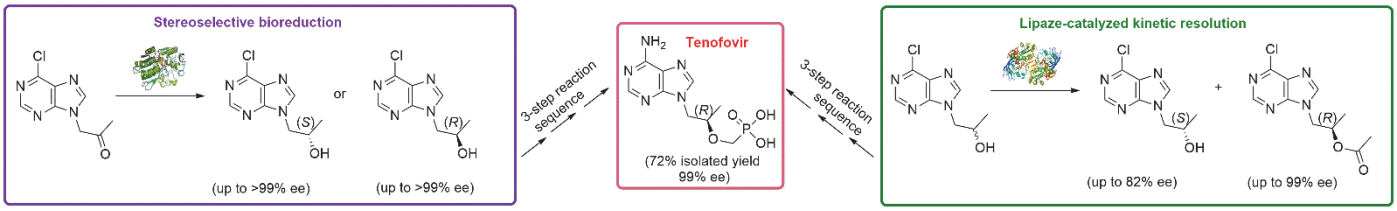
Tenofovir and its lipophilic prodrugs [i.e., tenofovir disoproxil fumarate (**TDF**, Viread®) and tenofovir alafenamide (**TAF**, Vemlidy®)] are powerful antiretroviral agents that have already gained the status of 'frontline drugs' for the treatment of HIV/AIDS infection and chronic hepatitis B caused by HBV [1-2]. The anti-HIV activity of tenofovir, resulting from competitive inhibition of HIV reverse transcriptase, is highly dependent on the absolute configuration of this medication. In this context, the (*R*)-configurated tenofovir is ca. 100-fold more active as a nucleoside reverse transcriptase inhibitor (NRTI) than its enantiomeric counterpart [3].

In this study, optimization of the reaction conditions for lipase-catalyzed kinetic resolution of racemic hydroxyl key-intermediate was performed. This task allowed us to select the most efficient biocatalytic system, which consisted of immobilized lipase from *Burkholderia cepacia* (Amano PS-IM) suspended in a mixture of vinyl acetate as an acyl donor and toluene as co-solvent. The corresponding optically pure (*R*)-acetate (>99% ee) was obtained on a 500 mg-scale (60 mM final conc. in 60 mL) in 47% yield when employing preparative silica-gel column chromatography at a purification step or in 31% yield when using chromatography-free procedure relying on a selective liquid-liquid extractive workup.

Alternatively, stereoselective bioreduction of prochiral ketone was performed. The most satisfactory result in terms of enantiomeric purity (>99% ee) and the isolated yield (86%) of the desired (*R*)-alcohol was obtained in the reaction catalyzed by lyophilized *E. coli* cells harboring recombinantly overexpressed variant of alcohol dehydrogenase (ADH) from *Lactobacillus kefir* (*E.coli*/Lk-ADH-Prince). The key (*R*)-configurated intermediate was further functionalized toward tenofovir in a three-step reaction sequence.

The total isolated yield of enantiomerically enriched tenofovir (99% ee) reached 72% after four steps. The elaborated enzymatic strategy might be applicable in the asymmetric synthesis of two other blockbuster antiretrovirals, such as **TDF** and **TAF**, respectively.



Scheme 1. Chemoenzymatic synthesis of tenofovir.

Acknowledgement

This research was funded by the National Science Center (NCN) of Poland grant SONATA 15 (No: 2019/35/D/ST4/01556). B.Z. is grateful to the IDUB project ('Scholarship Plus' Programme) for providing a research fellowship.

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P-110

Design and synthesis of small molecule inhibitors targeting UPF1 in the NMD pathway for anticancer activity

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Regulation of RNA metabolism, in order to ensure its proper function, requires the existence of various quality control processes. During the process of protein biosynthesis, only properly synthesized, complex, and modified mRNAs can serve as templates. Inside the cell, an important surveillance mechanism exists that enables rapid recognition and elimination of transcripts containing inappropriate PTC (Premature Termination Codons) codons. This mechanism is known as the NMD (Nonsense-Mediated mRNA Decay) pathway.[1.2] The activation of the NMD pathway involves an important factor, the UPF1 (Up-Frameshift) protein, which acts as the main effector element.[3] Therefore, UPF1 may represent a novel therapeutic target that has yet to be investigated. Based on the results of computer simulations, chemical structures were selected that possess the potential to interact with the ATP binding site in the UPF1 enzyme.[4] The poster presents synthesis of potential anticancer compounds that target the functions of this protein. The main scaffold of the chemical molecules obtained is 2,3,4,9-tetrahydro-1H-carbazole. The Fischer indolization method was chosen to close the core of this group of carbazoles. Further studies also included dichloroaminophenol and triazole derivatives.

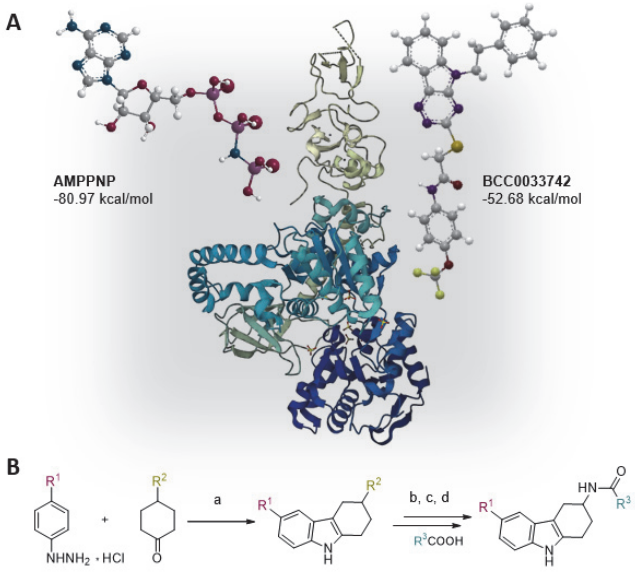

Figure.1.A. Comparison of docking of the AMP-PNP molecule with the BCC0033742 derivative **B.** Proposed synthesis paths of derivatives of 2,3,4,9-tetrahydro-1H-carbazole with the modification position

Acknowledgement

This research was funded by the *National Science Centre Poland: «The impact of UPF1 ATP mimetics on the mutant immunopeptidome»; 2020/39/B/NZ7/02677. Host institution: The International Centre for Cancer Vaccine Science (ICCVS).*

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P-111

Voltammetric study of selected pesticides on boron-doped diamond electrode

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Pesticides constitute a diverse group of chemical compounds used to protect crops, among other things, from fungi (fungicides). Currently, the most commonly used fungicides in agriculture are modern fungicides from the succinate dehydrogenase inhibitor (SDHI) group, which exhibit a broad spectrum of action and are highly effective against diseases in grains, fruits, and vegetables even at low doses.[1] The first generation of SDHI fungicides, such as carboxin and oxycarboxin, was introduced in the late 1960s, but they did not find widespread use in agriculture due to their moderate effectiveness.[2] In the last few decades, a new generation of broad-spectrum SDHI fungicides has been introduced to the market, such as boscalid, bixafen, fluopyram, isopyrazam, penthiopyrad, benzovindiflupyr, flutolanil, penflufen, fluxapyroxad, sedaxane, and mepronil.[3]

The objects of my research were selected fungicides from the SDHI group, such as penflufen and mepronil, which are widely used in agriculture to combat fungal diseases in potato, cereal, rapeseed, corn, and soybean crops.[4] [5] Apart from their beneficial effects, these fungicides can have a harmful impact on the human body (they can disrupt oxidation and reduction processes occurring in living organisms). Therefore, it is essential to determine their redox properties.

