XXI INTERNATIONAL SYMPOSIUM „ADVANCES IN THE CHEMISTRY OF HETEROORGANIC COMPOUNDS”

Centre of Molecular
and Macromolecular Studies
Polish Academy of Sciences

Section
of Heteroorganic Chemistry
Polish Chemical Society

ŁÓDŹ
November 23, 2018

XXI INTERNATIONAL SYMPOSIUM „ADVANCES IN THE CHEMISTRY OF HETEROORGANIC COMPOUNDS”

ORGANIZED BY

Centre of Molecular
and Macromolecular Studies
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Section of Heteroorganic Chemistry
Polish Chemical Society

in cooperation with

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Faculty of Mathematics
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XXI International Symposium
"Advances in the Chemistry of Heteroorganic Compounds"

is dedicated to

Professor
Tadeusz Gajda

and

Professor
Janusz Zakrzewski

on the occasion of their 70th birthday

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

Programme

Friday, November 23		
9:00 – 9:30	**OPENING**	
SESSION I – chairman: **Tadeusz Gajda**		
9:30 – 10:15	PL-1	**Stefano Menichetti** *University of Florence, Italy* Synthesis and selected properties of heterohelicenes: A new twist on our chemistry
10:15– 11:00	PL-2	**György Keglevich** *Budapest University of Technology and Economics, Hungary* Microwave irradiation and catalysis in organophosphorus chemistry – green synthesis of organophosphorus compounds
11:00 – 11:20	**COFFEE BREAK**	
11:20 – 12:50	**POSTER SESSION**	
12:50 – 13:50	**LUNCH**	
SESSION II – chairman: **Janusz Zakrzewski**		
13:50 – 14:35	PL-3	**Peter Metz** *Technische Universität Dresden, Germany* Total Synthesis of Diterpene Natural Products
14:35 – 15:20	PL-4	**Claudio Santi** *University of Perugia, Italy* Organoselenium Compounds in Catalytic Reactions
15:20– 16:05	PL-5	**Masaichi Saito** *Saitama University, Japan* Expansion of Aromaticity: From π-Aromaticity to σ+π-Double Aromaticity
16:05 – 16:35	PL-6	**Luca Sancineto** *Centre of Molecular and Macromolecular Studies* *Polish Academy of Science, Poland* *University of Perugia, Italy* An Organoselenium Catalyzed Strategy for Oxidation Reactions Compounds
16:35 – 16:50	**CLOSING**	
PL - plenary lecture		

PLENARY LECTURES

PL-1

Synthesis and selected properties of heterohelicenes: A new twist on our chemistry

Stefano Menichetti and Caterina Viglianisi

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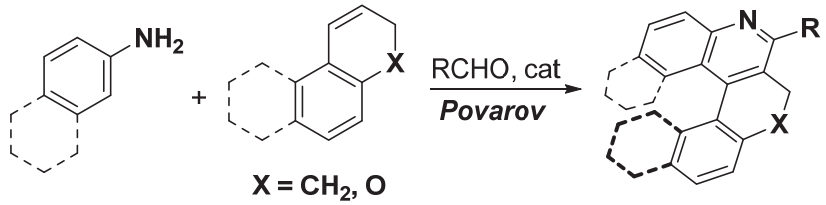
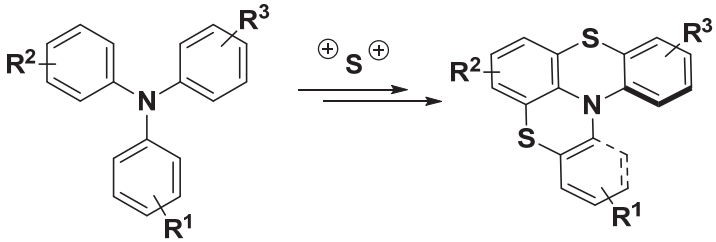
Helicenes and heterohelicenes are challenging chiral structures that continuously stimulate new interest and find new applications. From just a chemical curiosity related with their inherent chirality, these compounds are now commonly used in asymmetric synthesis, medicinal chemistry and, above all, material science.[1] In the last years we became interested in the chemistry of heterohelicenes and we described new approaches for their synthesis. For example, we demonstrated that with the proper design of the reagents, the Povarov reaction can be exploited for the synthesis of [4], [5] and [6]azahelicenes.[2]



At the same time we showed that thia-bridged triarylamine[4]helicenes can be prepared using consecutive regioselective electrophilic sulfur insertions on triarylamines or *N*-arylphenothiazines.[3] Due to the length of the four carbon-sulfur bonds, these peculiar systems belong to the valuable family of stereochemically stable [4]helicenes with racemization barriers as high as 31-32 Kcal/mol.



In this communication, scope and limitation of the above procedures as well as preliminary investigations of the properties of these heterohelicenes will be discussed.

References

[1] a) Y. Shen, C-F. Chen *Chem. Rev*. **2012**, *112*, 1463–1535; b) M. Gingras *Chem. Soc. Rev*. **2013**, *42*, 968-1006.

[2] C. Viglianisi, C. Biagioli, M. Lippi, M. Pedicini, C. Villani, R. Franzini, S. Menichetti, *Eur. J. Org. Chem*. **2018**, DOI: 10.1002/ejoc.201801489.

[3] a) G. Lamanna, C. Faggi, F. Gasparrini, A. Ciogli, C. Villani, J. P. Stephens, J. F. Devlin,; S. Menichetti, *Chem-Eur. J.*, **2008**, *14*, 5747-5750. b) S. Menichetti, C. Faggi, M. Onori, S. Piantini, M. Ferreira, S. Rocchi, M. Lupi, I. Marin, M. Maggini, C. Viglianisi, *Eur. J. Org. Chem*. **2018**, DOI: 10.1002/ejoc.201801493.

PL-2

Microwave irradiation and catalysis in organophosphorus chemistry – green synthesis of organophosphorus compounds

Dedicated to Prof. Marian Mikołajczyk on the occasion of his 80th Birthday

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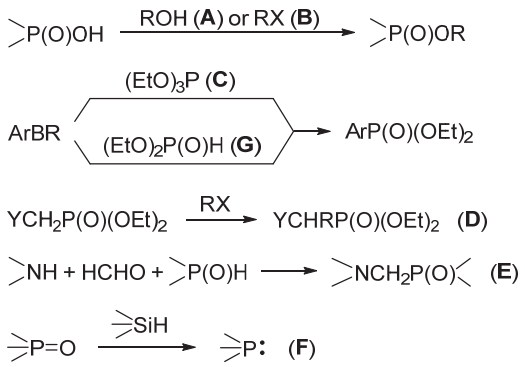
The microwave (MW) technique has become an important tool in organophosphorus chemistry [1–3]. In this paper, the advantages of MWs in different catalytic reactions are surveyed. The first case is, when the MW-assisted direct esterification of phosphinic acids becomes more efficient in the presence of an ionic liquid catalyst (**A**) [4]. The second instance is, when catalytic reactions, such as the phase transfer catalyzed (PTC) O-alkylation of phosphinic acids (**B**), or the Arbuzov reaction of aryl bromides (**C**) are promoted further by MW irradiation. It is also an option that MWs may substitute catalysts, such as in the PTC alkylation of active methylene containing P-derivatives (**D**) [5], in Kabachnik–Fields condensations (**E**) [6], and in reluctant P=O deoxygenations (**F**) [7]. Another valuable finding of ours is that in the Hirao P–C coupling applying $Pd(OAc)_2$ as the catalyst, the slight excess of the >P(O)H reagent may substitute the usual P-ligands (**G**) [8].



It is also the purpose of this paper to elucidate the scope and limitations of the MW tool [2,3], to interpret the special MW effects, and to model the distribution and effect of the local overheatings [9,10]. All these considerations were possible on the basis of the results of our quantum chemical calculations, and utilizing the pseudo first order kinetic equation and the Arrhenius equation.

References

[1] G. Keglevich, E. Bálint, N. Z. Kiss, in: *Milestones in Microwave Chemistry – SpringerBriefs in Molecular Science*, Ed.: G. Keglevich; Springer, Switzerland, **2016**, pp. 47-76.
[2] G. Keglevich, N. Z. Kiss, A. Grün, E. Bálint, T. Kovács, *Synthesis*, **2017**, *49*, 3069.
[3] G. Keglevich, *Chem. Rec.*, **2018**, in press.
[4] N. Z. Kiss, G. Keglevich, *Tetrahedron Lett.*, **2016**, *57*, 971.
[5] G. Keglevich, E. Bálint, A. Grün, *Catalysts*, **2015**, *5*, 634.
[6] G. Keglevich, E. Bálint, *Molecules*, **2012**, *17*, 12821.

[7] T. Kovács, G. Keglevich, *Curr. Org. Chem.*, **2017**, *21*, 569.
[8] G. Keglevich, R. Henyecz, Z. Mucsi, N. Z. Kiss, *Adv. Synth. Catal.*, **2017**, *359*, 4322.
[9] G. Keglevich, I. Greiner, Z. Mucsi, *Current Org. Chem.*, **2015**, *19*, 1436.
[10] G. Keglevich, N. Z. Kiss, Z. Mucsi, Milestones in microwave-assisted organophosphorus chemistry. *Pure Appl. Chem.*, **2016**, *88*, 931.
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PL-3

Total Synthesis of Diterpene Natural Products

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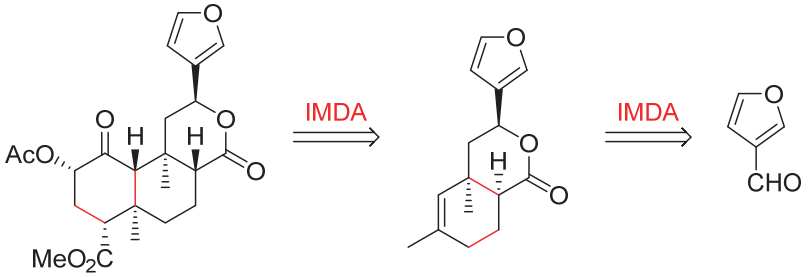
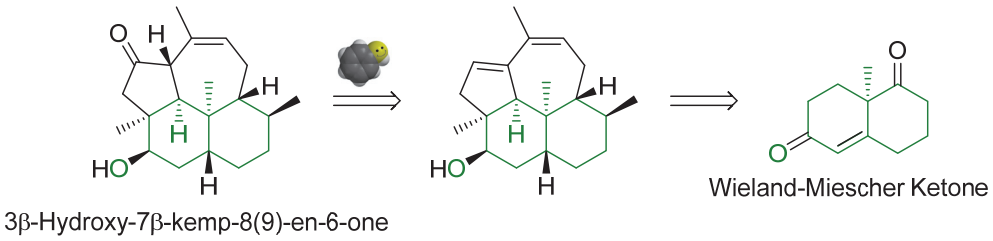
A concise total synthesis of the neoclerodane diterpene salvinorin A, isolated from the leaves of the Mexican medicinal plant *Salvia divinorum*, was achieved commencing with 3-furaldehyde (Scheme 1). Two highly diastereoselective intramolecular Diels–Alder reactions (IMDA) were used as the key transformations.[1]



Scheme 1.

The first total synthesis of the diterpene 3β-hydroxy-7β-kemp-8(9)-en-6-one, isolated from the soldier defense secretion of higher termites, has been accomplished starting from the Wieland-Miescher ketone (Scheme 2). A diastereoselective sulfa-Michael addition enabled the generation of the delicate β,γ-unsaturated ketone moiety, while the tetracyclic kempane skeleton was readily constructed through domino metathesis.[2]



Scheme 2.

Acknowledgements
This work was supported by the Deutsche Forschungsgemeinschaft (ME 776/20-2, ME 776/17-2).

References

[1] Y. Wang, P. Metz, *Org. Lett.*, **2018**, *20*, 3418-3421.
[2]Y. Wang, A. Jäger, M. Gruner, T. Lübken, P. Metz, *Angew. Chem.*, **2017**, *129*, 16076-16081; *Angew. Chem. Int. Ed.*, **2017**, *56*, 15861-15865..

PL-4

Organoselenium Compounds in Catalytic Reactions

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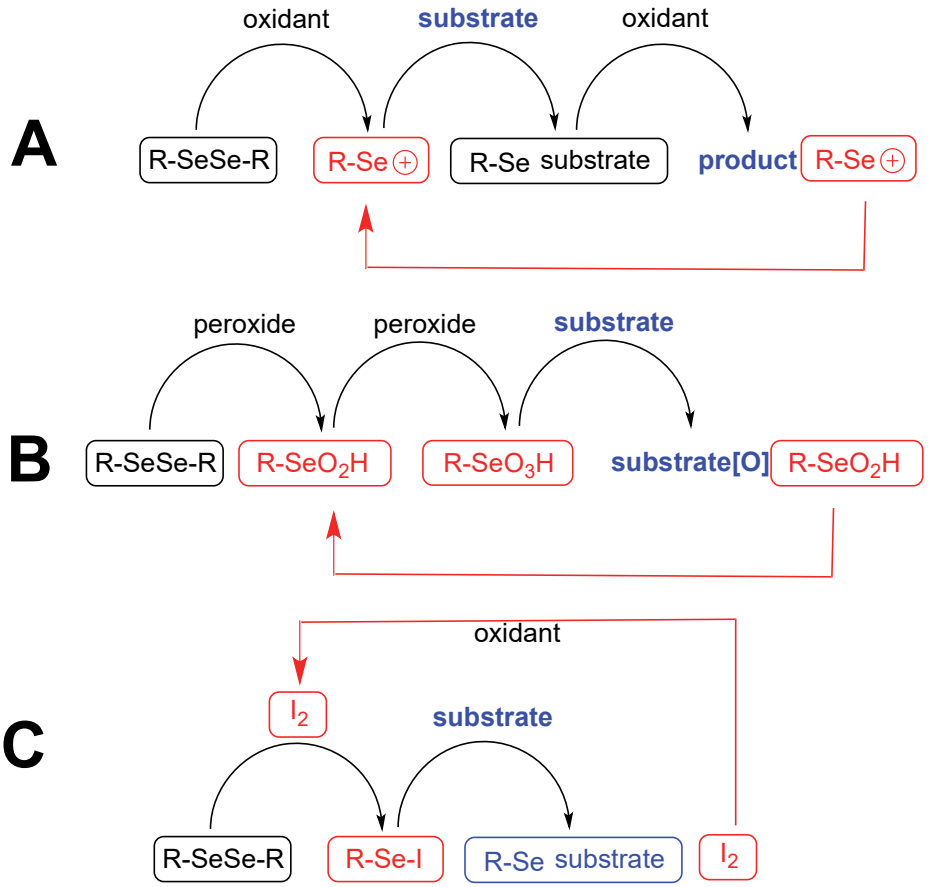
One of the most interesting aspect of organoselenium chemistry is the possibility to perform functional group conversions or selenofunctionalization under catalytic conditions. Electrophilic selenation-deselantion (A), oxygen transfer reactions (B) and iodine catalysed selenofunctionalization (C) will be here discussed focusing the attention on the most recent results using non-conventional conditions and the first examples of selenium catalysed processes under flow conditions.[1]



Scheme 1.

References

[1] E. J. Lenardao, C. Santi, L. Sancineto *New Frontiers in Organoselenium Compounds*, **2018**. Springer International Publishing (Springer Nature).

PL-5

Expansion of Aromaticity: From π-Aromaticity to σ+π-Double Aromaticity

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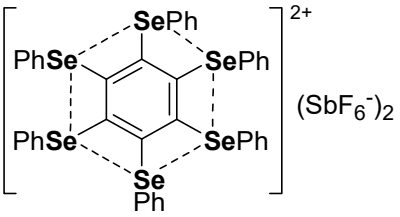
Since the discovery of benzene, aromaticity has been utilized to explain unique properties of benzene and its derivatives. The aromaticity arises from delocalized π-orbitals composed of (4 *n* + 2) π-electrons and is found to be retained even in lead-bearing cyclic compounds.[1, 2] However, aromaticity is not limited to that derived from π-electrons, which is denoted as π-aromaticity. Nowadays, σ- and δ-aromaticity arising from (4 *n* + 2) σ- and δ-electrons, respectively, have already been discovered by theoretical predictions and experimental studies.[3] From a fundamental curiosity to expand the aromaticity, we decided to elucidate whether different types of aromaticity coexisted in a single molecule. Since theoretical prediction on a hypothetical molecule possessing σ- and π-double aromaticity was reported by Schleyer in 1979,[4] experimental evaluation based on bench-stable σ- and π-double aromatic compounds has remained targeted.[5] Inspired by the previous report on the synthesis of a hexaiodobenzene dication,[6] though, which is still controversial,[7] we independently designed a hexaselanylbenzene dication as a possible σ- and π-double aromatic compound. Our previous quantum-chemical calculations of a model compound predicted its σ- and π-double aromatic character.[8] Based on this molecular design, we herein report the synthesis of dication salt of hexakis(phenylselenyl)benzene **1** and its X-ray characterization.[9] The σ- and π-double aromatic character of **1** is also discussed.



1

References

[1] M. Saito, M. Sakaguchi, T. Tajima, K. Ishimura, S. Nagase, M. Hada, *Science*, **2010**, *328*, 339-342; M. Saito, M. Nakada, T. Kuwabara, M. Minoura, *Chem. Commun*., **2015**, *51*, 4674-4676.

[2] For a review, see: M. Saito, *Coord. Chem. Rev.*, **2012**, *256*, 627-636.

[3] For examples of reviews, see: I. A. Popov, A. A. Starikova, D. V. Steglenko, A. I. Boldyrev, *Chem. Eur. J.*, **2018**, *24*, 292-305; D. Y. Zubarev, B. B. Averkiev, H-J. Zhai, L-S. Wang, A. I. Boldyrev, *Phys. Chem. Chem. Phys*., **2008**, *10*, 257-267.

[4] J. Chandrasekhar, E. D. Jemmis, P. v. R. Schleyer, *Tetrahedron Lett.*, **1979**, *20*, 3707–3710.

[5] M. Unverzagt, G. Subramanian, M. Hofmann, P. v. R. Schleyer, S. Berger, K. Harms, W. Massa, A. Berndt, *Angew. Chem.*, *Int. Ed.*, **1997**, *36*, 1469–1472.

[6] D. J. Sagl, J. C. Martin, *J. Am. Chem. Soc.*, **1988**, *110*, 5827–5833.

[7] M. J. Molski, D. Mollenhauer, S. Gohr, B. Paulus, M. A. Khanfar, H. Shorafa, S. H. Strauss, K. Seppelt, *Chem. Eur. J.*, **2012**, *18*, 6644-6654.

[8] M. Hatanaka, M. Saito, M. Fujita, K. Morokuma, *J. Org. Chem.*, **2014**, *79*, 2640-2646.

[9] S. Furukawa, M. Fujita, Y. Kanatomi, M. Minoura, M. Hatanaka, K. Morokuma, K. Ishimura, M. Saito, *Commun. Chem.*, **2018**, *1*, Article number 60. **(Highlighted in C&EN)**

PL-6

An Organoselenium Catalyzed Strategy for Oxidation Reactions

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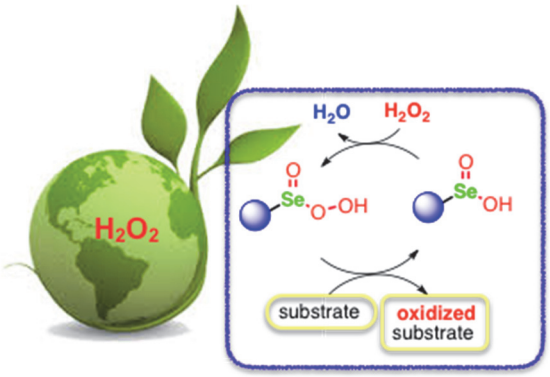
As a result of our efforts to develop new sustainable and eco-friendly oxidative procedures [1,2] here we report some examples of selenium-catalyzed transformations. The talk will be about the conversion of aldehydes into carboxylic acids and esters using a highly efficient and ecofriendly procedure [1]. Furthermore, the first general method for the benzeneseleninic acid–catalyzed cyclofunctionalization of alkenoic acids and alkenols will be detailed. The procedure is efficient in "on water" conditions [3] using stoichiometric amounts of hydrogen peroxide as a green oxidant giving the products in very good yields and diastereoselectivities, which however depend on the nature of the substrate. Finally, preliminary results on a heterogeneously catalyzed approach will be presented.



Scheme 1. General concept of selenium-catalyzed for oxidation reactions.

References

[1] Sancineto, L.; Tidei, C.; Bagnoli, L.; Marini, F.; Lenardão, E. J.; Santi, C. Selenium Catalyzed Oxidation of Aldehydes: Green Synthesis of Carboxylic Acids and Esters. *Molecules* **2015**, *20* (6).

[2] Santoro, S.; Azeredo, J. B.; Nascimento, V.; Sancineto, L.; Braga, A. L.; Santi, C. The Green Side of the Moon: Ecofriendly Aspects of Organoselenium Chemistry. *RSC Adv.* **2014**, *4* (60).

[3] Santi, C.; Jacob, R. G.; Monti, B.; Bagnoli, L.; Sancineto, L.; Lenardão, E. J. Water and Aqueous Mixtures as Convenient Alternative Media for Organoselenium Chemistry. *Molecules* **2016**, *21* (11)..

POSTERS

P-001

Influence of Lewis-acid catalyst on the molecular mechanism of thermal decomposition of nitroalkyl carboxylates

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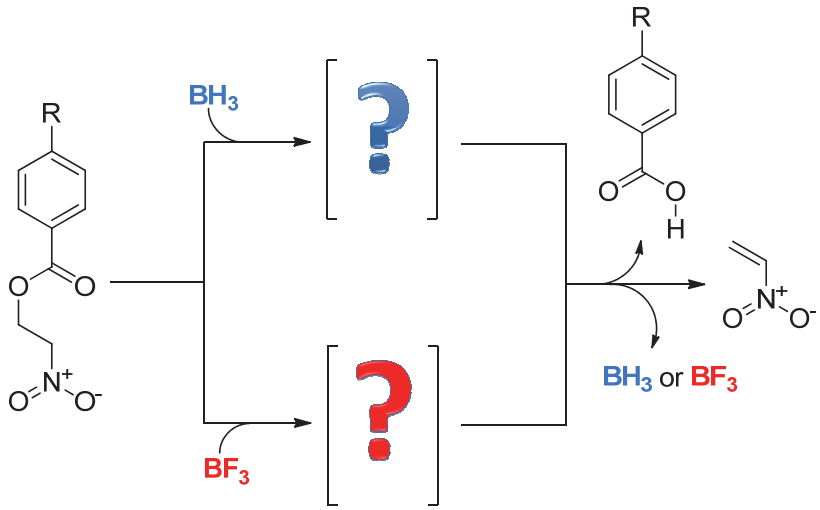
The molecular mechanisms of the decomposition reactions of nitroethyl carboxylates catalyzed by Lewis Acids (LAs) based on boron element – borane (BH_3) and boron trifluoride (BF_3) – was studied using Density Functional Theory (DFT) methods.[1] Our quantum chemical study proved that the LA – BH_3 catalyzed decomposition reactions of nitroethyl benzoates proceed via a polar one-step mechanism. However, the presence of fluorinated Lewis acids has a unique influence on the molecular mechanism. In the case of decomposition reactions catalyzed by BF_3, a change from a one-step mechanism to a two-step one involving a zwitterionic intermediate is observed. These decomposition reactions, catalyzed by LAs – BH_3 and BF_3 – take place much faster than the same reactions process without the catalyst.[2,3]



Scheme 1. Decomposition reaction of nitroethyl benzoates catalyzed by the LA.

References

[1] A. Kącka-Zych, LR. Domingo, R. Jasiński, *Res. Chem. Int.*, **2018**, *44(1),* 325-337.
[2] A. Kącka, R. Jasiński, Heteroatom Chem., **2016**, *27(5),* 279-289.
[3] R. Jasiński, A. Kącka, J. Mol. Model., **2015**, *21*, 59-65..

P-002

Regioselectivity of [3+2] cycloaddition between benzonitrile N-oxide and 3-nitroprop-1-ene

Barbara Mirosław[1], Dmytro Babyuk[2], Agnieszka Łapczuk-Krygier[3], Agnieszka Kącka-Zych[3], Oleg M. Demchuk[4], Radomir Jasiński[3]

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4,5-Dihydroisoxazoles (Δ^2-isoxazolines) are heterocycles with many important practical applications in veterinary medicine, has anti-cancer activity and in organic synthesis.[1,2] There are many efficient methods for preparation of nitrosubstituted 4,5-dihydroisoxazoles; the most universal one is [3+2] cycloaddition (32CA) between nitrile N-oxides as three atom components (TACs) and conjugated nitroalkenes (CNA). At the same time, nitromethyl-substituted 4,5-dihydroisoxazole is very poorly studied.

5-(Nitromethyl)-3-phenyl-4,5-dihydroisoxazole was obtained as a product of a high-yielding [3+2] cycloaddition reaction of in situ-generated benzonitrile N-oxide and 3-nitroprop-1-ene. For the first time, the regiochemistry of this reaction was unambiguously proven by X-ray structural analysis (Fig 1). The quantum-chemical calculation performed at the M06-2X/6-31G(d) (PCM) theoretical level affords a basis for explaining the course of reaction as well as the nature of transition states. The results obtained provide a valuable background for understanding of the chemistry of nitromethyl-4,5-dihydroisoxazoles. They are also useful for better understanding of other 32CA processes involving nitroallylic systems.[3]

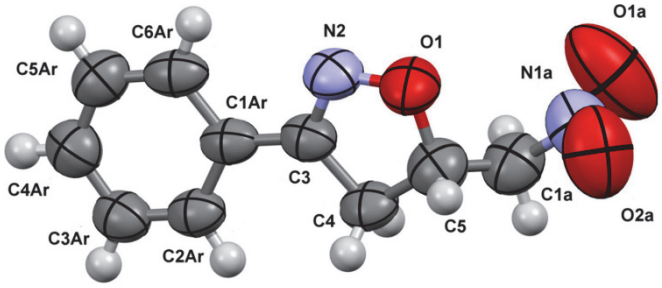

Fig.1 Molecular structure of 5-(nitromethyl)-3-phenyl-4,5-dihydroisoxazole.

References

[1] Banday AH, Giri AK, Parveen R, Bashir N, **2014**, Steroids 87:93
[2] Kara YS , **2015**, Spectrochim Acta. Part A Mol Biomol Spectrosc 151:723
[3] Jasiński R, **2015**, J Heterocycl Chem 52:185

P-003

Regio- and stereoselectivity of [3+2] cycloadditions between 3-nitroisoxazoline N-oxide and monosubstituted ethenes

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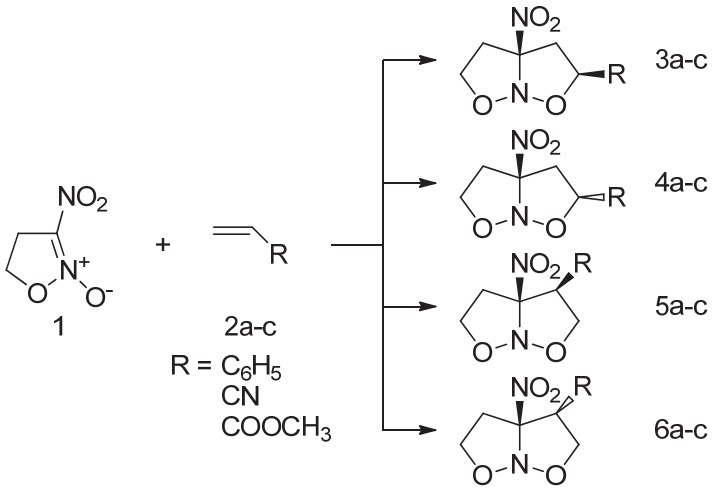
Studied 3-nitroisoxazoline N-oxide is a example of five-membered cyclic nitronate, which has been first synthesized in 1964 [1]. Thanks to its TAC [2] nature it can undergo [3+2] cycloaddition to monosubstituted ethenes yielding regio- and stereosomeric 3(4)-R-5-nitro-1-aza-2,8-dioxabicyclo[3.3.0]octanes. [3] At time of first synthesis of these compounds its stereoselectivity could not be determined due to apparatus restrictions. In our work we isolated and full characterized synthesized cycloadducts by CHN elemental analysis, IR spectroscopy as well as also H^1 and C^{13} NMR spectroscopy. Stereoisomerism has been determined in detail using 2D NMR techniques such as COSY and NOESY. We also conducted prediction of biological activity by PASS software analysis.



Scheme 1. Possible products of 3-nitroisoxazoline N-oxide [3+2] cycloaddition to monosubstituted ethenes.

References

[1] V. A. Tartakovskii, I. E. Chlenov, S. S. Smagin, S. S. Novikov, *Russ. Chem. Bull.*, **1964**, 13, 549.

[2] L. R. Domingo, M. Ríos-Gutiérrez, P. Pérez, *Tetrahedron* **2016**, 72, 1524-1532.

[3] В. А. Тартаковский, А. А. Онищенко, В. А. Смирнягин, С. С. Новиков, *Ж. Орг. Хим.*, **1966**, 2, 2225-2231.

A DFT computational study about [3+2] cycloadditions between sterically crowded diazocompounds and selected 2-R-nitroethenes

Karolina Kula, Agnieszka Fryźlewicz, Agnieszka Łapczuk-Krygier, Radomir Jasiński

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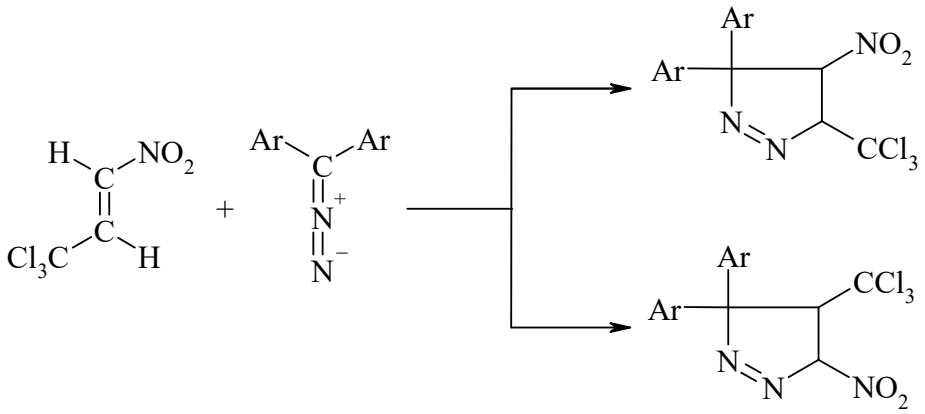
Reaction between diazocompounds and alkenes is actually one of the popular method of synthesis Δ^1-pyrazolines. The processes generally are realized under mild conditions and with full atomic economy [1]. Application of conjugated nitroalkenes as 2π-components in these type reactions give the possibility of preparation of nitrosubstituted Δ^1-pyrazolines.

In present work, mechanistic aspects of reactions between (E)-3,3,3-trichloro-1-nitroprop-1-ene and homogeneous series of diaryldiazomethanes has been examined using DFT computational methods. This work is a continuation of our comprehensive study on the participation of allenyl-type three atom components (TACs) in cycloaddition reactions with electrophilic dipolarophiles.



Scheme 1. Theoretically possible paths of reaction between diaryldiazomethanes and (E)-3,3,3-trichloro-1-nitroprop-1-ene.

Acknowledgements

The quantum-chemical calculations were performed on the SGI-Altix-3700 computer at the Cracow Computing Center "CYFRONET" (grant no. MNiSW/Zeus_lokalnie/PK/009/2013).

References

[1] R. Jasiński, *Reakcje 1,3-dipolarnej cykloaddycji: aspekty mechanistyczne i zastosowanie w syntezie organicznej*, **2015**, RTN, Radom.

[2] I. Jastrzebska, J.W. Morzycki, Some observations on solasodine reactivity, *Steroids* 127, 13-17, **2017**.

P-005

Parent thionitrone in [3+2] cycloaddition with conjugated nitroalkenes

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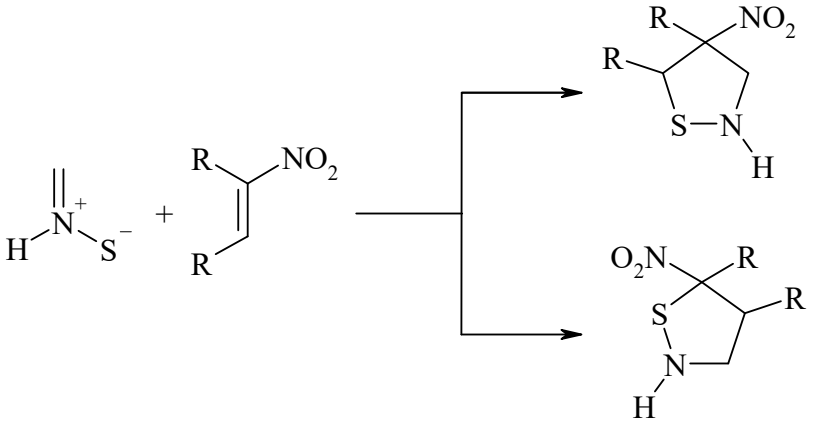
Five-membered heterocycles are widely used as biologically active compounds.[1] Heterocyclic compounds with two different heteroatoms particularly are the object of growing research interest of chemists. In particular, compounds bearing the thiazole ring in the molecular structure, such as isothiazolidines or isothiazolines, have antitumor, anti-allergic, anti-diabetic, anti-inflammatory, anthelmintic and anti-HIV activity [2-4].

Nitroisothiazolidines can be prepared via [3+2] cycloaddition reaction involving thionitrones and conjugated nitroalkenes as addents. A molecular mechanism of these type [3+2] cycloaddition has been explored using various DFT theoretical levels. It was found that the reaction proceeds via transition states with different synchronicity, but no intervention of the theoretical possible zwitterionic intermediates.



Scheme 1. Theoretically possible paths of [3+2] cycloaddition reactions of parent thionitrone with nitroethene and their substituted analogs.

References

[1] N. Khurana, M. P. S. Ishar, A. Gajbhiye, R. K. Goel, *Eur. J. Pharmacol.*, **2011**, *662*, 22-30.
[2] A. Aitha, S. Yennam, M. Behera, J. S. Anireddy, *Tetrahedron Lett.*, **2017**, *58 (6)*, 578-581.
[3] V. O. Sinenko, S. R. Slivchuk, V. S. Brovarets, *Current Chem. Lett.*, **2018**, *7 (1)*, 1-8.
[4] P. Chaudhary, K. Sharma, A. Sharma, J. Varshney, *Int. J. Curr. Pharm. Res.*, **2010**, *2 (4)*, 5-11.

P-006

Conversion of metal contaminated biomass into polymetallic catalysts and their application in the synthesis of heteroorganic compounds

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Catalysis established as the 9th of the twelve Principles of Green Chemistry is sometimes referred to as the ‘‘foundational pillar’’ of Green Chemistry [1]. The use of catalytic reagents is a means of achieving lower energy requirements, reduced waste, and improved atom economy, and thereby, catalysis touches on several of the other Principles of Green Chemistry. While it is common for catalysts to be optimized for turnover rates and selectivity, additional Green Chemistry considerations would include toxicity, hazard [2], and relative abundance of metals used [3]. Recently, the term “metal criticality” was established to evaluate metals beyond their relative abundance to include environmental implications of mining operations and supply risk [4]. In line with those new trends in catalysis and in Green Chemistry, new solutions are sought to provide metals resources in an environmentally benign fashion.

We show that metal contaminated biomass from plants used in phytoremediation of metal contaminated sites or rhizofiltration of metal contaminated water can serve as alternative source of metals. This biomass can be used for production of polymetallic catalysts suitable for application in organic synthesis and preparation of a variety of heteroorganic compounds with high added value [5,6].

References

[1] H. C. Erythropel, J. B. Zimmerman, T. M. de Winter, L. Petitjean, F. Melnikov, C. H. Lam, A. W. Lounsbury, K. E. Mellor, N. Z. Jankovic, Q. Tu, L. N. Pincus, M. M. Falinski, W. Shi, P. Coish, D. L. Plata, P. T. Anastas, *Green Chemistry* **2018,** *20*, 1929-1961.
[2] K. S. Egorova, V. P. Ananikov, *Angew. Chem., Int. Ed.*, **2016**, *55*, 12150–12162.
[3] X. Lim, *Nature*, **2016**, *537*, 156–158.
[4] T. E. Graedel, E. M. Harper, N. T. Nassar, P. Nuss, B. K. Reck, *PNAS*, **2015**, *112*, 4257– 4262.
[5] V. Escande, T.K. Olszewski, E. Petit, C. Grison, *ChemSusChem* **2014**, *7*, 1915-1923.
[6] G. Clave, C. Garel, C. Poullain, B.-R. Renard, T.K. Olszewski, B. Langeen, S. Mylor, M.-P. Faucon, C. Grison**,** RSC Advances **2016**, *6*, 59550-59564

P-007

Determination of sulfate ions with 2,4,6-triphenylpyrylium tetrafluoroborate in natural sulphide water using HPLC/UV-VIS technique

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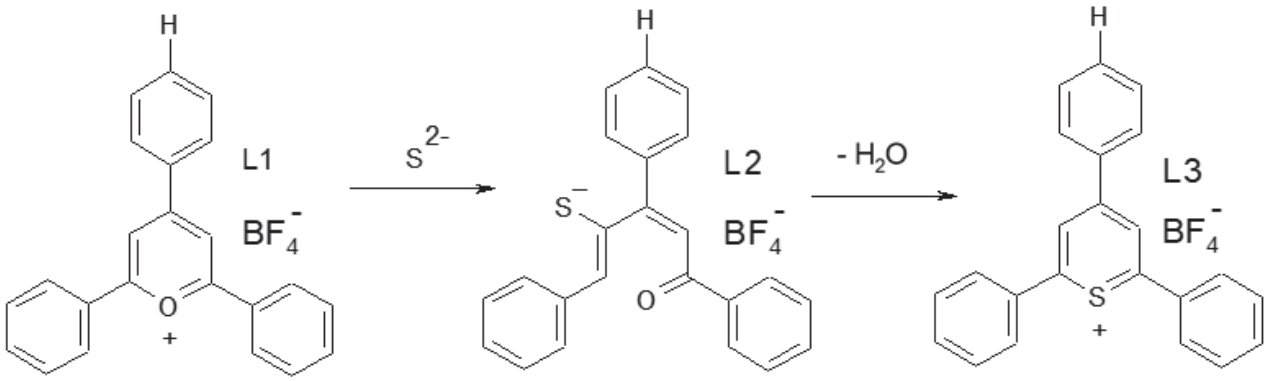
Sulphide ion is commonly found in nature. It is present in water, soil, air, rocks and organic matter. It is used in many branches of industry and agriculture. Compounds containing sulphide ion are used, among others, in tanneries, for the production of sulfuric acid (VI), dyes and cosmetics.

The aim of the research was to develop a method based on the determination of sulphide ions using the salt of pyridyl tetrafluoroborate 2,4,6-triphenylpyril (L1) in samples of sulphide water originating from the health resorts of Busko Zdrój and Uniejów. The technique, which was carried out experiments, was high performance liquid chromatography (HPLC) with a UV-VIS detector. The developed method was subjected to the validation process on the basis of which it can be stated that it is simple, sensitive, repeatable and precise [1-3].



Scheme 1. Proposed scheme for derivatisation reactions sulphide ion using L1.

References

[1]. D. Jiménez, R. Martínez-Máñez, F. Sancenón, J.V. Ros-Lis, A. Benito, J. Soto*, J. Am. Chem. Soc.,* **2003**, *125*, 9000–9001.

[2]. Ż. Rembisz, D. Bzdurska, J. Obiedzińska, R. Martínez-Máñez, R. Zakrzewski, *J. Chromatog A,* **2015**, *1407*, 184–192.

[3] Ż. Rembisz, R. Zakrzewski, W. Ciesielski, M. Skowron, R. Martínez-Máñez, *J. Planar Chromat.,* **2014**, *27*, 240..

P-008

Study The Reactivity Of Santi's Reagent- The Synthesis Of Selenosteroids

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In the last few years, the organochalcogen compounds have emerged as important reagents in modern organic syntheses, in particular, has been demonstrated that various functional groups can be selectively introduced into complex molecules under very mild reaction conditions by using nucleophilic selenium reagents [1].

Among these, PhSeZnCl (Santi's reagent) emerged as the first bench-stable selenium nucleophilic agent showing the great versatility of use [2].

Therefore the aim of this work has been focused on its reactivity on different steroids analogues with at least an electrophilic center. In this respect, several synthetic attempts have been done employing different reaction conditions. The best results have been obtained with the "one pot reaction" in which the PhSeZnCl, is formed *in situ*, immediately react with the appropriate starting material.

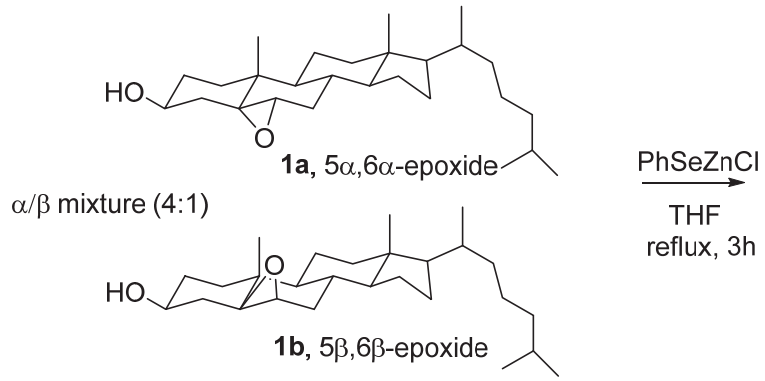

Figure 1. Reaction of 3β-hydroxy-5ζ,6ζ-epoxycholestanes (**1a** and **1b**) with PhSeZnCl.

Acknowledgements

Financial support from the National Science Center, Poland within the project UMO-2015/17/B/ST5/02892 is gratefully acknowledged.

References

[1] a) A. Krief, L. Hevesi, Organoselenium Chemistry, vol. 1, SpringerVerlag, Berlin, **1988,** b) ed. T. Wirth Organoselenium Chemistry: Synthesis and Reactions, Wiley-VCH Verlag, **2011**.

[2] C. Santi, S. Santoro, B. Battistelli, L. Testaferri, M. Tiecco *Eur. J. Org. Chem* **2008**, 5387, b) G. Bellino, M. Scisciani, J. Pinto Vargas, L. Sancineto, L. Bagnoli, F. Marini, D. S. Ludtke, E. J. Lenardao, C. Santi Journal of Chemistry, **2016**, Article ID 2849140, 8 pages.

P-009

Synthesis of C-substituted derivatives of N-phosphonomethylleucine

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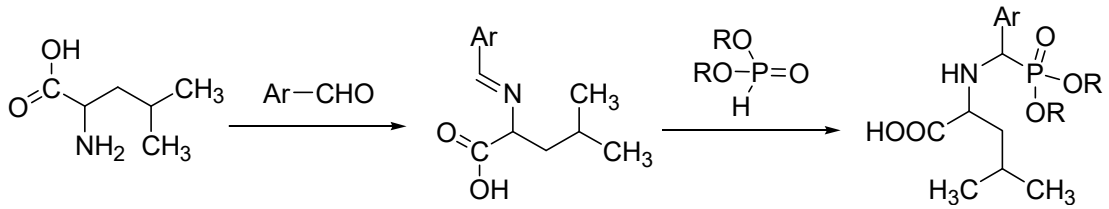
The project presented here aimed at the preparation of a series of the *C*-substituted derivatives of *N*-phosphonomethylleucine, namely: dialkyl *N*-(1-methoxycarbonyl-3-methylbutyl)amino(aryl)-methylophosphonates [1,2]. These compounds are *C,C'*-disubstituted derivatives of phosphonomethylglycine, which is much better known as glyphosate.