The aim of my research was to investigate the electrochemical activity of penflufen and mepronil. The electrochemical studies of these compounds were conducted in a wide pH range of supporting electrolyte (Britton-Robinson buffer) from 2.0 to 12.0 employing the cyclic voltammetry (CV) technique with a boron-doped diamond electrode (BDDE). The next stage of the research involved examining the nature of the currents and electrochemical processes of the studied fungicides at the optimal pH of the supporting electrolyte, also using CV on BDDE at various scan rate values ranging from 5 to 500 mV s^{-1}.

Acknowledgement

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P-112

π-Extended Discotic Mesogens of Flat Benzo[1,2,4][*e*]triazin-4-yl radical: Development of synthetic access

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Multifunctional materials especially paramagnetic liquid crystals based on stable organic radicals are increasing importance in the technological advances. Thus, the exceptional stability, spin π-delocalization, narrow electrochemical window and low excitation energies made benzo[e][1,2,4]triazin-4-yl derivatives attractive for application in organic batteries, molecular electronics, spintronics, photodetectors, and liquid crystalline photoconductors.[1] There are many reports on the stable organic radicals but the discotic liquid crystalline radicals are still rare.[2] Herein, we report the synthesis, liquid crystalline and magnetic properties of the full disc and half disc planar Blatter radicals. For the synthesis of the radicals all the three procedure, Pschorr-type cyclization, Photocyclization (Halogen lamp irradiation) and Bu_3SnH- and TMS_3SiH-assisted cyclizations were considered. Liquid crystalline properties were investigated by the combination of differential scanning calorimetry, polarizing optical microscopy and powder XRD analysis. Both the compounds are mesogenic and showing the columnar hexagonal mesophase below the room temperature.

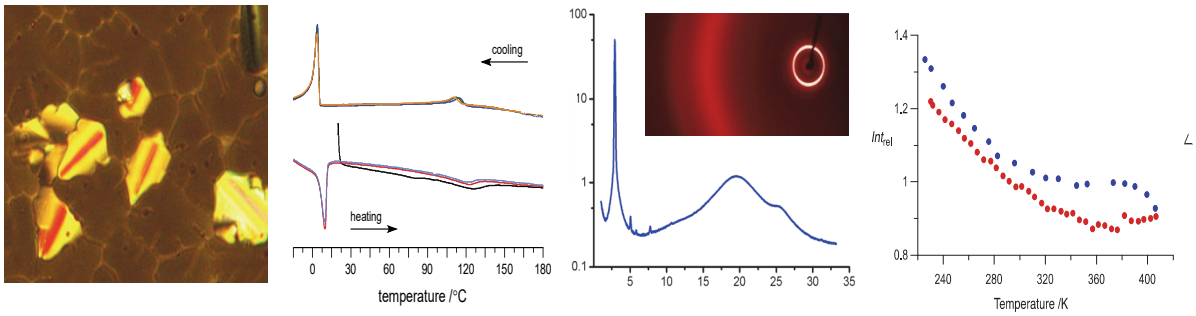

Figure1. POM image, DSC, XRD and intensity of solid-state EPR signal of discotic mesogen.

Acknowledgement
This work is supported by the *NCN (*2020/38/A/ST4/00597*).*

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P-113

Synthesis and physicochemical studies of new planar benzo[*e*][1,2,4]triazinyl diradicals

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In recent years, we have witnessed a rapid increase in interest in open-shelled organic molecules based systems for organic electronics and spintronics. The Blatter radical (Fig. 1.) and recently discovered planar Blatter radical [1] belong to this group of compounds. They are high stable molecules with π-delocalization of spin and wide absorption band in visible light, applicable in self-organizing materials, energy storage systems [2] and OLEDs [3]. Recently, Blatter radical has been utilized as a building blocks for high-spin organic diradical materials [4, 5], which opens possibilities for further exploration of this group of compounds.

The main goal of our research is the synthesis of a new planar benzo[*e*][1,2,4]triazinyl diradicals **1** and **2** (Fig. 1). In this context, it is planned to utilized two synthetic methods: photocyclization [6] and cyclization of aryl iodides supported by TMS_3SiH [7]. Synthesized diradical materials will be investigated for their spectroscopic (UV-vis, EPR), electrochemical, and magnetic (SQUID) properties.

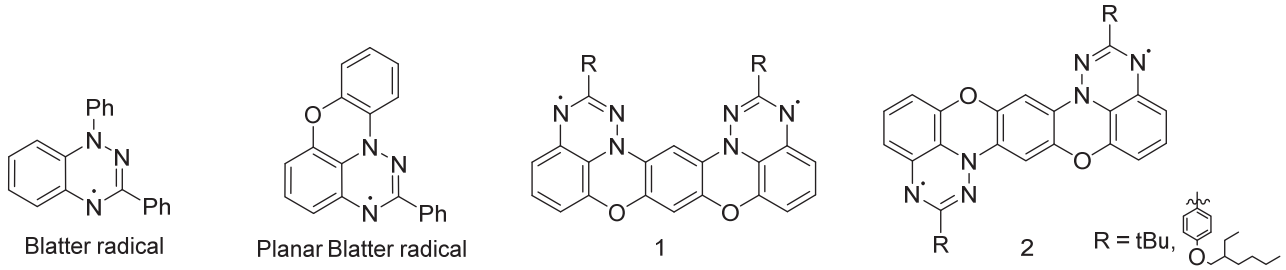

Figure 1. Blatter radical, planar Blatter radical and benzotriazinyl diradicals planned to obtain.

Acknowledgement
The research was financed by a Student Research Grant from the University of Lodz.

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P-114

Synthesis and *in vitro* study of anticancer activity of novel *N*-(4-cyano-1,3-oxazol-5-yl)sulfonamide derivatives

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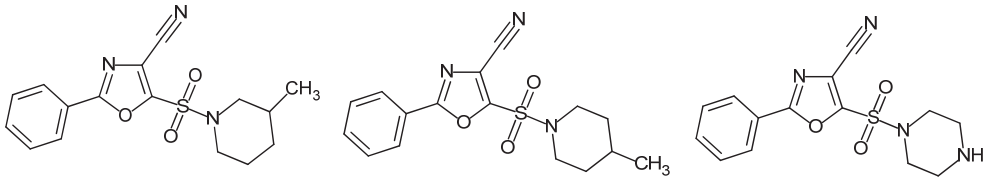
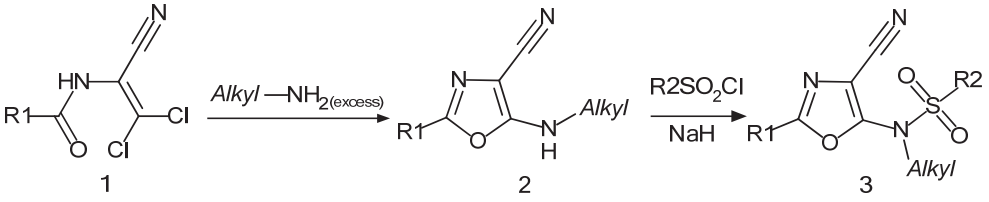
1,3-Oxazolesulfonamides are considered as perspective anticancer agents [1,2]. In [3] the influence of sulfonamide group linked to oxazole ring is discussed to explain the mechanism of pharmacological activity. As you can see, the sulfonamide group in these structures is directly connected to the oxazole ring:



The logical continuation of these works is the synthesis and study of the biological activity of new representatives of such structures, as well as compounds with a sulfonamide group in the side chain. The available dichloroacrylonitriles **1** were chosen as the starting compounds [4] for the synthesis of 4-cyano-5-amino-1,3-oxazoles **2** (Scheme 1) [4]. The reaction of a series of sulfonyl chlorides with 5-amino-1,3-oxazoles **2** occurs in the presence of sodium hydride with forming of oxazolesulfonamides **3** in yields of 68–81%.



Scheme 1. Synthesis of novel *N*-(4-cyano-1,3-oxazol-5-yl)sulfonamide derivatives **3.**

The novel series of synthesized *N*-(4-cyano-1,3-oxazol-5-yl)sulfonamide derivatives **3** displayed different anticancer activity. Among them two compounds (*N*-(4-cyano-2-phenyl-1,3-oxazol-5-yl)-*N*,4-dimethylbenzenesulfonamide and *N*-(4-cyano-2-(thiophen-2-yl)-1,3-oxazol-5-yl)-*N*,4-dimethylbenzene-sulfonamide) displayed inhibitory activity within GI_{50} parameter in five dose analyses. But their cytostatic activity was observed against only several cancer cell lines and cytotoxic concentration was outside the maximum used, i.e. > 100 μM. Therefore, in view of the positive results N-(4-cyano-1,3-oxazol-5-yl)sulfonamides may be promising for further functionalization to obtain more active compounds.

Acknowledgement
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P-115

Synthesis of organometallic analogues tariquidar

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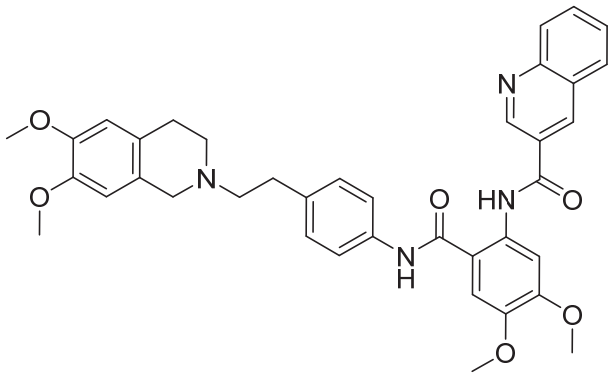
One of the factors responsible for the failure of chemotherapy in treating cancer is the overexpression of ABC transporters, particularly ABCB1, ABCG2, and ABCC1. Inhibiting their activity with a low-molecular-weight inhibitor can sensitize resistant cancer cells to commonly used chemotherapeutics. We have shown that introducing a ferrocenyl substituent into the cytotoxic molecule of plinabulin turned out the organometallic analogue to ABC proteins inhibitor[1]. Continuing our research in developing new organometallic inhibitors of ABC proteins, we synthesized a series of organometallic analogues of Tariquidar (Figure 1). In this presentation, we will discuss the synthesis of organometallic analogs of tariquidar and present the results of biological activity studies of the obtained compounds.



Tariquidar

Figure 1. The structure of Tariquidar.

Acknowledgement

This research was financially supported by the National Science Centre (NCN) grant 2018/29/B/ST5/01736.

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P-116

Electrochemical studies of metallocarbonyl complexes with imides

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The chemistry of organometallic transition metal complexes of biologically important ligands is a field of research within the relatively new branch of organometallic chemistry and bioorganometallic chemistry.

Succinimides have a diverse range of biological functions, which is of interest to many scientists. In my university laboratory, methods of introducing the $CpFe(CO)_2$ group ($Cp=\eta5\text{-}C_5H_5$) into such ligands containing acidic NH bonds were developed, based on the photochemical substitution of iodide in $CpFe(CO_2I)$ leading to the formation of 3-substituted metallocarbonyl complexes (Fe, Ru) with maleimide and succinimide ligands (Fpm, Rpm and Fps). These complexes were obtained in the presence of K_2CO_3 during the reaction of oxa-Michael $CpM(CO)_2$ (1-maleimidato) (M = Fe, Ru) with alcohols (MeOH, EtOH). Metallocarbonyl complexes containing succinimides can serve as modern compounds overcoming antibiotic resistance. One of the ways of pharmacological action of this type of compounds are redox reactions leading to the disruption of cellular processes.

One of the commonly used electrode materials for the electrochemical analysis of organic compounds is glassy carbon. Glassy carbon is electrochemically inert, dense and hard as glass, impervious to gases and liquids, and has a large potential window.

The aim of the presented work was to determine the electrochemical activity of newly synthesized imide complexes such as Fpm, Rpm and Fps.

The characteristics of the working glassy carbon electrode were determined in a solution of the standard Fe(III)/Fe(II) redox system using cyclic voltammetry (CVC) and electrochemical impedance spectroscopy (EIS). Determination of the topographic properties of the GC electrode surface was carried out using an atomic force microscope (AFM). The electrochemical properties of the imide complexes were studied in Britton-Robinson buffer solutions at different pH 5, 7 and 10 using cyclic voltammetry (CVC) and electrochemical impedance spectroscopy (EIS).

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P-117

Structural studies of darifenacin free base hydrate

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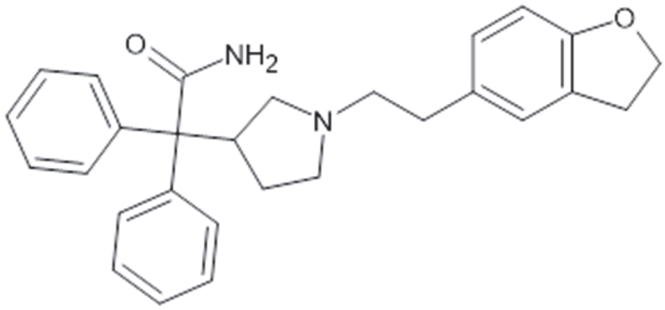
Among benzofuran derivatives, we can find many compounds with high biological activity. They are widely used as antidepressants, anticancer, antifungal, and heart drugs [1]. One of the benzofuran derivatives is darifenacin, which is used to treat overactive bladder [2]. In the literature, we find only one solved crystal structure of darifenacin, where darifenacin occurs in the form of hydrobromide. The remaining known crystal forms are the toluene solvate and the hydrate, but they are characterized only by IR spectroscopy, powder diffraction, and differential scanning calorimetry. Darifenacin free base occurs in an amorphous form.