Glyphosate is a herbicidal agent killing terrestrial higher plants by inhibiting 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase, and is efficient when applied as the herbicidal preparation (Roundup®). Recent reports on harmful impact of glyphosate itself as well as its commercial preparation [3], prompted us to look for new compounds having herbicidal properties. Derivatization of glyphosate seemed to us the most convenient point to start with. That is why we performed the preparation of title compounds.



Scheme 1. The method for synthesis of phosphonic derivatives of leucine.

Acknowledgements

Anna Kowalczyk wishes to thank the University of Łódź for awarding her the student grant.

References

[1] J. Lewkowski, R. Karpowicz, *Heteroatom Chem.*, **2010**, *21*, 326-331.

[2] J. Lewkowski, R. Karpowicz, *Heteroatom Chem.*, **2012**, *23*, 395-398.

[3] N. Defarge, J. Spiroux de Vendômois, G.E. Séralini, *Toxicology Reports*, **2018**, *5*, 156–163

The final *comptes-redus* on the NCN grant implementation. In a search for a New Herbicide, have we reached Nowhere?

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Synthesis of about 150 compounds (or even more), their purification to obtain the degree of purity suitable for biological studies, carrying out phytotoxicological tests, which must be conducted precisely following the prescribed procedures, testing the selectivity towards one type of plants, performing ecotoxicological evaluation of each compound – are all these actions sufficient to lead the scientific project to the successful end? Is the lack of a spectacular success a defeat? Is publishing the grant results in a form of 10 scientific articles [1,2] a sufficient achievement, or is it a disaster not to find a 100% proper candidate for a herbicide?

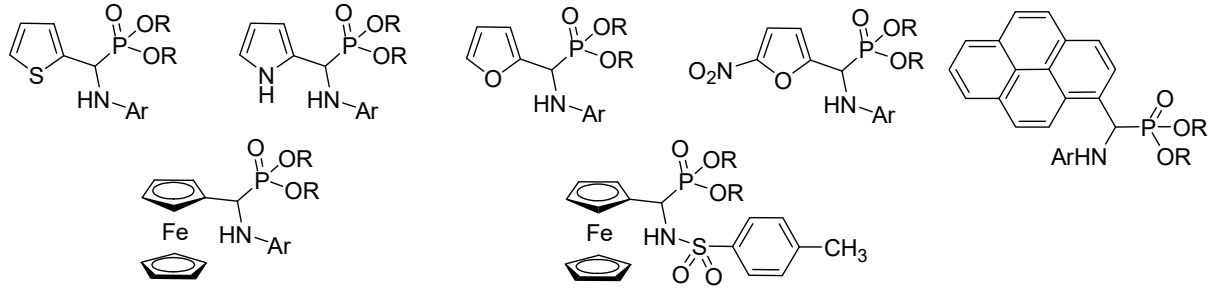

Figure 1. General formulas of investigated compounds.

Although, it is not easy to summarize the three-years project in a B1 poster, I will try to answer all the questions, which were asked above.

Acknowledgements

The studies were funded by Narodowe Centrum Nauki (NCN) grant no. 2014/13/B/NZ9/02418.

References

[1] J. Lewkowski, M. Morawska, R. Karpowicz, P. Rychter, D. Rogacz, K. Lewicka, *Chemosphere*, **2017**, *188*, 618-632.

[2] J. Lewkowski, R. Karpowicz, M. Morawska, P. Rychter, D. Rogacz, K. Lewicka, P. Dobrzynski, *RSC Adv.*, **2017**, *7*, 38399-38409..

P-011

Anthracene-thymine conjugates for confocal microscopy bio-imaging applications

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Anthracene derivatives are widely used as luminescent probes in biology.[1] We report the synthesis of luminescent anthracene-thymine conjugates **1** and **2** (Fig. 1).

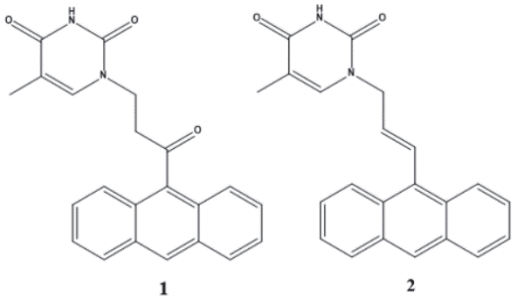

Figure 1. luminescent anthracene-thymine conjugates **1** and **2**.

We have used compounds **1** and **2** as luminescent probes for confocal microscopy bioimaging studies in living HeLa cells. Dyes showed photo stability and lack of photo toxicity which are both required for molecules to be a luminescent bioimaging probes. Furthermore, we have found that structural alternations of the linker group enable us to control accumulation of the dye in the selected cellular compartments. Accordingly, compound **1** predominantly stains nucleus and nucleoli of the HeLa cells (Fig. 2) while **2** accumulates in mitochondria and plasmatic membranes (Fig. 3).

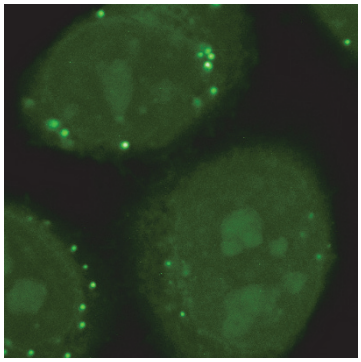

Figure 2. Confocal microscopy view on **1** in living HeLa cells

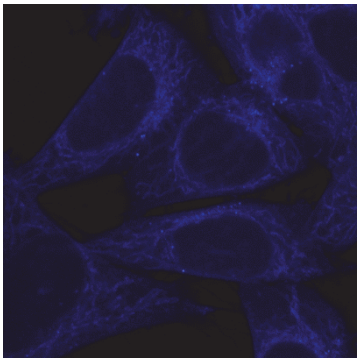

Figure 3. Confocal microscopy view on **2** in living HeLa cells

References

[1] R. Martinez-Máñez, F.Sancenón, Chem. Rev., 2003, 103, 4419-4476.

P-012

Synthesis of novel bis-dipyridothiazines

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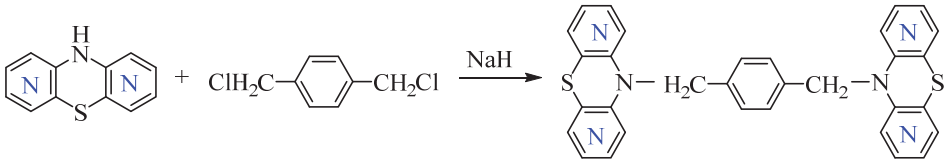
Cancer has now become a global problem and ranked the top leading cause of death worldwide after cardiovascular disease, tuberculosis and malaria combined. Chemotherapy has been still improved in cancer therapy and the survival has been greatly increased but there is need to discover and develope new more potent antitumor agents with better selectivity and reduced side effects [1]. Phenothiazines are important class of heterocyclic compounds with wide spectrum of biological properties. Recent reports showed promising anticancer, antiplasmid, antibacterial, anti-inflammatory and immunosuppressive activities of classical and new phenothiazines [2]. Previously synthesized dipyridothiazine derivatives (1,6-, 1,8-, 2,7- and 3,6-diazaphenothiazines) were shown to possess interesting antiproliferative, anticancer, antioxidant and immunosuppressive activity [3-6]. In continuation of our search we obtained new derivatives of dipyridothiazines – bis-dipyridothiazines in the reactions of selected dipyridothiazines with α,α`-dichloro-p-xylene.



Using 1H and 13C NMR two-dimensional spectroscopy (1H-1H COSY, ROESY, HSQC, HMBC), mass spectrometry (HR MS) the right structure of the products were determined.

For those compounds, the anticancer action on selected tumor lines (SNB-19, Caco-2, A549, MDA-MB231) will be investigated.

Acknowledgements

The studies were supported by The Medical University of Silesia in Katowice grant KNW-1-072/K/8/O.

References

[1] R. L. Siegel, K. D. Miller, A. Jemal, Cancer Statistics, 2015, CA Cancer J. Clin 65, 5–29 (2015).
[2] K. Pluta, B. Morak-Młodawska, M. Jeleń, *Eur. J. Med. Chem*., 138, 774 (2017).
[3] B. Morak-Młodawska, K. Pluta, A. N. Matralis, A. P. Kourounakis, *Archiv Pharm.*, 343, 268 (2010).
[4] B. Morak-Młodawska, K. Pluta, M. Zimecki, M. Jeleń, J. Artym, M. Kocięba, *Med. Chem. Res.* 24, 1408 (2015).
[5] M. Zimecki, J. Artym, M. Kocięba, K. Pluta, B. Morak-Młodawska, M. Jeleń, *Cell. Mol. Biol. Lett.* 14, 622(2009).
[6] B. Morak-Młodawska, K. Pluta, M. Latocha, K. Suwińska, M. Jeleń, D. Kuśmierz. *J. Enzyme Inhib. Med. Chem.* 31 (2016) 1512-1519..

P-013

Synthesis, anticancer activities & lipophilicity of novel dipyridothiazines with 1,2,3-triazole substituents

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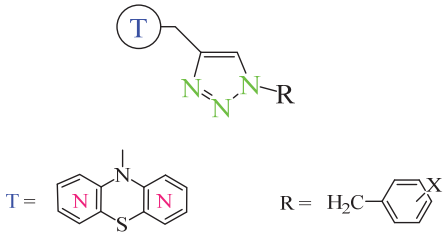
Lipophilicity has been long considered as a vital component of drug discovery and development. It is crucial physicochemical parameter which is important for *in vivo* distribution of organic compounds by influencing their solubility, cell uptake, blood-brain penetration and rationalizing a number of biological events as membrane penetration and permeability [1,2]. A review of the literature demonstrates that compounds that display lipophilicity (log*P*) between one and three appear to be optimal for achieving appropriate physicochemical characteristic to ensure downstream drug success [3]. For this reason, a quantitative assessment of lipophilicity is an important tool in quantitative structure–activity relationship studies [4,5].

In the continuation of the search of bioactive azaphenothiazines, the synthesis, analysis of structure and biological activities of new 2,7-diazaphenothiazines with 1,2,3-triazole substituents was presented.



2,7-DIAZAPHENOTHIAZINE

Some of these compounds exhibit promising and significant *in vitro* antiproliferative acivity. The aim of this project was examination of the lipophilicity of new series of 10-substituted 2,7-diazaphenothiazines determined experimentally by RP-TLC and calculated with computer programs, as well as search for relationships between their lipophilicity, structure and biological activity.

Acknowledgements

The studies were supported by The Medical University of Silesia in Katowice grant KNW-1-072/K/8/O.

References

[1] J.A. Arnott, S.L. Planey, *Exp. Op. Drug Disc.*, 7, 863 (2012).
[2] A. Toma, D. Hapa, et all. *J. Chromatogr. Sci.*, 52, 1302 (2014).
[3] M. J. Waring, *Exp. Op. Drug Disc.,* 5, 235 (2010).
[4] Z. Mazerska et all., *Anti-Cancer Drug Des.,* 11, 73 (1996).
[5] B.Mora-Młodawska, K. Pluta et all., *J. Enzyme Inhib. Med. Chem.,* (2016); doi: 10.3109/14756366.2016.1151014.

P-014

Study of the interaction between cucurbituril Q7 and metoclopramide in aqueous solution

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Cucurbiturils (CB) are a relatively new class of macrocyclic compounds. Their name is derived from the latin word *cucurbitaceae*, because they have a similar shape to a pumpkin. They are made from glycoluril residues connected by methylene groups. Inside the macrocycle there is a cavity capable of hosting smaller molecules - including medicaments. Cucurbiturils can be used as nano-transporter of toxic drugs.

Metoclopramide is a medication used with anticancer drugs to improve the comfort of treatment. Metoclopramide is commonly used to treat nausea and vomiting associated with chemotherapy. The use of the drug is limited because of its low stability inside living organism and many side effects.

Cucurbiturils are well tolerated by organism. These oligomers might be used to reduce its toxicity and improve bioavailability of many drugs, including metoclopramide. The object of this work is to investigate the effects of interactions between cucurbituril Q7 and metoclopramide in aqueous environment.

Results of the equilibrium dialysis experiments show that the molecule of metoclopramide forms a guest-host complex with two molecules of cucurbituril Q7. The complexation process is reversible and has spontaneous character.

Acknowledgment
The work was partially founded by the University of Lodz from the project “Student Research Grant 2018”.

P-015

A facile synthesis of novel 9-substituted 2,3,4,9-tetrahydro-1*H*-xanthen-1-ones

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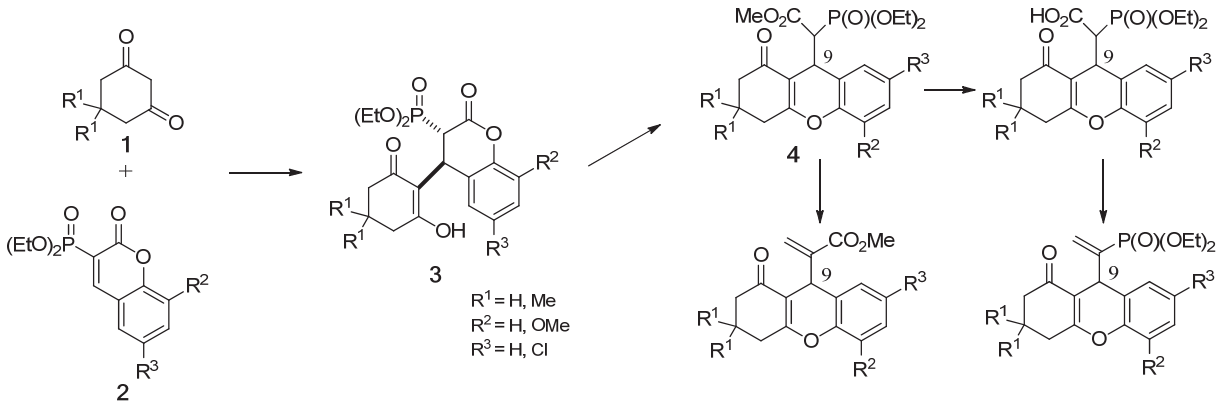
Heterocycles bearing 2,3,4,9-tetrahydro-1*H*-xanthen-1-one scaffold are constituents of natural and unnatural products, some of which display pronounced biological activities.[1-3] Therefore, the synthetic methods for this class of compounds are highly desirable. In this communication a strategically new approach to 9-substituted 2,3,4,9-tetrahydro-1*H*-xanthen-1-ones **4** is presented. The protocool includes TMG promoted, conjugate addition of cyclohexane-1,3-diones **1** to 3-(diethoxyphosphoryl)coumarins **2** and domino transesterification-cyclodehydration reaction of the adducts obtained **3**. Modifications of the substituent at C-9 position of tetrahydroxanthenone core are reported for the first time. These transformations were realized using previously described procedures. [4,5]



References

[1] A. Kumar, S. Sharma, R.A. Maurya, J. Sarkar, *J. Comb. Chem.* **2010**, *12*, 20-24.

[2] D.L. da Silva, S.B. Terra, M.R. Lage, A.L.T. Góis Ruiz, C.C. da Silva, J.E. de Carvalho, J.W. de Mesquita Carneiro, F.T. Martins, S.A. Fernades, A. de Fatima, *Org. Biomol. Chem*. **2015**, *13*, 3280-3284.

[3] G.L. Goud, S. Ramesh, D. Ashok, V.P. Reddy, P. Yogeeswari, D. Sriram, B. Sakrishna, V. Manga, *Med. Chem. Commun*. **2017**, *8*, 559-570.

[4] H. Krawczyk, J. Koszuk, R. Bodalski, *Pol. J. Chem*. **2000**, *74*, 1123.

[5] H. Krawczyk, Ł. Albrecht, J. Wojciechowski, W.M. Wolf, *Tetrahedron* **2008**, *64*, 5051-5054..

P-016

Theoretical study of oxidation of formic acid on boron-doped diamond electrode

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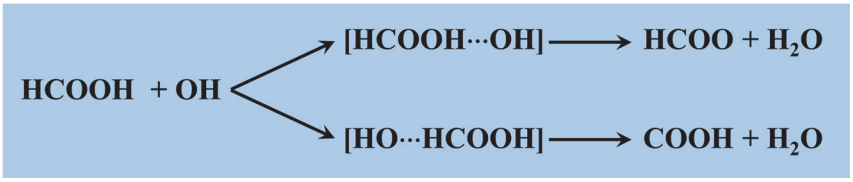
Electrochemical oxidation of organic compounds plays an increasing role in treating wastewater from organic contaminants. These processes are based on in situ generation of highly reactive oxidants, such as the electrogenerated OH radicals, which can trigger the mineralization of organic compounds to CO_2, water and ions. At special inert electrodes characterized by low adsorption properties, such as the boron-doped diamond (BDD) electrode, the hydroxyl radical generation and incineration of carboxylic acids can proceed via the outer sphere mechanism, i.e. without adsorption of intermediates [1,2].

Formic acid is one of intermediates of the oxidative degradation of various organic substrates. In the poster we present results of our MP2/aug-cc-pVTZ calculations performed for the initial steps of the reaction of formic acid with hydroxyl radical in aqueous solution, in which first the HCOOH forms with OH a hydrogen-bonded adduct, followed by the carboxylic or formyl hydrogen abstraction. The latter yields $HCOO+H_2O$ or $COOH+H_2O$, which also form hydrogen-bonded complexes. The structures of the prereactive adducts, product complexes and the transition states between them are shown along with their relative energies.



Scheme 1. Two possible pathways of a hydrogen abstraction from formic acid by OH radical in water.

Acknowledgment

The authors acknowledge support by the state of Baden-Württemberg through bwHPC and by the Deutsche Forschungsgemeinschaft through grants: DFG FOR1376 and SCHM 344/50-1. E.S. acknowledges PIP-CONICET 112-201001-00411 and PICT- 2012-2324 (Agencia Nacional de Promoción Científica y Tecnológica, FONCYT, préstamo BID). E.S. and W.S. acknowledge continuous support from CONICET Argentina. Some calculations have been carried out using resources provided by Wroclaw Centre for Networking and Supercomputing (http://wcss.pl), grant No. 443

References

[1] A. Ignaczak, E. Santos, W. Schmickler, T. F. da Costa, *J. Electroanal. Chem.*, **2018**, *819*, 410-416.

[2] J. L. A. Queiroz, A. R. L. Silva, D. C. Moura, D. R. Silva, C. A. Martínez-Huitle, *J. Electroanal. Chem.*, **2017**, *794*, 204-211.

P-017

Luminescent *fac*-[Re(CO)$_3$(phen)] carboxylato complexes with non-steroidal anti-inflammatory drugs

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Non-steroidal anti-inflammatory drugs (NSAIDs) are a very important group of medications with anti-inflammatory, analgesic and antipyretic activity. Acetylsalicylic acid (aspirin), which is a key NSAIDs family member, shows also a antiplatelet and cancer prevention activity. Cyclooxygenases (COX-1 and COX-2) are molecular targets for NSAIDs. These enzymes catalyze the transformation of arachidonic acid into prostaglandins which are mediators of inflammation and are also involved in other biological processes such as angiogenesis. Poster presentation shows the synthesis, structure, luminescence and biological properties of *fac*-[Re(CO)$_3$(phen)(L)] complexes with the ancillary ligands L being medicinally active NSAIDs: aspirin (**A**), (*S*)-(+)-ibuprofen (**B**), (*S*)-(+)-naproxen (**C**) and indomethacin (**D**; Figure 1).

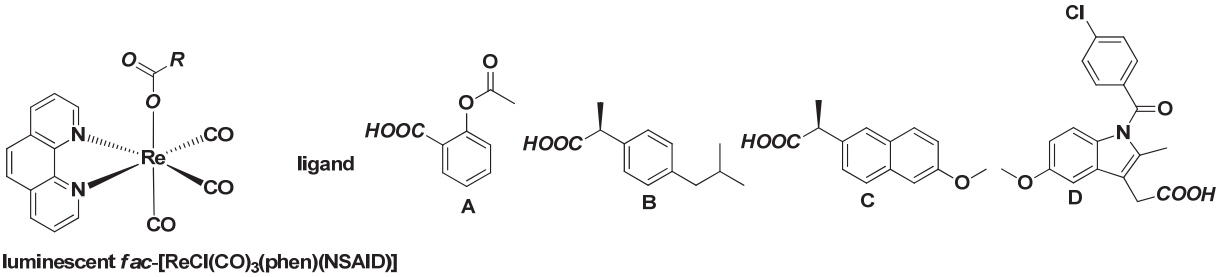

Figure 1. *fac*-[Re(CO)$_3$(phen)(NSAID)] complexes.

fac-[Re(CO)$_3$(phen)(aspirin)] complex showed activity profile derived from its molecular constituents. Similar to aspirin drug, the Re-aspiryn complex inhibits COX-2 enzymes. The luminescent *fac*-[Re(CO)$_3$(phen)]$^+$ unit localize in mitochondria of HeLa cells as shown by confocal microscopy studies (Figure 2). Furthermore it elevates ROS concentration, disturb cell cycle and induce apoptosis.

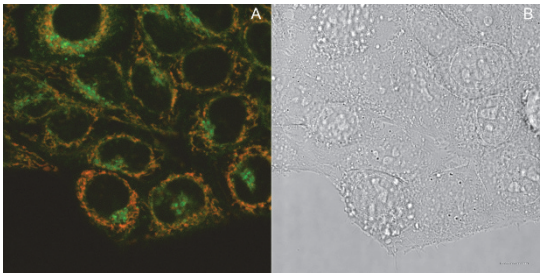

Figure 2. Confocal microscopy view on *fac*-[Re(CO)$_3$(phen)(Aspirin)] complex in living HeLa cells.

P-018

Intermolecular interactions in the structure of pentachloropyridine *N*-oxide

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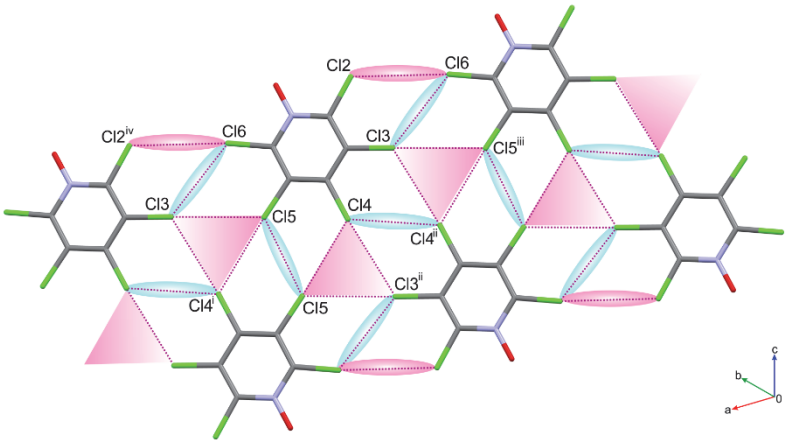
Recently, an increased interest in pyridine *N*-oxide, due to their use. Pyridine *N*-oxides are components of antifungal, antiviral, anti-inflammatory and bacteriostatic substances, as well as being used as drugs for cancer chemotherapy [1-3]. Here, in the continuation of our research, we present the results of the synthesis of a new crystal stabilized by halogen bonds, pentachloropyridine *N*-oxide. The title compound, crystallizes in the monoclinic group P21/c with one molecule in a general position. In the crystal structure, molecules are linked by C - Cl…Cl halogen bonds into infinite ribbons extending along the crystallographic [100] direction. These molecular aggregates are further stabilized by very short intermolecular *N*-oxide – *N*-oxide interactions into herringbone motifs [4]. Computations based on quantum chemistry methods [5] allowed for a more detailed description of the *N*-oxide – *N*-oxide interactions and Cl…Cl halogen bonds. For this purpose, the many-body approach to interaction energy were applied.



Scheme 1. The scheme of intermolecular interactions of (I), with halogen bonds shown in pink and Cl…Cl interactions shown in cyan within a single ribbon of molecules.

References

[1].W.A. Denny Curr. Med. Chem. Anti-Cancer Agents **2004** 4, 395– 399.

[2].J.R. Amsden, P.O. Gubbins, S. McConnell, E. Anaissie Antimicrob. Agents Chemother. **2013** 57, 3420–3423.

[3].J.C. Villalobos-Rocha, L. Sánchez-Torres, B. Nogueda-Torres, A. Segura-Cabrera, C.A. Garcia- Pèrez, V. Bocanegra-Garcia, I. Palos, A. Monge, G. Rivera Parasitol. Res. **2014** 113, 2027–2035.

[4].K. Wzgarda-Raj, A. J. Rybarczyk-Pirek, S. Wojtulewski, M. Palusiak Acta Cryst. **2018** C74, 113-119.

[5]. M. J. Frisch *et al.* **2009**: GAUSSIAN09. Gaussian Inc., Wallingford, CT, USA.

P-019

Modern Mannich-type reaction of 1-(*N*-acylamino)alkyltriphenylphosphonium salts with silyl enolates: A new catalyst-free approach for the synthesis of β-amino carbonyl compounds

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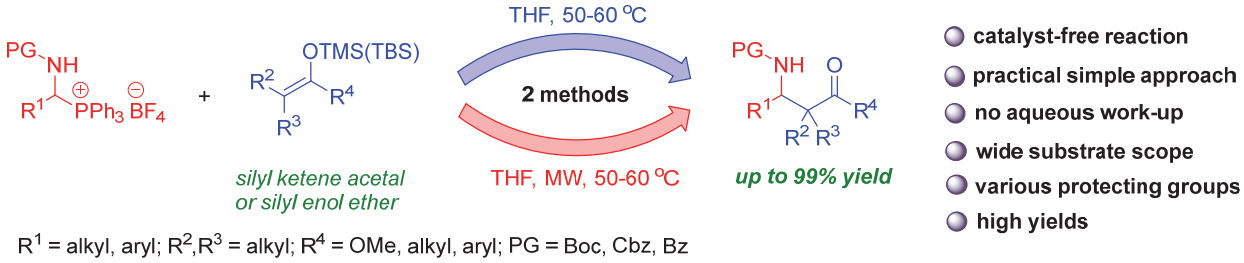
The Mannich reaction and its further modifications play an important role in organic synthesis. β-Amino carbonyl compounds, which are obtained in these reactions, display various biological activities. Moreover, these compounds are versatile building blocks that are often utilized in the synthesis of nitrogen-containing natural products. [1-3]

Herein we present a new catalyst-free Mannich-type reaction of 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborates with silyl enolates as an alternative approach for the synthesis of β-amino carbonyl compounds (Scheme 1).



R^1 = alkyl, aryl; R^2,R^3 = alkyl; R^4 = OMe, alkyl, aryl; PG = Boc, Cbz, Bz

Scheme 1

The developed method provides ready access to a variety of *N*-protected β-amino esters as well as *N*-protected β-amino ketones. In addition, our protocol offers many practical advantages, such as a simple and efficient reaction procedure, high reaction yield and the possibility to effect a significant reduction of reaction time by microwave irradiation. Moreover, the starting 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborates are readily available from *N*-protected α-amino acids. [4] From this point of view, the reported approach can be considered a new strategy for the α-homologation of *N*-protectedα-amino acids to prepare β-amino acid derivatives (with silyl ketene acetals as nucleophiles).

References

[1] G. Roman, *Eur. J. Med. Chem.,* **2015**, *89*, 743-816.
[2] M. Liu, M. P. Sibi, *Tetrahedron*, **2002**, *58*, 7991-8035.
[3] M. Arend, B. Westermann, N. Risch, *Angew. Chem. Int. Ed.*, **1998**, *37*, 1044-1070.
[4] R. Mazurkiewicz, J. Adamek, A. Październiok-Holewa, K. Zielińska, W. Simka, A. Gajos, K. Szymura, *J. Org. Chem.*, **2012**, *77,* 1952-1960.

P-020

Mechanistic aspects of the Michaelis-Arbuzov-type reaction of 1-(*N*-acylamino)alkyltriarylphosphonium salts with phosphorus nucleophiles

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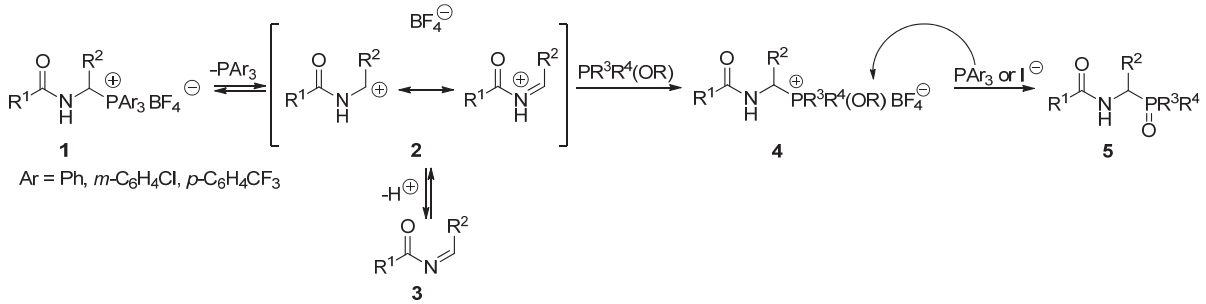
In 2013, we described a plausible mechanism of the Michaelis-Arbuzov-type reaction of 1-(*N*-acylamino)alkyltriphenylphosphonium salts **1** (Ar = Ph) with phosphorus nucleophiles wherein the *N*-acyliminium cation **2** (or *N*-acylimine **3**) generated from phosphonium salt **1** reacts with phosphorus nucleophile to form alkoxyphosphonium salt **4** – a characteristic intermediate of the Michaelis-Arbuzov reaction. The final step of the reaction is the dealkylation of the alkoxyphosphonium salt **4** and may occur directly with triphenylphosphine (see Scheme 1). However, we have not been able to isolate or even observe the formation of postulated intermediate product **4**.[1]

Recently, we reported the synthetic application of 1-(*N*-acylamino)-alkyltriarylphosphonium salts with weakened C_α-P^+ bond strength.[2] We synthesized triarylphosphonium salts derived from EWG-substituted triarylphosphines **1** (R = *m*-C_6H_4Cl or *p*-$C_6H_4CF_3$) and investigated their reactivity in the Michaelis-Arbuzov-type reaction with phosphorus nucleophiles. Detailed NMR (^1H and ^{31}P NMR) and HR-MS analysis confirmed that alkoxyphosphonium salt **4** was present in the reaction mixture. Moreover, we isolated and fully characterized the intermediate product of the Michaelis-Arbuzov reaction **4** (R^1 = *t*-Bu, R^2 = Me, R = Et).



Scheme 1. α-Amidoalkylation of *P*-nucleophiles by 1-(*N*-acylamino)alkyltriarylphosphonium salts **1** - a plausible mechanism.

Acknowledgment

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References

[1] Adamek, J.; Październiok-Holewa, A.; Zielińska, K.; Mazurkiewicz, R. *Phosphorus, Sulfur Silicon Relat. Elem.* **2013**, *188*, 967-980.

[2] Adamek, J.; Węgrzyk, A.; Kończewicz, J.; Walczak, K.; Erfurt, K. *Molecules* **2018**, *23*, 2453.

P-021

Preparation and synthetic application of 1-(*N*-acylamino)-1-triphenylphosphoniumalkylphosphonates

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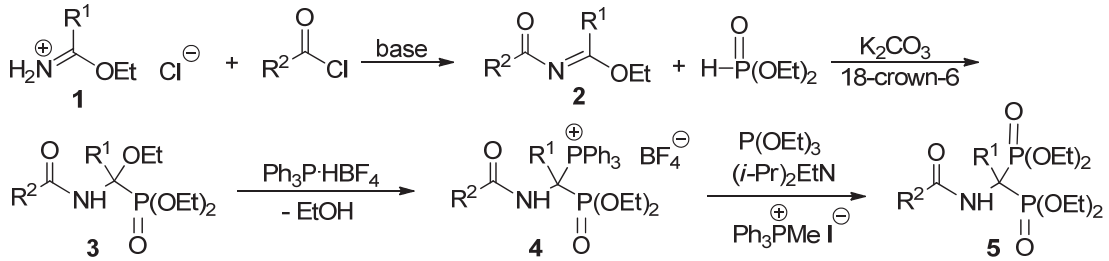
Recently we described a new method for synthesis of α-phosphonium derivatives **4** of α-aminophosphonates (R^1 = H, Me, Ph; R^2 = Me, Bn) from imidate hydrochlorides **1** readily available from nitriles. The starting compounds may be effectively converted into target phosphonium salts *via* a three-step transformation involving acylation of the imidate hydrochloride **1** with an acyl chloride, the Michaelis–Becker-like addition of diethyl phosphite to the *N*-acylimidate **2** in a PTC system and finally nucleophilic substitution of the ethoxy group of the 1-ethoxyphosphonate derivative **3** with triphenylphosphonium tetrafluoroborate.[1]

Then our efforts were concentrated on further extending the utility of this new, promising method for α-phosphonium derivatives **4** of other phosphonates (R^1 = Bn, *i*-Pr, *i*-Bu) possessing an amino group protected with easily removable acyl group, such as *e.g.* Cbz group. In the studies on the reactivity of the obtained compounds it turned out that these practically unknown phosphonium salts were in fact convenient materials in some further transformations due to increased electrophilicity of their α-carbon. Thus, we have demonstrated the possibility of performing the Michaelis–Arbuzov-like reaction with phosphorus nucleophile, such as triethyl phosphite, to give α-aminobisphosphonate derivatives **5**, that are used in the treatment of osteoporosis and other related bone diseases.[2-4]



R^1 = H, Alk, Ar; R^2 = Me, *t*-Bu, Bn, OBn

References

[1] A. Kuźnik, R. Mazurkiewicz, M. Zięba, K. Erfurt, *Tetrahedron Lett.*, **2018**, *59*, 3307-3310.
[2] P. Kafarski, B. Lejczak, *Curr. Med. Chem.- Anti-Cancer Agents*, **2001**, *1*, 301-312.
[3] R. Graham, G. Russell, *Bone*, **2011**, *49*, 2-19.
[4] V. D. Romanenko, V. P. Kukhar, *Arkivoc*, **2012**, *4*, 127-166.

P-022

SW-AdSV using the BiF/GCE as a sensor is the first analytical method allowing the quantitative determination of a new anticancer agent

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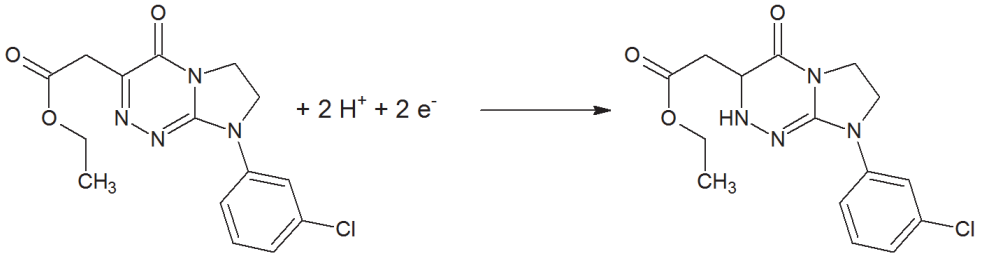
A square-wave adsorptive stripping voltammetric protocol (employing the bismuth film modified glassy carbon electrode – BiF/GCE – as a reusable sensor) was extensively optimized allowing the quantitative determination of an unknown anticancer agent, e.g. ethyl [4-oxo-8-(3-chlorophenyl)-4,6,7,8-tetrahydroimidazo[2,1-*c*][1,2,4]triazin-3-yl]acetate (ETTA) in its pure form and in serum. This novel molecule has been patented previously as useful in the treatment of two human multiple myelomas (resistant and susceptible to thalidomide) as well as human solid tumours of cervix and breast [1]. Furthermore, ETTA has been shown to evoke much higher necrosis rates in human tumour cells in comparison to that detected in normal cells [2].

The developed electroanalytical procedure with a significant innovation proved to be particularly suitable for the determination of ETTA in spiked serum samples – at concentration ranges typically measured in medicated patients – after removing the interfering components by solid phase extraction. This procedure is based on the adsorptive accumulation of this small molecule at the surface of the prepared sensor (BiF/GCE) as well as the reductive behaviour of this electroactive compound during the analytical stripping step. The electron gain mechanism at the developed sensor, characterizing the electrochemical behaviour of ETTA was clarified for the first time. Under experimental conditions a well-defined single cathodic peak was observed due to a two proton and two electron reduction of the electroactive –N(2)=C(3) double bond of azomethine-type in the triazinone ring of test analyte resulting in its dihydro-derivative with –NH–CH grouping. This reduction mechanism was confirmed by cyclic voltammetry.



References

[1] K. Sztanke, M. Sztanke, inventors. Medical University of Lublin, assignee. Polish Patent 219424, April 30, 2015.
[2] M. Sztanke, J. Rzymowska, K. Sztanke, *Bioorg. Med. Chem*. **2013**, *21*, 7465-7480.

P-023

NMR Studies of heptacoordinated organosilicon compounds

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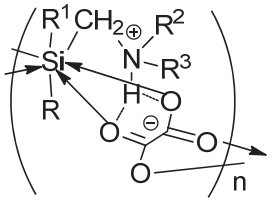
Hypercoordinated (λ^{5-7}) organosilicon compounds are intensively studied by many research groups due to their interesting structure and synthetic usability.[1]

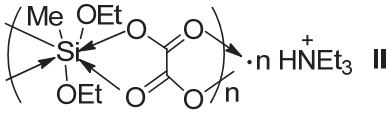
The presented research deals with the NMR studies of heptacoordinated organosilicon compounds. Goshchava silanates (**I**) are neutral, soluble in water and DMSO heptacoordinated silicon compounds.[2] When dissolved in water, compounds **Ia**,**b** hydrolyze to corresponding derivatives **Ic**. That is why the investigations of compounds **I** were carried on in dry DMSO-d6.



I a - e

R, R^1 = H (**Ia**), OEt (**Ib**), OH (**Ic**),
$CH_2C_6H_5$, H (**Id**), 2-furyl (**Ie**)

It is shown that for studied heptacoordinated compounds **Ia-b** the values of the chemical shift of silicon are from 169.0 to 174.7 ppm. On the other hand, the difference between chemical shifts of **Ib** and heptacoordinated derivative of ammonium type **II** is 11.2 ppm.



II

Abnormal ^{13}C chemical shifts reveal 2-furyl groups in compound **Ie**. For C-4 and C-5 of the ring the ^{13}C chemical shifts remain practically unchanged as compared to unsubstituted furan, while chemical shifts of carbon atoms C-2 and C-3 are considerable moved downfield (the carbon atoms deshielding is 17.5 and 19.4 ppm, correspondingly). The nature of these specific properties will be discussed.

References

[1] V. Y. Lee, *Organosilicon Compounds: Experiment (Physico-Chemical Studies) and Applications*, **2017**, Academic Press.

[2] N.P. Erchak, K. Pypowski, E.E. Liepinsh, *Russ. J. Gen. Chem*., **2007**, *77*, 2210-2211..

P-024

Conformational analysis of the cellobiose derivative of azacrown ether

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The search for new compounds which can find practical applications in various areas of life is an extremely important branch of supramolecular chemistry. Particularly noteworthy are the molecules of biological importance: potential drugs, as well as their selective transporters (receptors). The latter, by formation of a complex with a drug, can significantly change the absorption, distribution and excretion of excess of drugs, as well as their interactions with other pharmaceuticals. Drug carriers may be macrocyclic compounds, such as cyclodextrins, calixarenes or cucurbiturils. Also crown ethers and azacrown ethers, as well as their derivatives, may play this role. In the Faculty of Chemistry, University of Lodz the team of prof. B. Kryczka and dr hab. S. Porwański managed to synthesize new compounds, in which cellobiose groups are linked to azacrown ethers through urea bridges. One of these compounds is 1,10-*N,N'*-Bis-(β-D-ureidocellobiosyl)-4,7,13-trioxa-1,10-diazacyclopentadecane.[1]

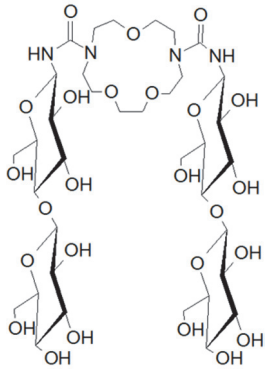

Figure 1. Structure of 1,10-*N,N'*-Bis-(β-D-ureidocellobiosyl)-4,7,13-trioxa-1,10-diazacyclopentadecane

Since no crystallographic data for this molecule is available, to determine its most stable structures a thorough conformational analysis has been performed at the Density Functional Theory.

On the poster are presented five lowest energy structures of this compound found from the B3LYP-GD2/6-31G(d,p) calculations performed in water described by Polarizable Continuum Model, and are analyzed their relative energies. For the most stable conformer the IR and NMR spectra are also shown and compared to the experimental data available.

Acknowledgment
Calculations have been carried out using resources provided by Wroclaw Centre for Networking and Supercomputing (http://wcss.pl), grant No. 443.

References

[1] M. Pintal, B. Kryczka, A. Marsura, S. Porwański, *Carbohyd. Res.*, **2014**, *386*, 18-22.

P-025

Synthesis of new heterocyclic system – oxazolo[4,5-*c*][1,5,2] oxazophosphepine-1-oxide

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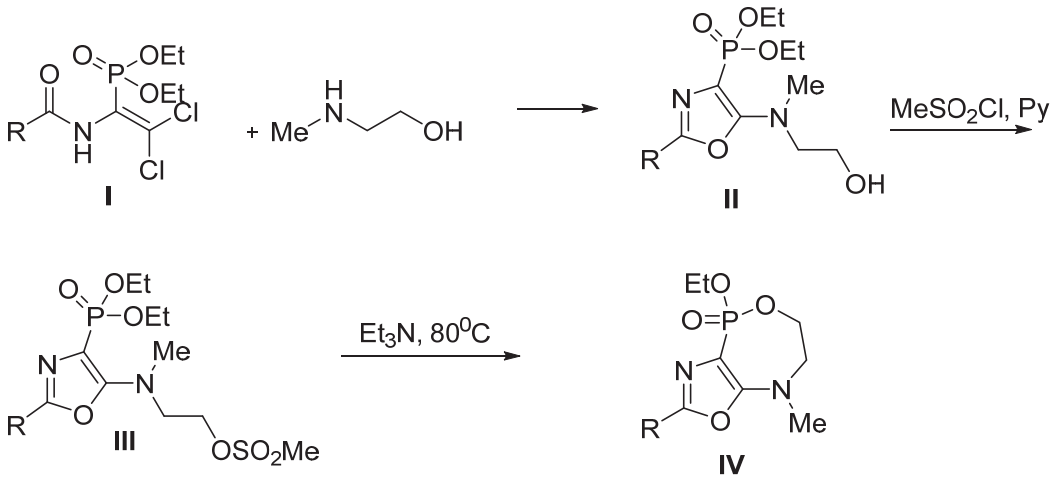
It is known that interaction of diethyl esters of 1-acylamino-2,2-dichloroethenylphosphonic acids (I) with amine alcohols leads to formation of 4-phosphorylated derivatives of 1,3-oxazole (II) containing aminoalkanol substituents in position 5 [1] . It turned out that these compounds are promising for further cyclocondensations. In particular, we have found treating oxazols (II) with methanesulphochloride leads mainly to compounds (III) in high yields, which in turn are converted into derivatives of new heterocyclic system oxazolo[4,5-*c*][1,5,2]oxazophosphepine-1-oxide (IV) when heated in the presence of triethylamine.



R = Me, Ph, 4-Tl, 4-$O_2NC_6H_4$

Compounds (IV) are stable solids. Their structure well correlates with the results of elemental analysis, ^1H , ^{13}C, ^{31}P NMR spectroscopy and mass spectrometry.

References

[1] Abdurakhmanova E. R., Lukashuk E.I., Golovchenko A.V., Brovarets V.S. *Russ. Jorn. Gen. Chem*., **2016**, *86*, 1206-1208..

P-026

Synthesis of polymers derived from the complex of (±)-trans-N, N'-bis (salicylidene) -1,2-cyclohexanediamine (II) and kinetics of electrode processes

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The complexes of nickel with salen and it's derivatives under current conditions undergo polymerization. Electrodes modified with such polymers find application in the catalysis of reactions oxidation or reduction[1,2]. The aim of the presented research is electrosynthesis of a polymer (polyNisalhd) derived from the complex Ni(II) with (±)-trans-N,N'-bis(salicylideno)-1,2-cycloheksanediamine and investigating the kinetics of the processes occurring on electrodes modified with films of this polymer. This may allow future use of these electrodes for electrocatalysis.

PolyNisalhd modified electrodes were obtained based on cyclic voltammetry, during registration of 1 - 25 cycles on a platinum electrode, immersed in a complex solution in AN, against tetraethylammonium perchlorate (TBAP). As a result of this process, yellow polymer films were obtained on the surface of the electrodes. Diffusion coefficients are a measure of the kinetics of electrode processes. Kinetic studies by cyclic voltammetry showed decreasing diffusion coefficients along with the increase in the thickness of polymer films. Only in thin films obtained as a result of 1-5 electropolymerization cycles kinetic limitations don't occur. Kinetics were also examined by electrochemical quartz crystal microbalance (EQCM). Such experiments allow to determine the size of the mass transported into polymeric films. The mass of ions and solvent transported into the film begins to increase from the oxidation potential of the polymer, which can be seen from the decreasing frequency. During anode processes, it decreases with the increase of polymer film, frequency indicates the increase in the mass of ions transported into films. For thicker films, obtained as a result of more than 5 polymerization cycles, the increase in the mass transported is clearly limited, which confirms the limitations in the transport of cargo by these films. The dependence of charge on potential also indicates kinetic difficulties in thicker films. The reason for the restrictions in the transport of the load is most likely the compact structure of the cross-linked conductive polymer. Optimal kinetics for films obtained as a result of 3-5 electro-polymerization cycles predestines these films for electrocatalytic applications.

References

[1] E.R. Wagoner, C.P. Baumberger, B.H.R. Gerroll, D.G. Peters, Electrochim. Acta, 2014, 132, 545-556,

[2] P.G. Cozzi, Chem. Soc. Rev., 2004, 33, 410-432..

P-027

Catalysis on the electrode modified with the manganese-2,2'-bipyridine complex

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The interest in Mn(II) complexes is related to the role of this element in anodic catalysis. However, the tendency to undergo the disproportionation process of thermodynamically unstable Mn(III) ions in the aqueous environment complicates these processes. Counteracting this process can be achieved by using excess Mn(II) ions, maintaining low pH, complexing or by partially isolating the catalyst from the aqueous environment by binding it to, for example, the polymer.

The aim of the study was to assess how the binding of the catalyst to a hydrophobic-hydrophilic polymer film (Nafion) and partial separation from the aqueous environment will reduce the tendency to disproportionation process of Mn(III) ion and thus influence the stabilization of electrode and electrocatalytic processes.

A glassy carbon electrode was modified by embedding Nafion with incorporated in its structure Mn(II) complexes with 2,2'-bipyridine (*2,2'-bpy*). The electroactivity was tested by multiple recording of cyclic voltammetry curves in the solution of the supporting electrolyte. The instability of peak currents in the initial cycles is a consequence of ions movement.

The characteristic of the anodic process was evaluated on the basis of voltammograms recorded at increasing sweep rates. A single anodic peak, moving along with the increase of sweep rate towards higher potentials and a wide, complicated cathodic peak, splitting with increasing scan rate, as well as value of $i_{pk} / i_{pa} < 1$ indicate that the investigated process proceeds according to EC mechanism, with poorly marked disproportionation reaction of anodic product.

The electrocatalytic properties were analyzed against glycolic acid. The change in the area of both catalyst reduction peaks indicates the participation of both products of the disproportionation reaction in the electrocatalysis process. On the other hand, the increase in the anodic peak potentials in the electrocatalysis reaction is a result of the weakening of the interaction of the complex with the sulfone groups of Nafion by a competitive anion such as the reducer. This conclusion results from the values of E_f, which in the polymer environment are lower than the values determined in the water-alcohol solution of the complex, which results from the interaction of the complex with Nafion.

References

[1] B.S. Lane, K. Burgess, *Chem. Rev.* **2003**, *103*, 2457-2483.

P-028

Synthesis of quinoline glycoconjugates with potential anticancer activity using azide-alkyne 1,3-dipolar cycloaddition

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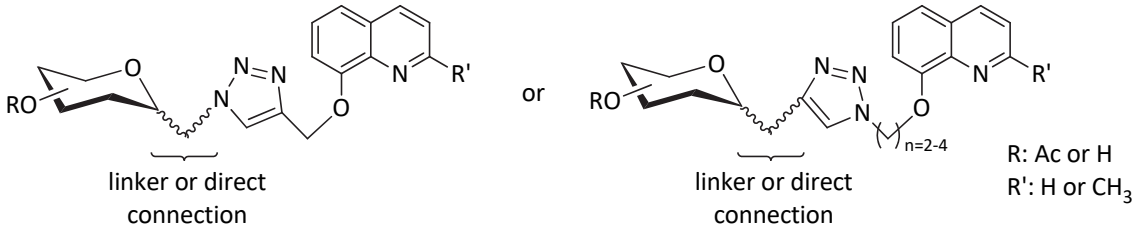
8-Hydroxyquinoline (8HQ) is a heteroaromatic compound used in designing a new active agents with therapeutic potential. One of the possible methods for derivatization of the 8HQ scaffold is formation of glycoconjugates. Experimental results indicate that the mechanism of anticancer activity of 8HQ derivatives is associated with their abilities to chelate of copper(II) ions, that are necessary for cancer growth and angiogenesis. However, the presence of a sugar moiety prevents the undesirable systemic chelation of copper(II) ions by 8HQ and thus reduced toxicity effect of anticancer agents.[1,2]

In our research group, we design and synthesize glycoconjugates of 8HQ derivatives as well as test their anticancer activity. Our research shows that the presence of both: a sugar unit as well as a heteroaromatic ring in the glycoconjugates structure improves the antiproliferative activity of the test compounds against a wide bunch of cancer cell lines compared to the aglycons.[3]

In this work we present simple and effective approach for the synthesis a series of glycoconjugates derivatives of 8HQ. Different sugar derivatives substituted in the anomeric position with a substituent containing the azide moiety or triple bond were connected with quinoline derivatives by functionalizing their 8-OH moiety. For the synthesis of these compounds, we used the copper(I)-catalyzed azide-alkyne 1,3-dipolar cycloaddition as an example of the innovative *click chemistry* concept (Scheme 1). This type of reaction in a simple, easy and inexpensive way leads to products with high yield, purity and selectivity.[4] The structures of all obtained compounds were confirmed by means of NMR and MS spectra.



Scheme 1.

References

[1] V. Prachayasittikul, S. Prachayasittikul, S. Ruchirawat, V. Prachayasittikul, *Drug Des. Dev. Ther.*, **2013**, *7*, 1157–1178.

[2] E. C. Calvaresi, P. J. Hergenrother, *Chem. Sci.*, **2013**, *4*, 2319–2333.

[3] G. Pastuch-Gawołek, K. Malarz, A. Mrozek-Wilczkiewicz, M. Musioł, M. Serda, B. Czaplińska, R. Musioł, *Eur. J. Med. Chem.*, **2016**, *112*, 130-144.

[4] H. C. Kolb, K. B. Sharpless, *DDT*, **2003**, *8*, 1128-1137.

P-029

Reduction of P=O bond in bicyclic phosphine oxides using borane complex

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Transition metal catalysts are very useful in many reactions performed at laboratory and industrial scale. Their use allows to increase efficiency of the reaction, reduce the reaction time and lower the cost of processes. Among wide group of catalysts complexes of transition metals with phosphine ligands are successfully used in various catalytic transformations, both achiral and stereoselective.

During our studies devoted towards the synthesis of bicyclic phosphines we attempted the synthesis of new phosphine ligands possessing benzophospholane or benzophosphorinane skeleton. Recently the synthesis of benzophospholane and benzophosphorinane oxides has been described by our research group [1]. Phosphine oxides were reduced using the literature protocol. Benzophosphole oxides were submitted to a reaction with borane dimethylsulfide complex affording phospine-boranes with excellent yields and selectivity. In the case of benzophosphorinane oxides reduction with phenylsilane was necessary and the formed free phosphines were protected as their borane complexes. Phosphine-boranes were next used as a precursors of rhodium complexes.

References

[1] Wlodarczyk K.; Stankevic M., *Tetrahedron,* **2016**, *72*, 5074-5090.

P-030

Microwave-promoted synthesis of s-tetrazine-1,3,4-oxadiazole derivatives

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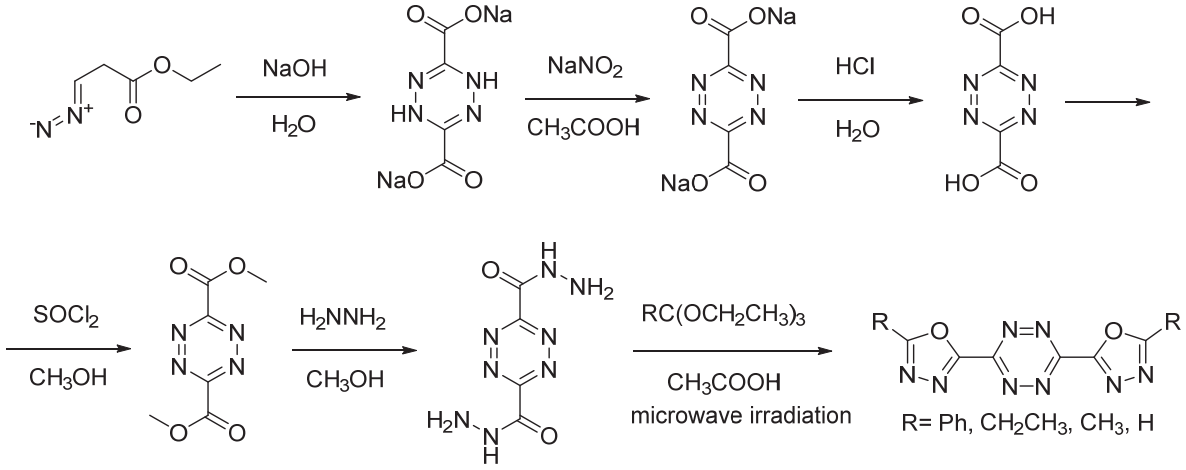
Derivatives of *s*-tetrazine and 1,3,4-oxadiazole are very popular among scientists due to the wide range of potential applications. Both systems exhibit excellent optoelectronic properties, which allows their use inter alia in the production of OLEDs.[1,2] In addition, the compounds of both types often show biological activity.[3,4] That is why it seems to be particularly advantageous to combine *s*-tetrazine system with 1,3,4-oxadiazole derivatives.

Considering the importance of both systems to different branches we report here the efficient path of obtaining *s*-tetrazine derivatives containing 1,3,4-oxadiazole scaffold. The final products were obtained in a six-step reaction sequence, including the synthesis of dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate described in literature, conversion of this compound into 1,2,4,5-tetrazine-3,6-dicarbohydrazide and reaction with triethyl ortoesters. The last step required the use of microwave assistance. Fluorescent and spectroscopic properties were measured for the desired products.



Scheme 1. Synthesis of the title compounds

References

[1] M. Moral, A. Garzón, Y. Olivier, L. Muccioli, J.C. Sancho-García, J. M. Granadino-Roldán, M. Fernández-Gómez, *J. Phys. Chem. C*, **2015**, 119, 18945–18955.

[2] Y. Tao, Q. Wang, C. Yang, Q. Wang, Z. Zhang, T. Zou, J. Qin, D. Ma, *Angew. Chemie - Int Ed*. **2008**, 47, 8104–8107.

[3] H. Wu, S. C. Alexander, S. Jin, N. K. Devaraj, *J. Am. Chem. Soc*., **2016**, 138, 11429-11432.

[4] V. B. Iyer, B. Gurupadayya, V. S. Koganti, B. Inturi, R. S. Chandan, *Med. Chem. Res.,* **2017**, 26, 190–204.

P-031

Anionic Ring-Opening Polymerization of *β*-Butyrolactone initiated with sodium phenoxides

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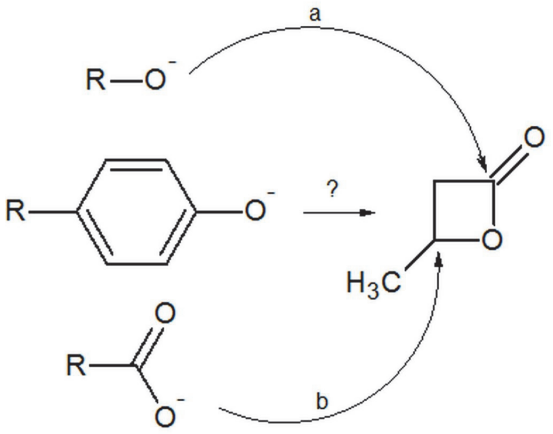
Poly([R]-3-hydroxybutyrate) (PHB) is a biopolymer produced by microorganisms as a carbon and energy source. PHB is a biodegradable and biocompatible aliphatic polyester considered as future „green" engineering plastics for biomedical, food package or drug delivery applications. Poly(3-hydroxybutyrate) is synthesized by biotechnological processes, applying bacterial fermentation of substrates such as sucrose, corn, cane sugar *etc.* or as a result of a chemical reaction*, i.e.* by the polymerization of *β*-butyrolactone (4-methyl-2-oxetanone, BL), in coordination, cationic or anionic ring-opening polymerization.

Ring-opening in the anionic polymerization of *β*-lactones (AROP) strongly depends on the structure of the monomer and the initiator used. Ring-opening of the monomer can occur at the acyl-oxygen or alkyl-oxygen positions. In the reaction of *β*-lactones with an initiator which is weak nucleophile, *e.g.* an alkali metal carboxylate, the attack occurs on the C4 carbon (Scheme 1. b) of the lactone ring and subsequent alkyl-oxygen bond scission occurs. The carboxylate ion formed in this reaction is the center of the chain growth. If a strong nucleophile, *e.g.* an alkali metal alcoholates are used as initiator, the attack occurs at C2 carbon (Scheme 1. a) with cleavage of the acyl-oxygen bond and alkoxide anion formation. However, the polymer chain growing centers (alcoholate or carboxylate) strongly depends on the *β*-lactone structure, *i.e.* the presence of hydrogen at C3 carbon. The communication proposes a mechanism of *β*-butyrolactone AROP initiated with various sodium phenoxides and reveals the effect of the initiator basicity on the position of the attack in the monomer.



Scheme 1.

P-032

Synthesis and structures of new chemiluminogens based on acridinium derivatives

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Medical diagnostic is a very fast developing section of science. Numerously research groups are looking for a new methods which determine concentration of human blood or tissue components. Chemiluminometric methods are interesting in this field, because of cognitive and utilitarian nature. As far as it is known chemiluminescence has very wide perspectives of application.[1] It can be used in biochemical, chemical and medical analysis to quality and quantity determination of concentration of enzymes, hormones, antibiotics and others.[2,3] One of the most extensively explored and promising group of compounds showing the ability to chemiluminescence are acridinium derivatives.

Chemiluminescent properties of acridinium derivatives are known since 1970's.[4] High intensity and quantum efficiency of acridinium derivatives initiated investigations of a new chemiluminogens with better chemiluminescenct properties. For now one of the most examined acridinium derivatives are 10-methyl-9-(phenoxycarbonyl)acridinium derivatives, which have limit detection at the level of 10^{-19} mole of analyte or below. In this communication will be present methods of synthesis and structure determination of 10-methyl-9-(thiophenoxycarbonyl)acridinium derivatives.

Acknowledgment

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References

[1] Cormier M.J., Hercules D.M., Lee J., *Chemiluminescence and bioluminescence*, Springer Science + Business Media, LLC, **1973**, 1–6.
[2] Roda A., Guardigli M., *Anal. Bioanal. Chem.,* **2012**, *402*, 69–76.
[3] Ren L., Cui H., *Luminescence*, **2014**, *29*, 929–932.
[4] McCapra F., *Clin. Chem.,* **1983**, *29*, 1474–1479.

P-033

Mechanism of chemiluminescence of new acridine derivatives

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Acridone/acridine analogs are one of the most studied heterorganic compounds with a very wide range of biological activity. On the other hand acridine derivatives are chemiluminogens that independently emits light in the presence of H_2O_2 and alkaline media [1-3]. Efficient chemiluminogens are N-substituted acridine derivatives that have been used in immunological diagnostics as luminogen fragment of chemiluminescent labels [4].

It is extremely important to know the mechanism of reaction leading to the generation of light by chemiluminogens. Chemiluminescence of acridinium begins with the nucleophilic attack of peroxide ion in the alkaline environment. The main pathway of the chemiluminescence reaction ("light pathway") leads to formation of the electronically excited product – 10-methyl-9-acridinone. The computational studies present two concurrent pathways ("dark pathway"), which do not lead to the formation of electronically excited product: the first is the hydrolysis of the 10-methylacridinium molecule and the second one is the formation of so–called "pseudobase" and the products its transformation.

In the communication will be presented mechanism of chemiluminescence of new acridine derivatives.

Acknowledgment

This study was financed from the Research of Young Scientists grant no. 538-8220-B776-17/18. The calculations were done on computers of the Wroclaw Centre for Networking and Supercomputing (grant no. 215).

References

[1] I. Beheshti, F. McCapra, A. K. Campbell, J. S. Woodhead, *Clin. Chem*., **1983**, *29*, 1474–1479.

[2] G. Zomer, J.F.C. Stavenuiter, *Anal. Chim. Acta*., **1989**, *227*, 11-19.

[3] J. Czechowska, A. Kawecka, A. Romanowska, M. Marczak, P. Wityk, K. Krzymiński, B. Zadykowicz, *J. Luminescence.*, **2017**, *187*, 102-112.

[4] A. Natrajan, D. Wen, *Org. Biomol. Chem*., **2015**, *13*, 2622–2633.

P-034

Structure considerations on novel acridinium thioesters

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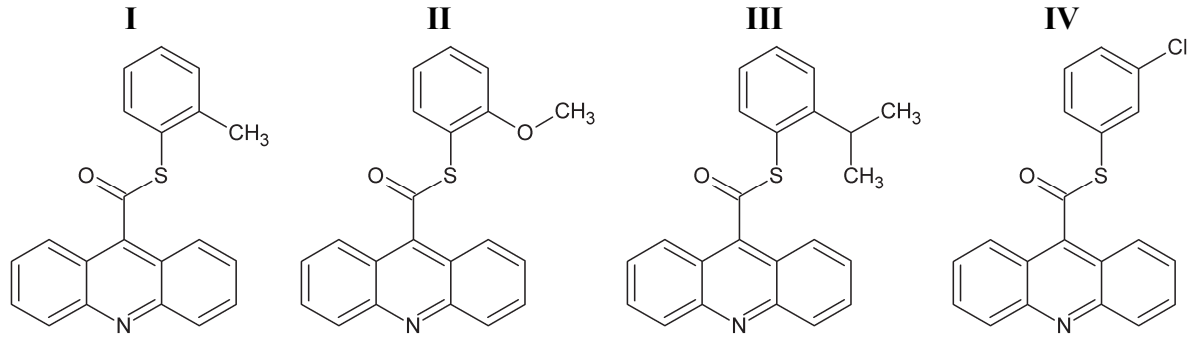
The 10-methylacridinium-9-carboxylic acid derivatives are extensively used as reagents for chemiluminescence labeling of biological molecules (e.g. antigens, antibodies, hormones).[1] They can serve as tracers in the assays of oxidative entities (e.g., hydrogen peroxide, peroxide anion) and other nucleophilic individuals in environmental, biological, or pharmaceutical samples.[2] Quantitative analyses utilizing aromatic esters of 10-methylacridinium-9-carboxylic acid (acridinium esters) are regarded as some of the most sensitive analytical methodologies available nowadays, enabling analytes to be detected even at the subattomole level.[3] The enhancement of their luminogenic properties can be achieved through the exchange of the oxygen atom in the carboxylic group with an sulfur atom creating esters of acridine-9-carbothioic *S*-acid (acridinium thioesters). These compounds exhibit higher chemiluminescent yield in comparison to acridinium esters , which may contribute to their use as biological markers and indicators.

Herein we present the crystal structure, intermolecular interactions and Hirshfeld Surfaces studies of four acridinium thioesters: (**I**) 9-((2-methyl)-thiophenoxycarbonyl)acridine, (**II**) 9-((2-methoxy)-thiophenoxycarbonyl)acridine, (**III**) 9-((2-isopropyl)-thiophenoxycarbonyl)acridine, and (**IV**) 9-((3-chloro)-thiophenoxycarbonyl)acridine



Scheme 1. Structure of investigated compounds.

References

[1] L. M. Campos, C. L. B. Cavalcanti, J. L. Lima-Filho, L. B. Carvalho Jr., E. I. C. Beltrão, *Biomarkers*, **2006**,11, 480–484.

[2] D. W. King, W. J. Cooper, S. A. Rusak, B. M. Peake, J. J. Kiddle, D. W. O'Sullivan, M.L. Melamed, C.R. Morgan, S. M. Theberge, *Anal. Chem.*, **2007**, 79, 4169–4176.

[3] L. J. Kricka, *Anal. Chim. Acta*, **2003**, 500, 279–286.

P-035

Computational methods in investigations of 9-substituted acridines and their *N*-methylated salts

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An interesting group of acridine derivatives are those capable of chemiluminescence. This ability is displayed by acridinium cations alkyl-substituted at the endocyclic nitrogen atom and containing electron-attracting substituents at C9; this latter atom is thus susceptible to the attack of anionic oxidants [1]. Oxidation gives rise to electronically excited N-alkyl-9-acridinones. Their relaxation is accompanied by the emission of light, i.e. chemiluminescence [1,2]. The efficiency of chemiluminescence, no greater than a few per cent [1], can be affected by the presence of various substances in the medium, including nucleophilic species, competing with oxidants for substitution at C9 [3,4]. This effect is utilized in the assay of oxidants, nucleophiles or other entities, and in such cases acridinium cations serve as chemiluminogenic indicators [1,3]. Acridinium chemiluminogens can also be linked via a spacer (e.g. alkyl chain) to an active group able to react with appropriate fragments of macromolecules; such chemiluminescent labels are widely used in medical, biological and environmental analyses [1].

The compounds on which this communication focuses are the chemiluminogenic substituted acridinium trifluoromethanesulphonates and their precursors, 9-substituted acridine derivatives. The aim of the investigations was to examine the properties of these compounds by combining experimental methods with appropriately selected computational ones [2–5]. A further aim was to discover whether and to what extent the stability and behaviour of the compounds investigated affect their utilitarian potency.

Acknowledgment

The calculations were done on computers of the Wroclaw Centre for Networking and Supercomputing (grant no. 215).

References

[1] C. Dodeigne, L. Thunus, R. Lejeune, *Talanta*, **2000**, *51*, 415-439.
[2] K. Krzymiński, A. Ożóg, P. Malecha, A.D. Roshal, A. Wróblewska, B. Zadykowicz, J. Błażejowski, *J. Org. Chem.*, **2011**, *76*, 1072-1085.
[3] B. Zadykowicz, J. Czechowska, A. Ożóg, A. Renkevich, K. Krzymiński, *Org. Biomol. Chem.*, **2016**, *14*, 652-668.
[4] J. Czechowska, A. Kawecka, A. Romanowska, M. Marczak, P. Wityk, K. Krzymiński, B. Zadykowicz, *J. Luminescence*, **2017**, *187*, 102-112.
[5] B. Zadykowicz, P. Storoniak, *J. Therm. Anal. Calorim.*, **2017**, *129*, 1613-1624.

P-036

Imidazolines bearing the hydrazino function as antioxidant agents

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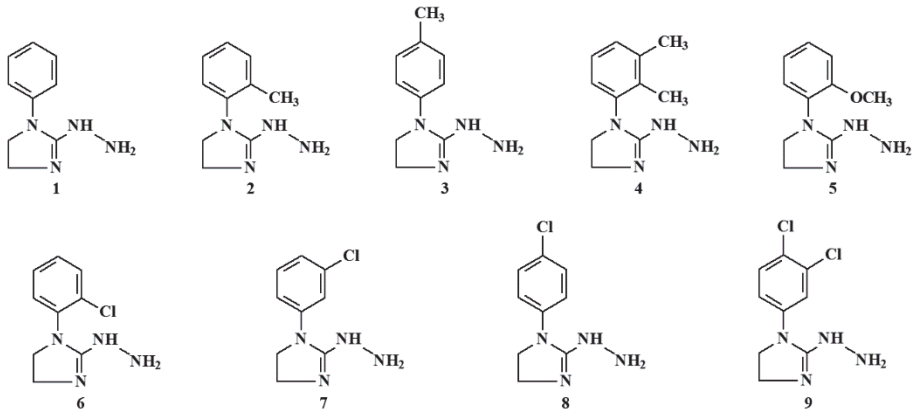
Strong antioxidant properties of structurally related imidazolines (**1-9**), bearing the hydazino function and the aromatic phenyl moiety unsubstituted or substituted by electron-donating (e.g. alkyl, dialkyl or alkoxy) or electron-withdrawing (e.g. chloro or dichloro) groups, are disclosed for the first time. The studied heterocyclic compounds have been resynthesized for current research needs *via* successful hydrazinolysis of 1-aryl-2-methylsulfanyl-4,5-dihydro-1*H*-imidazoles. Their structures have been confirmed by combined spectroscopic data, DEPT, 2D NMR experiments and elemental analyses. In previous investigations the title compounds revealed significant antibacterial activities. In addition, these chemically and biologically important molecules have been previously utilized as the starting nucleophiles in synthesis of important fused azaisocytosine-containing molecules (including *inter alia* anticancer agents and a novel antagonist of A_{2A} adenosine receptors useful as a medicine for liver diseases).



DPPH$^{\bullet}$, GOR, NO and H_2O_2 scavenging properties of the investigated compounds are presented for the first time. For all the tested 5-membered nitrogen heterocycles a particular importance of the hydrazino function in an antioxidant effect was confirmed and the most likely DPPH$^{\bullet}$ and GOR scavenging mechanisms were proposed. The strongest DPPH$^{\bullet}$ scavengers proved to be molecules **2-4** with methyl or dimethyl substitutions at the phenyl moiety (revealing the potency superior to that of butylated hydroxyanisole – BHA, butylated hydroxytoluene – BHT, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid – Trolox, propyl gallate – PG and ascorbic acid – AA). Furthermore, hydrazinoimidazolines **2-4** revealed strong NO neutralising potencies – better than that of BHA (**2-4**), Trolox (**2** and **3**), BHT (**2** and **3**) and AA (**3**). Compound **5**, bearing 2-methoxy group at the phenyl moiety, proved to be an excellent scavenger of GOR, NO and H_2O_2 with the potency superior or comparable to the majority of antioxidants used, whereas **9** (with 3,4-dichloro substitution at the phenyl ring) and **4** were found to be effective in the neutralisation of H_2O_2 and GOR, respectively. Additionally, all the investigated imidazolines revealed the reducing power higher than that of BHT.

Finally, five hydrazino-containing imidazoline structures (**2-5** and **9**), revealing excellent or good antiradical activities, could be utilized as promising antioxidant candidates.

P-037

Synthesis of optically pure *N*-diphenylphosphino(phosphinoyl)alkyl(aryl)aziridines and their application in enantioselective reactions

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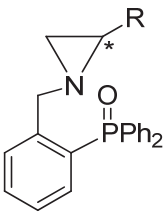
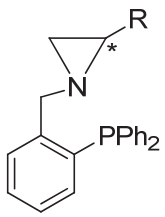
Asymmetrical synthesis is currently one of the most important directions in the development of research in organic chemistry. Its importance is increased by the fact of industrial demand for methods and technologies leading to optically pure organic compounds with defined physicochemical (new materials) and biological properties (active substances for new drugs, intermediates for the chemical, cosmetics and food industries, etc.).

The selection of a suitable optically active catalyst, affecting both the stereochemistry of the products obtained, as well as chemical performance and optical purity, is a key issue in modern asymmetric synthesis. For this reason, further research focusing on the synthesis of new, effective catalysts for stereocontrolled synthesis remains of interest to many research groups.

Therefore, the main objective of the work was the synthesis of new catalysts based on optically pure aziridine ring containing additionally diphenylphosphinoyl (A) or diphenylphosphino (B) moiety.



A



B

It should be emphasized that such derivatives have not yet gained place in asymmetrical synthesis, because they have never been tested in stereocontrolled reactions.

On the basis of our experience learned as well as preliminary studied we can claim that such compounds have potentially more possibilities of playing a significant role in this field.

Such type of catalysts also allow to extend the scope of the studies with a large group of asymmetric reactions in the presence of palladium.

Acknowledgment

Projekt zrealizowany w ramach programu Studenckie Granty Badawcze na Uniwersytecie Łódzkim.

P-038

Synthesis, anticancer and pharmacokinetic properties of 8-aryl-3-ethyl-7,8-dihydroimidazo[2,1-*c*][1,2,4]triazin-4(6*H*)-ones

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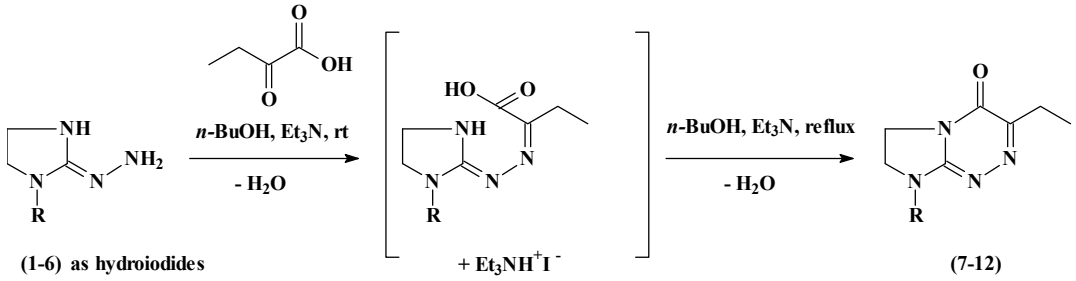
In continuation of our persistent search for innovative antimetabolites with much less toxic effects in normal cells and better biopharmaceutical properties, a class of title small molecular weight compounds (**7-12**) was synthesized. For this purpose equimolar ratios of 1-aryl-2-hydrazinylideneimidazolidine hydroiodides (**1-6**) were subjected to condensation with ethyl 2-oxobutanoic acid in *n*-butanol containing a small molar excess of triethylamine to yield the ring-opened ketimine intermediates (such as 2-[(1-arylimidazolidin-2-ylidene)hydrazinylidene]butanoic acids) with a concomitant elimination of water molecule and a simultaneous formation of triethylammonium iodide as a by-product of alkylation. Next, all the intermediates (having a protonated *endo*-nitrogen in the imidazolidine centroid) that were formed underwent a successive intramolecular cyclization under basic conditions in refluxing primary solvent medium, yielding the title compounds (**7-12**) with a simultaneous loss of water molecule. Structures of all the obtained compounds were confirmed by NMR methods and DEPT experiments. Their high purities were assessed using the HPLC technique and the retention times were determined for the first time on



1,7: R = C_6H_5; 2,8: R = 4-MeC_6H_4; 3,9: R = 2-ClC_6H_4; 4,10: R = 3-ClC_6H_4; 5,11: R = 4-ClC_6H_4; 6,12: R = 3,4-$Cl_2C_6H_3$.

various reversed-phase materials imitating biosystems.

The title molecules showed strong anticancer effects against human solid tumours of lung, cervix, breast and ovary in the assay BrdU-based. Several compounds in the same bioassay were found to be less cytotoxic towards non-cancerous cells of the same epithelial origin. The statistically significant relationships were found between the experimental log *k* factors of the majority of compounds and their *in silico* pharmacokinetic descriptors (such as: $P_{e,\ jejunum}$ and log BB – in the case of all the molecules, Caco-2, $f_{u,\ brain}$ and log P_{HSA} – in the case of **7**, **8**, **10**, **11**, **12**, and %F – in the case of **7**, **8**, **10**, **11**) predicting optimal biopharmaceutical properties *in vivo*. Noteworthy is that all the studied representatives in this series revealed much higher inhibitory effects on the growth of epithelial solid tumour cells in comparison with that shown by a commonly used antimetabolite – pemetrexed. Primarily, compounds **10** and **12** exhibited the best selectivity indices. However, several structures demonstrated better selectivity than pemetrexed in tumour cell lines of lung (**7**, **10**, **12**), cervix and breast (**9**, **10**, **11**, **12**) after 24-, 48- and 72-h incubation periods. Therefore, they may be promising candidates with prospective anticancer utility and therefore should be utilized in further more advanced investigations.

P-039

Effect of boron cluster substitution on electronic properties of purine chromophore in adenosine nucleosides

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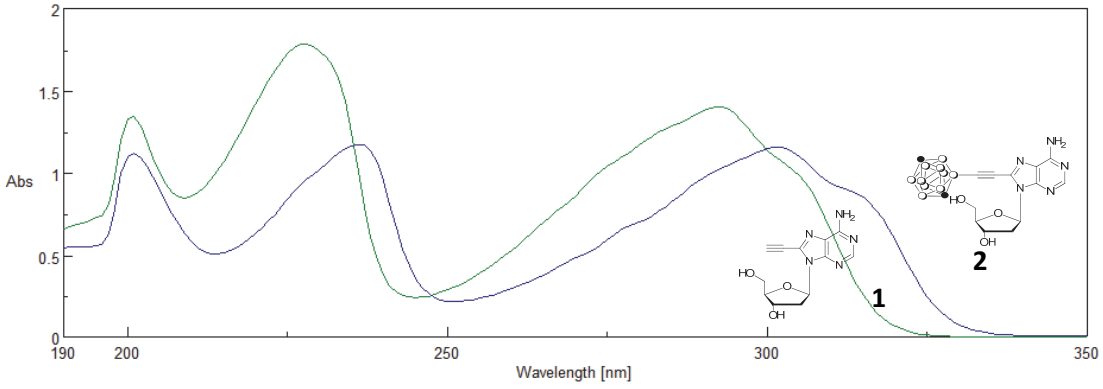
Adenosine plays important roles in various biological processes. There is also a range of adenosine derivatives used in in clinical practice as cardioprotective, anticancer or antiviral drugs. In spite of advantages there are also limitations of adenosine drugs such as low stability *in vivo,* low selectivity or low affinity towards protein target. [1] Introduction of cycloalkyl, phenyl, boron cluster or other highly lipophilic substituent can improve stability, selectivity and bioavailability of drug molecule. [2,3]

Although UV spectroscopy is not sufficient to determine compound structure it is useful for molecule characterisation due to spectrum-structure relationships. Using reference nucleosides enables obtaining valuable information on the structural characterisation of nucleosides. [4]

In the present communication we describe an effect of boron cluster modification on UV spectra of series of adenosine and deoxyadenosine derivatives substituted at position 2 or 8 through rigid ethynyl linker. Spectra of unmodified nucleosides and ethynyl- or phenylethynyl-modified molecules were studied for comparison. An electronic properties of the boron cluster modification relevant for the observed phenomenon are discussed.



Scheme 1. UV spectrum of ethynyl- (1) and boron cluster-modified deoxyadenosine (2).

Acknowledgment

This work was supported by National Science Center (grant 2015/16/W/ST5/00413) and statutory fund of IBM PAS.

References

[1] F. Issa, M. Kassiou, L. M. Rendina, *Chem. Rev*., **2011**, 111, 5701-5722.

[2] V. Ralevic, G. Burnstock, *Pharmacol. Rev*., **1998**, 50 (3), 413-492.

[3] Z. J. Leśnikowski, *J. Med. Chem*. **2016**, 59, 7738.

[4] C. W. Gehrke, K. C. T. Kuo, *Analytical Methods for Major and Modified Nucleosides - HPLC, GC, MS, NMR, UV and FT-IR,* Elsevier, **1989**.

Catalytic role of fluoride anion in hydrolysis of substituted alkylalkoxysilanes – theoretical study

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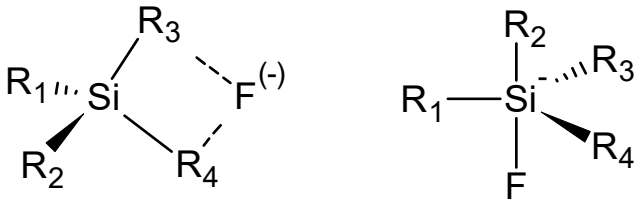
Hydrolysis of substituted silanes is one of the most important class of reactions silicon-containing molecules can undergo. Leading to many important precursors of polymers, this reaction type was extensively studied theoretically.[1] It is a well-known fact, that fluoride anon acts as a catalyst for such reaction and the latter issue prompted many researcher teams to investigate the impact $F^{(-)}$ possesses on the reaction mechanism and energetics.[2] Yet, in spite of researchers' long-lasting efforts, the exact role of fluoride anion in the process is at best elusive and still holds many mysteries to be explained.

Substituted alkylalkoksysilanes of various number of alkyl, alkoxyl and hydroxyl groups in combination with $F^{(-)}$ were investigated in order to explain impact $F^{(-)}$ can exert on energetics (and mechanism) of silanes hydrolysis. Two types of junction of such moieties, shown in scheme 1, were investigated: loose ion-dipole complexes (left) and pentacoordinated transition anions (right). Hydrolysis of substituted silanes without any catalyst was taken as the reference frame.

Compounds taken into account were:

- $Me_3Si(OMe)$ – trimethylmetoxysilane;
- $Me_2Si(OMe)_2$ – dimethyldimetoxysilane;
- $MeSi(OMe)_3$ – methyltrimethoxysilane;
- $MeSi(OMe)_2(OH)$ – methyldimethoxysilanol;
- $MeSi(OMe)(OH)_2$ – methylmethoxysilanediol;
- $(MeO)_2Si(OH)_2$ – dimethoxysilanediol;



Scheme 1. Two exemplary types of junction of $F^{(-)}$ with substituted silanes considered – ion-dipole complexes and pentacoordinate transition anions.
R_1, R_2, R_3, $R_4 \in$ {-Me; -OMe; -OH}

Results obtained suggest barrier heights dependence on $F^{(-)}$–junction form and presence of hydroxyl group in compounds investigated.

References

[1] Trinh, T. T., et al.; *J Phys Chem B*, **2006**, *110*, 23099; Liu, Y.,et al.; *ChemPhysChem*, **2012**, *13*, 2392

[2] Liu, Y., et al.; *New Journal of Chemistry*, **2013**, *37*, 1371.

P-041

A MEDT computational study on the [3+2] cycloaddition reactions of (Z)-diarylnitrones with 2-methyl-1-nitroprop-1-ene

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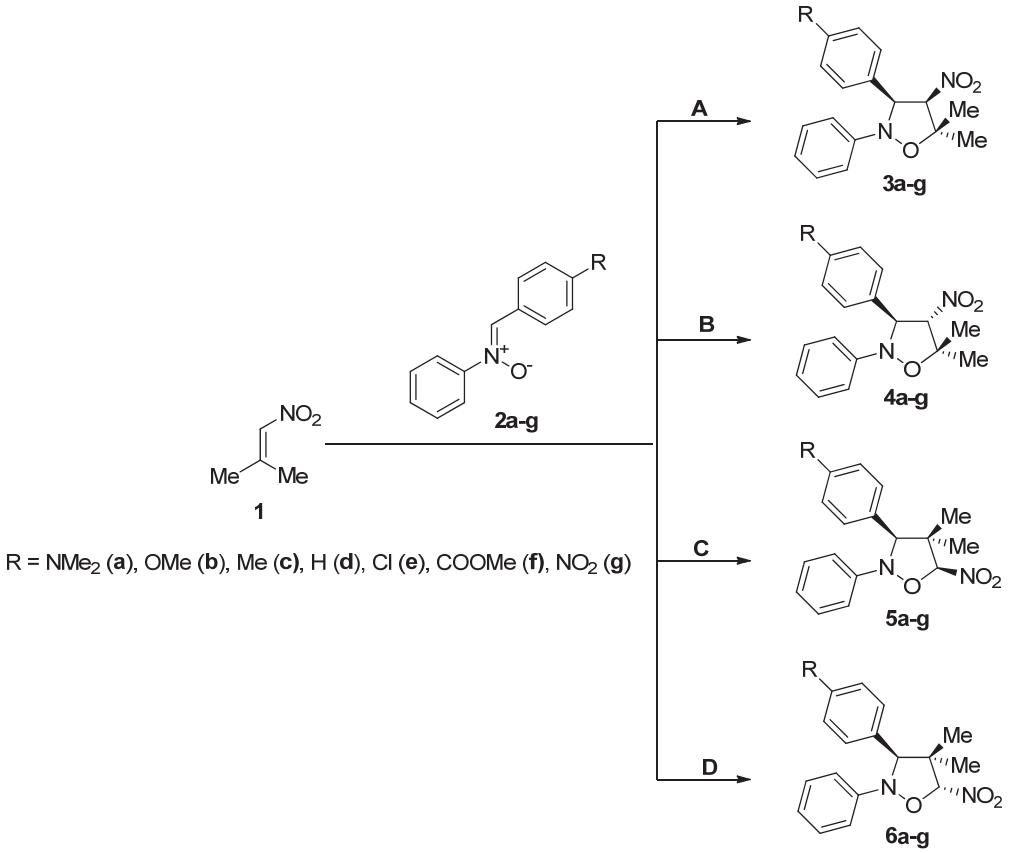
Theoretically possible reaction paths of [3+2] cycloaddition (32CA) between homogenous group of (Z)-C-aryl-N-phenylnitrones and 2-methyl-1-nitroprop-1-ene were explored in detail using B3LYP/6-31G(d) level of theory. All the considered 32CA processes are initiated by attack of the most nucleophilic oxygen atom in nitrone molecule to the most electrophilic beta-carbon atom in nitroethylene moiety. These types of interactions favour formation of 4-nitro substituted cycloadducts. Additionally, in the light of Molecular Electron Density Theory (MEDT), the 32CAs in question should be considered as polar processes with asynchronous transition states (TSs). However, the asynchronicity of localised TSs is unexpectedly low and evidently insufficient to enforce a stepwise, zwitterionic mechanism.



P-042

Synthesis and antitumor activity of selected selenoorganic compounds

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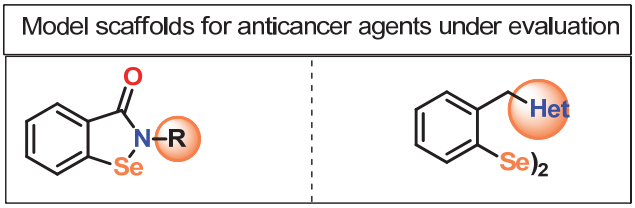
Among the selenoorganic compounds, Ebselen synthesized by Lesser and Weiss[1] as early as 1924 attracted a considerable interest in pharmacology research field. In 1984 it was found to serve as mimic of glutathione peroxidase (GPx), later on, the studies on its biological profile showed its antimalarial, antitubercular, and neuroprotective activities[2]. The second representative of benzisoselenazolones, Ethaselen (BBSKE) has shown good antitumor effects in many cancer models and currently is in phase I clinical trial for the treatment of TrxRd overexpressing advanced nonsmall cell lung cancer[3]. Diselenides, in turn, were found to be synthetically useful precursors for electrophilic, nucleophilic, radical species or precatalysts with a large applicability in organic synthesis. Apart from already known antimicrobial and antioxidant properties of diselenides, a cytotoxic profile for the examples of this class compounds has been tested in MCF-7 cells, and among them, 1,2-bis(chloropyridazinyl) diselenide was found to possess a significant activity obtained at low micromolar concentrations[4]. As there is still a lack of the detailed investigations based on a poor knowledge of their antitumor properties we wanted to contribute to the synthesis of a set of ebselen-like compounds and a series of diversely functionalized diaryl diselenides, with the aim of evaluating their antiproliferative activity.



Acknowledgment

Acknowledgement for the financial support from the Polish National Science Center (Polonez 2 to LS (Reg. No: 2016/21/P/ST5/03512)).