Scheme 1. The structural formula of darifenacin free base.

In this work, I present two methods of preparing darifenacin hydrate and the crystal structure determined by X-ray analysis of single crystals. What's more, there the attempt to thermal removal of the water molecule from darifenacin hydrate controlled by PXRD is shown.

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P-118

2,7-diadamantylpyrene as a precursor of new fluorophores

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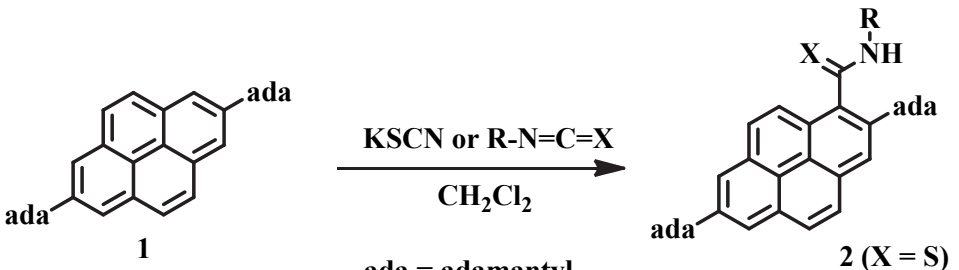
Pyrene and its derivatives are among the fluorophores with unique physicochemical properties - high quantum efficiency of fluorescence or emission dependent on the environment surrounding the fluorophore. Moreover, they show strong fluorescence in living cells with very low cytotoxicity, which means that they can be used as fluorescent probes. [1]

The above-mentioned photophysical properties, both in solution and in solid state, make pyrene derivatives one of the most promising fluorophores for the preparation of organic optoelectronic materials, as well as for applications in fluorescence microscopy or as an environmental probes [2].

In this communication, we want to present the synthesis, photophysical and biological studies of new derivatives based on the 2,7-diadamantylpyrene skeleton. We have shown that 2,7-diadamantylpyrene, similarly to 2,7-ditertbutylpyrene [3], undergoes a modified Friedel-Crafts-type reaction with isocyanates or isothiocyanates in the presence of triflic acid, giving amides and thioamides in high yields (Scheme 1.). The obtained compounds show a number of interesting photophysical properties that may be attractive in the design of new organic materials emitting light of a specific color and may be used in fluorescence microscopy as fluorescent probes or pH sensors, as well as for the visualization of biologically active compounds in cells.



ada = adamantyl
X = O, S
R = -H, -Et, -*i*Pr, -n-Bu, -*t*-Bu, -n-hexyl, -cyclohexyl, -Ph;

Scheme 1.

Acknowledgement
This research was funded by University of Lodz, grant number 4/DGB/2022.

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P-119

The use of triflic acid in the synthesis of new pyrene fluorophores

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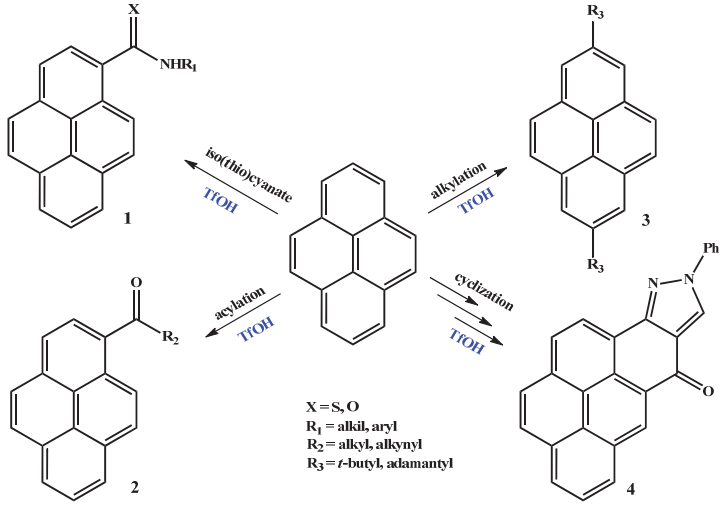
Pyrene and its derivatives have found application in many areas of science, technology and life. Due to the high application potential, methods of modification the pyrene system which leads to new derivatives are still being sought [1]. In recent years, we have proposed several solutions to obtain new pyrene fluorophores with interesting photophysical properties, both in solutions and in solid state. Trifluoromethanesulfonic acid (CF_3SO_3H, triflic acid, TfOH) turned out to be particularly useful for us in the synthesis of these pyrene derivatives (Scheme 1). Triflic acid, due to increased thermal stability and resistance to oxidation and reduction, is particularly useful as a reagent and solvent in organic synthesis. We have shown that the Friedel-Crafts reaction of pyrene or 2,7-di-*ter*t-butylpyrene with alkyl and aryl isocyanates and isothiocyanates, carried out in the presence of trifluoromethanesulfonic acid, allows obtaining the corresponding amides and thioamides **1** in high yields (85-95%) [2, 3]. In recent years, we have also demonstrated the great utility of TfOH in the acylation (**2**) and alkylation (**3**) of pyrene. In addition, triflic acid was used by us for the cyclization reaction, as a result of which we obtained type **4** of fluorophores.



Scheme 1. Application of triflic acid in the synthesis of pyrene derivatives.

Acknowledgement
This research was funded by University of Lodz, grant number 9/GNZPA/2022.