References

[1] a) R. Lesser, R. Weiss, Chem. Ber., **1924**, 57B, 1077–1082; b) D. Bartolini, L. Sancineto, A.F. de Bem, K.D. Tew, C. Santi, R. Radi, P. Torquato, F, Galli. *Adv. Cancer Res.* **2017**, *136*, 259.

[2] a) M. T. Harris, D. M. Walker, M. E. Drew, W. G. Mitchell, K. Dao, C. E. Schroeder, et al. *Antimicrob.Agents Chem*., **2013**, *57(8),* 3731–3737; b) L. Favrot, A. E. Grzegorzewicz, D. H. Lajiness, R. K. Marvin, J. Boucau, D. Isailovic, et al. Nat. Comm., **2013**, *4,* 2748; c) H. Koizumi, H. Fujisawa, E. Suehiro, S. Shirao, M. Suzuki, Neurologia Medico-Chirurgica (Tokyo), **2011**, *51(5),* 337–343.

[3] L. Wang, Z. Yang, J. Fu, H. Yin, K. Xiong, Q. Tan, et al. *Free Radic Biol Med.,* **2012**, *52(5),* 898–908.

[4] C. Kim, J. Lee, M. S. Park, *Arch Pharm Res.,* **2015**, *38(5),* 659–665.

P-043

Alkylation of the K-Region in a Sterically Hindered Pyrene Carboxamide via Directed Reaction with Alkyllithiums under Air

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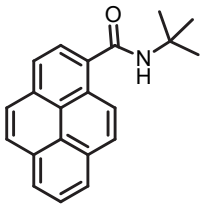
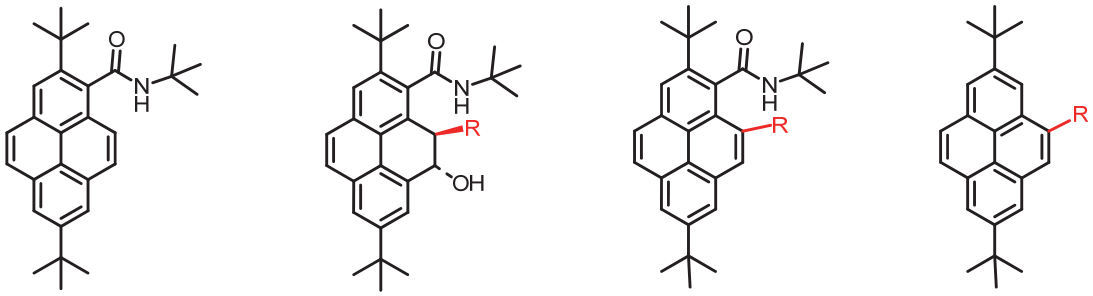
We have recently reported that secondary pyrene-1-carboxamide **1** undergoes regioselective directed lithiation at position 2- with *n*-BuLi/TMEDA, opening a route to 2-substituted derivatives.[1,2]



1

Sterically hindered *N*,2,7-tri-*tert*-butylpyrene-1-carboxamide **2** treated with *n*-BuLi, *iso*-BuLi, *sec*-BuLi and *n*-HexLi in THF in the presence of TMEDA and air afforded *trans*-*N,2,7*-tri-*tert*-butylpyrene-10-alkyl-9-hydroxy-9,10-dihydropyrene-1-carboxamides **3**. Trifluoroacetic acid promoted dehydration compounds **3** gave 10-alkyl derivatives **4**. The minor products of this reaction were deaminated compounds **5**.[3]



2 **3a-d** **4a-d** **5a-d**

R = **(a)** *n*-Bu; **(b)** *iso*-Bu; **(c)** *sec*-Bu; **(d)** *n*-Hex

References

[1] A. Wrona-Piotrowicz, M. Ciechańska, J. Zakrzewski, R. Métivier, A. Brosseau, A. Makal, *Dyes & Pigments*, **2016**, *125*, 331-338.

[2] A. Wrona-Piotrowicz, M. Ciechańska, J. Zakrzewski, A. Makal, *J. Photochem. Photobiol. A: Chem.* **2016**, *330*, 15-21.

[3] M. Ciechańska, A. Wrona-Piotrowicz, A. Makal, J. Zakrzewski, *J. Org. Chem.*, DOI: 10.1021/acs.joc.8b01024

P-044

Amide bond coupling between 3-amino-1,8-naphthalimides and 3-carboranylopropionic acids

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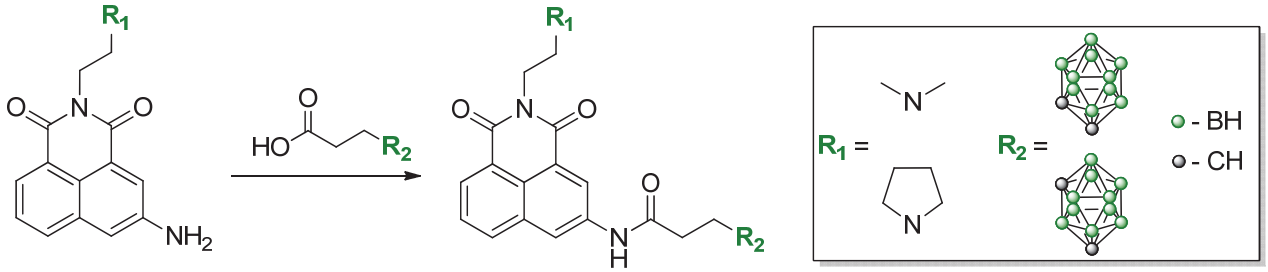
Amide bond formation is one of a most frequently occurring reactions in synthesis of biological active compounds.[1] Amide bonds play a major role in the elaboration and composition of biological systems, representing for example the main chemical bonds that link amino acid building blocks together to give proteins. There are not limited to biological systems and are indeed present in a huge array of molecules, including major marketed drugs: Atorvastatin, Lisinopril, Valsartan.[2] The prevalence of amide functionality sometimes gives the incorrect impression that there are no remaining synthetic challenges.

Naphthalimides are important aromatic heterocycles with immense pharmacological significance, as they serve as core scaffold for many antitumor, anti-inflammatory, antiprotozoal, antiviral agents. The tricyclic planar ring system of naphthalimide is primarily responsible for its intercalation with DNA to perturb the cellular events. Two of them mitonafide and amonafide were used in clinical trials.[3]

In our laboratory we have an on-going project entitled "*Molecules binding DNA – synthesis and properties of DNA intercalators containing boron clusters*". The goal of the research project is to obtain new, modified intercalators like naphthalimides modified with carborane cluster in various positions of the planar ring.

In the poster we will present the preparation of 3-aminonaphthalimide derivatives bearing carborane clusters obtained by amide bond formation (Scheme 1). Different methods for synthesis of the desired compounds will be discussed.



Scheme 1. Synthesis of boron cluster containing naphthalimide derivatives.

Acknowledgment

This study was supported by the National Science Centre, Poland (grant 2014/14/E/ST5/00577).

References

[1] D. G. Brown, J. Bostrom, *J. Med. Chem.*, **2016**, *59*, 4443-4458

[2] E. Valeur, M. Bradley, *Chem. Soc. Rev.*, **2009**, *38*, 606-631

[3] A. Kamal. N. R. Bolla, P. S. Srikanth, A. K. Sirvastava, *Expert Opin. Ther. Patents*, **2013**, *23*, 299-317.

P-045

Zeolite catalysts for lactic acid and ethyl lactate production from DHA

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Developing efficient catalysts for the conversion of bio-renewable feedstocks to selected key chemicals such as lactic acid esters (Figure 1), which would be an alternative to the currently used techniques of obtaining them from non-renewable resources, is the main issue for scientists working in the field of catalysis. Lactic acid is used in the food industry and for the production of other chemicals and polymers; its production is about 2.7 Mton/year [1]. The urgent needs for a more sustainable production of chemicals from renewable feedstock, like biomass, have caused intensive research efforts in search for novel porous nano-materials [2].

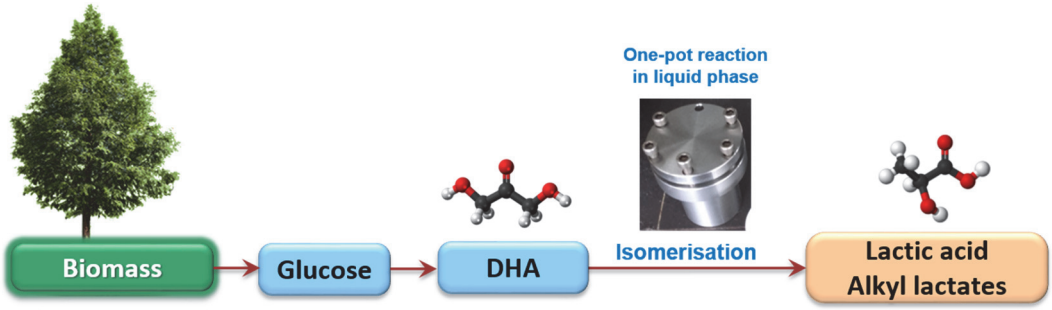

Figure 1. Scheme illustrating the targeted product (lactic acid) from biomass via DHA.

In the present study, we are interested in designing one-pot approach for the production of lactic acid (LA)/alkyl lactates from dihydroxyacetone (DHA) over zeolite catalysts (synthetic and natural clinoptilolite). Various synthetic BEA zeolites modified with metals (Sn, Cu, Na, Zn and Fe) were prepared using ion exchange. The catalysts were tested in liquid phase using one-pot periodic autoclave (3 h, 120°C).

The investigated catalysts trends in following byproduct formation: lactic acid, ethyl lactate, ethyl acetate, acetic acid or acetaldehyde. The best selectivity towards lactic acid was achieved using the Cu-modified natural clinoptilolite (only 16%). The best yield towards ethyl lactate was obtained using Na-BEA zeolite (50%).

Acknowledgment

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No. 665778 (Polonez-1 no. 2015/19/P/ST4/02482 of National Science Centre, Poland).

References

[1] I. Czekaj, N. Sobuś, *Technical Transactions*, **2018**, *8*, 35–58.
[2] A. Corma, S. Iborra, A. Velty, *Chem. Rev.*, **2007**, *107*, 2411-2502..

P-046

A new method for synthesis and synthetic applications of ethyl 1-(*N*-acetylamino)-1-ethoxyalkylphosphinates

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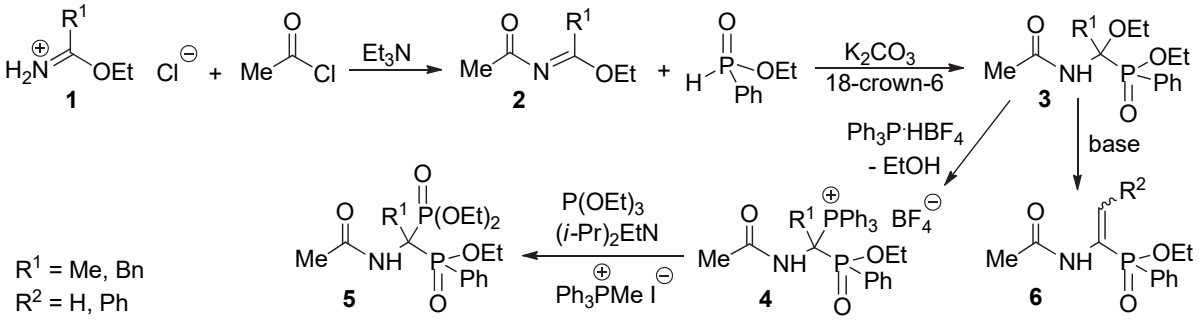
In 2015, we published a few-stage transformation of *N*-acyl-α-amino acid derivatives into phosphonate derivatives α-functionalised with nucleofugal methoxy group, that was introduced by electrochemical alkoxylation.[1] However, one of the drawback of this method was the inability to undergo electrochemical oxidation of phosphinate analogues of the starting α-amino acids.

Recently we described a completely new approach for synthesis of α-alkoxy derivatives of α-aminophosphonates from imidate hydrochlorides **1**. The starting compounds were effectively transformed into α-ethoxyphosphonates *via* acylation of their amino group with an acyl chloride followed by the Michaelis–Becker-like addition of diethyl phosphite to *N*-acylimidates **2** in a PTC system.[2] Therefore, to overcome the above-mentioned problem of the lack of ability to electrochemically oxidize phosphinate analogues of α-amino acids, in further studies we have attempted to perform an analogous Michaelis–Becker-like reaction involving ethyl phenylphosphinate. As a result of these investigations we have isolated the expected α-ethoxyphosphinates **3** in the form of separated diastereoisomers. In the further studies on the reactivity of the obtained compounds, it was shown that subsequent displacement of the ethoxy group by the triphenylphosphonium group provided unknown phosphonium derivatives **4** of α-aminophosphinates, that were successfully converted into biologically active α-aminobisphosphoric compounds **5** *via* the Michaelis–Arbuzov-like reaction with triethyl phosphite. It was also possible to subject the α-ethoxyphosphinates **3** to a β-elimination reaction in the presence of a base, which resulted in the formation of α,β-dehydro-α-aminophosphinate derivatives **6** used for the asymmetric hydrogenation.[3]



References

[1] A. Kuźnik, R. Mazurkiewicz, M. Grymel, et al., *Beilstein J. Org. Chem.,* **2015**, *11,* 1418–1424.

[2] A. Kuźnik, R. Mazurkiewicz, M. Zięba, K. Erfurt, *Tetrahedron Lett.*, **2018**, *59*, 3307-3310.

[3] A. Kuźnik, R. Mazurkiewicz, N. Kuźnik, *Curr. Org. Synth.*, **2013**, *10*, 411–424.

P-047

Synthesis of 1,2-dihydrothieno-1λ^5-[2,4,1]oxazaphosphine

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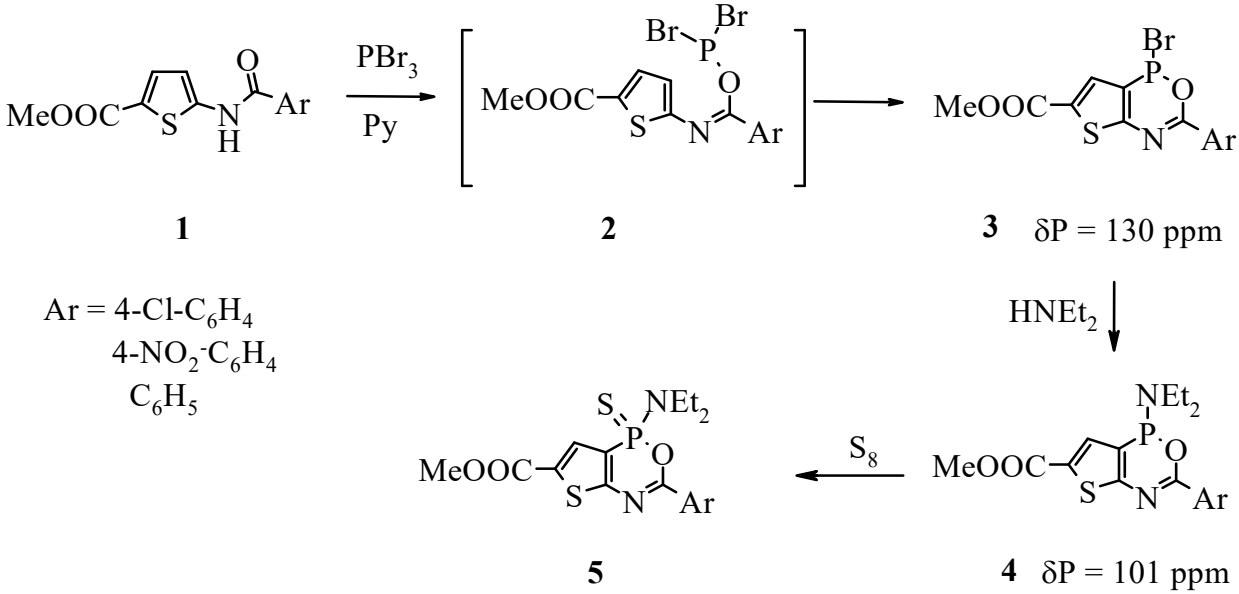
Carboxylic acid amides known to be functionally active with respect to phosphorus (III) halides [1-4]. N-acylated 2-aminothiophene derivatives **1**, containing an exocyclic O-nucleophilic atom in its structure, are phosphorylated with phosphorus(III) bromide to form a bicyclic system containing phosphorus atom, namely, dihydrothieno[2,4,1]oxazaphosphine **3**. The reaction proceeds with the participation of two centers, namely, the endocyclic thiophene C3-atom and the exocyclic oxygen atom of amide group (Scheme 1).



1 **2** **3** **4** **5**

Ar = 4-Cl-C_6H_4
4-NO_2-C_6H_4
C_6H_5

Scheme 1. Phosphorylation of N-acylated 2-aminothiophene derivatives with phosphorus(III) bromide.

Due to the higher nucleophilic reactivity of O-atom of the exogroup compared to the sp^2-hybridized C-center, perhaps, phosphorylation of compound **1** begins from the O-center of the amide group. As a result, an intermediate acyclic structure **2** is formed. The subsequent intramolecular interaction between functional group PBr_2 and C nucleophilic center in the third position of the thiophene ring proceeds to form an energetically favorable six-membered cyclic structure, containing endocyclic P atom, namely, [2,4,1] oxazaphosphine. Three- and four-coordinated phosphorus derivatives **4**, **5** were synthesized on the basis of bromoanhydride **3** formed.

References

[1] M. Porada, E. Budzicz, J. Graczyk, W. Pakulska, *Acta Pol. Pharm.*, **1993**, *50, 2-3,* 173-178.
[2] K. Kostka, M. Porada, J. Graczyk, *Arch. Pharm.* **1994**, *327*, 4, 233-236.
[3] Д. М. Маленко, Л. И. Нестерова, С. Н. Лукьяненко, А. Д. Синица, *ЖОХ,* **1990**, *60,* 5, 1186-1187.
[4] D. Volochnyuk, A. Pushechnikov, D. Krotko, G. Koydan, A. Marchenko, A. Chernega, A. Pinchuk, A. Tolmachev, *Synthesis*, **2003**, *6*, 906–914.

Alkylation of phosphinous and phosphonous acid-boranes using α-hydroxyalkyl group as protecting group for P-H bond

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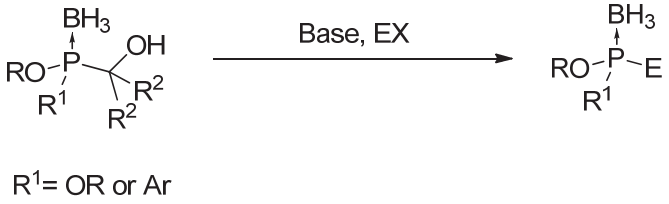
In the past few years, a steadily increasing interest in α-hydroxyalkylphosphorus compounds as substrates for transformations of organophosphorus compounds is observed.[1] Recently, α-hydroxyalkylphosphonates were applied in palladium-catalyzed phosphonation of C(sp^2)-H bonds[2] and in direct arene phosphorylation vis C-H activation using rhodium(III) catalyst.[3] Simultaneously, Hayashi and coworkers presented palladium-catalyzed P-C coupling reaction using (hydroxymethyl)diphenylphosphine sulphide as an equivalent of $Ph_2P(S)H$.[4]

Rapid progress in reduction of P=O bond opened an access to α-hydroxyphosphine–boranes.[5] Very recently, it was shown that α-hydroxyalkyl moiety could be used as a masking group for P-H bond in an alkylation of phosphine–boranes with both high yields and enatioselectivity.[6]

Herein, we wish to present our results concerning an alkylation of (α-hydroxyalkyl)phosphinous and phosphonous acid-borane derivatives available via chemoselective P=O bond reduction in α-hydroxyalkylphosphonates and phosphinates (Scheme 1).[7]



Scheme 1

References

[1] K. V. L. Crèpy, T. Imamoto, *Tetrahedron Lett.,* **2002**, *43*, 7735-7737.
[2] M. Min, D. Kang, S. Jung, S. Hong, *Adv. Synth. Catal.*, **2016**, *358*, 1296–1301.
[3] C. Li, T. Yano, N. Ishida, M. Murakami, *Angew. Chem. Int. Ed.*, **2013**, *52*, 9801–9804.
[4] M. Hayashi, T. Matsuura, I. Tanaka, H. Ohta, Y. Watanabe, *Org. Lett.,* **2013,** *15*, 3, 628-631.
[5] (a) M. Kwiatkowska, G. Krasiński, M. Cypryk, T. Cierpiał, P. Kiełbasiński, *Tetrahedron: Asymmetry*, **2011**, *22*, 1581-1590. (b) S. Sowa, M. Stankevič, A. Szmigielska, H. Małuszyńska, A. E. Kozioł, K. M. Pietrusiewicz, *J. Org. Chem.,* **2015**, 80, 1672-1688.
[5] S. Lemouzy, M. Jean, L. Giordano, D. Herault, G. Buono, *Org. Lett*., **2016**, ***Błąd! Nie zdefiniowano zakładki.***, 18, 140-143.
[6] S. Sowa PhD thesis, **2015**, UMCS, Lublin. S. Sowa, K. M. Pietrusiewicz *submitted.*

P-049

Synthesis of new derivatives of 5-alkylamino-4-cyanooxazoles

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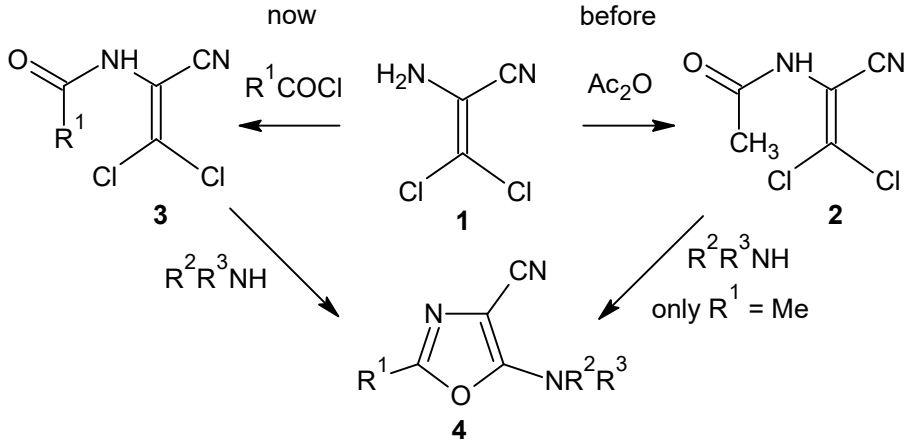
The chemistry of derivatives of 5-alkylamino-4-cyanooxazoles **4** is quite diverse [1],[2],[3], moreover, many biologically active substances have been found. With the aim of developing a synthesis of new derivatives of 5-alkylamino-4-cyanooxazoles **4**, we proposed to use the approach previously described by Matsumura [4], through acylation of 2-amino-3,3-dichloracrylonitrile **1**, which leads to **2**. Previously, the authors of the article were limited to using only acetic anhydride. We showed that 2-amino-3,3-dichloroacrylonitrile **1** is able to react with various acid chlorides, with formation **3**, which in turn makes it possible to obtain the corresponding derivatives of 5-alkylamino-4-cyanooxazoles via reactions with aliphatic amines.



R^1 = C(O)OEt, $CH_2C(O)OMe$, $CH_2CH_2C(O)OEt$, CH_2OAc, CH_2CN, CH=CH-C(O)OEt;
R^2R^3NH = Me_2NH, $MeNH_2$, $PhCH_2NH_2$, pypy, morpholine

References

[1] Kozachenko A.P., Shablykin O.V., Vasylenko A.N., Brovarets V.S. J. Gen. Chem., 2010, 80(1), 133-139.
[2] Kozachenko A.P., Shablykin O.V., Brovarets V.S, Drach B.S. J. Org. Pharm. Chem., 2010, 8(3), 24-41
[3] Kozachenko A.P., Shablykin O.V., Vasylenko A.N., Rusanov E.B., Brovarets V.S., Drach B.S. J. Gen. Chem., 2010, 80(5), 824-830.
[4] Matsumura K., Saraie T., Hashimoto N. Chem. Pharm. Bull., 1976, 24(5), 912-923.

Application of 3,3,3-trifluoro-1-diazopropanone in the synthesis of (fluoroalkyl)thiazoles

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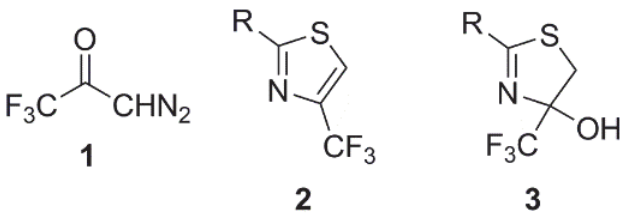
Synthesis of fluorinated heterocyclic compounds is current problem of modern organic synthesis [1,2]. Particular interest is focused on compounds containing small fluoroalkyl groups *e.g.* CF_3. Diazo ketones are interesting building blocks for preparation of many heterocycles e.g. β-lactams, thiazoles, oxazoles. [1,3]-Thiazole or[1,3]-oxazole scaffolds are structural motifs present in many biologically active compunds [3].

The goal of studies was to applied 3,3,3-trifluoro-1-diazopropanone (**1**) as fluorinated building block for the synthesis of selected heterocycles such as thiazoles and oxazoles. Synthesis of **1** via reaction of trifluoroacetic anhydride with diazomethane were described in few papers [4], but to the best of our knowledge application of **1** for preparation of heterocyclic products was not described in the literature.

Reactions of thioamides with **1** performed in the presence of BF_3 or $Cu(OTf)_2$ led to formation of thiazoles **2** (R = Ar) and hydrated heterocycles **3**. Reaction of thiourea with **1** gave thiazole (R = NH_2) as sole product. Amides were not reactive in this reactions. Heterocycles **3** are intermediates in mechanism that explains formation of thiazoles **2**. Derivatives **3** upon treatment with dehydrating agents $MsCl/Et_3N$ or P_2O_5 were converted in thiazoles **2**. Direct preparation of thiazoles **2** from thioamides and **1** performed in the presence of BF_3 was achieved under microwave conditions.



References

[1] In *Fluorine Heterocyclic Chemistr*y, V. G. Nenajdenka Ed., Springer International Pub., Berlin **2014**.

[2] P. Kirsch, *Modern Fluoroorganic Chemistry*, Wiley-VCH, Weinheim, **2013**.

[3] J. S. Yadav, B. V. Subba Reddy, Y. Gopala Rao i A.V. Naraiah, *Tetrahedron Letters* **2008**, *49*, 2381-2383.

[4] P.Strazzolini, A. G. Giumanini, A. Gambi, G.Verardo i G. Cerioni, *Can. J. Chem*. **1996**, *74*, 1348-1359.

P-051

The interaction of disubstituted β-dicarbonyl compounds with silicon chlorides

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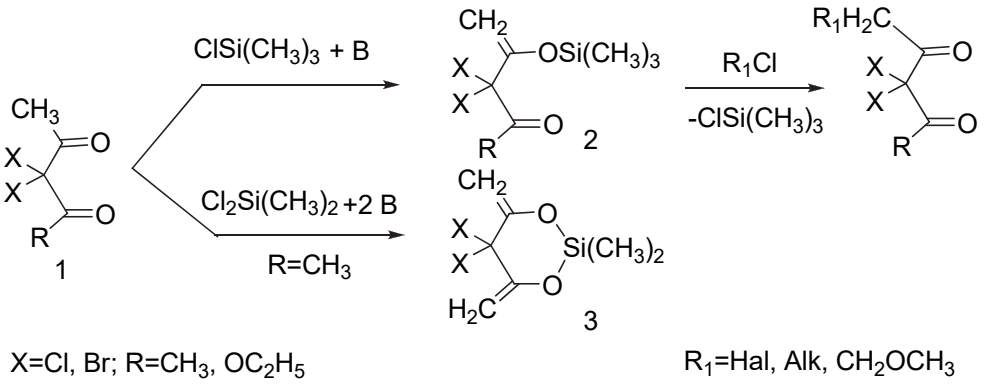
It was shown that β-dicarbonyl compounds that do not contain protons in the methylene group **1** react with silicon chlorides with deprotonation of the methyl group of the acetyl fragment. The reaction takes place in the presence of a base [1]. Depending on the silicon chlorides used, one or both acetyl groups (in the case of acetylacetone derivatives) can be involved in the reaction with the formation of linear **2** or cyclic products **3**.



O-silyl-substituted enols **2** were successfully used as starting reagents for introducing substituent into the acetyl group of β-dicarbonyl compounds.

References

[1] D. M. Malenko, L. A. Repina, N.V. Simurova, A.D. Sinitsa, *Journal of general chemistry of the USSR*, **1992**, *62*, 966-967.

P-052

The synthesis of double functionalized bibenzyls

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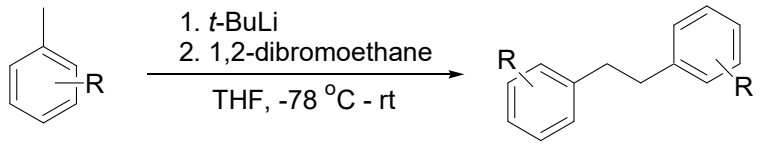
In organic chemistry, the synthetic methodology plays a crucial role as it allows the preparation of the specified molecules in an efficient way using the optimized pathway. Therefore, the development of new synthetic methodologies leading to new but also known compounds is constantly growing area in synthetic organic chemistry.

It is well known, that a treatment of methyl or alkyl-substituted arenes with a strong base affords the corresponding benzyl carbanion, which may undergo a reaction with an electrophile yielding the corresponding modified products. Another way, surprisingly little explored in organic synthesis, is based on the homocoupling of benzyl carbanions. In this case the reaction proceeds with the formation of compounds possessing C_2 symmetry.

Herein, results concerning homodimerization of functionalized benzyl carbanions will be presented along with attempted synthesis of non-symmetrical double functionalized bibenzyls.



up to 99%

R = $S(O)NR_2$, $CONR_2$, $P(O)R_2$

Scheme 1

P-053

Ionization mode of P-BH_3-type compounds in RP-HPLC-HRMS system

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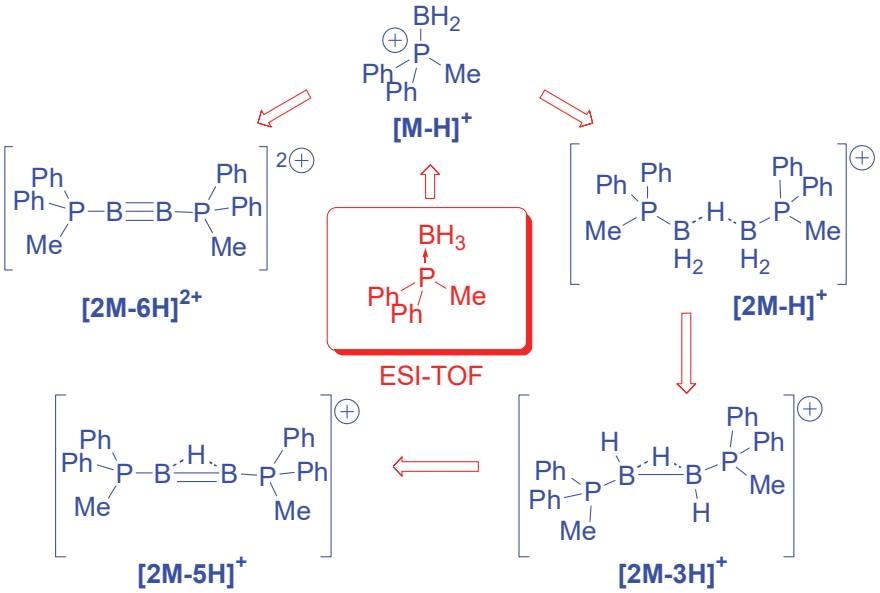
The presence of weak phosphorus-boron bond frequently rises the problem of the complete analysis of phosphine–boranes especially when the data are collected during the preparation of the manuscript for publication. Contrary to NMR which is regarded as non-destructive analytical method, the MS analysis, and especially the coupled LC–MS or GC–MS techniques, cause predominantly the cleavage of P–B bond leading to the corresponding free phosphines during measurement. The latter may undergo oxidation affording the completely different compound which enters the mass analysis. As a consequence, additional statement should be included and the presence of other molecular ions should be pointed out.

Herein, we would like to discuss the results concerning the HRMS analysis of a set of structurally different phosphine–boranes using RP–HPLC–HRMS technique along with some interesting consequences associated with the discussed observations.



Scheme 1

P-054

New method of synthesis vinyl disulfanes

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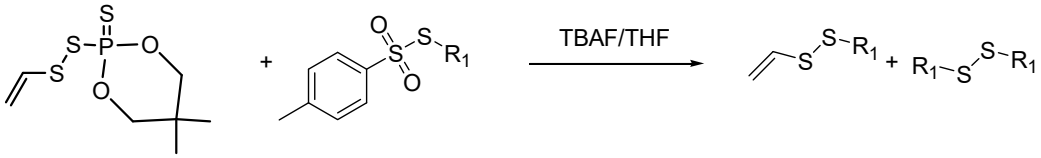
Disulfanes have a wide range of applications in the industry, in organic synthesis, biotechnology or nanotechnology [1]. Unsymmetrical vinyl disulfanes can make this group more interesting with strong bioactivity against bacteria, fungus and viruses [2]. Naturally vinyl disulfanes are present in garlic and onion. The most known vinyl disulfane is Ajoene, firstly isolated by E. Block in 1984 [3]. *Z*-Ajoene is more active than its *E*-isomer as an anti-thrombotic agent, and some studies on anticancer treatments have focused primarily on the *Z*-isomer [4].We developed new method of unsymmetrical vinyl disulfanes synthesis and are planning to show its pros and cons.



Scheme 1. Method of unsymmetrical vinyl disulfanes synthesis .

References

[1] B. P. Zambrowicz, et al., *Nat. Rev. Drug Discovery*, **2003**, 2, 38.
[2] H. A. Perez, M. De La Rosa, R. Apitz, *AAC,* **1994**, 38 337
[3] E. Block and S. Ahmad, *J. Am. Chem. Soc*., **1984**, 106, 8295
[4] Kaschula, C. H., Hunter, R., Parker, M. I.; *Biofactors*. **2010**, 36, 78.

P-055

Bioorthogonal reactions between metallocarbonyl norbornenes and tetrazine derivatives

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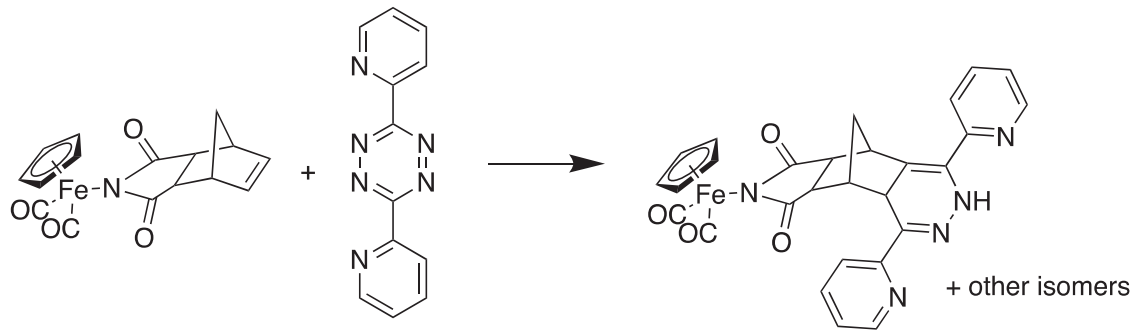
Bioorthogonal reactions refer to chemical reactions that can be carried out in complex biological settings without interfering with native biochemical processes. Recently bioorthogonal methods have been widely applied to protein modification / labeling via reaction of non-natural aminoacids [1]. In the past decade, a variety of reactions has been identified to be suitable for the conjugation of biomolecules using different ligation concepts. One of them is the inverse electron demand Diels-Alder reaction (iEDDA) between 1,2,4,5-tetrazines and olefins or strained alkynes [2].



The aim of this study was to synthesize half-sandwich metallocarbonyl complexes containing a norbornene handle [3]. These complexes display unique spectroscopic properties since they absorb in the mid-IR spectral region allowing them to be detected by IR spectroscopy. iEDDA reactions between metallocarbonyl norbornenes and model 3,6-dipyridyl tetrazine (scheme) as well as tetrazine incorporated in Bovine Serum Albumin were extensively investigated .

References

[1] Z. Mengmeng, L. Zheng, P. Zhang, J. Li, Y. Zhang, *Molecules*, **2015**, 20, 3190-3205.
[2] A. C. Knall, C. Slugovc, *Chem. Soc. Rev*., **2013**, 42, 5131-5142.
[3] B. Rudolf, M. Palusiak, J. Zakrzewski, *J. Organomet. Chem.,* **2009**, 694 1354-1358.

P-056

Metallocenyl biconjugates of monastrol – synthesis and anticancer activities

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Human kinesin Eg5 plays an essential role in mitosis by establishing the bipolar spindle.[1] Inhibition of Eg5 prevents centrosomal separation and mitotic spindle assembly, thus leading to the formation of monopolar spindles. Inhibitors of Eg5 arrest only mitotic cells (cancer cells) and are not expected to affect non-proliferating cells (normal cells). Because of this, inhibitors of Eg5 may not have the severe side effects associated with traditional antimitotic agents. Human kinesin, HsEg5, a member of the kinesin-5 family, is currently under investigation as a prospective cancer drug target. It is worth noticing that Eg5 is overexpressed in many neoplastic tissues (cancer cells), including leukemia, breast, lung, ovarian, bladder and pancreatic cancers,[2] while in non-proliferative tissues Eg5 is almost undetectable.[3] We will present out achievement in a synthesis and study of biological properties of metallocenyl bioconjugates of the first low-molecular-mass inhibitor of kinesin-5, monastrol (Figure 1).

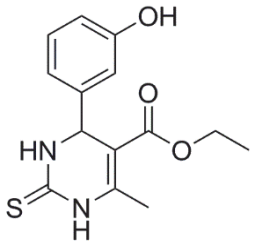

Figure 1. Monastrol

Acknowledgements

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References

[1] Hirokawa, N. *Science* **1998**, 279, 519

[2] Castillo, A.; Morse III, H.C.; Godfrey, V.L.; Naeem, R.; Justice,M.J. *Cancer Res*. **2007**, 67, 10138.

[3] El-Nassan,H.B. *Eur. J. Med. Chem*. **2013,** 62, 614.

P-057

The influence of protecting groups on cytotoxic activity of new gemcitabine 5'-phosphoramidates

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Gemcitabine (2'-2'-difluorodeoxycytidine, dFdC) is widely used for the treatment of solid tumours. It is for instance used to treat metastatic cancer of the pancreas. However, the basic mechanisms of gemcitabine resistance include intracellular transport as well as biochemical processes occurring in the intracellular space which are controlled by kinases [1]. Therefore, gemcitabine pronucleotides seem to be interesting derivatives, as in the form of masked 5'-*O*-phosphate they allow the improvement of the pharmacodynamic and pharmacokinetic parameters. Herein, we report interesting dFdC prodrugs which are the phosphoramidates of gemcitabine. Their masking groups are 4-chlorophenyl and aminoalkyl moieties. Moreover, in the synthesis we applied a protecting group for 3' and 4-*N* position of gemcitabine. In our statement we present the results of cytotoxic activity assessment depending on the group used. We used benzoyl (Bz), *tert*-butoxycarbonyl (Boc) and benzyloxycarbonyl (Cbz) group. The synthesis of our target compounds is based on the modified Reese method [3]. Our phosphorylating agent was 4-chlorophenyl phosphoroditriazolide. It was prepared by reaction of 4-chlorophenyl phosphorodichloridate with 1,2,4-triazole in the presence of triethylamine in acetonitrile [2]. The new 5'-phosphoramidates of dFdC were tested for their cytotoxic activity in six human cancer cell lines: cervical (HeLa), nasopharyngeal (KB), liver (HepG2), lungs (A-549), glioblastoma (U87), and normal human dermal fibroblast cell line (HDF).

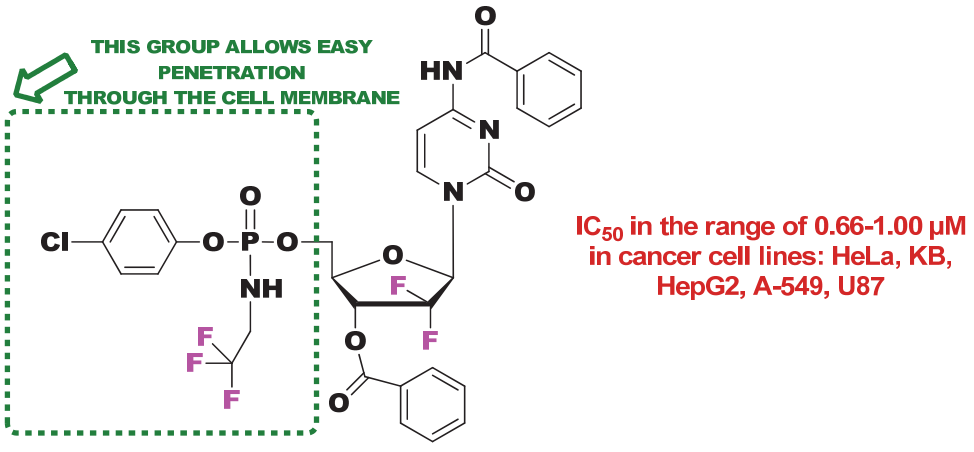

Figure 1. An example of gemcitabine 5'-phosphoramidate.

References

[1] F. Schinazi *et al*, *Chem. Rev.*, **2016**, *116*, 14379-14455.
[2] M. Lewandowska *et al*, *Bioorg. Med. Chem.*, **2016**, *24*, 2330-2341.
[3] J.B. Chattopadhyaya, C.B. Reese, *Teatr. Let.*, **1979**, *52*, 5059-5062..

P-058

Imidazole-doped Polymeric Proton Conductor Based on Pure Cellulose Fibers

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In our previous studies, we synthesized and characterized properties for different proton conducting composites based on microcrystalline and nanocrystalline cellulose with different concentration of imidazole as a dopant. [1-3] The aim of present study was the synthesis and characterize physico-chemical properties of a new composite based on cellulose fibers (CMF) doped with imidazole molecules (Im). The combination of a natural polymer such as cellulose with heterocyclic molecules containing nitrogen atoms is the strategy, which allows to find new, biodegradable proton conducting polymeric materials, which can be used in the temperature range above 100 ^{O}C. [1-4] Materials such as polymeric proton conductors can be used, e.g., in fuel cells – electrochemical devices, which convert the energy from chemical reactions into electricity and do not produce contamination.

The newly synthesized polymeric composite containing imidazole molecules (3.5CMF-Im) and pure, non-functionalized cellulose polymer matrix were comprehensively studied in terms of structural, thermal, and electrical properties. The composite was examined with elemental analysis to determine its chemical composition. The crystallinity index for pure cellulose fibers and the obtained composite were checked with X-ray diffraction (XRD). Utilizing differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) tests were carried out to examine the stability and thermal decomposition of studied materials. In order to determine the temperature dependences of electrical conductivity, the impedance spectroscopy was used.

The obtained results have shown the differences between properties of polymer matrix – pure cellulose fibers, and 3.5CMF-Im composite. The resulting composite reveals close to four orders of magnitude higher value of conductivity in the temperature range above the boiling point of water. Newly synthesized polymeric composite 3.5CMF-Im is inexpensive to obtain, non-hazardous, environmentally friendly and can be considered as a solid electrolyte for application in electrochemical devices.

Acknowledgments

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References

[1] I. Smolarkiewicz et al., *Electrochim. Acta*, **2015,** 155, 38-44.
[2] I. Smolarkiewicz et al., *Eur. Polym. J.,* **2016** 78, 186-194.
[3] J. Tritt-Goc et al., *Cellulose,* **2018**, 25, 281-291.
[4] I. Jankowska et al., *Carbohydr. Polym.*, **2018**, 200, 536-542.