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P-120

Synthesis of metallocarbonyl derivatives of bisphosphonates and bisphosphonic acids

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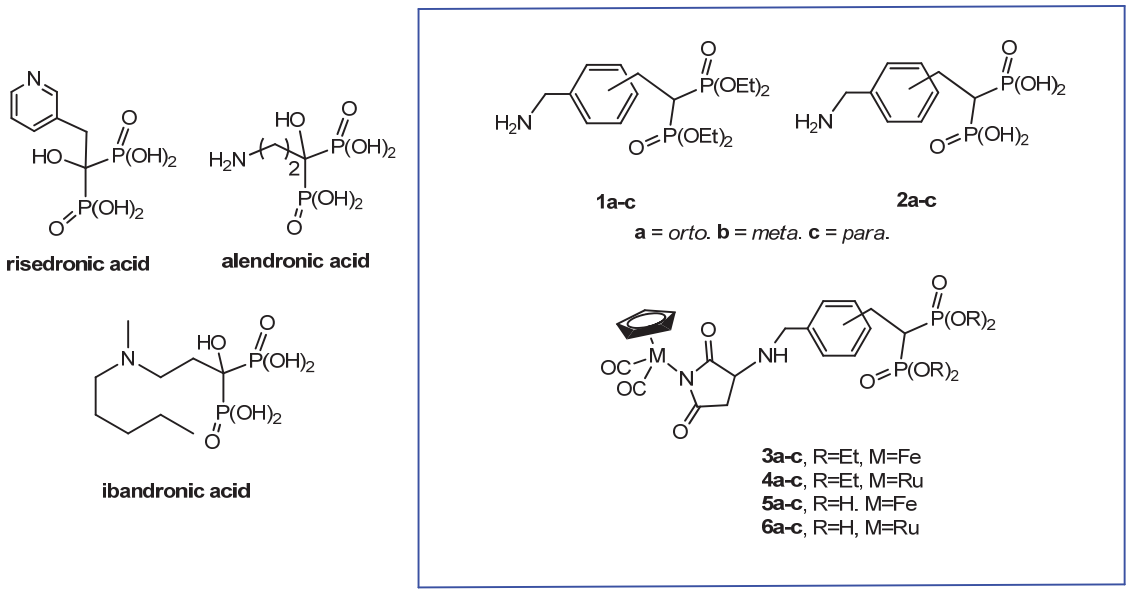
Organophosphorus compounds, which include bisphosonans and bisphosonic acids, are characterized by high biological activity. Thanks to this, they are used as drugs for osteoporosis, Paget's disease, bone metastases and multiple myeloma. Bisphosphonates used in medicine include: etidronate, alendronate and risendronate, alendronate, ibandronic acid, etc. Unfortunately, they can cause quite serious side effects, ranging from jaw necrosis through atrial fibrillation, excessive inhibition of bone remodeling, hypocalcemia, inflammatory reactions in muscles and bone ache. For this reason, new therapeutic molecules that do not cause such severe side effects are constantly being sought.[1]

Therefore, it seems advisable to introduce an organometallic group into the structure of bisphosphonates or bisphosphonic acids, which may change their physicochemical properties and biological activity.



Scheme 1. Bisphosphonic acids used in medicine and their new analogues.

Acknowledgement
This research was funded by University of Lodz, grant no. IDUB 38/2021.

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P-121

Acylation of electron-rich arenes with unprotected amino acids

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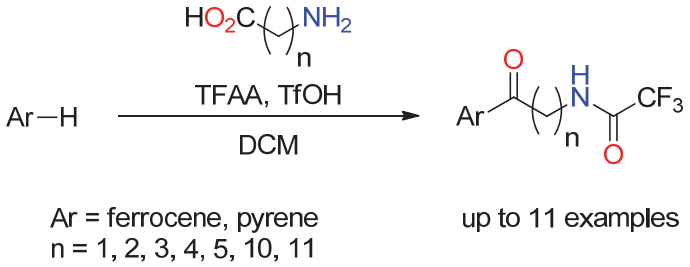
Aminoketones are an important class of organic compounds. They play an important role as a high-value synthons in synthetic and medicinal chemistry. The most notable examples are Bupropion, Amfepramone, Tolperisone and Oxyfedrine [1,2]

Herein we reported the synthesis of the *N*-trifluoroacetyl amidoketones by direct acylation of electron-rich arenes (ferrocene and pyrene) with unprotected amino acids. The acylation is achieved with the use of trifluoroacetic anhydride/triflic acid system, previously used for functionalization of ferrocene and pyrene with carboxylic acids.[3, 4]

We postulate mechanism that includes in situ conversion of unprotected amino acids to reactive *N*-trifluoroacetamides mixed anhydride species. Protonated by triflic acid they generate appropriate carbocations which attacks the electron-rich arenes to form *N*-trifluoroacetic amidoketones.

The obtained *N*-trifluoroacetyl amidoketones can be easily deprotected and converted to corresponding aminoketones. Both ferrocenyl and pyrenyl amidoketones can be used as versatile building blocks for syntheses of more complex compounds, like molecular probes or optoelectronic materials.



Scheme 1. Acylation of electron-rich arenes with unprotected amino acids.

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P-122

Fujiwara-Moritani reaction of ferrocene and chalcones containing a *"push-pull"* system in the molecule

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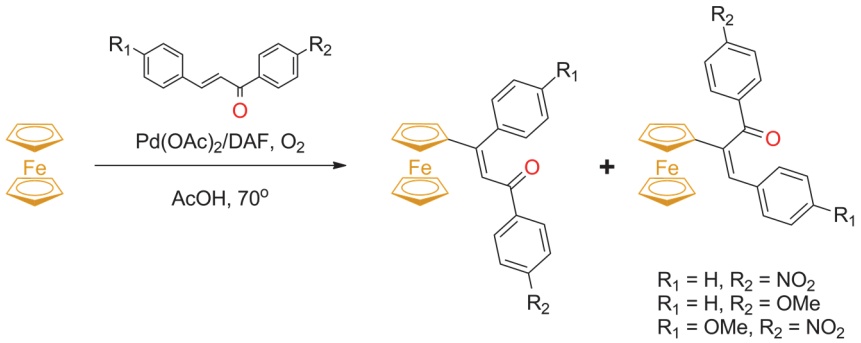
Compounds exhibiting nonlinear optical properties (NLO) are widely used in fields such as photonics, nanophotonics and electro-optics. Among the compounds exhibiting nonlinear optical properties, an important place is occupied by ferrocene derivatives containing the so-called *"push-pull"* system, i.e. electron-donating and electron-withdrawing groups connected by a system of conjugated π bonds.[1] This communication presents the synthesis of new chalcone derivatives of ferrocene with potential non-linear optical properties, using the Fujiwara-Moritani reaction, which is an oxidative variant of the Heck reaction.[2 ,3]

X-ray structural tests were carried out for the obtained products, which allowed to confirm the structure of the obtained *"push-pull"* systems.



Scheme 1. Synthesis of ferrocene and chalcone derivatives with electron-donating and electron-withdrawing substituents.

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P-123

Reactions of elemental sulfur and sulfur donors with selected organophosphorus derivatives under mechanochemical conditions

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In the times of "greening and reducing the level of pollution" in synthetic organic chemistry mechanochemical solvent-free reactions by milling, grinding or other types of mechanical action have emerged as a viable alternative to reactions carried out in solution [1]. Extending our very recent research on the synthetic and stereochemical aspects of transformation of achiral and chiral heterorganic derivatives under mechanochemical conditions [2] we started experiments on the use of this methodology in the transformation of basic phosphorus-containing functional groups. Preliminary results of experiments on the reactions of elemental sulfur and sulfur donorswith several model organophosphorus derivatives will be presented in this communication.

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P-124

Attempts at enzyme-promoted addition of nitromethane to nitrones and iminium salt

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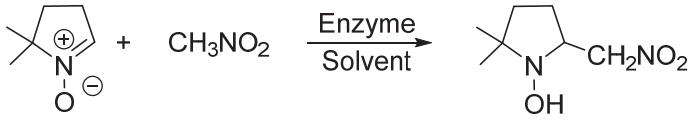
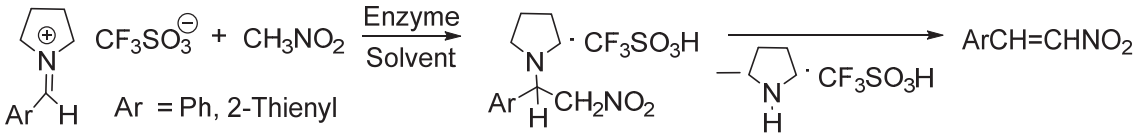
Enzyme catalytic promiscuity is a remarkable property that enables a single enzyme active site to catalyze multiple chemical transformations, including those that differ from natural processes.[1,2] Our recent report on the enzyme-catalyzed addition of nitromethane to aldimines (the aza-Henry reaction) produced highly valuable β-nitroamines. However, we were disappointed to find that this reaction is non-stereoselective.[3]

Looking for other solutions, we decide to use various types of imine analogues. Initially, we added nitromethane to several nitrones, but only one of them (illustrated in Scheme 1) was effective. Moreover, the yield and enantiomeric excess were not satisfactory.



Scheme 1. Enzyme promoted addition of nitromethane to nitrones.

Next, we focused our attention on iminium salts. Their reaction with nitromethane yielded not only the desired adduct but also unexpected by-products, among them 2-nitroethenylarenes resulting from the retro-Michael elimination of the ammonium salt (Scheme 2).



Scheme 2. Enzyme promoted addition of nitromethane to iminium salts.

Ongoing investigations are being conducted to prevent the subsequent reaction. The results will be discussed.

Acknowledgement

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P-125

Additive Effects of Copper-Catalyzed Addition of Aryl Boronic Acid to Benzoquinones

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The p-quinol moiety is a key structural motif found in numerous natural products (ie Trigonochinene B isolated from Trigonostemon heterophyllus), pharmaceutically relevant compounds (ie Denudatin B, antiplatelet activity and high selectivity to inhibit of cyclooxygenase 1 (COX1), or Robutaside D, antimalarial activity against resistant Plasmodium falciparum), and synthetic building blocks (Figure 1). In particular, both low molecular Graviquinone and Jacaranone, as well as high molecular Robutaside, expose selective and high cytotoxicity against cancer cell lines [1].

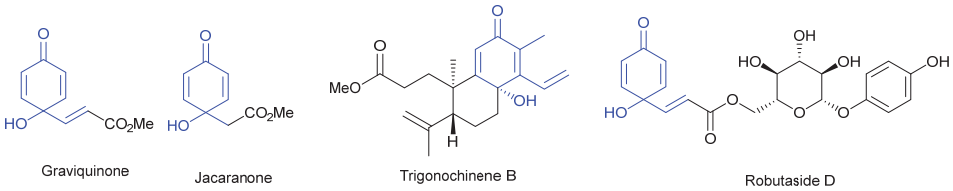
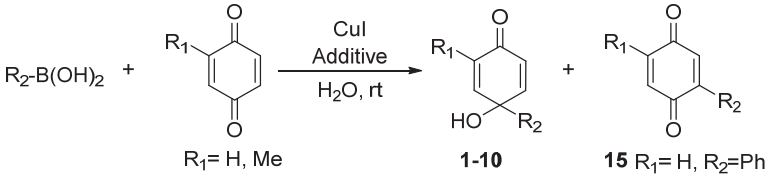


Figure 1. Examples of biologically active p-quinol derivatives.

Recently, we have published a sustainable method for the synthesis of p-quinols based on the copper-catalysed addition of phenylboronic acid to quinone that leads to carbon-carbon bond formation under aqueous conditions [2,3]. However, the target products were obtained with moderate yields. Additionally, formed side-products hampered. The mild and efficient protocol for the synthesis of p-quinols under aqueous conditions was developed [4]. The pivotal role of additives on copper-catalyzed addition of aryl boronic and heteroaryl boronic acids to benzoquinones was observed (Scheme 1).



Scheme 1. Copper catalyzed 1,2-addition of boronic acid derivatives to 1,4-benzoquinones.

The results of our studies on additivies impact on the reaction course leading to the target *p*-quinols will be presented (Scheme 1) [4]. The influence of the reaction conditions, reaction media and additive type on the reaction course will be discussed.

Acknowledgement
The work was supported by the National Science Centre, Poland, under research project Opus no 2019/33/B/ST4/01118.

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P-126

Synthesis and modifications of fluorescent 10-antrylphosphonates

Łucja Knopik[1,2], Marek Koprowski[1], Bogdan Dudziński[1], Krzysztof Owsianik[1], Vivek[1,2], Piotr Bałczewski[1,3], Ewa Różycka-Sokołowska[3]

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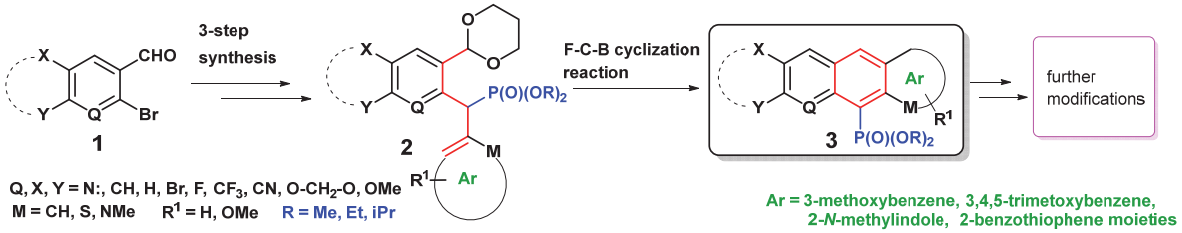
Phosphonates play an important role in many fields of chemistry [1]. Anthrylphosphonates, in which the phosphorus atom of the phosphonate group is directly bonded to the aromatic carbon atom of anthracene, are becoming increasingly useful in materials chemistry [2]. Despite the promising properties of the compounds discussed, anthrylphosphonates and their derivatives have not been sufficiently explored. Moreover, such systems with a high degree of substitution are practically unknown.



Scheme 1. A new method of synthesis of dialkyl 10-anthrylphosphonates.

In this communication, we introduce a new phosphorus variant of the Friedel-Crafts-Bradsher cyclization reaction which enables the preparation of multiply substituted 10-antrylphosphonates **3** (Scheme 1), as well as further modifications of these compounds. We also present, the photophysical properties of the obtained phosphonates and show that introducing various functional groups of highly differentiated electron properties onto the anthracene ring using the F-C-B reaction allows these properties to be modified. As a result, the highest photoluminescence quantum yields were obtained in this group of compounds.