P-059

Theoretical and experimental investigations of electrical conductivity of 1H-1,2,4-triazol-4-ium hydrogen oxalate

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Our research aims to create new, organic, highly conductive proton conductor. Kreuer *et al.* have proposed materials composed of amphoteric nitrogen-containing heterocyclic molecules as existing alternatives to polymer membrane electrolyte fuel cells (PEMFCs) [1]. To design proton conductors with the desired conductive values, it is important to study the hydrogen bond network and to analyze its influence on the conductivity properties [2]. The object of our research is the new proton conductor, 1H-1,2,4-triazol-4-ium hydrogen oxalate ($C_2H_4N_3^+$, $C_2HO_4^-$), which is based on the 1,2,4-triazole and oxalic acid molecules.

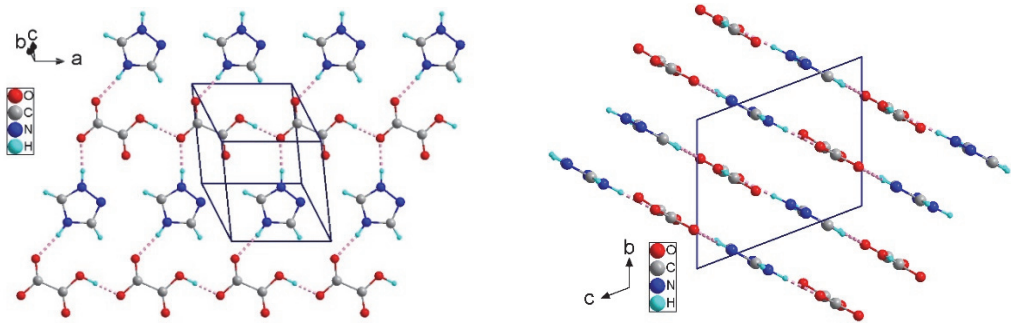

Figure 1. Molecular structure of 1H-1,2,4-triazol-4-ium hydrogen oxalate (a) hydrogen bonds on (0-11) plane (b) parallel layers

We present the thermal properties (DSC and TGA) and conductivity studies of 1H-1,2,4-triazol-4-ium hydrogen oxalate. The crystal is thermally stable to the temperature of 450 K. The value of the conductivity equals 5.3 Sm^{-1} at 450 K. The activation energy of proton conductivity obtained from dielectric spectroscopy is 1.94 eV. We compare this value with the results of quantum mechanical DFT calculations of proton motion in the hydrogen bond network to fully explain the transport mechanism occurred in the studied system. In the solid proton conductors, the way of proton transport is described by Grotthuss mechanism. Transport is provided by rotating the molecules and transfer the proton through the hydrogen bridges between the molecules. We calculated the possible pathways of protons in the system using Potential Energy Scans (PES) analysis. The energy needed to rotate the triazole is rather small compared to the energy necessary to transport the proton through the oxygen atoms between the oxalic acid molecules.

References

[1] K.D. Kreuer, A. Fuchs, M. Ise, M. Spaeth, J. Maier, *Electrochim. Acta*, **1998**, *43*, 1281.
[2] M. Widelicka, K. Pogorzelec-Glaser, A. Pietraszko, P. Ławniczak, R. Pankiewicz, A. Łapiński, *PCCP*, **2017**, *19*, 25653..

The synthesis of new chiral 2-(aminoalkyl)aziridine derivatives and their applications in asymmetric synthesis

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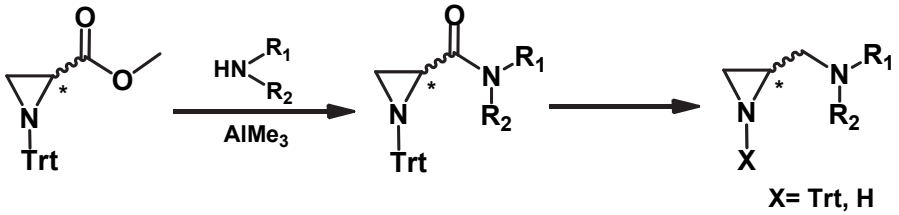
Aziridines, the smallest nitrogen-containing heterocycles, are important building blocks in organic synthesis. The efficient synthesis of aziridines is of importance as a result of their extensive biological activities as well as their potential as chiral ligands for the asymmetric synthesis [1].

The main goal of our research was the synthesis of optically pure 2-(aminomethyl)aziridine derivatives. Reactions of chiral ester of aziridinyl-2-carboxylic acid with corresponding amines provided the secondary and tertiary amides. Prepared compounds were reduced to the corresponding optically pure amines. Desired optically active 2-(aminomethyl)aziridine derivatives were obtained in good chemical yields. We proved that all the newly synthesized aziridine derivatives are versatile catalysts, exhibiting high catalytic activity in asymmetric reactions (in the presence of zinc ions) like asymmetric arylation, addition of diethylzinc to benzaldehyde or asymmetric epoxidation of chalcone [2].



Scheme 1. Synthesis of 2-(aminomethyl)aziridine derivatives.

Acknowledgements

Author is grateful to National Science Centre, Poland for financial support of research (Grant PRELUDIUM 8 UMO-2014/15/N/ST5/02897)

References

[1] S. Leśniak, M. Rachwalski, A. M. Pieczonka *Current Organic Chemistry* **2014**, *18*, 3045-3065.

[2] S. Jarzyński, S. Leśniak, M. Rachwalski Tetrahedron Asymmetry **2017**, *12*, 1808-1816.

Reactivity of aminophosphonic acids. 2.1.[1] Stability in solutions of acids and bases

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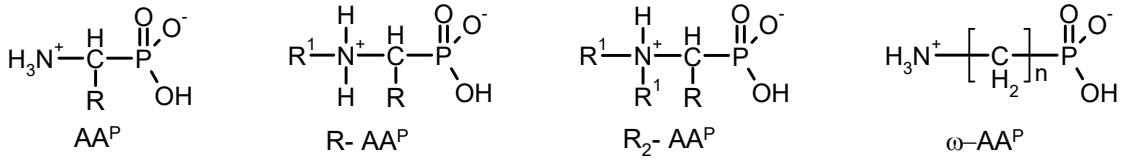
Aminoalkylphosphonic acids (AA^P, R-AA^P, R_2-AA^P, ω-AA^P) due to remarkable biological potential and have found numerous applications in industry, pharmacology and biomedical sciences, and also in agro-chemistry.[2] Due to their importance the study of the synthesis of aminoalkylphosphonic acids and derivatives,[3] and their reactivity (e.g. [4]) constitute an important topic in chemistry and biochemistry.[2]



Scheme 1. Recommended aminophosphonic acids abbreviations [5]

Recently we have published on the hydrolytic stability of *N*-acylaminoalkylphosphonic acids. [6,7] In this communication we present the results on the hydrolytic stability of selected types of aminoalkylphosphonic acids supported by quantum chemical calculations.

References

[1] Part 2.: M.H. Kudzin, J. Drabowicz, F. Jordan, Z.H. Kudzin, P. Urbaniak, *Phosphorus Sulfur Silicon Relat Elem.*, **2018** *(in press)*.

[2] *Aminophosphonic and Aminophosphinic Acids: Chemistry and Biological Activity*. V.P. Kukhar, H.R. Hudson, Eds.; John Wiley & Sons, Ltd., Chichester, New York, 2000.

[3] Z.H. Kudzin, M.H. Kudzin, J. Drabowicz, C. Stevens, *Curr. Org. Chem*., **2011**, *15*, 2015-2071.

[4] J. Drabowicz, F. Jordan, M.H. Kudzin, Z.H. Kudzin, P. Urbaniak, C. Stevens, *Dalton Transaction*, **2015**, *45*, 2308-2317.

[5] J. Drabowicz, H. Jakubowski, M.H. Kudzin, Z.H. Kudzin, *Acta Biochim. Pol*., **2015**, *62*, 139-150.

[6] M. Cypryk, J. Drabowicz, B. Gostynski, M.H. Kudzin, Z.H. Kudzin, P. Urbaniak, *Phosphorus Sulfur Silicon Relat Elem.*, **2017**, *192*, 651-658.

[7] M. Cypryk, J; Drabowicz, B. Gostynski, M.H. Kudzin, Z.H. Kudzin, P. Urbaniak, *Molecules*, **2018**, *23*, 859-877.

P-062

Influence of the terminal functional group on induction of the smectic A phase in mixtures of nematic liquid crystals

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Induction of the liquid crystalline smectic A phase is an example of non-additive behavior in mixtures of nematic liquid crystals. [1] This work concerns establishing the dependence of polar terminal group of four-ring nematics (Fig. 1) on induction of the smectic A phase. [2] Each compound I-II.X.4 was mixed with compound A.5.5 and the temperatures of phase transitions were measured using polarizing optical microscope to construct phase diagrams for investigated systems. The lengths of molecules and dipole moment were calculated using Scigress. The strongest induction was observed in systems with compounds containing terminal trifluoromethoxy group. The presence of isothiocyanate group in the terminal position causes weaker induction. The weakest induction was in the case of compounds terminated with a fluorine atom.

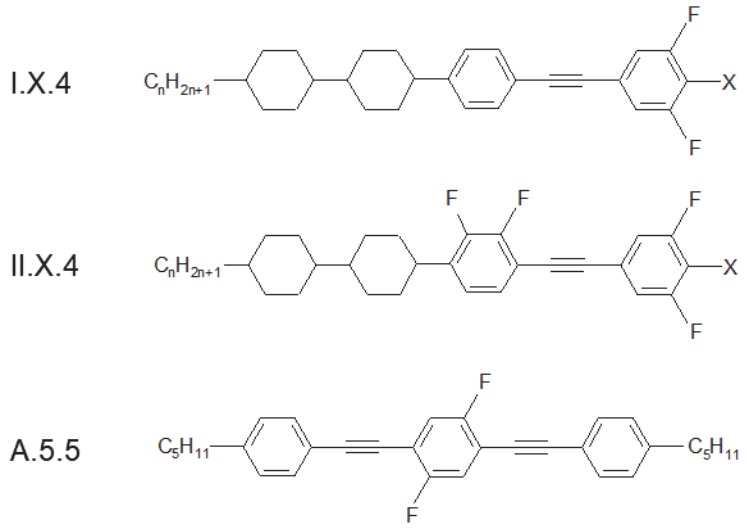

Figure 1. The structure of investigated compounds, where X=OCF_3, NCS, F; n=4.

References

[1] R. Dąbrowski, K. Czupryński, Induced Smectic and Nematic Phases and Re-entrant Phenomena, Modern Topic in Liquid Crystals, World Scientific Publishing, Singapore, **1993**, 125-160.

[2] M. Celiński, Nematyczne ciekłe kryształy dla techniki podwójnego adresowania – synteza i badanie właściwości, PhD thesis, Warsaw, **2014**.

P-063

Studies of lipophilicity and drug-likeness for few 3-carboxyalkylrhodanine acids derivatives with the use of chromatographic and in-silico methods

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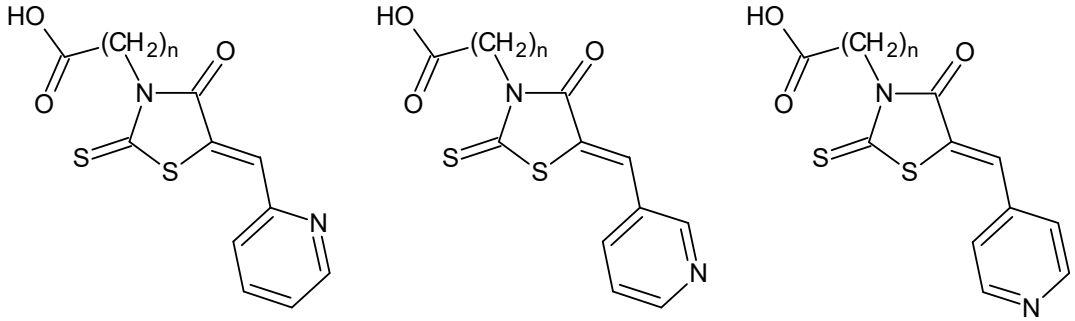
Hydrophobicity of the twelve 3-carboxyalkylrhodanine acids derivatives was determined experimentally by TLC and predicted by means of commercially available programmers. R_M values were determined by RP-TLC with using water and organic modifier (methanol, acetonitrile, acetone, propan-2-ol, 1,4-dioxane) mixtures. The physicochemical parameters including octanol partition coefficients (miLogP), molecular mass (MW), number of hydrogen bonds donors (NOHBD) and number of hydrogen bond acceptors (NOHBA) were calculated with the use of Molinspiration Software using molinspiration server. These results were used to assess the drug-likeness of the studied compounds using the Lipinski's rule of five. On this basis, preliminary conclusions have been drawn as to whether they have a biological effect and therefore whether they can be used as e.g. potential medicines.



Scheme 1. Structural formulas of the tested 3-carboxyalkylrhodanine acids derivatives; n = 3, 4, 5 or 10.

References

[1] T.L. Oprea, *J. Comp. Aided Mol. Des.*, **2002**, *16*, 325-334.
[2] R. Zakrzewski, P. Urbaniak, A. Nowicki, W. Tejchman, *J. Chromatogr. Sci.*, **2018**, *56(8)*, 709-715.
[3] G. L. Biagi, A. M. Barbaro, M. F. Gamba, M. C. Guerra, *J. Chromatogr. A*, **1969**, *41(3)*, 371-379.

P-064

Synthesis of 1-phenyl-3-(pyren-1-yl)-1*H*-pyrazole-4-carbaldehyde and its triflic acid–promoted cyclization

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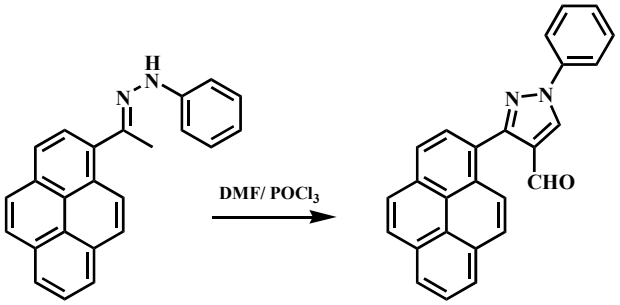
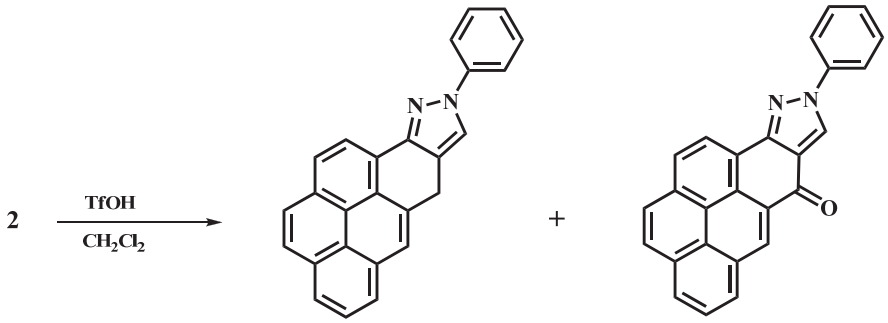
We have recently reported that the reaction of 1-acetylpyrene phenylhydrazone (**1**) with Vilsmeier-Haack reagent afforded 1-phenyl-3-(pyren-1-yl)-1*H*-pyrazole-4-carbaldehyde (**2**) in good yield [1].



1 **2**

Compound **2** underwent triflic acid-promoted cyclization yielding two strongly fluorescent compounds **3** and **4**.



3 **4**

The structures of compounds **3** and **4** were determined by spectroscopic methods and X-ray crystallography. Their luminescence properties were also studied. The results of this study will be presented and discussed.

References

[1] R. Flamholc, A. Wrona-Piotrowicz, A. Makal, J. Zakrzewski, *Dyes and Pigments*, **2018**, *154*, 52-61.

P-065

Ionic liquid crystals based on the [*closo*-$B_{10}H_{10}$]$^{2-}$ cluster

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Ionic liquid crystals (ILC) are of interest for applications in contemporary technologies, such as electrolytes for batteries and photovoltaic cells [1]. Materials for the latter occasionally involve photoinduced intermolecular charge transfer. In this context we focused on photoactive ionic liquid crystalline derivatives of [*closo*-$B_{10}H_{10}$]$^{2-}$ anion. Initially, we developed a convenient and efficient synthetic access to iodo derivatives, [*closo*-$B_{10}H_9$-1-I]$^{2-}$ and [*closo*-$B_{10}H_8$-1,10-2I]$^{2-}$ [2], which allowed further functionalization of the {*closo*-B_{10}} cage and opened entry to 1-aryl and 1,10-diaryl derivatives **1** and **2**. A judicious choice of the aryl group Ar and the counterion Q^+ leads to induction of lamellar phases in these derivatives and appearance of intermolecular charge-transfer bands.

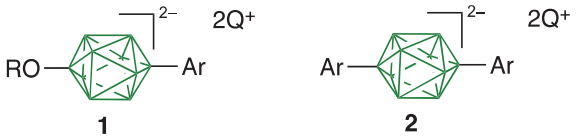

Figure 1. New derivatives of {*closo*-B_{10}} cage.

Acknowledgements

This work was supported by the FNP (TEAM/2016-3/24) and NCN OPUS (2015/17/B/ST5/02801) grants.

References

[1] K. Gossens, K. Lava, C. W. Bielawski, K. Binnemans, *Chem. Rev.* **2016**, *116*, 4643–4807.
[2] E. Rzeszotarska, I. Novozhilova, P. Kaszyński, *Inorg. Chem.* **2017**, *56*, 14351–14356.

Modified Phosphates as Models for Backbone-to-base Hole Transfer

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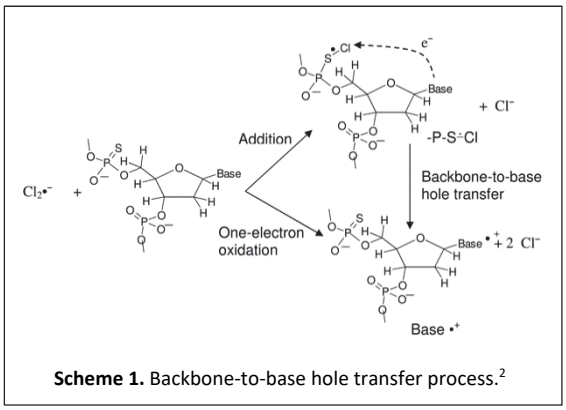
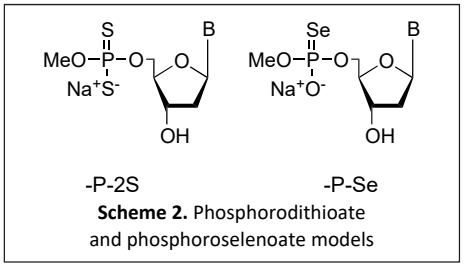
To investigate regulation of gene expression, phosphoromonothioate incorporated DNA-oligomers (S-oligomers) are extensively employed as antisense DNA-oligomers.[1] Employing S-oligomers and phosphoromonothioate model compound, diisopropyl phosphorothioate, and using ESR spectroscopy, for the first time we showed that a phosphorothioate (PO_3S^-) substitute for a phosphate in the DNA backbone is an effective hole trap for the study of the sequence dependence and of the rates of hole transfer from backbone-to-base (scheme 1).[2] Therefore, combining our approach of synthesis and ESR spectroscopy, we have determined whether phosphorodithioates and phosphoroselenoates (scheme 2) could be employed to study backbone-to-base hole transfer process. In order to obtain model compounds, 3'-acyl-protected nucleosides were combined with chlorodithiaphospholane or chlorooxathiaphospholane. The oxidation of tricoordinate phosphorus intermediates to the corresponding 2-thio-1,3,2-dithiaphospholanes or 2-seleno-1,3,2-oxathiaphospholanes was accomplished with the use of elemental sulfur or selenium. Key intermediates reacted with methanol in the presence of a base, following by deprotection. The resulting phosphorodithioates or phosphoroselenoates were converted into their sodium salts illustrated in scheme 2. As outlined in scheme 1, employing phosphoroselenoate model compound (scheme 2), formation of the two-center three-electron σ^2-σ^{*1}-bonded adduct radical (-P-Se∴Cl) via addition of $Cl_2^{\bullet-}$ to phosphoroselenoate was observed for the first time. However, -P-Se∴Cl could not oxidize G in contrast to our observation of one-electron oxidation of G by -P-S∴Cl [2]. Therefore, we predict that backbone-to-base hole transfer process by ESR is not possible in Se-oligomers. However, employing synthesized phosphorodithioate containing G as the base (G-2S, scheme 2) and ESR spectroscopy, we have observed one-electron oxidation of G by -P-2S∴Cl at low concentration of G-2S (0.5 mg/mL). Whereas, formation of the dimer anion radical [-P-2S∴2S-P-]$^-$ is found at high concentration of G-2S (6 mg/mL). *Supported by*: NIH NCI (Grant R01CA045424), Research Excellence Fund (REF), Center for Biomedical Research, and Statutory Funds of CMMS PAS.



Scheme 1. Backbone-to-base hole transfer process.[2]



Scheme 2. Phosphorodithioate and phosphoroselenoate models

References

[1] Wang, S.; Allen, N.; Vickers, T. A.; Revenko, A. S.; Sun, H.; Liang, X.-H.; Crooke, S. T. *Nucleic Acids Res*. **2018**, *46*, 3579–3594. [2] Adhikary, A.; Kumar, A.; Palmer, B. J.; Todd, A. D.; Sevilla, M. D. *J. Am. Chem. Soc.* **2013**, *135*, 12827–12838.

Synthesis and SDE via achiral chromatography studies of β-amino-α,α-difluorophosphonic acids

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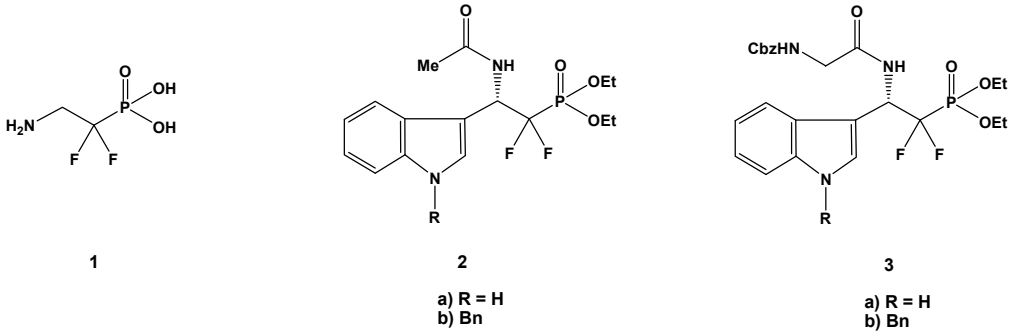
The self-disproportionation of enantiomers (SDE) is a ubiquitous phenomenon observed for non-racemic samples of chiral compounds when subjected to standard purification via achiral column chromatography as well as during other physicochemical transformations such as sublimation or distillation. Indeed, the SDE under chromatographic conditions has been found to be a useful and convenient method for the enantiopurification of organic compounds [1].

Aminophosphonic acids possess unique biological properties, for example, they can mimic the transition state in peptide bond cleavage, they can act as hydrogen bond acceptors, etc. Moreover, 2-amino-1,1-difluoroethylphosphonic acid (**1**) with two fluorine atoms in the α position is known to be a potent phosphoglycerate kinase (PGK) inhibitor [2].

In our poster we will present the SDE results via chromatography obtained for amide derivatives **2** and **3**, model compounds derived from β-amino-α,α-difluorophosphonic acid.



Scheme 1. The structures of the model compounds.

Acknowledgement

We are grateful for financial support from the German Research Foundation (DFG, grant RO 362/75-1).

References

[1] V. A. Soloshonok, Ch. Roussel, O. Kitagawa, A. E. Sorochinsky, *Chem. Soc. Rev.*, **2012**, 41, 4180–4188.

[2] Y. Xu, J. Aoki, K. Shimizu, M. Umezu-Goto, K. Hama, Y. Takanezawa, S. Yu, G. B. Mills, H. Arai, L. Qian, G. D. Prestwich, *J. Med. Chem.,* **2005**, 48, 3319–3327.

P-068

The new isoniazid-carborane derivatives and their anti-tuberculosis activity

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Mycobacterium tuberculosis (*Mtb*) is a gram-positive bacterium causing tuberculosis (TB) in human. Tuberculosis is one of the most widespread infectious diseases on Earth. Despite the availability of therapy, it is estimated that around 9 million people suffer from tuberculosis every year and 1.5 million die. Multidrug resistant TB (MDR TB) (MDR: resistant at least to isoniazid (INH) and rifampicin (RMP)) is increasing in prevalence, and threatens the ability of standard control measures to contain the global TB epidemic.[1]

Isoniazid, also called isonicotinic acid hydrazide, is a synthetic compound first prepared in 1912, that anti-TB activity was first reported in 1952. INH is a prodrug. In order for INH to be effective against *MtB* it needs to be activated by the multifunctional catalase-peroxidase enzyme KatG into a range of activate species such as an isonicotinoyl radical, that can acylate numerous compounds.[2] The main mechanism of resistance to isoniazid resides in the presence of mutations in its activator, KatG, product of the *katG* gene.[3]

The disturbing emergence of MDR-TB has been driving the scientific community to urgently search for new and efficient anti-tubercular drugs. Despite the various drugs currently under evaluation, INH is still the key and most effective component in all multi-therapeutic regiments recommended by WHO.

The focal point of our research was to recognize the potential of boron clusters (dicarba-*closo*-dodecaboranes ($C_2B_{10}H_{12}$), as prospective building blocks in the design of anti-tuberculosis agents, derived from INH core structure. In the poster we will present the synthesis and *in vitro* anti-mycobacterial activity studies of carborane

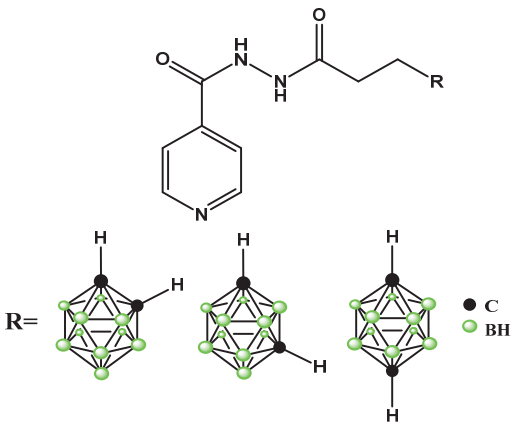

Fig. 1. Structure of INH derivatives containing carborane

Acknowledgment

This study was supported by the National Science Centre, Poland (grant 2014/14/E/ST5/00577) and statutory found of IBM PAS.

References

[1] World Health Organization. Global tuberculosis report. *WHO Report,* **2014**.
[2] K. Johnsson, P. G. Schultz, *J. Am. Chem. Soc*., **1994**, *116*, 7425-7426.
[3] Y. Zhang, B. Heym, B. Allen, D. Young, S. Cole, *Nature*, **1992**, *358*, 591-593.

Optimization of the Heck Reaction – Functionalization of α-Phosphonocarboxylates

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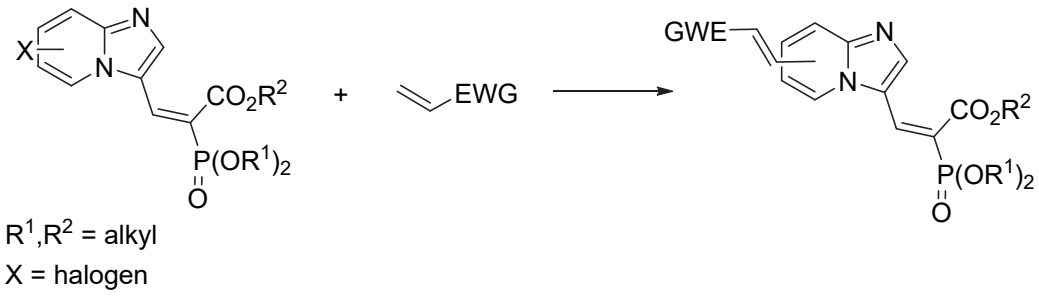
The abnormal activity of Rab geranylgeranyl transferase (RGGT) – an enzyme responsible for the post-translational modification of Rab GTPases, is related to many medical disorders. These observations ignited the search for selective inhibitors of RGGT. The α-phosphonocarboxylates containing imidazo[1,2-a]pyridine ring (IP) turned out to be one of the most potent RGGT inhibitors of this class. The Heck reaction was applied to modify the IP ring with a carbon chain equipped with a group ready for further functionalization. A range of conditions, such as time, solvents, bases etc., were tested leading to the optimized synthetic route.



Scheme 1.

References

[1] Whitcombe, N. J.; Hii, K. K.; Gibson, S. E. *Tetrahedron,* **2001**, *57*, 7449 – 7476.

[2] Kaźmierczak, A.; Kusy, D.; Niinivehmas, S. P.; Gmach, J.; Joachimiak, Ł.; Pentikäinen, O. T.; Gendaszewska-Darmach, E.; Błażewska, K. M. *J. Med. Chem*., **2017**, *60* (21), 8781 – 8800.

P-070

Exceedingly Strong Antiviral Effect of Third Generation Polyanionic, Heterorganic Dendrimer Against Human Immunodeficiency Virus

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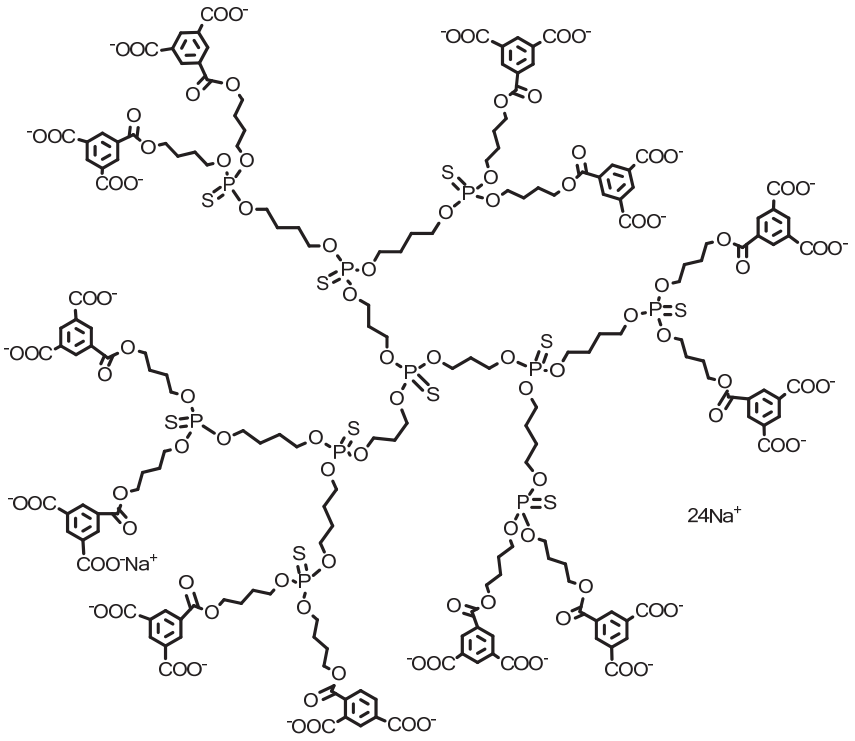
Even though HIV/AIDS was identified almost forty years ago, neither effective therapy nor protective vaccine that efficiently controls or eliminates the spread of HIV virus, have been developed despite all the efforts of the scientific community. Therefore, the development of novel compounds to prevent HIV-1 infection is of superior significance. On the other hand the quickly growing number of newly synthesized macromolecular compounds, including dendrimers is not necessarily followed by the information about their properties and possible applications. In particular, the biological and pharmaceutical aspects need to be explored sufficiently. The aim of this study was to examine the potential antiviral activity together with cytotoxicity of medium-sized, water-soluble, phosphorus-based dendrimers with carboxylate functions on the surfaces. We have found that polyanionic, thiophosphate dendrimer (generation 3, theoretical Mw 5283.7) exhibited very strong activity against HIV-1 virus, even in picomolar concentration, a way below its cytotoxicity.



In this communication, a simple and efficient synthesis leading to the title dendrimer as well as some antiviral testing results will be presented.

P-071

Synthesis of the new hydrazide hydrazones with fluorescent properties

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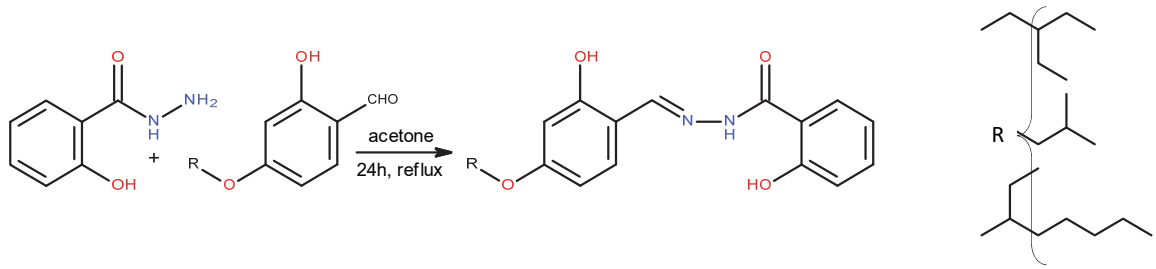
The aim of the study was the synthesis of organic compounds, derivatives of carboxylic acid hydrazides, having the ability to produce polycrystalline layers with fluorescent properties. The main concept was to find such chemical compounds, whose chemical structure would allow to obtain a strong fluorescence effect, as well as to produce thin films of appropriate thickness. A series of reactions were carried out using the carbohydrazides as the main substrates. The corresponding hydrazide hydrazones derivatives of salicylaldehyde having a branched, aliphatic substituent were obtained (Scheme 1). Hydrazide hydrazones were characterized by different properties, e.g. the ability to form polycrystalline layers or the effect of fluorescence, observed under the microscope. Thanks to the cooperation with the Laboratory of Biosensors and Organic Electronics, photos were taken using a metallographic microscope. Photographs taken with different techniques, that is: in a dark field, in polarized light or in UV light, they facilitated the analysis of the properties of the thin films made by the spin-coating technique. Despite the diverse nature of the products obtained and the different emission of light, some of them can be used not only as the main emission layer in the construction of OLEDs, but also as other layers necessary to produce an organic light-emitting diode.



Scheme 1.

P-072

Synthesis of 2-substituted 1-acyl-3-diethoxyphosphoryl-2,3-dihydroquinolin-4(1*H*)-ones

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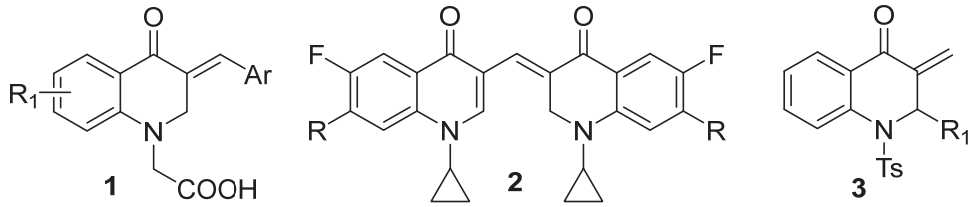
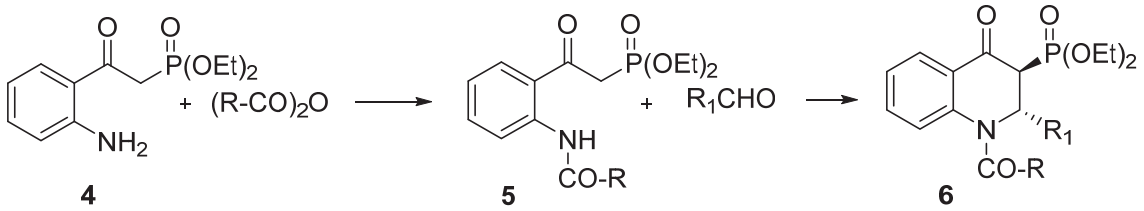
3-Alkylidenequinolin-4-ones are very important class of azaheterocycles which are widely used in medicinal and synthetic chemistry. For example 1-carboxymethyl-3-arylidene-2,3-dihydroquinolin-4-ones **1** are glutathione S-transferase P1-1 inhibitors [1], whereas alkylidenequinolinones **2** and **3** possess high cytotoxic activity [2], [3].



In this communication, we present synthesis of various 1-acyl-3-diethoxyphosphoryl dihydroquinolinones **6** which can be a convenient precursors for the synthesis 3-alkilidene-2,3-dihydroquinolin-4(1*H*)-ones, via Horner-Wadsworth-Emmons olefination.



The title compounds were synthesized in a three step reaction sequence which started with acylation of β-ketophosphonate **4** with various anhydrides. The obtained *N*-acyl-β-ketophosphonates **5** were next treated with aldehydes and underwent Knoevenagel condensation followed by intramolecular Michael addition.

References

[1] J. Wang, S. J. Wang, D. D. Song, et al., *Med. Chem. Res.,* **2012**, *21*, 2823-2826.
[2] L. Yang, D. Yong, A. Hui et al., Patent CN1043700812 A, 2015.
[3] J. Koszuk, T. Bartosik, J. Wojciechowski, et al., *Chem. Biodiversity,* **2018**, *15*, e1800242.

P-073

An experimental and theoretical study of alkylation/acylation products of uracil and its derivatives

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While working on our recent research project, we selected the Boc–protecting group as the most efficient for the U (uracil), T (thymine), and 6–MU (6-methyluracil) intermediates, as it was stable in comparison to most nucleophiles and bases [1] and could be removed under neutral conditions in a clean and selective manner.[2]
Due to the incomplete and inconsistent data concerning the Boc protection of U, T and 6–MU, we have decided to validate the hypothesis of different chemical reactivity of these structurally similar nucleobases with this acylation reagent. As a continuation of this investigation, we have also tested the course of the alkylation reaction with EtI by comprehensively analyzing the separated products.
We have studied the following parameters, which may control regioselectivity: the molar concentration ratio of the substrate and alkylation agent, the presence/absence of the catalyst (in this case DMAP), the temperature of the reaction (ambient, elevated).
We have isolated different acylation/alkylation products of three pyrimidine bases: U, 6–MU and T and discovered a new product containing the *N*–Boc–pyridinium moiety at the C^5–position of 6–MU.
All the obtained compounds were isolated and fully characterized by various NMR and HRMS techniques. Numerous quantum mechanical calculations within the density functional theory (DFT/B3LYP) were performed to support the experimental results and discuss product structures.

References

[1] (a) A. Sarkar, S.R. Roy, N. Parikh, A.K. Chakraborti, *J. Org. Chem*, **2011**, *76*, 7132–7140. (b) E.A. Englund, H.N. Gopi, D.H. Appella, *Org. Lett*, **2004**, *6*, 213–215. (c) R. Moumne, S. Lavielle, P. Karoyan, *J. Org. Chem*, **2006**, *71*, 3332–3334. (d) D.M. Shendage, R. Froehlich, G. Haufe, *Org. Lett*, **2004**, *6*, 3675–3678.
[2] J.R. Hwu, M.L. Jain, S–C. Tsay, G.H. Hakimelahi, *Tetrahedron Lett.*, **1996**, *37*, 2035–2038.

P-074

Synthesis and antibacterial properties of novel metallocenyl-7-ADCA conjugates

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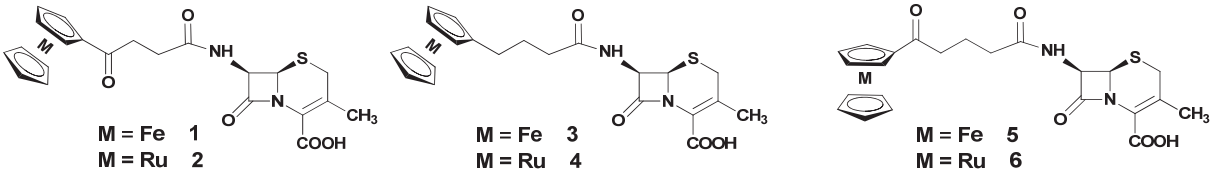
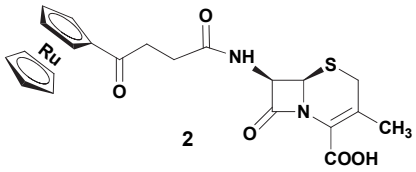
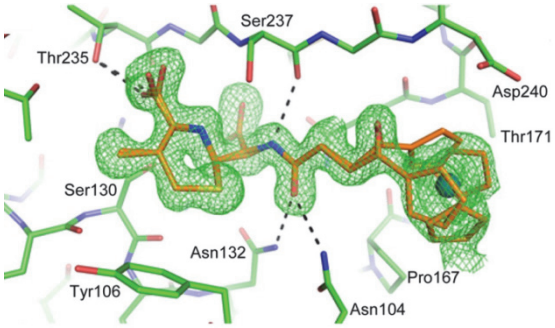
The β-lactam antibiotics are widely use antibacterial agents with a broad spectrum of activity against Gram negative and Gram positive pathogens. The β-lactams antibiotics inhibit Penicillin Binding Proteins (PBPs), a enzymes involved in bacterial cell wall synthesis. Main bacterial resistance mechanisms against β-lactam antibiotics involves PBP structure alternations and hydrolysis by β-lactamases [1]. In an attempt to overcome bacterial resistance novel metallocene 7-aminodesacetoksycephalosporanic (7-ADCA) compounds **1-6** have been obtained (Fig. 1) [2]. In this poster presenatation we show the synthesis, antibacterial and structural properties of ferrocenyl and ruthenocenyl 7-ADCA conjugates.







Scheme 1. Structures 1-6 and X-ray crystal structure of Rc-β-lactam **2** binds to bacterial CTX-M β-lactamase in its active site [2].

References

[1] S. E. Rossiter, M. H. Fletcher, W. M. Wuest, *Chem. Rev,.* **2017**, *117*, 12415-12474.

[2] E. M. Lewandowski, Ł. Szczupak, S. Wong, J. Skiba, A. Guśpiel, J. Solecka, V. Vrček, K. Kowalski, Y. Chen, *Organometallics,* **2017**, *36*, 1673-1676..

P-075

Synthesis and cytotoxic activity of 6,6-disubstituted 3-methylidene- tetrahydropyran-4-ones

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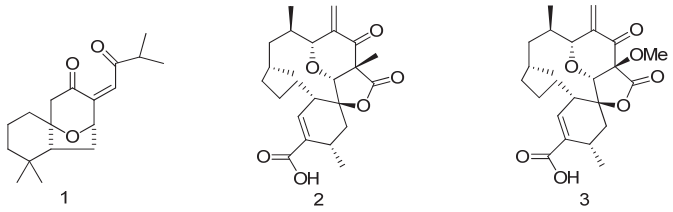
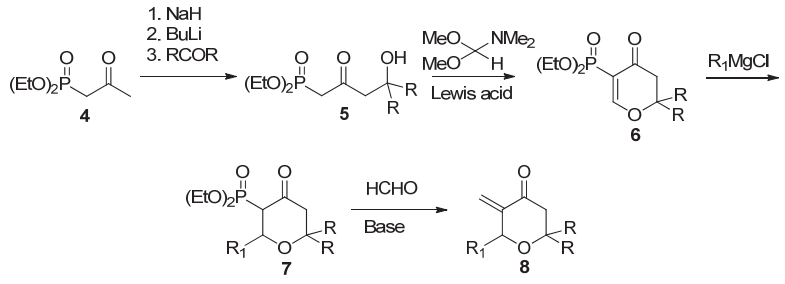
The 3-methylidenetetrahydropyran-4-one skeleton occurs in many compounds, which are common in nature and display many valuable biological properties. For example, norperovskatone **1** has *anti*-HBV activity, whereas (+)–Okilactomycin **2** and Chrolactomycin **3** have anticancer properties. [1-3]



In this report, we present the results of research on the synthesis and biological properties of 6,6-disubstututed 3-methylidenetetrahydropyran-4-ones **8**. Title compounds were obtained in a four-step reaction sequence comprising addition of dianion formed from diethyl 2-oxopropylphosphonate **5** to symmetrical ketones, cyclization leading to 6,6-disubstituted 3-diethoxyphosphoryldihydropyran-4-ones **6**, addition of Grignard reagents to **6** and Horner-Wadsworth-Emmons olefination of the obtained adducts. Final 6,6-disubstututed 3-methylidenetetrahydropyran-4-ones **8** were tested for cytotoxic activity against HL-60, NALM-6 and MCF-7 cancer cell lines.