Acknowledgement

This research was funded by the National Science Center, grant number UMO-2019/33/B/ST4/02843.

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P-127

Highly Substituted 10-Phosphinoyl Anthracenes *via* the P-O-C to P(=O)-C Rearrangement and the *phospho*-Friedel-Crafts-Bradsher Reaction

Vivek[1,2], Marek Koprowski[1], Krzysztof Owsianik[1], Łucja Knopik[1,2], Ewa Różycka Sokołowska[3], Piotr Bałczewski[1,3]

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A series of unknown 10-phosphinoyl anthracenes (**ANT 1-10)** was synthesized *via* the P-O-C to P(=O)-C rearrangement and the *phospho*-Friedel-Crafts-Bradsher reaction, and fully characterized. All the anthracene derivatives (**ANT 1-10)** were synthesized in a one-pot, three-step reaction. Initially, the process involved the conversion of the dibenzylic alcohols **3(a-j)** into the phosphinite intermediates **4** using NEt_3 and PPh_2Cl, which were then rearranged to phosphine oxide **5** using trimethylsilyl trifluoromethanesulfonate.[1] Subsequently, the mixture underwent cyclization through the novel *phospho*-Friedel-Crafts-Bradsher reaction (*phospho*-F-C-B) under acidic conditions.[2] The obtained group of compounds will be further investigated to assess their viability in organic optoelectronics by analyzing their photophysical, photochemical, and thermal properties

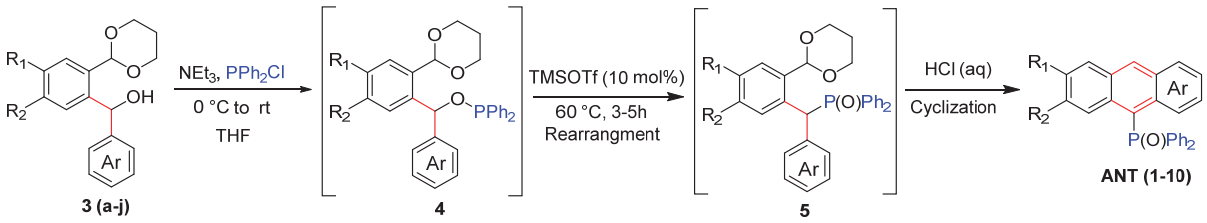

Figure 1. Synthesis of 10-phosphinoyl anthracenes **ANT(1-10)** from the dibenzyl alcohol **3(a-j)**.

Acknowledgement

This research was funded by the National Science Center (Poland), grant number 2019/33/B/ST4/02843 (2019–2024). And, I would like to acknowledge the Bio-Med-Chem Doctoral School at the University of Łódź and Łódź Institutes of the Polish Academy of Sciences for sponsoring this conference.

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P-128

Asymmetric addition of phenylboronic acids to aldehydes catalyzed by modified amino alcohols from (+)-α-pinene

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The addition reactions of Grignard and organolithium compounds to aldehydes and ketones are an effective method for forming carbon-carbon bonds to give secondary and tertiary alcohols. Unfortunately, controlling the enantioselectivity of such reactions remains a major challenge. [1] For zinc-organic compounds, methods have been developed for their activation with chiral ligands and asymmetric additions of alkyl, aryl and alkynyl groups. [2]

Enantioselective arylation of aldehydes in the presence of chiral ligands gives optically active diarylmethanols, important precursors of pharmacological compounds such as antihistamines ((*R*)-neobenodine, (*S*)-carbinoxamine), antiarrhythmics, antidepressants, laxatives and anticholinergics ((*R*)-orphenadrine) (Fig. 1). Other compounds with similar structural features also demonstrate biological activity. [3]

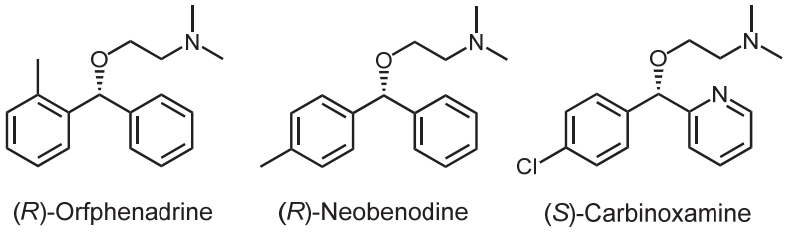

Figure 1. Structures of (R)-orphenadrine, (R)-neobenodine, and (S)-carbinoxamine.

In the presented research, phenylboronic acid addition reactions to aldehydes were carried out in the presence of diethyl zinc and 10% of the catalyst, which were modified β-amino alcohols obtained from (+)-α-pinene. The influence of the structure of aldehyde and boronic acid on the enantiomeric excesses of the obtained alcohols was examined. The enantioselectivity of the reaction was determined by HPLC analysis on chiral stationary phase columns.

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P-129

Application of modified Still-Gennari type reagents for highly *Z*-selective synthesis of trisubstituted alkenes

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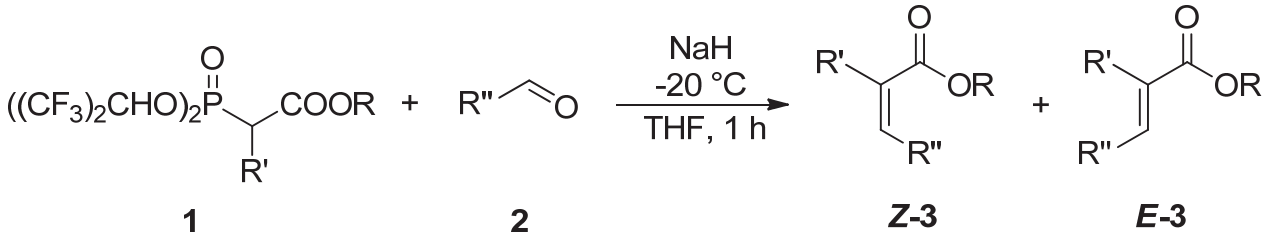
Z-selective Still-Gennari modification of typically *E*-selective Horner-Wadsworth-Emmons (HWE) reaction is a widely applied, highly stereoselective olefination method allowing access to *Z*-olefins by carbonyl group transformation.[1,2] The procedure is based on application of bis(2,2,2-trifluoroethyl) phosphonates for the olefination of carbonyl group at low temperature, in presence of strong base – typically KHMDS with 18-crown-6 additive at -78 °C.

In this communication we would like to present application of novel Still-Gennari type reagents (bis(1,1,1,3,3,3-hexafluoroisopropyl) phosphonates) for the synthesis of trisubstituted alkenes. A series of trisubstituted alkenes was obtained using these reagents with very high stereoselectivity and very good yields.



Scheme 1. New Still-Gennari type reagents for *Z*-selective synthesis of trisubstituted alkenes.