References

[1] Jiang, Z-Y.; Zhou, J.; Huang, C-G.; Hu, Q-F.; Huang, X-Z.; Wang, W.; Zhang, L-Z.; Li, G-P.; Xia, F-T. *Tetrahedron* **2015**, *71*, 3844.

[2] Imai, H.; Suzuki, K.; Morioka, M.; Numasaki, Y.; Kadota, S.; Nagai, K.; Sato, T.; Iwanami, M.; Saito, T. *J. Antibiot.* **1987**, *40*, 1475.

[3] Nakai, R.; Kakita, S.; Asai, A.; Chiba, S.; Akinaga, S.; Mizukami, T.; Yamashita, Y. *J. Antibiot.* **2001**, *54*, 836.

P-076

Trifluoroacetonitrile imines chemistry - challenges and recent progress

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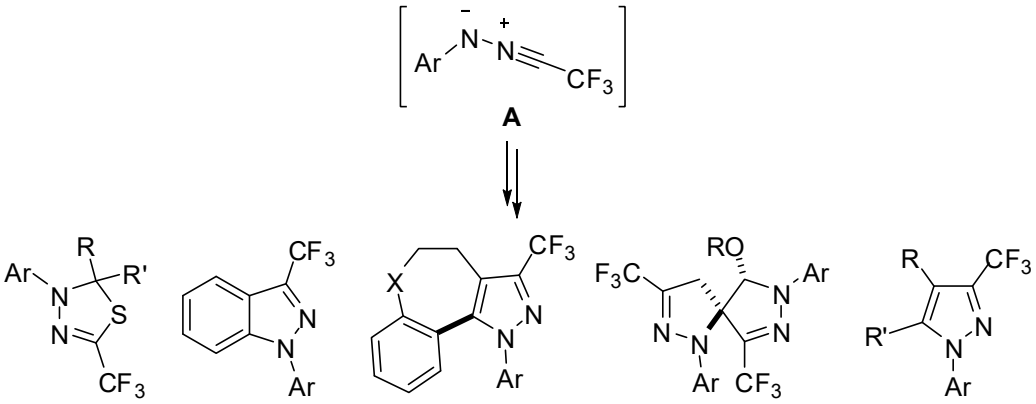
During last decades a large number of organofluorine compounds have been demonstrated as an attractive products for practical applications e.g. in the field of pharmaceutical and materials industry. In this context, (3+2)-cycloaddition reactions (so-called Huisgen reactions) of appropriate fluorinated components are considered extremely useful strategy towards five-membered, polyfunctionalized heterocyclic compounds. We paid special attention to the chemistry of trifluoroactonitrile imines of type **A**, recognized as readily available class of fluorinated 1,3-dipoles, generated *in situ* by base-induced dehydrohalogenation of the respective hydrazonoyl bromides. The title nitrile imines opened up straightforward access to CF_3-heterocyclic systems including polycyclic derivatives.[1]



Scheme 1. Application of nitrile imines **A** in the synthesis of fluorinated heterocyclic compounds.

Acknowledgment

Financial support by the National Science Centre (Poland; grant PRELUDIUM no 2016/21/N/ST5/01254) is gratefully acknowledged.

References

[1] (a) G. Mlostoń, *et al*., *J. Fluorine Chem.,* **2016**, *192*, 147-154; (b) G. Utecht, *et al*., *J. Fluorine Chem.,* **2017**, *201*, 68-75; (c) G. Utecht, *et al., Org. Biomol. Chem.,* **2018**, *16*, 1252-1257; (d) G. Utecht, *et. al*., *Synlett,* **2018**, *29*, 1753-1758.

P-077

Synthesis, structure and spectroscopic properties of novel 2-(1*H*-indol-2-yl)acrylonitrile derivatives as antimicrobial and anticancer agents

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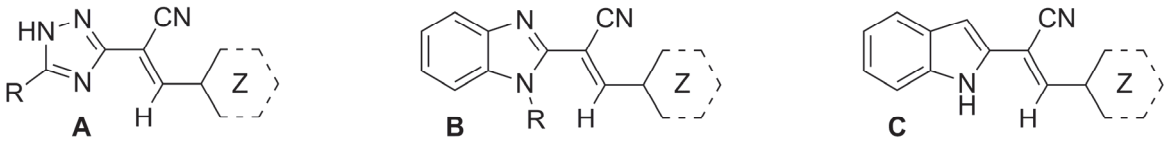
2,3-Disubstituted acrylonitriles have attracted considerable attention for many years in the development of compounds with pharmacologically useful properties including spasmolytic, hypotensive, antioxidative, tuberculostatic, insecticidal and anticancer activities.

Recently, we have reported that 3-arylacrylonitrile with either triazole (Structure **A**) or benzimidazole (Structure **B**) substituents in position 2 of the acrylonitrile have pronounced cytotoxic activity on human cancer cells. The exceptionally high activity of 2-benzimidazole **B** prompted us to further modify their structure, including replacement of the benzimidazole ring for indole ring (Structure **C**).



R = H, alkyl, acyl; **Z** = aryl, heteroaryl

The target acrylonitriles of type **C** were prepared by Knoevenagel condensation reaction of the 2-(1*H*-indol-2-yl)acetonitrile with either aryl- or heteroaryl aldehydes. Structures of the newly prepared compounds were confirmed by IR, NMR spectroscopy and mass spectrometry (MS). The *Z*-configuration of these heteroarylacrylonitriles was confirmed by X-ray crystal analysis (Fig. 1).

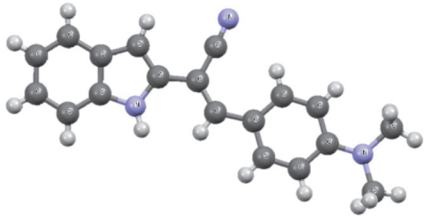


Figure 1. X-ray structure of (*Z*)-3-[4-(dimethylamino)phenyl]-2-(1*H*-indol-2-yl)acrylonitrile

All the compounds prepared were screened for antimicrobial and cytotoxic activities on a panel of the 60 tumour cell lines. Additionally, the compounds depicted as **C** were investigated for their fluorescent properties.

References

[1] Sączewski F. et al. *J. Med. Chem*. 47 (2004) 3438-3449.
[2] Sączewski F. et al. *Eur. J. Med. Chem*. 43 (2008) 1847-1857.

P-078

Total Synthesis of β-(+)-Valienamine

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Carbasugars are a wide group of carbohydrate mimetics in which the ring oxygen had been replaced by methylene group [1]. High importance of these compound is related to theirs interesting biological and pharmacological properties which are the matter of current studies.

N-alkyl derivatives of *β*-valienamine such as *N*-octyl-*β*-(+)-valienamine or *N*-octyl-*β*-(-)-valienamine are potent inhibitor of lysosomal enzymes and find application in the treatment of Gaucher disease [2].

Due to the fact of increasing application of carbasugars is not surprisingly that much effors has been put in the synthesis of these highly functionalized cyclohexene derivatives.

In our work a concise, six-step synthesis of carbasugar from naturally occurring D-xylose is presented. The one-pot *seleno*-Michael reaction connected with intramolecular aldol reaction is a key step of the carbasugar core asymmetric synthesis. Further transformation of obtained carbasugar moiety led to *β*-(+)-valienamine.

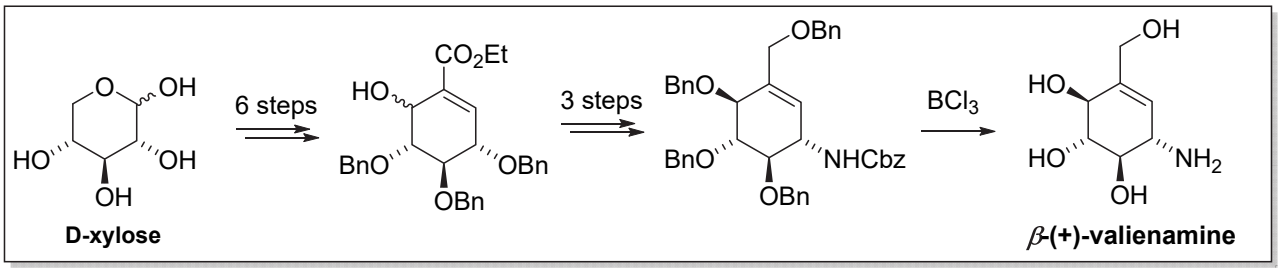

Figure 1. Synthesis of *β*-(+)-valienamine.

Tandem *seleno*-Michael reaction conjugated with oxidation/elimination step of *in situ* generated nucleophile have been described few years ago in intermolecular variant [3]. In our work, we present the first example of this reaction in intramolecular way which leads to previously inaccessible cyclic product of Morita-Baylis-Hillman reaction [4]. Conducted experiments allowed to receive cyclic products with high yields and good diasteroisomeric excess.

Acknowledgment

This work was financed by Polish National Science Center (Grant No. 2015/17/D/ST5/01334).

References

[1] 1. O. Arjona, A. M. Gómez, J. C. López, J. Plumet, *Chem. Rev*. **2007**, 107, 1919.

[2] N. F. Brás, N.M.F.S.A. Cerqueira, M. J. Ramos, P. A. Fernandes, *Expert Opin Ther Pat.*, **2014**, 24, 857

[3] B. A. Sousa, A. A. Dos Santos, *European J. Org. Chem*. **2012**, 18, 3431.

[4] P. Banachowicz, J. Mlynarski, S. Buda, *J. Org. Chem.* ***2018***, 83, 11269.

P-079

Antimicrobial activity of chiral ricinoleic and 3-hydroxynonanoic acids derivatives

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Hydroxy fatty acids (HFAs) occupy a significant position among lipids, however, their industrial use is limited principally by their poor availability. (*R*)-ricinoleic acid (RA) [(*R,Z*)-12-hydroxyoctadec-9-enoic acid] is the only one available in sufficient quantities representative of this group of compounds. It is an important feedstock commonly used in different fields of industry and its most important source is castor oil, in which it represents about 80–90% of all fatty acids. RA is characterised by the presence of hydroxy group in the homoallilic position and one double bond in the *cis* configuration making it a great raw material for chemical and biochemical syntheses [1]. Transformations of RA lead to different compounds and many of them show interesting biological activity. For instance, amides of ricinoleic acid exhibited significant anticancer and antimicrobial activity [2–5].

Two hydroxy fatty acids, *i.e.* ricinoleic acid and 3-hydroxynonanoic acid were the objects of our interests. In the form of chiral methyl esters they constituted starting materials for the preparation of amide derivatives. Having at disposal both forms of ricinoleic acid methyl esters, we decided to obtain analogous esters of (*R*)- and (*S*)-3-hydroxynonanoic acid by a multistage process involving ozonolysis and oxidation of castor oil and methyl (*S*)-ricinoleate, respectively. Then, all of the obtained compounds were transformed into corresponding chiral derivatives, *i.e.* amides and hydroxamic acids. Different methods for their preparation were developed during our study, including chemical and biochemical processes. We drew our attention to fatty acid amides and hydroxamic acids because they have recently raised special interest as biologically active compounds.

Then, the obtained amide derivatives of (*R*)- and (*S*)-ricinoleic acids and (*R*)- and (*S*)-3-hydroxynonanoic acids were tested in terms of antimicrobial activity. The minimal inhibitory concentration (MIC) against 13 different microorganisms was determined using microdilution method. The results were very interesting. Some of the tested derivatives showed significant antimicrobial potential and they may be considered as compounds of potential pharmacological significance. Moreover, in some cases differences in the activity of enantiomers were observed.

References

[1] S. Pabiś, J. Kula, *Curr. Med. Chem*. **2016**, *23*, 4037-4056.
[2] C.R.M. D'Oca, T. Coelho, T.G. Marinho, et al., *Bioorg. Med. Chem. Lett.* **2010**, *20*, 5255–5257.
[3] D.S. Dos Santos, L.A. Piovesan, C.R.M. D'Oca, et al., *Bioorg. Med. Chem.* **2015**, *23*, 340–347.
[4]S. Matysiak, A. Chmiel, J. Skolimowski, J. Kula, A Błaszczyk, *Chirality* **2017**, *29*, 1–7.
[5] S. Matysiak, J. Zabielska, J. Kula, A. Kunicka-Styczyńska, *J. Am. Oil Chem. Soc.* **2018**, *95*, 69–77.

P-080

Organocatalytic synthesis of enantiomerically enriched polyheterocyclic tetrahydrothiophene derivatives

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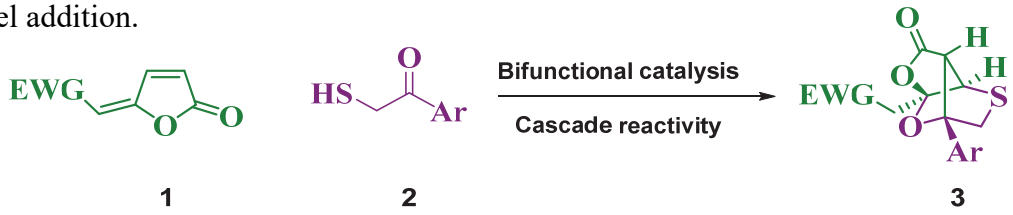
Stereoselective synthesis of complex heterocyclic compounds constitute an important target in organic chemistry. [1] Herein we present the highly stereoselective synthesis of tetrahydrothiophene derivatives **3**. In this approach mercaptoacetophenones **2** and furanones **1** were used as starting materials and the reaction was carried out using cinchona-alkaloid-derived bifunctional catalyst. Polyheterocyclic products **3** were efficiently obtained with great stereoselectivity in a cascade involving: thia-Michael addition followed by aldol and oxa-Michael addition.



Scheme 1. Organocatalytic synthesis of tetrahydrothiophene derivatives.

Acknowledgment

This project was realized within the Sonata Bis programme (grant number: 2015/18/E/ST5/00309) from the National Science Centre, Poland

References

[1] A. P. Taylor, R. P. Robinson, Y. M. Fobian, D. C. Blakemore, L. H. Jones and O. Fadeyi, *Org. Biomol. Chem.,* **2016**, 6611-6637

P-081

Coupling reactions as a tool in the synthesis of luminescent compounds

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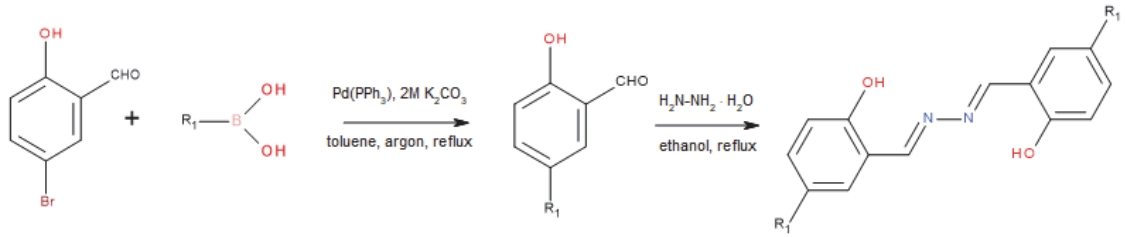
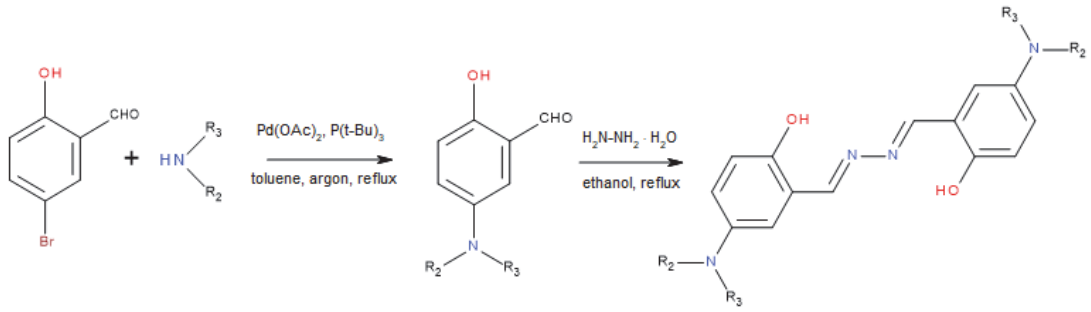
One of the most useful reactions to modify the molecule are coupling reactions. Owing to them, we can create a new C-C or C-N bond. The introduction of conjugated aromatic or aminoaromatic substituents into the backbone of the azines can significantly affect the absorption, solubility or the ability to organize molecules in a thin layer of a solid. In order to modify was use a Suzuki coupling reaction. A corresponding salicylaldehyde derivative containing the bromine substituent was reacted with a substituted boronic acids esters or boronic acids (*Scheme 1*). In this way, large aromatic systems were introduced into the backbone of the azines. Buchwald's coupling reaction allowed the introduction of aminoaromatic substituents (*Scheme 2*) [1] [2]. In conclusion, owing to the use of coupling reactions in the synthesis, were obtained a number of new organic compounds with interesting physicochemical properties.



Scheme 1



Scheme 2

References

[1] Ł. Skórka et al. *Synthetic Metals,* **2017**, 228, 1–8

[2] X. Ma, J. Cheng, J. Liu, X. Zhou, H. Xiang, *New J. Chem*, **2015**, 39, 492-500.

P-082

Spectroscopic study of the interaction between selected fungicides with α-cyclodextrin in water

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Plant protection products play a very important role in agriculture. The use of fungicides is necessary, where high humidity and favorable temperature cause rapid development of many species of plants. In most cases these fungicides are sparingly soluble in water. It is often an auxiliary substance, which in combination with cyclodextrin further improves the desired physicochemical, chemical and transport properties of a given fungicide [1]. Among them, the most common are α, β- and γ-cyclodextrin, which consist of 6, 7 and 8 glucose units respectively. The shortened conical cyclodextrin have a hollow, conical cavity with a depth of 0.79 nm, while both the upper and lower diameters increase with the number of glucose units. The main goal of our research was to investigate the effect of α - cyclodextrin on increasing the solubility of 4-Phenylphenol and 2-Phenyleneol in water. To determine the increase in solubility of fungicides in water caused by the presence of α-cyclodextrin, aqueous solutions of the cyclic oligosaccharide were prepared in a concentration range from 2 mM (α-CD) to 90 mM (α-CD) to which an excess of solid fungicides. The concentration of fungicides (ligand) caused by the increase in the concentration of α-cyclodextrin (receptor) indicate an increase in the solubility of the fungicide. The solubility of 4-Phenylphenol and 2-Phenylphenol in the aqueous solution of α-cyclodextrin increased 4 and 2.5 times for the concentration of α-cyclodextrin receptor (α-CD) 30 mM and 90 mM.

References

[1] Sergey V. Kurkov, Thorsteinn Loftsson, *International Journal of Pharmaceutics*., **2013**, 453, 167– 180.

P-083

Synthesis of tetramethyl [(alkylamino)(aryl)methylene bisphosphonates

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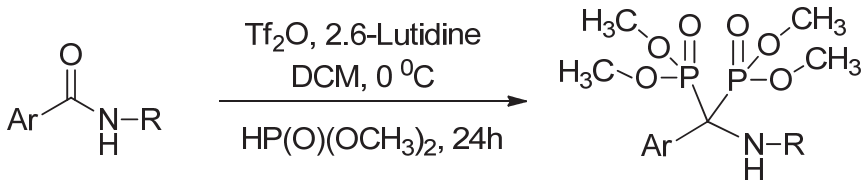
Bisphosphonates are organic compounds with a structure similar to inorganic pyrophosphates. They are of great importance due to their significant biological activity, *i.e.* bactericidal or regulating bone mineralization properties. Bisphosphonates are used as medicines in a treatment of several bone diseases, *e.g.* in osteoporosis, congenital malformations of the skeletal system, Paget's disease. These organophosphorus compounds inhibit hydroxyapatites dissolution and also inhibit bone resorption by selective adsorption to mineral surfaces and further internalization by osteoclasts. Nitrogen bisphosphonates, *i.e.* alendronate, pamidronate, risedronate, more strongly inhibit the action of osteoclasts than bisphosphonates that do not contain a nitrogen atom in their structure, *e.g.* ethidronate, clodronate. [1] This work will present the results of studies on the preparation of diversely functionalized nitrogen bisphosphonates (Scheme 1) based on the bisphosphonylation of secondary amides using trifluoromethanesulfonic anhydride (Tf_2O). [2]



Scheme 1.

References

[1] M. T. Drake, B. L. Clarke, S. Khosla, *Medycyna po dyplomie*, **2010**, *2*, 80-81.
[2] A-E. Wang, Z. Chang, W-T. Sun, P-Q. Huang, *Org. Lett.*, **2015**, *17*, 732−733.

P-084

Influence of azomethine model compounds chemical structure on their optical and thermal properties

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The simplicity of synthesis process, which consists of a polycondesation reaction, together with the simple purification of the obtained product make polyazomethines a potential counterpart for currently utilised conjugated polymers in optoelectronic systems. Even though a considerable quantity of polyazomethines has been already reported and described, there is only a brief investigations of the relationship between chemical structure of the azomethine molecule and its optical and thermal properties.

This paper presents a complex investigation on the effect of chemical structure of building blocks such as diphenylmethane, benzene, biphenyl, diphenyl oxide, naphthalene, fluorene and 1-(naphthalen-1-yl)-2-phenyldiazene on thermal and optical properties of compounds consisting of such moieties. Each of these units has been used as central unit, to which have been attached either phenylene- or thiophene- arms. Use of such synthesised model compounds allowed to neglect the impact of polymer chain length. After confirmation of chemical structure with ^{1}H-NMR and mass spectroscopy, the thermal properties have been investigated using differential scanning calorimetry (DSC). Melting and glass transition temperatures have been designated and considered for different structures of model compounds. Optical measurements of azomethines' solutions in chloroform were taken on the UV-Vis spectrophotometer. Absorbance spectra of different model compounds were presented and on the basis of the position and intensity of the $\pi \rightarrow \pi^*$ transition absorption band, the conjugation and conformation of investigated molecules were discussed. Herein presented results of thermal and optical investigations of azomethine model compounds may be useful for design of suitable polyazomethines, with desired properties.

Vinylogous Nucleophiles in the Allylic-Allylic Alkylation of Morita-Baylis-Hillman Carbonates

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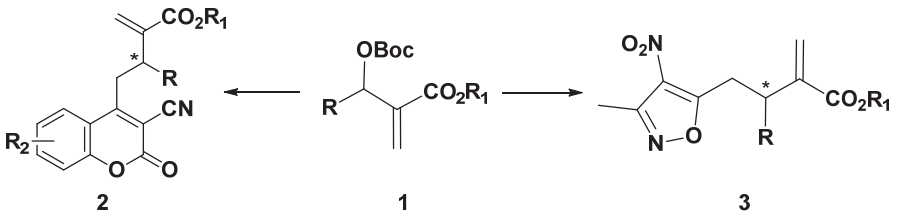
Vinylogous reactivity of organic compounds constitutes an important and challenging area in the contemporary organic chemistry. It allows for a transfer of nucleophilic or electrophilic properties of a given position to a remote reaction site through the conjugated double bonds system. This is a convenient manner to achieve new reactivities of organic compounds.[1]

Our studies demonstrate that vinylogous nucleophilies can be successfully employed in the allylic-allylic alkylation of Morita-Baylis-Hillman carbonates.[2] In such a manner a facile access to interesting products **2** and **3** is possible. Both developed approaches are promoted by readily available and cheap Lewis basic dimeric Cinchona alkaloid derivatives. Target products **2** and **3** bearing one stereogenic center are obtained in excellent yields in a highly enantioselective manner.



Acknowledgment

This project was realized within the Sonata Bis programme (grant number: 2015/18/E/ST5/00309) from the National Science Centre, Poland.

References

[1] Curti, C.; Rassu, G.; Zambrano, V.; Pinna, L.; Pelosi, G.; Sartori, A.; Battistini, L.; Zanardi, F.; Casiraghi G. *Angew. Chem. Int. Ed.* **2012**, *51*, 6200.

[2] a) Kowalczyk, D.; Albrecht, Ł. *Adv. Synth. Catal.* **2018**, *360*, 406; b) Kowalczyk-Dworak, D.; Albrecht Ł. submitted.

P-086

Reaction of secondary phosphine oxides with CCl_4 under flow conditions

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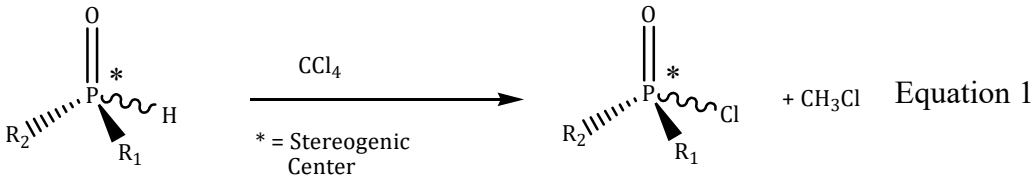
Phospinyl chlorides are a key substrate in the synthesis of wide range of other phosphinyl derivatives. [1] A few years ago during the measurements of the Vibrational Circular Dichroism (VCD) of optically active the secondary oxide of t-butylphenylphosphine, its conversion to tert-butylphenylphosphonyl chloride was observed, in experiments using carbon tetrachloride as a solvent. [2]

We will present our preliminary results of the research based on this observation on a very convenient procedure for the synthesis of phosphinyl chlorides as describe in general equation 1. Synthetic and stereochemical aspects for these reactions carried out in batch and under flow conditions will be discussed. [3]



Equation 1

Acknowledgment

This work was supported by The National Science Centre under Grant no UMO 2014/15/B/ST5/05329.

References

[1] J. Drabowicz et al. in *Science of Synthesis* Vol 42, Vol. Ed. F. Mathey, pp. 633-678.
[2] F. Wang et al. *J. Org. Chem*., **2000**, 65, 7561.
[3] T. Glasnov, Continuous-Flow Chemistry in the Research Laboratory, *Springer*, **2016**.

Liquid crystalline bis- and tris-radicals derived from the 1,4-dihydrobenzo[*e*][1,2,4]triazinyl

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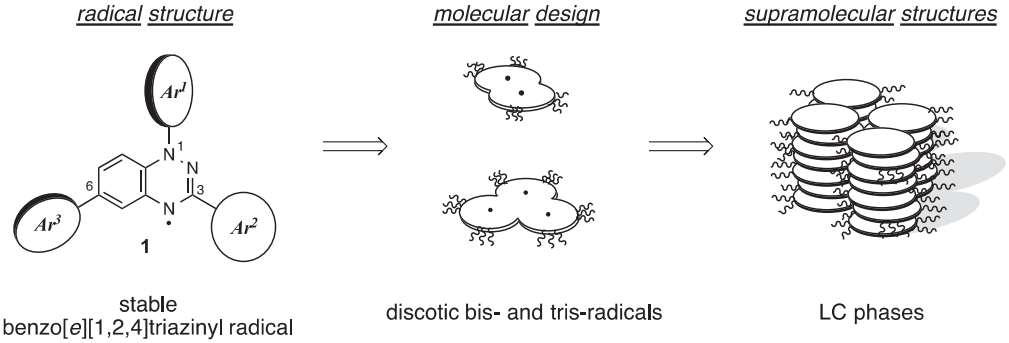
Self-organizing fluids, including liquid-crystalline derivatives of the benzo[*e*][1,2,4]triazinyl radical (BT) **1**, are used for easier control of magnetic properties of the crystalline state.[1,2] Our recent reports showed substituent-dependent magnetic interaction in discotic derivatives of type **1**,[2] and paramagnetic behaviour of the mesogenic bent-core structures.[3] In search for more organized phases, which can affect on more effective magnetic interactions, a series of bis- and tris-radical derivatives of the BT were designed and synthesized. Results, including synthesis and their mesogenic properties characterized by optical (POM) observation, thermal measurements (DSC) and X-ray diffraction (XRD) analysis will be presented.



Scheme 1. Benzo[*e*][1,2,4]triazinyl as a building block for polyradical liquid crystals.

Acknowledgement:

Financial support by the National Science Center (Preludium 2017/25/N/ST5/01805 and OPUS 2014/13/B/ST5/04525).

References

[1] J. S. Miller and M. Drillon, *Magnetism: Molecules to Materials II: Molecule-Based Materials*, WILEY-VCH Verlag GmbH, Weinheim, **2001**.

[2] M. Jasiński, J. Szczytko, D. Pociecha, H. Monobe, P. Kaszyński, *J. Am. Chem. Soc.* **2016**, *138*, 9421–9424.

[3] S. Kapuściński, A. Gardias, D. Pociecha, M. Jasiński, J. Szczytko and P. Kaszyński, *J. Mater. Chem. C*, **2018**, *6*, 3079-3088.

P-088

Phosphorus-containing isothiocyanate-derived mercapturic acids – a useful alternative for parental isothiocyanates

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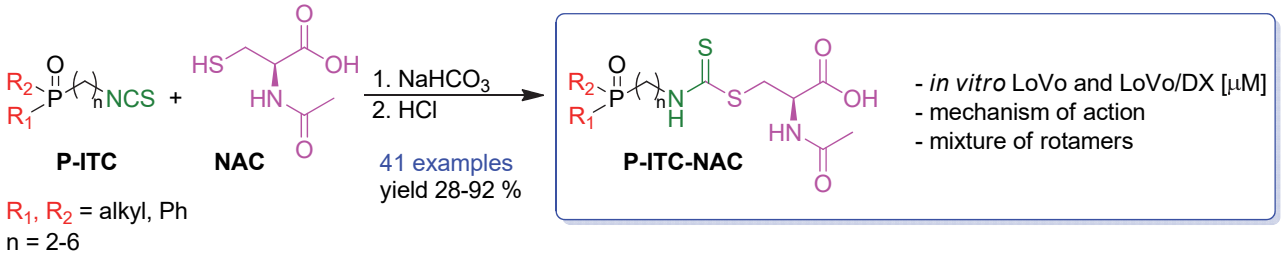
Inside cells isothiocyanates (ITCs) react with glutathione under the action of glutathione-*S*-transferases to form glutathione conjugates, which are converted to mercapturic acids (ITC-NACs) *via* mercapturic acid pathway. [1] The mercapturic acids and parental isothiocyanates exhibit comparable antiproliferative potential. ITC-NACs can be considered as convenient prodrugs as under physiological conditions they undergo a reverse reaction to parental isothiocyanates. [2]



Scheme 1. Synthesis of isothiocyanate-derived mercapturic acids

The aim of this project was to design and obtain a series of 41 phosphorus-containing isothiocyanate-derived mercapturic acids (P-ITC-NACs) with unbranched alkyl chains (n = 2–6), and with alkyl and phenyl substituents on phosphorus atom. Target P-ITC-NACs were prepared in 28–92% yields and with high purity (> 97%) in the reaction of the corresponding P-ITCs with *N*-acetyl-L-cysteine (NAC). All P-ITC-NACs were evaluated *in vitro* on human colon adenocarcinoma LoVo line and it's subline resistant to doxorubicin – LoVo/DX. [3]

Acknowledgement:

The authors gratefully acknowledge financial support from the Polish National Science Center (grant no. DEC 2011/03/B/ST5/01058).

References

[1] X. Wu, Q.-H. Zhou, K. Xu, *Acta Pharmacol. Sin.,* **2009**, *30*, 501.

[2] L. Tang, G. Li, L. Song, Y. Zhang, *Anticancer Drug,* **2006**, *17*, 297.

[3] M. Psurski, Ł. Janczewski, M. Świtalska, A. Gajda, T. M. Goszczyński, J. Ciekot, Ł. Winiarski, J. Oleksyszyn, J. Wietrzyk, T. Gajda, *Bioorg. Med. Chem. Lett.,* **2018**, *28*, 2611.

P-089

Synthesis of symetric oksadiazoles with luminescent properties

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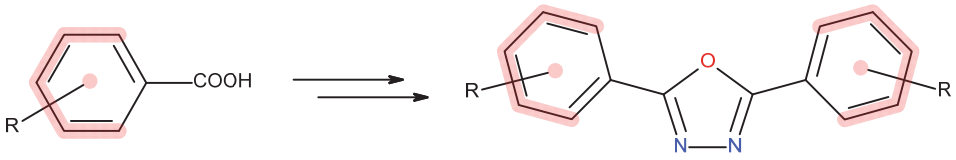
The purpose of this study was to obtain symmetric oxadiazoles with luminiscent properties and ability to form polycrystalline thin layers. During the conducted research two symmetric bis-hydrazides were obtained, displaying photoluminescence in solid. Symmetric oxadiazoles obtained from bis-hydrazides exibited much stronger luminescence in comparison to initial compounds (Scheme 1). All obtained derivatives were characterized by different properties, e.g. the ability to form polycrystalline layers or the effect of fluorescence, observed under the microscope (thanks to the cooperation with the Laboratory of Biosensors and Organic Electronics). Diverse properties of the products obtained and the different emission of light, can be used as the emission layer in the construction of an organic light-emitting diode (OLED).



Scheme 1.

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P-090

New naphthalene-based ferroelectric liquid crystals

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Synthesis of new chiral liquid crystalline molecules containing naphthalene in molecular core coupled with partially fluorinated or alkiloxy terminal chain (Fig.1) was planned and a class of the molecules was synthesized. There are many liquid crystals based on naphthoic ester core[1], some of them, with long enough alkiloxy terminal substituents, exhibit smectic phases SmA and SmC[2]. Partially fluorinated terminal chain was chosen to stabilize tilted smectic phases. Two different synthetic approaches were adopted depending on terminal substituent R_F. Received compounds were examined to determine phase transition temperatures, enthalpies and purity. Influence of terminal fluorinated chain length, bridge groups and lateral substituents on phase occurrence and temperature range was determined. Some of the compounds exhibit enantiotropic smectic phases SmC* and SmA* although compounds without mesophase were also discovered. Results allow to plan further synthesis of new molecules considering structural changes.

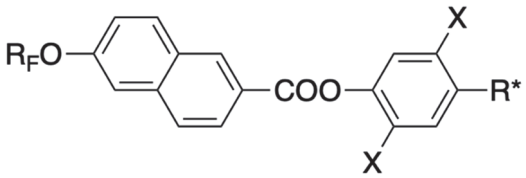

Figure 1. Schematic structure of synthesized compounds

References

[1] D. Coates, G. W. Gray, *Mol. Cryst. Liq. Cryst.*, **1976**, 37, 1, 249–262.
[2] D. Coates, G. W. Gray, *Mol. Cryst. Liq. Cryst.*, **1978**, 41, 7, 197–202.

P-091

Synthesis of new polar nematogenic compounds with a large dielectric anisotropy

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Highly polar nematic materials containing long molecular cores and possessing lower smectogenity are still highly desired. In our studies, we designed and synthesized new compounds containing a strongly polar substituent - a cyano group, which adequate positions favor bigger longitudinal dipole moment. Perpendicular polar effects are generated mostly by ester bridges but they are relatively small. The general structure of new compounds is shown below(Fig. 1). Similar structures were synthesized before but with a different molecular core[1]. Use of naphthalene as a part of a rigid core breaks the linearity of the molecule and shortens it. Phase sequence and phase transition temperatures were determined for synthesized molecules.

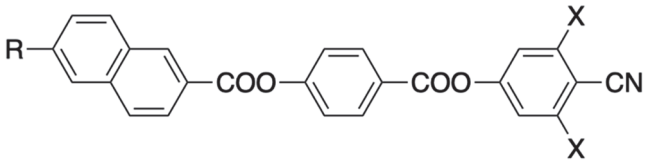

Figure 1. Schematic structure of synthesized molecules.

References

[1] D. Ziobro, J. Dziaduszek, M. Filipowicz, R. Dąbrowski, J. Czub, S. Urban, *Mol. Cryst. Liq. Cryst.*, **2009**, 502, 1, 258–271.

P-092

New azole *O*-benzyl oxime ethers derivatives of 2-acetylthiophene – synthesis and biological activity

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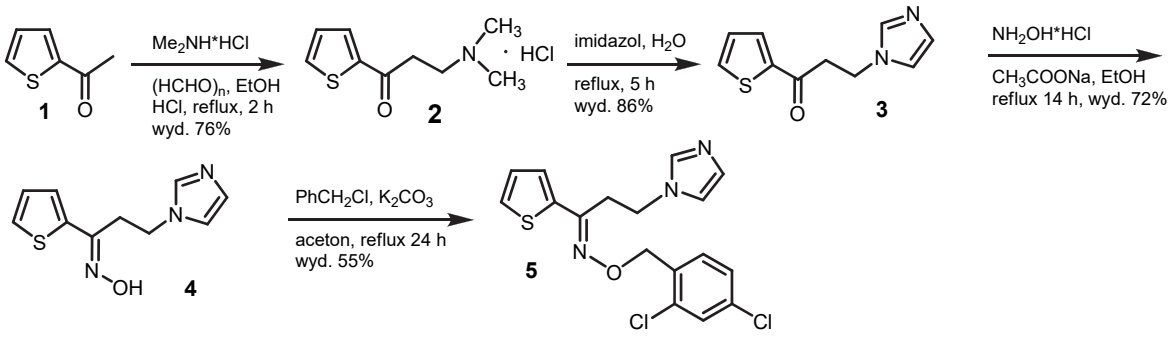
Oxime ethers are group of compounds with diverse biological activity. For example, fluvoxamine is an antidepressant, oxiconazole is an antifungal drug [1]. In our earlier studies, we synthesized selected *O*-benzyl ether derivatives of 2-acetylthiophene oxime [2] with moderate antifungal activities. We think that the introduction of the imidazole ring should significantly increase the biological activity.

In this work we prepared the oxime ethers containing the imidazole and thiophene rings. The final products were obtained from 2-acetylthiophene **1** in a four-step reactions. In the first stage we carried out the Mannich reaction, and into the obtained product **2**, we introduced the imidazole ring. The resulting aminoketone **3** was converted into the oxime **4** and then to the corresponding *O*-benzyl oxime ethers, on an example **5**. The obtained compounds are analogs of acetophenone esters derivatives with an imidazole embedded ring with antifungal activities [3].

The final products were tested against *C. albicans* and *M. furfur*.



Scheme 1. Synthesis of the final compound **5**.

References

[1] A. Zejc, M. Gorczyca, Chemia leków, Wydawnictwo Lekarskie PZWL **2004**.

[2] T. Kosmalski, J. Kutkowska, I. Dwojak, R. Studzińska, A. Sikora, B. Modzelewska-Banachiewicz, A. K. Gzella, *Heterocycles*, **2017**, *94*, 523-530.

[3] M. I. Attia, A. S. Zakaria, M. S. Almitairi, S. W. Ghoneim, *Molecules*, **2013**, *18*, 12208-12221.

P-093

Synthesis of chiral 1,2-diamine including proline and aziridine ring

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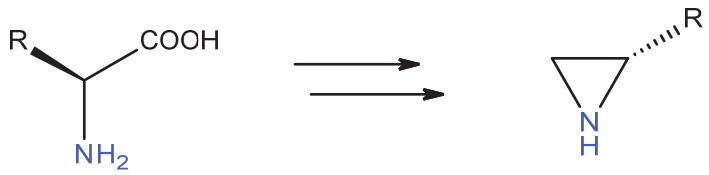
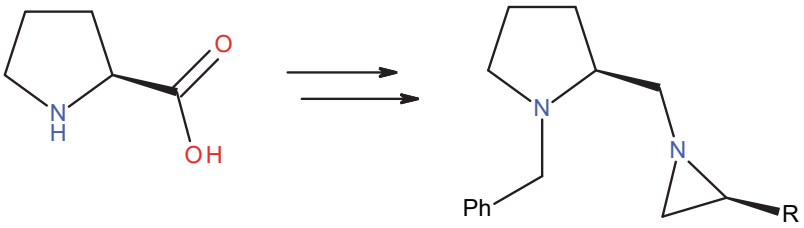
The main purpose of my research was the synthesis of aziridine derivatives using natural amino acids. Starting from natural *L*-valine, I received chiral, optically pure (*S*)-2-isopropylaziridine according to modified Wenker synthesis [1], with high yield (Scheme 1). I used the previously received *NH*-aziridine for the synthesis of (aminoalkyl)aziridine derivative starting from another amino acid – *L*-proline (Scheme 2). I obtained the target compound through aziridine-amide also with the high yield. The gained aziridine derivative will be used as bidentate, chiral catalyst in stereocontrolled synthesis.



Scheme 1.



Scheme 2.

References

[1] Xinyao Li, Ning Chen, Jiaxi Xu, *Synthesis* **2010**, *20*, 3423-3428.

P-094

Enhancing the solubility of selected fungicides through cyclodextrins complexation

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The fungicides are type of pesticides, which are used to controls fungal disease by specifically inhibiting and killing the fungus causing the disease. Thiabendazole, thiophanate methyl and carbendazim are systemic, benzimidazole fungicides, which are very poorly-water soluble compounds. For this reason, in commercially available plant protection products the harmful organic solvents are used.

Cyclodextrins are natural, non-toxic, cyclic oligosaccharides. The characteristic structure of cyclodextrins allows them to include poorly-water soluble molecules inside the hydrophobic cavity. The formation of an inclusion complex can change the properties of the ligand e.g. its solubility in water or bioavailability. The formation of host-guest complexes between cyclodextrins and fungicides could make these compounds much better soluble in water.

The aim of this study was to investigate the interactions between benzimidazole fungicides and natural α- and β-cyclodextrin by spectrophotometric method. As a result of the research, the maximum solubility increase of selected fungicides was determined. The stability constants of the formed complexes were compute using the Higuchi-Connors equation.

Acknowledgment

The work was partially founded by the University of Lodz from the project "Studenckie Granty Badawcze 2018" .

Structural studies on palladium complexes of new chiral polycyclic bisphosphanes derived from NORPHOS

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The contemporary asymmetric synthesis is often based on the utilisation of well-defined transition metal complex catalysts, usually derived from chiral phosphane and bisphosphane ligands. Such complexes are used to mediate wide pallet of crucially important asymmetric transformations: hydrogenations (Rh, Ru); allylic substitution (Pd); cross-couplings (Pd); hydroformylation (Co, Rh, Pt) and many other. The advanced experimental [1] and computational [2] studies on structure of the catalysts is crucial for better understanding their action and therefore for further design of new more efficient catalysts and conditions of the mediated reactions. The crystallographic analysis is an only a direct approach to elucidate the 3D structure of the catalysts.

Herein we would like to present the result of our studies concentrated on determination of the spatial structure of palladium complex of new rigid polycyclic bisphosphane, derived from highly efficient in asymmetric hydrogenation ligand NORPHOS.

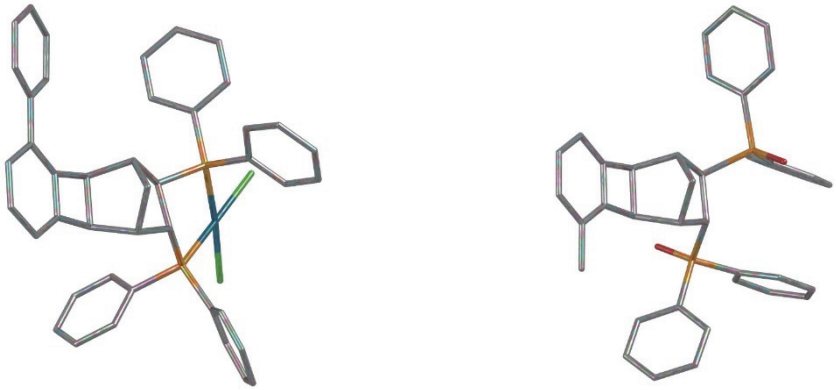

Figure 1. Crystallographic structures the palladium complex and oxide of two selected ligands.