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P-130

The “one-pot” synthesis method of tetrahydroquinolone derivatives

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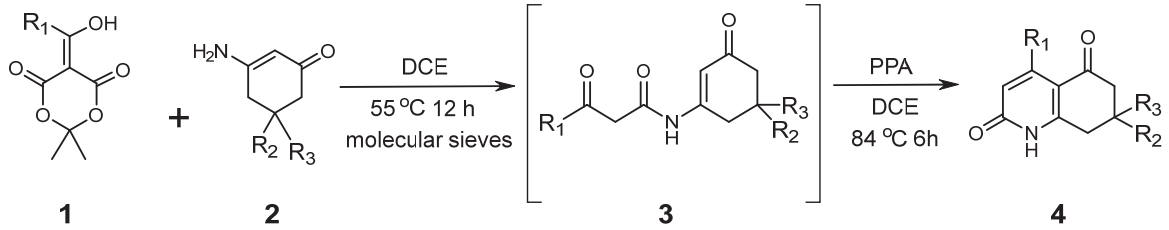
Quinolone derivatives constitute one of the most important drugs in medicine. These compounds are used in antibacterial, antimalarial, antifungal, and anticancer therapy. [1] In 2022, we published two works devoted to the design and synthesis of new 4-phenyl-5,6,7,8-tetrahydroquinolin-2(1H)-one derivatives. Several of them have shown attractive anticancer activity. [2,3] Our next project concerned the design and optimization of a "one-pot" synthesis method enabling the obtainment of the desired tetrahydroquinolone cores more quickly and cost-effectively. We proposed the condensation of acyl/aroyl Meldrum's acid derivatives (**1**) with enaminones (**2**), which resulted in the desired intermediates (**3**). Next, the obtained enamides were subjected to intramolecular cyclization without prior isolation. As a result, a series of the planned tetrahydroquinolone cores (**4**) was achieved. The yielding of the designed "one-pot" method ranged from 20 to 37% and was comparable or higher than the yielding of procedures known from the literature.



1 **2** **3** **4**

Scheme 1. The “one-pot” synthesis of tetrahydroquinolone cores.

Acknowledgement

The financial support to maintenance of research facilities used in these studies from Gdańsk University of Technology by the DEC--2/2021/IDUB/V.6/Si grant under the SILICIUM SUPPORTING CORE R&D FACILITIES “Excellence Initiative—Research University” program is gratefully acknowledged.

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No.	Presenting Author	Poster Title
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P002	Jusufi Kaltrina	*A Sustainable Method for Using Biosorbents for removal of organic dyes*
P003	Ismaili Mentor	*Examining the Fatty Acid Profile of the Calf Meat: Investigating the Relationship with Pasture and Food Farming Systems*
P004	Rozbicki Przemysław	*Oxidative halogenation of a thiol/disulfide containing a 1,2,4-triazine ring*
P005	Wzgarda-Raj Kinga	*X-ray studies of three 3,6-bis(pyridin-2-yl)-1,2,4,5-tetrazine cocrystals: an unexpected molecular conformation stabilized by hydrogen bonds*
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P015	Miksa Beata	*Yeast vehicles as templates for hybrid bioinspired poly(dopamine/phenosafranin) microparticles with immobilized Myoglobin retaining compromise activity*
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P017	Sowa Sylwia	*The fluorescent properties of 3-arylbenzo[b]phosphole oxides*
P018	Sowa Sylwia	*The investigation of the reactivity of benzophosph-3-yl triflates*
P019	Kawka Anna	*Synthesis and theoretical studies of new steroid bioconjugates containing 1,2,3–triazole rings*
P020	Hoelm Marta	*Theoretical search for the most stable structure of a potential drug carrier containing cellobiose units*
P021	Trzeciak Katarzyna	*Amorphization of Ethenzamide and Ethenzamide Cocrystals - Study of Single and Binary Systems Forming Low-Melting Eutectic Phases Loaded on/in Silica Gel*
P022	Olszewski Tomasz	*α-Amido sulphones as useful intermediates in the preparation of C-chiral α-aminophosphonates and α-aminophosphonic acids*

P023	Makieieva Natalina	*Theoretical characterization of structural and NMR parameters of coptisine alkaloid from Chelidonium majus L.*
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P026	Paprocka Renata	*Synthesis and antiproliferative activity on new cyclohex-3-ene-1-carboxylic acid derivatives*
P027	Piórecka Kinga	*Is acriflavine an efficient co-drug in chemotherapy?*
P028	Baumgart Szymon	*2-(cyclohexylamino)thiazol-4(5H)-one derivatives as 11β-hydroxysteroid dehydrogenase type 1 inhibitors – synthesis and in vitro studies*
P029	Milczarek Małgorzata	*Anticancer effect of 5-fluorouracyl and 4-isoselenocyanato-1-butyl 4'-fluorobenzyl sulfoxide combined treatment in in vivo model of triple negative breast cancer*
P030	Pogorzelska Anna	*Antitumour and antimetastatic activity of dietary dose of sulforaphane in the model of triple-negative breast cancer*
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P043	Fedorowicz Joanna	*Synthesis of 1,1-dialkylpiperazinium derivatives of 6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid with potential antibacterial and antibiofilm activity*
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P045	Jarończyk Małgorzata	*On Integral INICS Aromaticity of Pyridodiazepine Constitutional Isomers and Tautomers*

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P053	Jastrzębska Katarzyna	*Manual Solid-Phase and Solution-Phase Syntheses of P-stereodefined of morpholino dinucleoside 3',6'-thiophosphoramidates*
P054	Koronkiewicz Mirosława	*Study of the cytotoxic and antimicrobial activity of new rhenium complexes*
P055	Cal Dariusz	*A convenient synthesis of ω -hydrazinoalkylphosphonic acids*
P056	Kulik Katarzyna	*Reactivity of the tRNA wobble 5-methylaminomethyl-2-selenouridine under oxidative and reducing stress conditions.*
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P058	Demchuk Oleg M.	*Arylcyanomethylenequinone oximes the potent antifungal agents*
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P060	Kowalczyk Mateusz	*A Comparison of Reactivity of Enolizable Tetrazole-5-thiones and other Mercapto Azoles in Reactions with D-A cyclopropanes*
P061	Bartos Paulina	*New methods for the preparation of ring-fused π-delocalized stable radicals*
P062	Janczewski Łukasz	*Synthesis of 6-(isothiocyanatohexyl)phosphonates conjugated with Altretamine as a novel class of potential anticancer compounds*
P063	Banach Łukasz	*Synthesis and study of hemostatic and antibacterial activity of novel compounds containing ciprofloxacin and lysine analogues with hemostatic activity*
P064	Zaręba Przemysław	*New chlorinated N-(1,4-dihydroquinazolin-2-yl)naphthalene-1-sulfonamide as a new, low-basic 5-HT6R ligands*
P065	Tejchman Waldemar	*The unexpected effect of Biginelli's reaction*
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P090	Jędrzejczak Piotr	*Search for new selective drug delivery systems for lung cancer treatment - designing and synthesis of s-triazine - peptide conjugates*
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