The obtained results indicate that, despite a significant difference in structures, the key geometric features of palladium complexes and dioxides of ligands, which are belong to studied class, are notable common; this allows predicting the geometries, steric and electronic properties of other, structurally similar, catalysts, based on a limited crystallographic data and fast computer calculations only.

The details of the preparation, characterisation, comparison and analysis of new compounds will be presented.

References

[1] O. Demchuk, D. Arlt, R. Jasiński, K. Pietrusiewicz, *J. Phys. Org. Chem.,* **2012**, 25, 1006-1011

[2] R. Jasiński, O. M. Demchuk, D. Babyuk, *Journal of Chemistry,* **2017,** 3617527

New environmentally friendly synthesis of heteropolycyclic dyes

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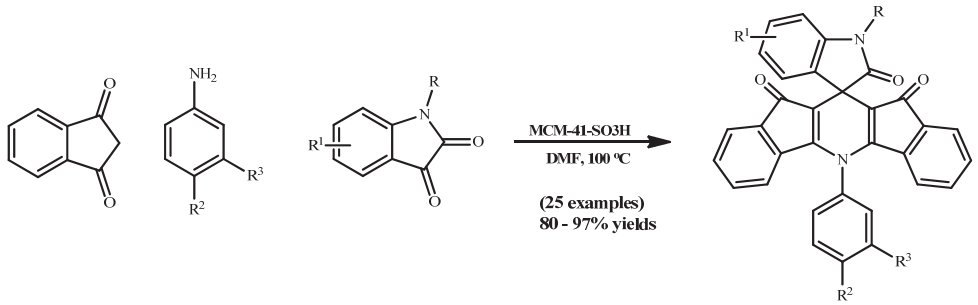
An efficient, metal-free and green method has been developed for efficient synthesis of novel dyes with potential pharmacological value. Substituted indenones and indenone merged heterocycles are well known as significant biological and medicinal skeleton for pharmaceuticals. Furthermore, the indenopyridine is the core structure of many pharmacological agents and natural alkaloids and are also useful in a wide range of biological applications, e.g. as antiprotozoal agents, fluorescent probes for biomolecular labeling, as well as nucleic acids (DNA and RNA) detection, photosensitizers for photodynamic therapy (PDT), tumor imaging contrasts and markers for flow cytometry. Despite well developed procedures of synthesis polyene dyes based on indenone core [1], a literature surveys indicates that methods for the synthesis of fused isatin-indenone based spiro compounds are still limited. In spite of several advantages, most of those reported methods have many drawbacks include the reactions under challenging conditions and utilisation of expensive and homogeneous catalysts (p-toluenesulfonic acid, sulfonated polyethylene glycol, acidic ionic liquid *N*-methyl-2-pyrrolidonium dihydrogen phosphate, etc) or toxic solvents.

Herein we would like to present new approach to synthesis of spiro(diindenopyridine)indolinnes, realised with utilisation of nano-ordered mesoporous silica catalyst, functionalized with SO_3H groups (MCM-41-SO_3H). The great advantages of our catalyst are nontoxicity, ease of preparation, and its recyclability and reusability [2]. The prepared spiro(diindenopyridine)indolinnes are red pigments, which could be used as indicator of basic pHs.



Scheme 1. Synthesis of the spiro(diindenopyridine)indolinnes.

The details of the preparation and characterisation our catalyst as well as it utilisation in the synthesis of important heteropolycyclic compounds will be presented.

References

[1] F. Azamifar, M. R. Naimi-Jamal, Oleg M. Demchuk, *Dyes and Pigments,* **2019**, *161,* 438–447

[2] E. Ali, M. R. Naimi-Jamal, M. G. Dekamin, *Sci. Iran*, **2013**, *20*, 592–597.

P-097

Synthesis of ulosonic acids via zinc- and-iron promoted asymmetric hetero Diels-Alder reaction

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Ulosonic acids (3-deoxy-aldonic acids) are family of naturally occurring sugar derivatives, which are synthesized by stereoselective enzyme catalyzed addition of phosphoenolpyruvate (PEP) to the corresponding aldoses. [1] All these acids are involved in many biologically important processes and thus they attract attention of many researchers.

Recently, we have showed that, these type of compounds can be obtained in biomimetic, stereocontroled aldol reaction. [2] However, alternative approach to this synthesis is the use of hetero Diels-Alder (HDA) reaction between diene and glyoxalates (Figure 1). Based on the current state of the art in enantioselective HDA reaction in the synthesis of ulosonic acids, [3] we would like to propose an innovative use of chiral zinc and iron complexes, which have not yet been widely used in this type of reaction.

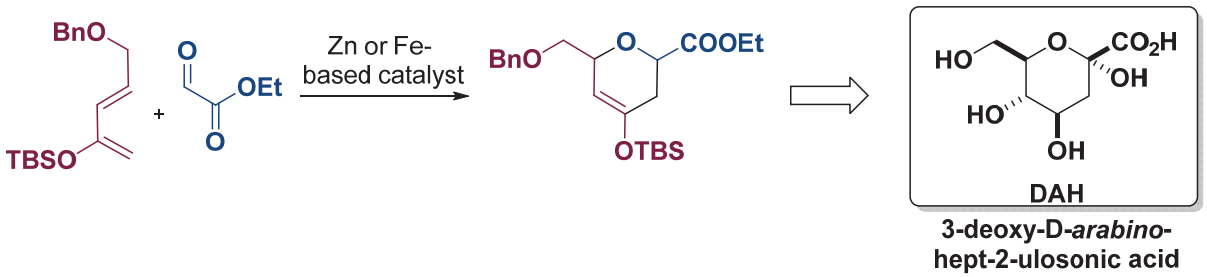

Figure 1. The hetero-Diels-Alder reaction in the synthesis of ulosonic acids derivatives.

In this work, we present the application of an enantioselective cycloaddition reaction of glyoxalate to dienes in stereocontroled construction of the pyranose system (Figure 1). This approach is the shortest synthetic route for ulosonic acids skeleton, therefore this reaction require enantioselective control by application of suitable catalysts.

Here, we present our effort towards high stereoselectivity of model reaction. We tested zinc and iron complexes with commercially available BOX and PyBOX ligands. Application of selected condition resulted in formation of derived pyranose ring with good overall yield (39 - 81%) and hight enantiomeric excess (58 up to 91% *ee)*.

References

[1] Machajewski T.D.; Wong C-H.; *Angew Chem Int Ed.* **2000**, *39*, 1352-1374.

[2] Molenda M.; Baś S.; El-Sepelgy O.; Stefaniak M.; Mlynarski J.; *Adv Synth Catal*. **2015**, *357*, 2098-2104.; El-Sepelgy O.; Mlynarski J.;. *Adv Synth Catal*. **2013**, *355*, 281-286; Molenda M.; Bas S.; Mlynarski J.; Eur *J Org Chem*. **2016**, 4394-4403.

[3]. X. Jang, R. Wang, *Chem. Rev.* **2013**, *113*, 5515–5546. 6. A. Lubineau, H. Arcostanzo, Y. Queneau, *J. Carbohydrate Chem.* **1995**, *14*, 1307-1328.

Effective Michaelis - Arbuzov rearrangement under flow conditions using catalytic amounts of alkyl halides

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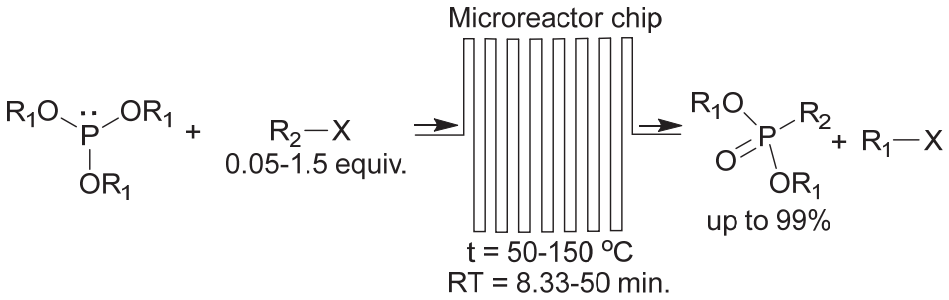
Alkyl phosphonates can be considered as one of the basic families of organophosphorus compounds that have found a broad spectrum of useful applications in the areas of industrial, agricultural and medicinal chemistry. Their importance stems from their diverse biological activity, as well as their utility as synthetic intermediates especially in the synthesis of other organophosphorus esters and amides including also biologically active molecules. The first solvent- and catalyst–free procedure for the Michaelis - Arbuzov reaction under flow conditions was developed (Scheme 1). [1] A variety of phosphonic esters could be obtained using this protocol starting from the corresponding phosphites and even catalytic amounts of alkyl halides with very short reaction times and excellent conversions. Thus, it provides a sustainable alternative to the existing methods for the preparation of alkylphosphonates. Isolation of the reaction products is fast and straightforward due to the lack of solvents and high purity of the obtained products.



Scheme 1. Continuous flow, solvent-free Michaelis-Arbuzov reaction.

Acknowledgment

The project was financed by the National Science Centre (NCN), Poland on the basis of the decision number UMO-2014/15/B/ST5/05329.

References

[1] J. Drabowicz, A. Jasiak, G. Mielniczak, M. Koprowski, K. Owsianik, E. Krawczyk-Sójka, D. Krasowska, Polish patent pending P. 425811 (April 4, 2018).

P-099

Application of gold electrode modified with a selected ferrocenyl derivative of metanothione to electrocatalytical determination of nitrates(III)

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Compounds containing nitrate ions(III) occur in food preservatives, fertilizers, corrosion inhibitors, detergents and industrial wastewater. Nitrates(III), when reacted with amines, can form nitrosamines, which are toxic and carcinogenic. High concentration of nitrates(III) in the human body increases the possibility of irreversible oxidation of hemoglobin to methemoglobin. For this reason, it seems important to develop new methods of detection and quantification of these compounds. Due to the fact that these compounds exhibit redox properties, it seems reasonable to apply electrochemical methods with the use of modified chemical electrodes, allowing for lower detection limits and higher selectivity. Considering the importance of ferrocenyl and heteroaryl fragments to obtain the desired material properties, a number of syntheses using Lawesson's reagent have been carried out and they resulted in corresponding new thioketone derivatives containing ferrocenyl and heteroaryl substituents that have been used as substances for chemical modification of gold electrode surface.

The aim of the studies was quantitative determination of nitrates(III) on a gold electrode modified with a newly obtained ferrocenyl derivative of the methanethione. The results implied that obtained monolayer of reduced form of selected ferrocenyl thioketone was an efficient electrocatalyst - mediator. The electrochemical and electrocatalytical properties as well as quantitative determination of nitrates(III) were studied with cyclic voltammetry and square wave voltammetry as well as the uv/vis spectroscopy.

The results of electrocatalytical activity of selected ferrocenyl thioketone immobilized on gold has been compared with those obtained for unmodified Au. The character of voltammetric plots is maintained even after 200 cycles. The immobilization of selected ferrocenyl thioketone on gold results in an increase of the oxidation peak currents of the investigated nitrates(III) in comparison to the same process on unmodified Au. The results point to the enhancement of the process efficiency and its selectivity in the presence of ferrocenyl thioketones immobilized on gold. The limit of detection and the limit of quantification of nitrates(III) on a gold electrode modified with a newly obtained ferrocenyl derivative of the methanethione were substantially improved which confirms the meditory activity of ferrocenyl thioketones immobilized on gold.

Acknowledgment

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Asymmetric bio-reduction of prochiral ketones using the catalytic potential of bioreagents

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Bio-reduction of prochiral carbonyl compounds is mainly carried out using the catalytic potential of NADH/NADPH dependent dehydrogenases (1.1.1.x.). Dehydrogenases belong to oxidoreductases, catalyzing the reaction of the oxidation of alcohols to the corresponding aldehydes or ketones. This protein is very common in cells of bacteria, fungi, animals and plants. In the reduction reaction, dehydrogenases transfer the hydride ion (pro-*S* or pro-*R*) from the cofactor to one of the prochiral sides of the carbonyl group (face *re* or *si*) to give pure enantiomerically or diastereomerically products. The necessity of employing expensive cofactors is one of the main limitations to the use of dehydrogenases. In contrast, the use of living organisms in the form of tissue cultures or whole microbial cells is a more effective method, because dehydrogenase, cofactor and regenerative system are found in the cell [1].

Baker's yeast is the most popular whole-cell biocatalyst for the asymmetric reduction of prochiral ketones, due to their unlimited availability, ease of growing, and low costs. For asymmetric bio-reduction of ketones, in addition to popular Baker's yeast, most often the cells of bacterial, fungal and plant tissue are used [2]. The use of bioreagents provides a whole range of chiral alcohols that can be successfully used as intermediates in the synthesis of biologically and pharmacologically important compounds. Not without significance is the fact that biocatalytic reactions are conducted under moderate conditions in aqueous solutions without the use of expensive and often toxic reagents. For this reason, they are environmentally friendly, which increases the scope of their applications.

In this work we presented the microbial biotransformation of unsymmetrical ketones in the reduction catalyzed by Boni Protect fungicide containing live cells of *Aureobasidium pullulans* and in the reaction catalyzed by Polyversum fungicide containing live cells of *Pythium oligandrium*.

The *P. oligandrium* fungus exhibits enantioselective properties in relation to unsymmetrical aryl-methyl ketones (80-99% ee). While the *A. pullulans* microorganism proved to be a more effective bioreagent in the reaction of reducing ketones with bulky substituents (96-99% ee) and α-, β-ketoesters (77-99% ee).

References

[1] K.T. Nakamura, R. Yamanaka, T. Mastuda, T. Harada, *Tetrahedron: Asymmetry,* **2003**, *14*, 2659-2681.

[2] Z.-J. Zhang, J. Pan, B.-D. Ma, J.-H. Xu, *Adv. Biochem. Eng. Biotechnol.,* **2016**, *155*, 55-106.

P-101

Aziridines as key compounds for the synthesis of *C*-glycosides

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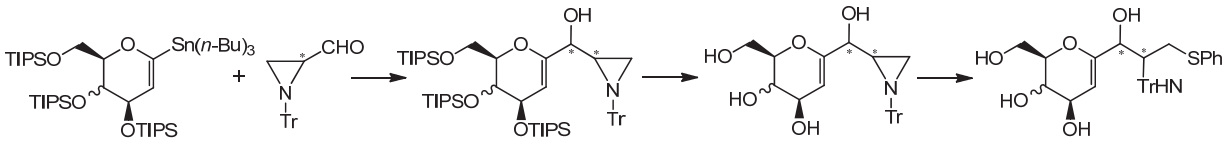
Thanks to plants, carbohydrates are an inexhaustible source of substrates for the synthesis of many chemical compounds. Understanding the role carbohydrates and glycoconjugates play in living organisms is the basis for the development of more and more effective therapeutic agents.An extremely important element in the construction of glycosides and glycoconjugates is the glycosidic bond, which is an essential part of such important substances as: antibiotics, antineoplastic drugs and cardiac glycosides. Therefore, research on glycosylation reactions is such an important research problem in carbohydrate chemistry. In nature, carbohydrate connections are based on *O*- and *N*-glycosidic bonds, but studies show that they are not stable enough under therapeutic conditions [1]. Replacement of this type of bonds with a *C*-glycosidic bond leads to derivatives with excellent chemical and enzymatic stability without negative influence on their biological properties [2]. The statement will present a synthesis path of new building blocks, which orginality is based on the use of aziridine as a connector with a defined configuration that combines an aminoacid with a saccharide.



Scheme 1.

References

[1] Ernst, B.; Magnani, J. *Nat. Rev. Drug. Disc.* **2009**, *8*, 661-667;

[2] (a) Sparks, M.; Williams, W.; Whitesides, M. *J. Med. Chem*. **1993**, *36*, 778-783; (b) Levy, D.E. *The Chemistry of C-Glycosides*, Pergamon, Oxford, **1995**.

The hydrophilic urea organocatalysts of carbohydrate derivatives; synthesis and application

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Looking through chemical literature we can observe growing interest in asymmetric synthesis. For this reason, an important aspect of this area of chemistry is the search for new, effective chiral catalysts that allow to conduct synthesis in an enantioselective manner[1]. Currently reaserch on catalysts are carried out. The catalysts are often chiral molecules that are capable of inducing asymmetric induction. Such promoters are much more stable than metal complexes, therefore they do not require reaction environment protection from oxygen or water. Additionally, products are not contaminated with heavy metals, which is important for the pharmaceutical industry.

While conducting research on the functionalization of sugars, we noticed that urea derivatives can play an effective role of organocatalysts in asymmetric synthesis giving high yields as well as enantiomeric excess[2].

The purpose of my work was synthesis of hydrophilic organocatalysts, urea derivatives of sugars. To achieve this goal it was necessary to obtain a series of azide saccharides which were then reacted with pyrrolidine derivatives. As a result of these reaction I received new organocatalysts with urea bridge. In the next stage I checked their effectiveness in the asymmetric aza-Henry reaction. In this reaction I checked also hydrophilic carbohydrate derivatives.

References

[1] (a) P. I. Dalko, L. Moisan; *Angew. Chem.*; **2004**; *43*; 5138-5175; (b) P. I. Dalko, L. Moisan; *Angew. Chem.*; **2001**; *41*; 3726-3748 (c) B. List; *Adv. Synth. and Cat.*; **2004**; *346*; 1021

[2] (a) S. Porwański; *Carbohydr. Res.*; **2014**; *394*; 7-12; (b) J. Robak, B. Kryczka, B. Świerczyńska, A. Zawisza, S. Porwański; *Carbohydr. Res.*; **2015**; *404*; 83-86.

P-103

The biological properties of the pyro- and hypophosphates for selected cancer and non-cancerous cells

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Pyrophosphate is a naturally occurring compound present in both the intra- and extracellular environments formed mainly as a product of hydrolytic degradation of nucleotide-5'-triphosphates and then used during their biosynthesis [1]. Nucleotide triphosphate hydrolysis and synthesis are the key processes for cell viability and health.

Hypophosphate as a pyrophosphate analogue lacking the bridge oxygen atom is an interesting research object due to the different interaction with the pyrophosphate recognition enzymes. Our studies indicate that the addition of hypophosphate to the extracellular environment has a significant effect on the cells survival. Moreover, obtained data shown, that pyro- and hypophosphate may differently affect cells, which is reflected in their different functioning and viability. The comparison of biological properties of pyro- and hypophosphate to cancerous and non-cancerous cells will be presented.

Acknowledgment

This project was financially supported by the grant for young scientists and state funds of the Centre of Molecular and Macromolecular Studies of the Polish c Academy of Sciences.

References

[1] R. Pawlowska, *Bioorg. Chem.*, **2016**, *67*, 110-115..

Additions of alkynes to nitrones in syntheses of fluorinated oxazolines

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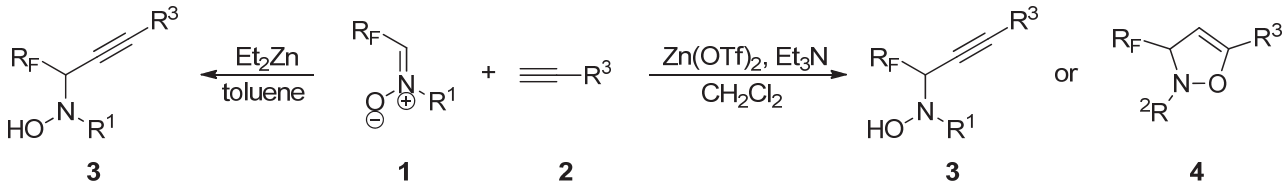
The synthesis of fluorinated organic compounds is one of the important tasks of modern organic synthesis. The presence of fluorine atoms or fluoroalkyl groups in the structure of organic compounds has a huge impact on their biological, physical and chemical properties. Compounds containing a trifluoromethyl or difluoromethyl group are of particular interest. [1]

The aim of research was to study the addition of terminal alkynes **2** to nitrones **1** derivatives of trifluoroacetic and difluoroacetic aldehyde in the presence of zinc compounds. The reactions were carried out using a catalytic amount of zinc triflate with a threefold excess of alkynes or diethylzinc with a stoichiometric amount of alkynes **2**. [2], [3] Fluorinated hydroxylamines **3** and isoxazolines **4** were obtained by the reactions.



Scheme 1. Addition of alkynes **2** to nitrones **1**.

References

[1] P. Kirsch, *Modern Fluoroorganic Chemistry*, Wiley-VCH, **2004**.

[2] B. Chandrasekhar, S. Ahn, J. S. Ryu, *Synthesis*, **2016**, *48*, A.

[3] P. Das, A. T. Hamme II, *Tetrahedron Lett.,* **2008**, *58*, 1086.

P-105

The application of bis(trifluoroethyl) phosphite in the Appel reaction

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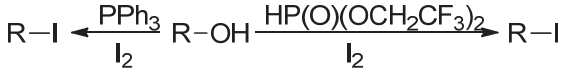
The Appel reaction is the reaction in which the alcohol reacts with methyl iodide or iodine in the presence of triphenylphosphine to form the corresponding alkyl iodide. [1] The main problem in carrying out this reaction is the formation of triphenylphosphine oxide which is difficult to remove. [2] In our method of synthesis of alkyl iodides, bis(2,2,2-trifluoroethyl) phosphite at first reacts with alcohol in the presence of pyridine and the formed mixed phosphite undergoes a reaction with molecular iodine. This method allows to obtain the appropriate alkyl iodides with good yields and also avoids the formation of hard-to-remove side products.



Scheme 1. Classical and modified version of Appel reaction

References

[1] M. Ueda, A. Ono, D. Nakao, K. Matsuno, T. Naito, O. Miyta, *Tetrahedron Rev.*, **2013**, *69*, 6866-6874.

[2] J. Cadogan, *Main Group Elements in Organic Synthesis*, **1979**.

6-Oxoverdazyl derivatives as a unique class of paramagnetic ionic liquid crystals

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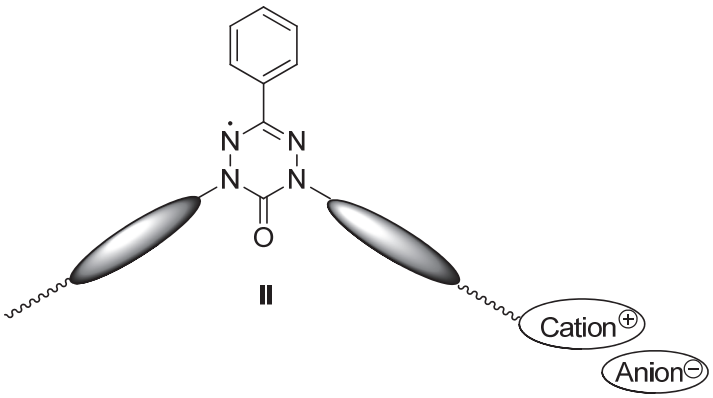
Ionic liquid crystals are materials with interesting properties, such as: red-ox, conductive, or luminescence, which is important from applications point of view.[1-2] So far, ionic liquid crystalline compounds with paramagnetic properties are unknown. Novel materials based on 6-oxoverdazyl as a paramagnetic unit have synthesized. This communication will present synthetic methodology and preliminary investigation of mesogenic properties.



II

Scheme 1. Ionic liquid crystalline 6-oxoverdazyl derivative.

Acknowledgment

Financial support by the National Science Center NCN grant no. 2016/21/N/ST5/03068 is gratefully acknowledged.

References

[1] Goossens K., Lava K., Bielawski C. W., Biennemans K., *Chem. Rev*. **2016**, *116*, 4643.
[2] Binnemans, K., *Chem. Rev.* **2005**, *105*, 4148.
[3] Kaszyński P, Jasiński M, Ciastek S, Kapuściński S, Gębicki K., *Arkivoc* **2017**, *part ii*, 345.

P-107

Synthesis of ferrocenyl analogs of folic acid

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Folic acid **1** is one of the essential vitamins required for biosynthesis of DNA and RNA. Folate deficiency or folate replacement by a similar, albeit biologically inactive molecule (antifolate, e.g. methotrexate **2**) inhibits this crucial process. Fast dividing cancer cells are the best target for the antifolate drugs because of their high need for nucleic acid synthesis. On the other hand, they are often able to overcome problems related to antifolate exposure due to specific resistance mechanisms [1,2]. We are attempting to break through the resistance mechanism by synthesizing novel antifolate analogues.

We are going to present the synthesis of a series of ferrocenyl analogs of folic acid.

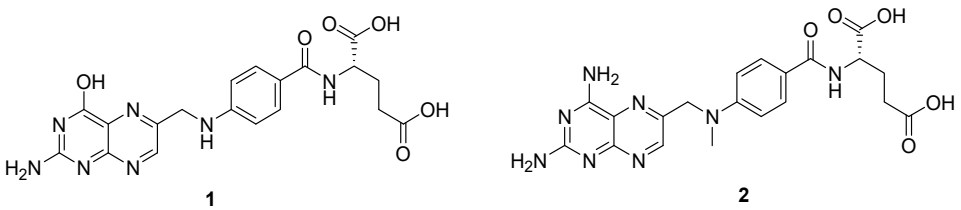

Figure 1. Structures of folic acid **1** and methotrexate **2**

Acknowledgement

This study is financially supported by the grant No. 2015/17/B/NZ7/03011 of the National Science Centre, Poland.

References

[1] N. Gonen, Y. Assaraf, *Drug Resistant Updates*, **2012**, *15*, 183

[2] J. Luo, M. Smith, L. Douglas, S. Wang, P. Fuchs, *J. Am. Chem. Soc.*, **1997**, *119*, 10004

Incorporation of the Thiocarbonyl Group in the Structure of Redox-Active Organoselenium Molecules

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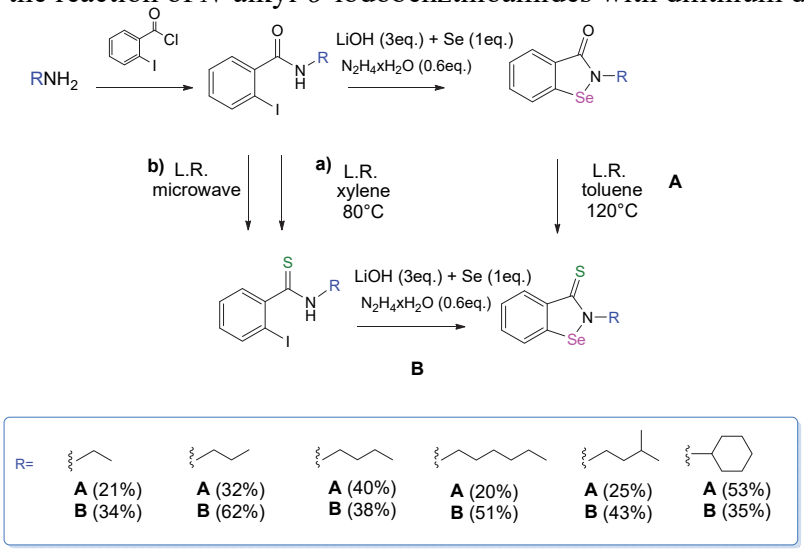
Sulfur is less electronegative than oxygen, but similar electronegative as carbon, therefore transformation of the carbonyl group into the thiocarbonyl group in the structure of benzisosenenazole-3-(2*H*)-ones changes the nature of the bond and can improve the antioxidant activity of the new derivatives.

This study presents convenient methods for the synthesis of benzisoselenazol-3(2*H*)-ones and corresponding thiocarbonyl derivatives. We have obtained *N*-alkylbenzisoselenazolthiones by two different two-step procedures. In the first method **A** we synthesized a series of *N*-alkyl-*o*-iodobenzamides that were further transformed by the reaction with dilithium diselenide to corresponding *N*-alkylbenzisoselenazolones.[1] Benzisoselenazol-3(2*H*)-thiones were prepared by the reaction of *N*-alkylbenzisoselenazolones with Lawesson's reagent in toluene at 120°C. In the second method **B** *N*-alkyl-*o*-iodobenzamides were transformed into the corresponding *N*-alkyl-*o*-iodobenzthioamides by two alternative methods. The first **a** based on the reaction of *N*-substituted *o*-iodobenzamides with Lawesson's reagent in xylene at 80°C.[2] The second **b** used analogous reaction, but without the presence of solvent under the influence of microwave radiation.[3] In the last step benzisoselenazol-3(2*H*)-thiones, were prepared by the reaction of *N*-alkyl-*o*-iodobenzthioamides with dilithium diselenide.[1]



Scheme 1. Synthesis of new thiocarbonyl derivatives of benzisoselenazol-3(2*H*)-ones

Acknowledgement

Work was supported from NCN grant nr UMO-2015/17/B/NZ7/03058.

References

[1] A. Pacuła, J. Ścianowski, K. Aleksandrzak, *RSC Adv.*, **2004**, *4*, 48959.
[2] S. Scheibye, J. Kristensen, S.O. Lawesson, *Tetrahedron*, **1979**, *35*, 1339.
[3] R.S. Varma, D. Kumar, *Org. Lett.*, **1999**, *1*, 697..

P-109

Synthesis and Applications of Gold (III) Pyridine Complexes

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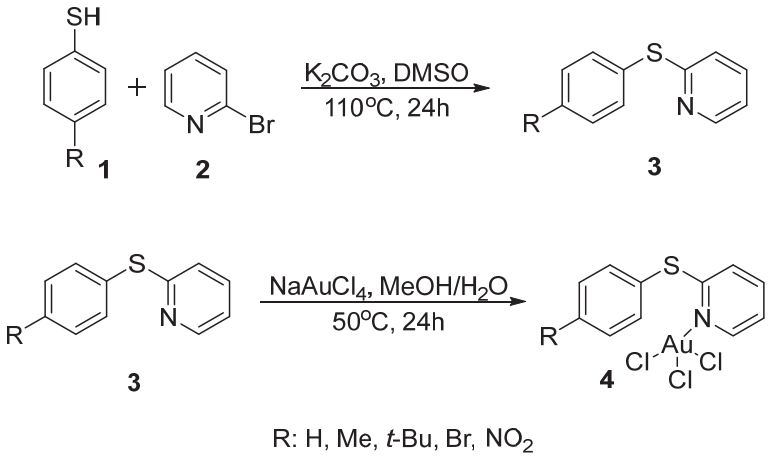
Gold compounds are widely used in medicine, mainly to reduce inflammation, and to slow down of the rheumatoid arthritis progression. [1] Thiazolopyridinium derivatives exhibit analgesic, anti-inflammatory, and hypoglycemic activity, and are used as surfactants and antistatic agents. [2] Furthermore, the compounds with benzothiazole moiety can be used in the diagnosis of Alzheimer's disease and they have many pharmacological applications, e.g. they act as immunosuppressive, anticonvulsants, anticancer, antibacterial, antimicrobial, and muscle relaxant agents. [3, 4]

Herein, we present a new methodology for the synthesis of sulfur containing Au (III) pyridine complexes and further modifications to benzothiazole derivatives. In the first step we have obtained a series of ligands **3** from commercially available 2-bromopyridine **2** and corresponding arenethiols **1**. The reaction of thioethers **3** with sodium tetrachloroaurate lead to complexes **4**. (Scheme 1.) In the next step, they were transformed to corresponding Au-salts.



Scheme 1. Synthesis of gold (III) pyridine complexes.

References

[1] A. A. Kerimova, M. Atalay, E. Y. Yusifov, S. P. Kuprin, T. M. Kerimov, *Pathophysiology*, **2000**, 7, 209-213.

[2] B. Blank, N. W. DiTullio, A. J. Krog, and H. L. Saunders, *J. Med. Chem.*, **1978**, 21, 489-492.

[3] R. M. Kumbhare, K. V. Kumar, M. J. Ramaiah, T. Dadmal, S. N. C. V. L. Pushpavalli, D. Mukhopadhyay, B. Divya, T. A. Devi, U. Kosurkar, M. Pal-Bhadra, *Eur. J. Med. Chem.*, **2011**, 46,4258 –4266.

[4] R. M. Kumbhare, T. Dadmal, U. Kosurkar, V. Sridhar, J. V.Rao*, Bioorg. Med. Chem. Lett.*, **2012**, 22, 453– 455..

P-110

POSS as a carrier of anticancer drugs – doxorubicin and daunorubicin

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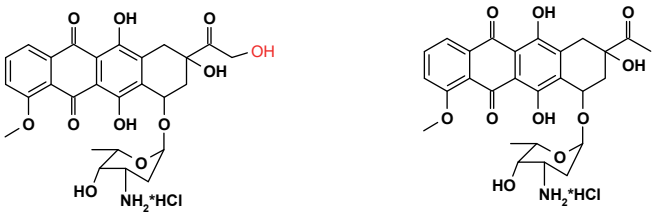
Anthracyclines (doxorubicin and daunorubicin) are widely administered and exhibit high effectiveness in treatment cancers of the bladder, breast, stomach, lung, ovaries, prostate, thyroid, soft tissue sarcoma, multiple myeloma as well in some leukemias and Hodgkin's lymphoma. However, prolonged treatment can lead to multidirectional cytotoxic effects, with cardiotoxicity being the most prominent.

In this work the main purpose is the synthesis of novel type of anthracycline nanoconjugates that can be used as effective molecular entities in anticancer therapy and are well soluble in water. The conjugates are based on silsesquioxane carriers (POSS – Polyhedral OligoSilSesquioxanes) bearing doxorubicin or daunorubicin.



Doxorubicin (DOX) Daunorubicin (DAU)

Scheme 1. Anthracycline

Acknowledgment

Financial support Grant UMO-2016/21/N/ST5/03360.

P-111

A novel *N*-substituted derivatives of 2-aminothiazol-4(5*H*)–one and their interactions with 11βHSD1 – synthesis, molecular modeling and *in vitro* studies

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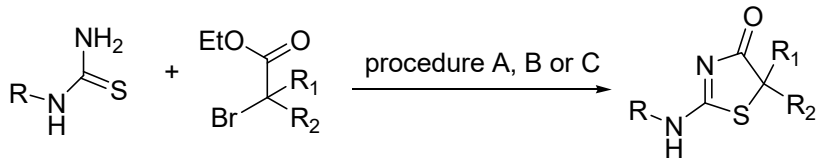
11β-Hydroxysteroid dehydrogenase type 1 (11β-HSD1) is an enzyme that catalyzes the conversion of inactive cortisone to physiologically active cortisol. Together with the isoform 2 – (11β-HSD2), it forms a system that regulates the level of cortisol in the body and thus the inhibition of its activity can be used in the treatment of diseases such as Cushing's syndrome, methabolic syndrome and type 2 diabetes. Therefore, from the therapeutic point of view it is important to search new compounds that would be selective 11β-HSD1 inhibitors.

Carrying out the research into the search for selective 11β-HSD1 inhibitors, we synthesized 19 new *N*-allyl or *N*-methyl derivatives of 2-aminothiazol-4(5*H*)–one differing in substituents at the 5 position of thiazole ring [1, 2] (Scheme 1) and tested their *in vitro* activity towards inhibition of both of the isoforms enzyme. Despite the higher probability of activity suggested by the PASS Online program, we found out that methyl derivatives are weaker inhibitors (up to 48%) of 11β-HSD1 in comparison to their allyl analogs (up to 71% at a concentration of 10 μM). Due to significant differences in the activity of methyl and allyl derivatives, molecular modeling was performed which was aimed at comparing the interaction between 11β-HSD1 and ligands differing substituent in the amino group (allyl *vs.* methyl). Modeling has shown that the absence of the allyl group can lead to the rotation of whole ligand molecule which can affect its interaction with the enzyme.



R - methyl, allyl
A - MeOH, MeONa, reflux, B - $CHCl_3$, room temp., C - EtOH, DIPEA, reflux

Scheme 1. Synthesis of *N*-substituted derivatives of 2-aminothiazol-4(5*H*)–one.

References

[1] R. Studzińska et al., *Monatsh. Chem.*, **2015**, *146*, 1673-1679.
[2] R. Studzińska et al., *Bioorg. Chem.*, **2018**, *79*, 115-121..

Synthesis of functionalized biodegradable (co)polymers for biomedical applications

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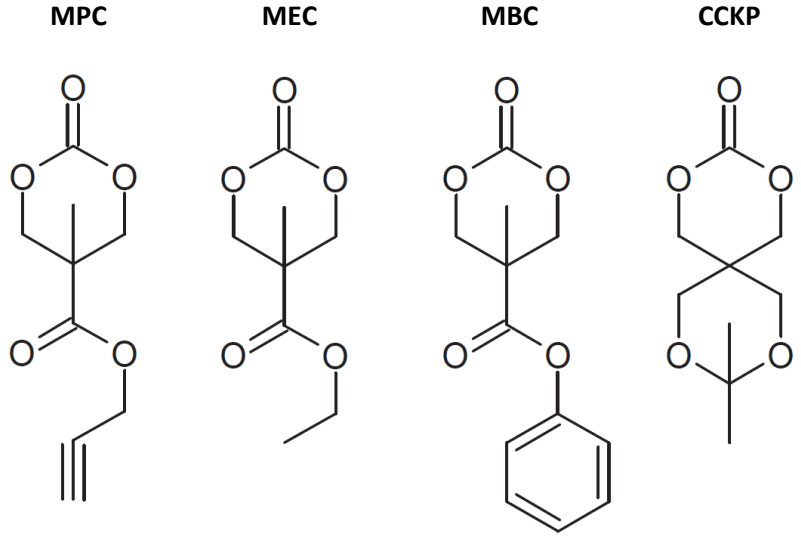
The ever-expanding biomedical and pharmaceutical industry such as tissue engineering, controlled drug release and regenerative medicine relies on improvement among advanced functional biomaterials. Polycarbonates own special properties like biocompatibility, biodegradability and approved appliances in biomedical devices.

A six-membered carbonates functionalized with propargyl (5-methyl-5-propargyloxycarbonyl-1,3-dioxan-2-one, MPC [1]), benzyl (5-methyl-5-benzyloxycarbonyl-1,3-dioxan-2-one, MBC [2]), ethyl (5-methyl-5-ethyloxycarbonyl-1,3-dioxan-2-one, MEC [2]) and ketal group (9,9-dimethyl-2,4,8,10-tetraoxaspiro[5.5]undecan-3-one, CCKP [3]) were synthesized, then homo- and copolymerized with L-lactide (LA), trimethylene carbonate (TMC) and ε-caprolactone (CL), respectively; using metal-free ring-opening polymerization technique. The study comprises application of various catalytic systems: TBD, DBU and (-)-sparteine/N-3,5-bis(trifluoromethyl)phenyl-N'-cyclohexylamine thiourea (SP/TU).



Scheme 1. Structure of (co)polymerized functional cyclic carbonates

References

[1] Lu C., Shi Q., Chen X., Lu T., Xie Z., Hu X., Ma J., Jing X. *J. Polym. Sci. Part A: Polym. Chem*. **2007**, *45*, 3204-3217.

[2] M. Kawalec, M. Pastusiak, J. Jaworska, P. Komar, P. Kurcok, P. Dobrzyński, *Eng. Biomater*., **2014**, *127*, 16-21

[3] E. J. Vandenberg, D. Tian, *Macromolecules*, **1999**, *32*, 3613-3619

P-113

New highly polar liquid crystalline aromatic cyanodiesters

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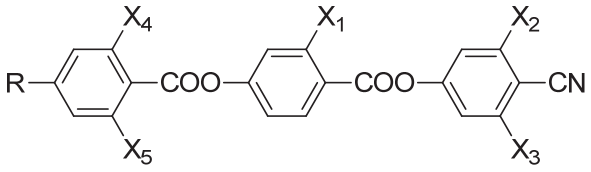
The new polar nematic three and four ring laterally fluorosubstituted cyanodiesters were synthesized. The polarity of synthesized nematogens is the result of molecular structure parts like ester linking group in rigid core, strongly polar cyano terminal group and fluorine atoms in lateral positions in the core of liquid crystalline compound. Presence of terminally substituted cyano group affects the presence of large longitudinal dipole moments. Phase transitions temperatures were measured by a polarising optical microscope. Synthesis route and basic physical properties of obtained compounds are presented. The general structure of synthesized compounds is shown below.



where R - alkyl or alkylcyclohexyl
X_1 to X_5 - F or H

P-114

An approach to direct synthesis of iminosugar-derived tetrazoles

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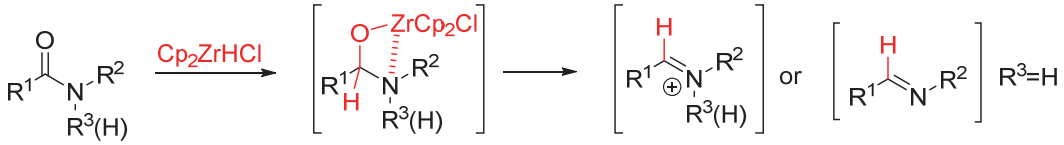
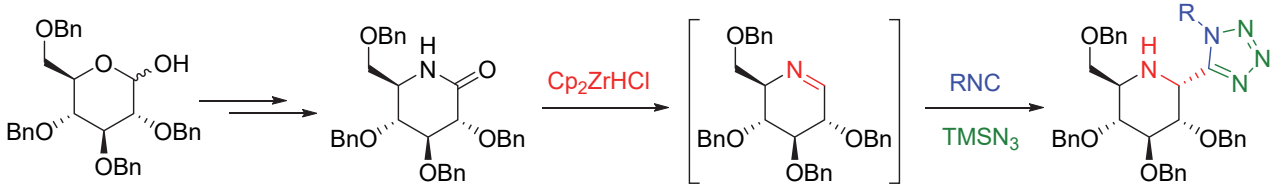
Amides are well-known for their reduced reactivity towards nucleophiles. Nevertheless it is possible to conduct such reactions by the use of appropriate activating agents. A preactivation step increases the electrophilicity of the amide moiety by diminishing the resonance effect of the amide nitrogen, e.g. via a transformation to an imide.[1]

A very interesting method, where zirconocene hydrochloride acts as an amide group reducing agent, has been proposed by Ganem.[2] Its uniqueness lies in its exceptional chemoselectivity, compared to other commonly used methods. It has been proven that Schwartz's reagent reduces secondary and tertiary amides, leading to formation of imines or iminium cations of high purity (Scheme 1).[2]



Scheme 1. An amide reduction with Schwartz's reagent.

This methodology is extensively studied in our group and appear to be a very convenient and effective tool for synthesis of functionalized amines.[3] Our latest efforts was focused on functionalizing sugar-derived lactams via one-pot Schwartz's reagent-mediated reduction and subsequent Azido-Ugi reaction with isocyanide and TMSN3. This stereoselective synthesis protocol leads to nojirimycin C-1 tetrazole derivatives (Scheme 2).



Scheme 2. The stereoselective synthesis of iminosugar derived tetrazoles.

Acknowledgment

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References

[1] (a) M. P. DeNinno, C. Eller, Tetrahedron Lett. 1997, 38, 6545. (b) M.P. DeNinno, C. Eller, J. B. Etienne, J. Org. Chem. 2001, 66, 6988.

[2] (a) D. A. Schedler, A. G. Godfrey, B. Ganem, Tetrahedron Lett. 1993, 34, 5035, (b) D. A. Schedler, J. Li, B. Ganem, J. Org. Chem. 1996, 61, 4115.

[3] (a) P. Szcześniak, S. Stecko, O. Staszewska-Krajewska, B. Furman, Tetrahedron, 2014, 70, 1880; (b) P. Szcześniak, S. Stecko, E. Maziarz, O. Staszewska-Krajewska, B. Furman, J. Org. Chem., 2014, 79, 10487; (c) P. Szcześniak, E. Maziarz, S. Stecko, B. Furman, J. Org. Chem., 2015, 80, 3621.

P-115

Biobased PHB plasticizers

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In recent years various publications have shown processing routes for the lab-scale production of PHBV using different carbon sources and strains of bacteria (e.g. A. latus., C. necator) [1]. However due to its limited mechanical properties, particularly a high brittleness, the PHBV polymer has not been used for demanding technical applications yet. In the past many publications have reported numerous options to improve the mechanical properties of PHBV by adding petrobased plasticizers e.g. dioctyl adipate, dioctyl phthalate, polyadipate, tri(ethylene glycol) bis(2-ethylhexanoate) [2, 3]. In order to result in fully biobased PHBV-formulations the addition of 100% biobased plasticizers is required. In this poster the use of modified vegetable oils (fatty acids) as plasticizers is investigated. It describes the modification for camelina oil, castor oil or rapeseed oil via chemical processing such as esterification, transesterification and epoxidation with the target to generate and provide functional groups which ensure the compatibility of the plasticizer with the polymer.

References

[1] G.-Q. Chen, Plastics from Bacteria, Natural Functions and Applications, Springer Berlin Heidelberg, **2010**.

[2] R.C. Baltieri, L. H. I. Mei, J. Bartoli, *Macromol. Symp.*, **2003**, *197*, 33-44.

[3] R. S. Kurusu, Ch. A. Siliki, É. David, N. R. Demarquette, C. Gauthier, J.-M. Chenal, *Industrial Crops and Products*, **2015**, *72*, 166-174.

P-116

Analogs of Sulforaphane – synthesis and biological activity

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Sulforaphane is a natural product belonging to the group of organic isothiocyanates. Research on the biological activity of this compound and some of its derivatives has been devoted to a large number of papers due to the established anti-cancer, anti-inflammatory and antioxidant properties. Looking for new analogs of sulforaphane with potentially better anti-cancer and chemopreventive properties, a number structural modifications was carried out [1-3].

The applied synthesis methods and results of *in vitro* tests of cytotoxic properties of new obtained compounds will be presented.

References

[1] P. Kiełbasiński, J. Łuczak, T. Cierpiał, J. Błaszczyk, L. Sieroń, K. Wiktorska, K. Lubelska, M. Milczarek, Z. Chilmończyk, *Eur. J. Med. Chem*. **2014**, 76, 332-342.

[2] T. Cierpiał, J. Łuczak, M. Kwiatkowska, P. Kiełbasiński, L. Śliwka, K. Wiktorska, Z. Chilmonczyk, M. Milczarek, K. Karwowska, *ChemMedChem* **2016**, 11, 2398-2409.

[3] "*Pochodne sulforafanu, ich prekursory oraz sposób ich wytwarzania*" T. Cierpiał, P. Kiełbasiński, J. Łuczak, Patent Polski Nr PL 220620 (B1) (14.12.2015).

P-117

Optimization of click reaction conditions on solid support for synthesis of oligofunctionalized carboranes

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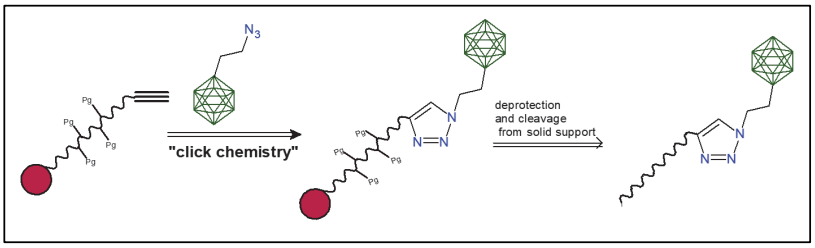
Boron cluster-modified therapeutic nucleic acids with improved properties are of interest in gene therapy and in cancer boron neutron capture therapy (BNCT) [1,2]. A post-synthetic Cu (I)-assisted "click" conjugation of alkyne-modified DNA-oligonucleotides with a boron cluster alkyl azide component have been described for the synthesis of electrochemically detectable probes targeted against avian influenza virus (AIV) [3] and boron cluster-loaded antisense oligonucleotides (ASOs) targeting epidermal growth factor receptor (EGFR) [4, 5]. Herein, we report an alternative and versatile method for the incorporation of various boron clusters into the structure of nucleic acids via Huisgen-Meldal-Sharpless azide-alkyne 1,3-dipolar cycloaddition ("click reaction") performed directly on solid support:



The corresponding alkyne modified oligomer was prepared on solid support by incorporating commercially available 5'-*O*-dimethoxy-trityl-2'-propargyluridine phosphoramidite monomer in the final coupling step of the automated oligonucleotide synthesis. The reactions of alkyl azide derivative of carborane cluster with alkene modified oligonucleotide on the solid support was carried out using the CuAAC click reaction conditions. The main advantages of this approach is that 1) it allows use of the oligonucleotide directly after automated solid phase synthesis without purification and 2) an excess reagents can be conveniently removed by simple washing of the solid support. We believe that the improved methodology presented here will facilitate application of boron cluster DNA conjugates as building blocks for nanoscale construction, in therapeutic nucleic acids area and in other fields.

Acknowledgment

This research was financially supported by The National Science Centre in Poland [Grant number 2015/16/W/ST5/00413 for years 2015–2019].

References

[1] Z. J. Leśnikowski, Eur. J. Org. Chem. 2003, 4489;
[2] A. Kwiatkowska et al., Bioconjugate Chem. 2013, 24, 1017;
[3] I. Grabowska, et al., Biosens. Bioelectron., 2014, *51*, 170;
[4] D. Kaniowski et al., Molecules 2017, 22(9), 1393;
[5] K. Ebenryter-Olbińska et al., Chem. Eur. J. 2017, 23, 16535.

Composites of Nucleic Acids and Oligofunctionalized Carboranes: synthesis, physicochemical and biological properties

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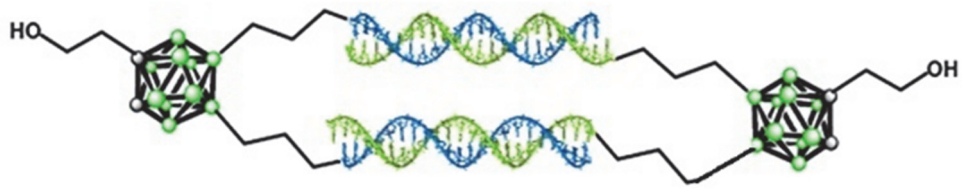
DNA nanotechnology is a branch of technology that exploits nucleic acids ability to self-assembly in order to construct nanostructures with specific properties. There are numerous potential applications of DNA nanostructures including those in diagnostics and therapy of human disorders.[1] Based on our previous studies on boron clusters as modifying units for nucleic acids[2,3] conjugates of the epidermal growth factor receptor (EGFR)-directed antisense DNA oligonucleotides modified with boron clusters [o-carborane, $C_2B_{10}H_{12}$; dodecacarborane, $B_{12}H_{12}^{2-}$; and metallacarborane, $[Fe(C_2B_9H_{11})^2]^-$] were obtained and tested as potential agents in antisense and BNCT therapy.[4,5]

In this communication, we present an application of DNA functionalized boron clusters (oligopods) as building blocks for nano-construction of therapeutic nucleic acid systems. Thus, tri-substituted *o*-carborane, bis-functionalized with EGFR-targeted sense or antisense oligonucleotides were obtained by solid phase method. The complementary dipods were self-assembled to nano-structured complexes which were visualized by the non-denaturating polyacrylamide gel electrophoresis (PAGE), atomic force microscopy (AFM) and cryo-transmission electron microscopy (Cryo-TEM). Their silencing activity, stability against exo- and endo-nucleases as well as melting properties were investigated.



Scheme 1. A schematic view of nanostructure formed by two complementary dipods (EGFR-sense and antisense oligonucleotides conjugated with boron-cluster)

Acknowledgment

This research was financially supported by The National Science Centre in Poland [Grant number 2015/16/W/ST5/00413 for years 2015–2019].

References

[1] DNA Nanotechnology, From Structure to Function, Springer-Verlag, 2013.
[2] Z. J. Leśnikowski, Eur. J. Org. Chem. 2003, 4489.
[3] A. Kwiatkowska et al., Bioconjugate Chem. 2013, 24, 1017.
[4] D. Kaniowski et al., Molecules 2017, 22(9), 1393.
[5] K. Ebenryter-Olbińska et al., Chem. Eur. J. 2017, 23, 16535..

P-119

Carbene-catalysed dihydropyridinone derivatives synthesis via *aza*-Claisen rearrangement

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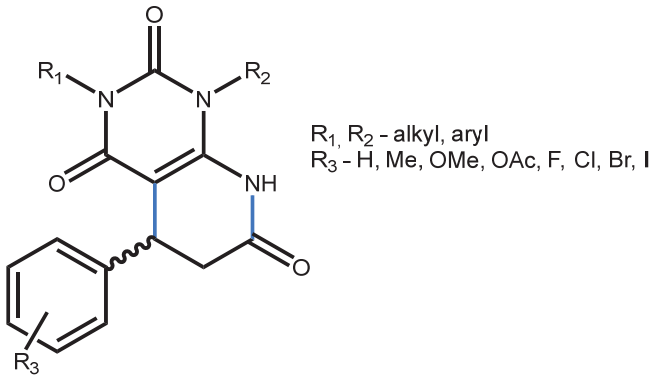
N-heterocyclic carbenes (NHC) are widely used in synthesis of various complex substances. Generated from appropriate salt NHC effects on the polarity reverse of carbonyl compound. This *umpolung* process effects in change of carbonyl carbon atom properties. Consequently, electrophilic carbon atom is transformed into synthetically appropriable nucleophile.[1] Moreover, it exists other way to use Breslow intermediate in organocatalysed reactions. It can be oxidized to acylazolium – very useful intermediate in esterification reactions and annulation reactions of α,β-unsaturated carbonyl compounds.[2]

Aza-Claisen rearrangement is example of [3,3]-sigmatropic reaction which can occur via NHC-catalysed annulation. In that kind of annulation 6-aminouracils derivatives and crotonaldehyde derivatives appears to be an attractive reagents to obtain bicyclic lactams with unprotected NH-amide group. This reaction model broadens the applicability of widely known thiazolium and triazolium salts and NHC precatalysts obtained in our team.[3-5]

The developed synthetic methodology leads to expected dihydropyridinones condensed with uracil ring for many different *N*,*N*'-disubstituted 6-aminouracils and crotonaldehyde derivatives. Moreover, products were obtained with very high yields and purities.



Scheme 1.

Acknowledgment

The project is co-financed by the National Science Center as part of the SONATA BIS program (UMO - 2016/22 / E / ST5 / 00469).

References

[1] D.M. Flanigan, F. Michailidis, N.A. White, T. Rovis, *J. Chem. Rev.*, **2015**, *115*, 9307-9387.
[2] C. Zhang, J. F. Hooper, D. W. Lupton, *ACS Catal.* **2017**, *7*, 2583-2596.
[3] Z. Rafiński, A. Kozakiewicz, K. Rafińska, *ACS Catal.* **2014**, *4*, 1404-1408.
[4] Z. Rafiński, A. Kozakiewicz, *J. Org. Chem.* **2015**, *80*, 7468-7476.
[5] Z. Rafiński, *ChemCatChem,* **2016**, *8*, 2599-2604.

P-120

NHC-catalysed enantioselective synthesis of chromanones

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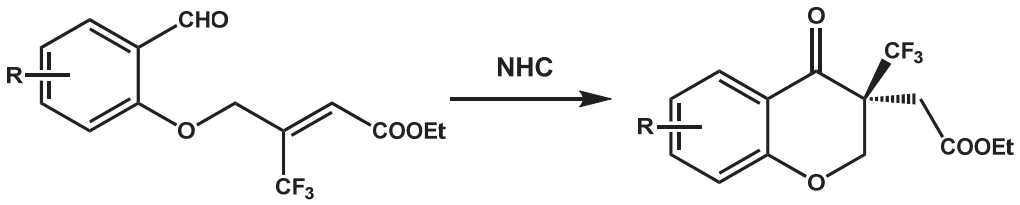
N-heterocyclic carbenes (NHC) are common used as organocatalysts in various *umpolung* reactions such as benzoin condensation or Stetter reaction. [1,2] NHC-catalysis is one of the most developed branch of organocatalysis which has become an important part of modern organic chemistry. Consequently, synthesis of chiral NHC catalysts caused development of sophisticated approach to synthesis of enantiomerically enriched substances. [3-5]

Aim of this work is synthesis of chromanones with trifluoromethyl group bonded to the quartenary stereogenic center. Products of intramolecular Stetter reaction were obtained with good yields and excellent enantiomeric excesses. The development of this synthetic approach is very interesting because of some chromanone derivatives exhibit a considerable biological and pharmacological activities such as antioxidant, antimicrobial, DNA binding, cleavage, anticancer, antiallergic, neuroprotective and pesticidal properties. [6]



Scheme 1. Reaction design

Acknowledgment

The project is co-financed by the National Science Center as part of the SONATA BIS program (UMO - 2016/22 / E / ST5 / 00469)

References

[1] D.M. Flanigan, F. Michailidis, N.A. White, T. Rovis, *Chem. Rev.,* **2015**, *115*, 9307-9387.
[2] J. L. Moore, T. Rovis, *Top Curr Chem,* **2010**, *291*, 77-144.
[3] Z. Rafiński, A. Kozakiewicz, K. Rafińska, *ACS Catal.* **2014**, *4*, 1404-1408.
[4] Z. Rafiński, A. Kozakiewicz, *J. Org. Chem.* **2015**, *80*, 7468-7476.
[5] Z. Rafiński, *ChemCatChem* **2016,** *8*, 2599-2604.
[6] B. Mayuri, P. Kavitha, S. Basavoju, G. Bhargavi, K.L. Reddy, *J. Mol. Struct.* **2017**, *1145*, 1-9..

P-121

Dynamic Light Scattering studies on polymeric carriers

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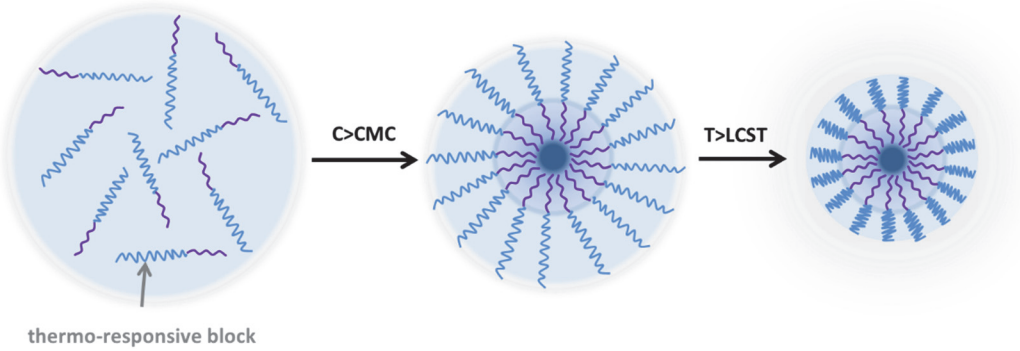
Dynamic light scattering (DLS) is a technique that can be used to determine the size distribution profile of small particles in suspension or polymers in solution.[1] DLS can also be used to determine the behavior of complex fluids such as concentrated polymer solutions.

In the recent years, "smart" materials such as stimuli-responsive polymers that can respond to an external stimulus have attracted considerable attention due to a wide range of applications. One of the most common and interesting are thermosensitive polymers, that change their physical properties with temperature.[2] Differences in size distribution of poly(*N*-isopropylacrylamide) and its block or statistical copolymers with different length of poly(*N*-ε-vinylcaprolactam) or acetylacetone derivative with complexing properties in PBS pH=7,4 and 0,9 % NaCl will be presented.



Scheme 1. Behavior of stimuli-responsive block copolymers in solution. CMC-critical micelle concentration, LCST-lower critical solution temperature.

References

[1] R. Pecora., *The Journal of Chemical Physics*, **1964**, *40*, 1604.
[2] A. S. Hoffman, *Artificial Organs*, **1995**, *19*, 458–467.

P-122

Gd-based nanoparticles as MRI contrast agents

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The development of magnetic resonance imaging (MRI) contrast agents with delicate sensitivity and advanced functionalities has recently received extensive interest.

Nanoparticle MRI contrast agents have been synthesized for various potential applications because of their unique properties, such as large surface area, surface modifications for multifunction, contrast enhancement, and conjugation with biomolecules for therapeutic and diagnostic applications. [1] New generation fluorophores, also termed upconversion nanoparticles (UCNPs), have the ability to convert near infrared radiations with lower energy into visible radiations with higher energy via a nonlinear optical process. [2]

Different Gd-based nanoparticles as MRI contrast agents will be presented.

References

[1] M.Wang, G. Abbineni, *Nanomedicine: NBM*, **2011**, *7*, 710–729.
[2] Z. Liu, F. Pu, S. Huang, Q. Yuan, J. Ren, X. Qu*, Biomater.*, **2013**, *34*, 1712–1721..

P-123

Planar Blatter Radical-Based Bent-Core Mesogens

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A series of bent-core mesogens **1[12,n]**, derived from planarized analogue[1] of prototypical Blatter radical[2] and possessing two different paraffinic tails, were synthesized and characterized by optical and thermal methods. The paraffinic tails were anchored sequentially on the functionalized planar Blatter radical by esterification reactions. Compound **1[12,12]** exhibits two liquid crystalline phases with the clearing temperature of 160 °C. Remarkably, compound **1[12,12]** easily supercools retaining the birefringent property of the mesophase even at room temperature. Different length of the alkyl chains and their partial fluorination are used to modulate the structure and stability of mesophases observed in series **1[12,n]**. Synthesis, thermal, optical, and powder XRD will be presented.

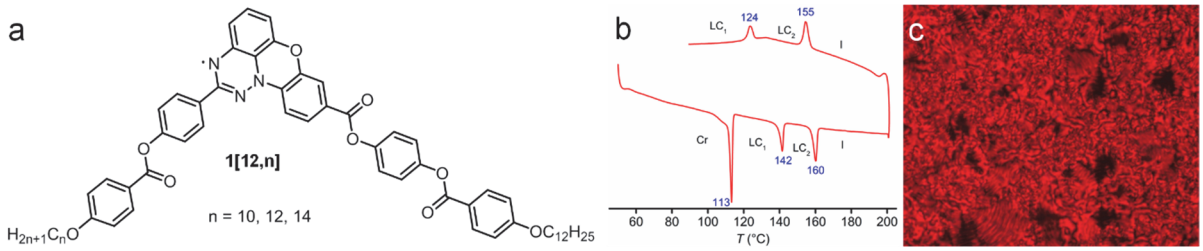

Figure 1. (a) The structure of bent-core mesogens **1[12,n]**; (b) DSC trace of **1[12,12]** obtained by heating and cooling the sample at 5 K/min; (c) Optical texture of a liquid crystalline phase obtained by cooling **1[12,12]** from the isotropic phase and observed in polarized light.

References

[1] P. Kaszyński, C. P. Constantinides and V. G. Young, *Angew. Chem. Int. Ed.*, 2016, **55**, 11149.

[2] H. M. Blatter and H. Lukaszewski, *Tetrahedron Lett.*, 1968, **9**, 2701..

P-124

A new approach to the Pictet–Spengler reaction

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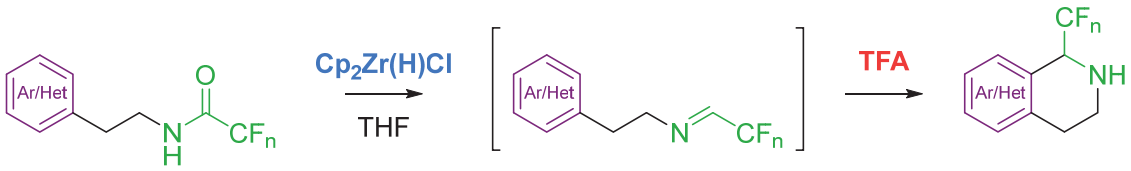
The Pictet-Spengler reaction is an intramolecular electrophilic aromatic substitution reaction that allows for the cyclization of β-arylethylamines. The reaction is most notably used in the synthesis of the isoquinoline and indole alkaloid frameworks. These structural scaffolds of an immense range of structurally complex synthetic products are key elements of thousands naturally occurring isoquinoline and indole alkaloids and several of them being of enormous physiological and therapeutic significance.[1] For that reason, the expanding of substrates pool for Pictet-Spengler cyclisation is highly relevant and the reaction has undergone continuous modifications.

A new prototype of the Pictet–Spengler reaction based on partial reduction of fluoroacetamides to imines by $Cp_2Zr(H)Cl$ (Schwartz's reagent) followed by electrophilic ring closure will be presented. The protocol allow to avoid expensive and hardly available aldehydes and as a source of fluorinated moiety propose amides easily obtained from fluoroacetic acids, esters or anhydrides. The cyclization conditions are milder than in the classical reaction variants and the whole transformation provides an alternative for well-known method and allow to introduce products inaccessible so far.



Scheme 1. A new approach to synthesis of fluorinated tetrahydroisoquinolines

References

[1] J. Stöckigt, A. Antonchick, F. Wu, H. Waldmann, Angew. Chem. Int. Ed., **2011**, *50*, 8538 – 8564..

The α-thio and β-γ-hypophosphate modified ATP analogs - synthesis and cytotoxicity

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Adenosine-5'-triphosphate (ATP) is a natural source of energy and signaling molecule present both inside the cells and in the surrounding area. The amount of extracellular ATP fraction is significantly higher in the tumor microenvironment in comparison with healthy tissue, which suggests its importance in the development and/or progression of cancer. However, in the extracellular environment nucleotides undergo rapid hydrolysis. The catabolism of extracellular ATP leads to the generation of adenosine-5'-diphosphate (ADP), adenosine-5'-monophosphate (AMP) and adenosine. To limit the possibility of ATP degradation, the modifications within the phosphate groups involving both bridged and non-bridged oxygen atoms were introduced and the new ATP analogs were used for testing the ATP-dependent processes in cancer cells.

ATP analogs containing β,γ-non-hydrolyzable hypophosphate P-P bond and a sulfur atom instead of one/or both, of the non-bridging oxygen atoms at the α-phosphate group were synthesized. The syntheses were performed based on the modified oxathiaphospholane method [1,2], where hypophosphate salt reacts with 5'-*O*-(2-thio)-1,3,2-oxathia(or dithia)phospholane derivative of adenosine. Two P-diastereomers of the β,γ-hypo-ATPαS were separated using RP-HPLC and designated as 'fast' and 'slow' in respect to their chromatographic mobility.

The new compounds were tested for their cytotoxicity for different cancer cell lines. The cytotoxicity measurements for diastereomerically pure ATP analogs and ATP were performed using MTT assay.

The *in vitro* biological tests demonstrated the differences between modified ATP analogs compared to their natural counterpart. Data obtained for individual diastereomers will be shown.

Acknowledgment

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References

[1] D. Blaziak, *Org. Biomol. Chem.*, **2010**, *8*, 5505-5510.
[2] R. Pawlowska, *Bioorg. Chem.*, **2016**, *67*, 110-115.

Structural modifications of Blatter radical

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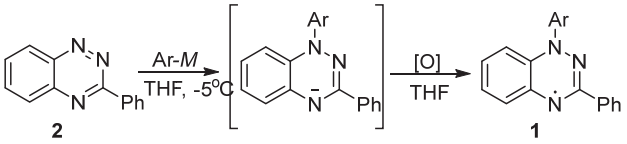
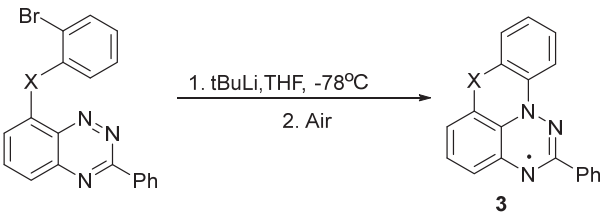
The Blatter radical and its derivatives are one of the prime scientific interests in recent years for their application in material science, due their fascinating properties like exceptional stability, spin π-delocalization, narrow electrochemical window and low excitation energies. In this context several synthetic methods for accessing this radical system have been recently improved and developed. As a contribution to the library of these methods, our group presented a one pot synthetic method to obatin the 1-aryl-3-phenyl-1,4-dihydrobenzo[*e*]-[1,2,4]triazin-4-yl radicals by addition of aryllithium to the readily available 3-phenylbenzo[e][1,2,4]triazine followed by aerial oxidation (*Scheme 1*).[1]



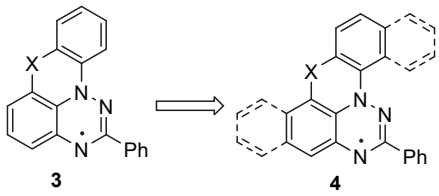
Scheme 1.

The general feature of all 1,4-dihydrobenzo[*e*][1,2,4]triazin-4-yl derivatives known to date is the presence of an aryl substituent at the N(1) position, such as Ph in the Blatter radical, which due to steric interactions between the C(8)-H and C(ortho)-H forms a large dihedral angle θ (38–82°) with the heterocycle.[2] This high torsion angle between the π planes limits spin delocalization from N(1) and affects molecular packing in the solid state, which in turn, impacts magnetic properties of the solids. A coplanar π substituent at N(1) would provide maximum spin delocalization, change in packing of the solid state, and offer a new platform for the design of functional materials. In this context, we described a simple and potentially wide-scope method for the preparation of planarized Blatter radical, such as in *Scheme 2*.[3]



Scheme 2.

The current work is focused on expanding the scope of this method and developing other methods for obtaining functionalized planar analogues of the Blatter radical in the context of molecular electronics and spintronic applications (*Scheme 3*).



Scheme 3

References

[1] C. P. Constantinides, E. Obijalska, P. Kaszyński *Org. Lett.* **2016**, 18, 916−919.
[2] A. Gardias, P. Kaszyński, E. Obijalska, D. Trzybiński, S. Domagała, K. Woźniak, J. Szczytko *Chem. Eur.J.*, **2018**, 24,1317 –1329.
[3] P. Kaszyński, C. P. Constantinides, V. G. Young, Jr. *Angew. Chem*. **2016**, 128, 11315-11318.

Electrochemical Polymerization and Analysis of Some Thiophene Derivatives

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Polythiophenes are one of the most important classes of conjugated polymers, with a wide range of applications, such as conducting films, electrochromics, and field-effect transistors [1, 2]. The literature reveals many references to electrochemical polymerization of thiophene. Conducting polymers can be generated both chemically and electrochemically. The electropolymerization method seem to be much better. However, the electropolymerization of thiophene is much more difficult than for pyrrole or aniline. This is due to the so-called „polythiophene paradox" - the oxidation potential of many thiophene monomers is higher than the oxidation potential of the resulting polymer. Futhermore, the substituents can significantly alter the processes of polymerization [3].

Electropolymerization is one of the most valuable techniques for obtaining oligomers and polymers. Spectroscopic and electrochemical characterizations were performed to highlight the structural attributes of the polymers. We would like to report our preliminary results devoted to the chemo- and electropolymerizaions of monomeric thiophene derivatives. Electropolymerization of monomers was carried out with use of cyclic voltammetry and electrochemical measurements were coupled in – situ with spectroscopic methods UV- Vis. The electrochemical cell used was the three – electrode type, working electrode for the cyclic voltammetric studies was a polycrystalline gold, platinum or glassy carbon. Voltammetric scanning of the molecules containing heterocyclic thiophene led to setting of conductive polymer layer on the surface of working electrode.

References

[1] K.Pekmez, N.Pekmez, A. Yildiz, *Tr. J. of Chem.*, **1998**, *22*, 47-53.
[2] I.F. Perepichka, D.F. Perepichka, H.Meng, F.Wudl, *Adv.Mater.* **2005,** *17,* 2281-2305.
[3] I. F. Perepichka, D. F. Perepichka, Handbook of Thiophene-based Materials, John Wiley and Sons, Ltd, Chichester, UK, **2009**.

P-128

Decarboxylative strategies in the synthesis of heterocyclic compounds

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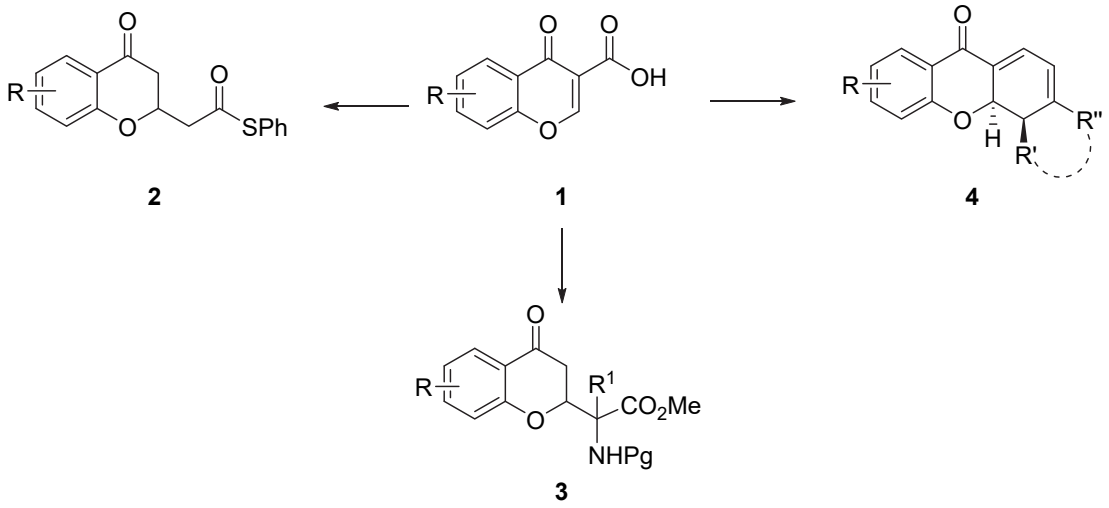
Development of stereocontrolled strategies leading to molecules of biological interest is of key importance in the contemporary organic chemistry.[1] A xanthone and chromanone ring system are key constituents of many natural products exhibiting diverse and useful biological properties.[2]

We have developed novel and straightforward approaches to chromanones **2, 3** and dihydroxanthone **4** based on a cascade reactivity of chromone-3-carboxylic acids **1** as key starting materials. The synthesis of chromanones **2, 3** has been performed using Cinchona alkaloid catalysis to afford target products **2**, **3** in good yield with enantioselectivity.[3] The synthesis of 4,4a-dihydroxanthone **4** has been realized under aminocatalytic conditions and involved the formation of dienamine intermediate that participated in the [4+2]-cycloadditon. Subsequent decarboxylative deamination was a key step of the cascade enabling the turnover of the aminocatalyst and the formation of the 4,4a-dihydroxanthone **4** derivatives.[4]



Scheme 1

Acknowledgment

This project was financially supported by the National Science Centre, Poland within the "Sonata" programme realized in the period 2017-2020, project number: UMO-2016/21/D/ST5/01668.

References

[1] a) E. N. Jacobsen, A. Pfaltz, H. Yamamoto, *Comprehensive Asymmetric Catalysis*, Springer, Berlin, **1999**; b) K. Mikami, M. Lautens, *New Frontiers in Asymmetric Catalysis*, Wiley-Interscience, New Jersey, **2007**;
[2] a) D. P. Kamat, S. G. Tilve, V. P. Kamat, J. K. Kirtany*, Org. Prep. Proc. Int.* **2015**, *47*, 1-79; b) K.-S. Masters, S. Bräse, *Chem. Rev.* **2012**,*112*, 3717-3776;
[3] A. Albrecht, *Eur. J. Org. Chem.* doi:10.1002/ejoc.201801110. [4] A. Albrecht, J. Bojanowski, *Adv. Synth. Catal.* **2017**, *359*, 2907–2911..

The Effect of Phosphates Ions on the Inclusion Complex Formation of β-cyclodextrin – NMR Titration Method

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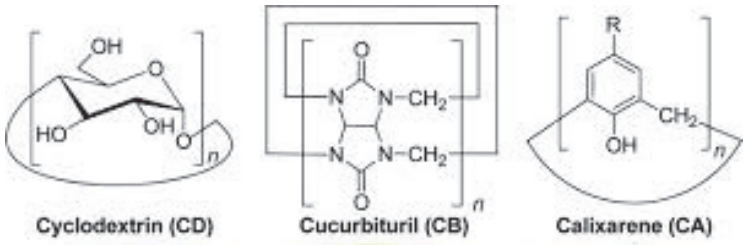
Macromolecules such as cyclodextrins (CD), cucurbiturils (CB) or calixarenes (CA) and their derivatives are tested as drug carriers or chemical sensors [1-4]. Drug molecule transport is possible as a result of inclusion complex formation. Organic molecule enters the cavity of the carrier ones.



Scheme 1. Cyclodextrins, cucrbiturils and calixarenes (n=5-8).

The competition of hydrophobic molecules for the cyclodextrin or cucurbituril cavities is well known in the literature. Much less attention is paid to interaction with inorganic molecules. The presence of inorganic molecules or ions may complicate the formation of inclusion complexes.

The aim of the presented poster was to investigate the influence of phosphoric acid and its ions on the formation of cyclodextrin complexes. The complexation has been studied by ^{1}H-NMR titration method in aqueous solutions. The investigations confirmed the interactions of phosphate ions or molecules of phosphate acid with β-cyclodextrin. The formation of complexes 1:1 was observed.

Based on results, the conditional stability constants of the inclusion complexes have been calculated.

References

[1] S.J.Barrow, S.Kasera, M.J.Rowland, J. del Barrio, O.A.Scherman, *Chem.Rev.*, **2015**, *115*, 12320-12406.
[2] O.A.Shpigun, I.A.Ananieva, N.Yu.Budanova, E.N.Shapovalova, *Russ.Chem.Rev.*, **2003**, *72*, 1035-1054.
[3] L.Szente, J.Szeman, *Anal.Chem,* **2013**, *85*, 8024-8030.
[4] J.Zhang, P.X.Ma, *Adv. Drug Delivery Rev.*, **2013**, *65*, 1215-1233.
[5] D.H.Macartney, *Isr.J.Chem.*, **2011**, *51*, 600-615..

P-130

Synthesis of benzofuryl compounds with potential antifungal activity

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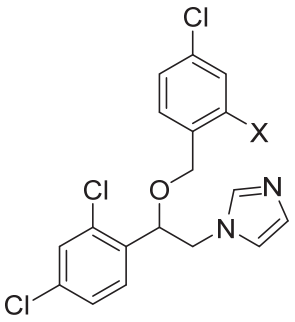
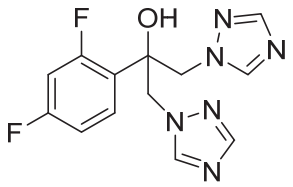
The azole derivatives including imidazoles, e.g. econazole **1**, miconazole **2**, and triazoles, e.g. fluconazole **3** inhibit the biosynthesis of fungal sterols through the inhibition of CYP51 and are used as first line drugs to treat *Candida* infections.[1] The main azole drugs possess at least two principal pharmacophoric groups: iron coordinating group - consisting of imidazole or triazole ring, able to interact with the heme iron, and hydrophobic group - typically aromatic, near the iron coordinating group. The aforementioned azole derivatives belong to *β*-amino alcohols which are useful structures in organic and medicinal chemistry. Moreover, chiral *β*-amino alcohols containing heteroaryl moieties are of great importance as a key intermediates for the synthesis of physiologically active compounds.[2] Benzofuran is considered as an important structure due to its diverse biological profile.[3]

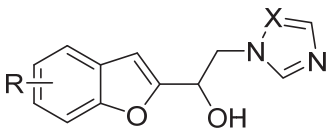
The aim of this project was the enantioselective synthesis of benzofuryl *β*-amino alcohols **4** possessing the azole skeleton. The asymmetric transfer hydrogenation of the corresponding *α*-amino ketones obtained from the appropriate *α*-halo ketones led to the chiral products **4** in high yields and excellent enantioselectivities (96-99%), as determined by chiral HPLC. Further studies are in progress to determine the antifungal activity of compounds **4**.



1 X = H Econazole
2 X = Cl Miconazole



3 Fluconazole



4 X = CH, N

References

[1] D. De Vita, et al. *Eur. J. Med. Chem.*, **2012**, *49*, 334-342.
[2] Y. Ohta, I. Shinkai *Bioorg. Med. Chem.*, **1997**, *5*, 465-466.
[3] R. J. Nevagi, S. N. Dighe, S. N. Dighe *Eur. J. Med. Chem.*, **2015**, *97*, 561-581.

P-131

Synthesis of γ,γ-Disubstituted Butenolides through a Doubly Vinylogous Organocatalytic Cycloaddition

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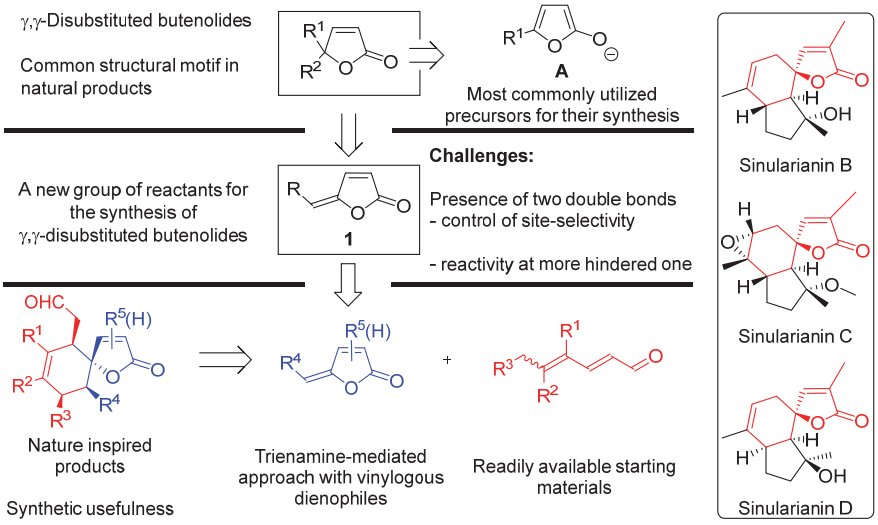
γ,γ-Disubstituted butenolides and related γ-lactones represents a common structural motif, found in wide variety of natural products relevant form the biological and medicinal chemistry point of view [1]. Therefore, much attention has been given to the development of synthetic methods allowing for their preparation, in a stereocontrolled manner. Within this research area, the asymmetric organocatalysis has proven highly useful, providing valuable solutions leading to enantiomerically enriched γ,γ-disubstituted butenolides [2].



Scheme 1

In this reaserch a new organocatalytic approach to the synthesis of γ,γ-disubstituted butenolides have been designed, employing a fully regioselective functionization of 5-alkilidenefuran-2(5*H*)-one [3]. The use of aminocatalytic strategy for the activation of α,β,γ,δ-diunsaturated aldehydes, allowed the reaction to proceed with high enantio- and diastereoselectivity. Furthermore, the synthesis benefits from a broad scope (26 examples) and the usefulness of the products have been shown in an example intramolecular Stetter reaction.

Acknowledgment

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References

[1] H. M. R. Hoffmann, J. Rabe, Angew. Chem. Int. Ed. Engl. 1985, 24, 94
[2] M. S. Manna, S. Mukherjee, Chem. Sci. 2014, 5, 1627;
[3] A. Skrzyńska, P. Drelich, S. Frankowski, Ł. Albrecht, *Chem. Eur. J.* **2018**, *article in press.*.

P-132

Synthesis of new chiral oxazoline-pyridines for applications in asymmetric synthesis

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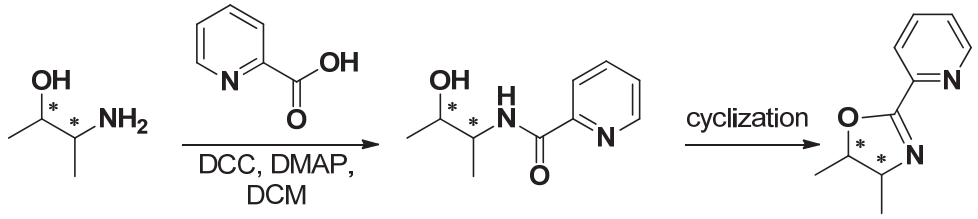
One of the most important goals of modern organic synthesis is the preparation of the compounds in optically pure form. In stereocontrolled synthesis, the most popular reactions are those catalyzed by transition metals with chiral ligands.

The aim of the research was the synthesis of chiral pyridine-oxazolines derived from (+)-α-pinene, (–)-β-pinene and (1*S*,2*R*)-1-amino-2-indanol[1]. These novel chiral compounds may be used as ligands with donor nitrogen atoms used in asymmetric catalysis with transition metals.



Scheme 1. Synthesis of chiral ligands.

The first step involved the synthesis of the appropriate terpene amino alcohols from (+)-α-pinene and (–)-β-pinene using known procedures.[2] Picolinic, nicotinic and isonicotinic acids were applied in the next step converting amino alcohols into amides by condensation reaction with DCC. The last step to prepare ligands involved cyclization of amides to oxazolines.[3]

References

[1] Aranda, C., Cornejo, A., M. Fraile, J., Garcia-Verdugo, E., Gil, M. J., Luis, S. V., Mayoral, J. A., Martinez-Merino, V., Ochoa, Z., *Green Chem.*, **2011**, *13*, 983.

[2] Krzemiński, M., Wojtczak, A, *Tetrahedron Lett.* **2005**, *46*, 8299.

[3] Kmieciak, A., Krzemiński, M. P., *Tetrahedron: Asymmetry* **2017**, *28*, 467.

P-133

Conversions of the in situ generated alkoxyimidazol-2-ylidenes into alkoxyimidazol-2-thiones via the reaction with elemental sulfur

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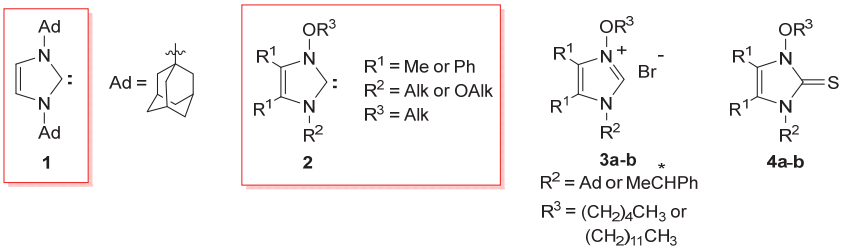
Nucleophilic heterocylic carbenes (NHC) are considered as an important class of reactive species, which changed in recent three decades from laboratory curiosities to synthetically useful tools (organic synthesis tools) [1]. In 1991, Arduengo demonstrated, that imidazole-2-ylidene **1** bearing two bulky adamantan-1-yl groups at N(1) and N(3) is stable enough to be isolated and stored for a longer time at ambient conditions [2].



The goal of the current project is the preparation of a series of new imidazole based nucleophilic carbenes of type **2** bearing alkoxy substituents attached to the N(3) or both, N(1) and N(3) atoms, starting with corresponding 2-unsubstituted imidazole *N*-oxides [3]. The isolated or only in situ generated alkoxyimidazol-2-ylidenes **2**, including some enantiopure representatives, will be tested in diverse reactions as new catalysts or ligands.

In a series of recent experiments we demonstrated that upon treatment with triethylamine NEt_3 in the pyridine solution, 3-alkoxyimidazolium salts **3a-b** can be converted into reactive 3-alkoxyimidazol-2-ylidenes **2**, which are able to trap the elemental sulfur yielding the corresponding 3-alkoxyimidazol-2-thiones **4a-b** in high yields.
Structures of all products were established based on spectroscopic data and elemental analysis.

Acknowledgement

The authors thank the National Science Center (PL-Cracow) for financial support within the projects *Beethoven-2* (Grant #2016/23/G/ST5/04115).

References

[1] a) M. Uzelac, E. Hevia, *Chem. Commun*. **2018**, *54*, 2455; b) W. A. Herrmann, J. Schütz, G. D. Frey, E. Herdtweck, *Organometallics*, **2006**, *25*, 2437.

[2] a) A. J. Arduengo III, R. L. Harlow, M. Kline, *J. Am. Chem. Soc.* **1991**, *113*, 311; b) A. J. Arduengo III, H. V. R. Dias, R. L. Harlow, M. Kline, *J. Am. Chem. Soc.* **1992**, *114*, 5530.

[3] G. Mlostoń, M. Jasiński, A. Wróblewska, and H. Heimgartner, *Curr. Org. Chem.*, **2016**, 20, 1359..

P-134

Chiral NORPHOS derived ligands for palladium-catalyzed allylic alkylation reaction

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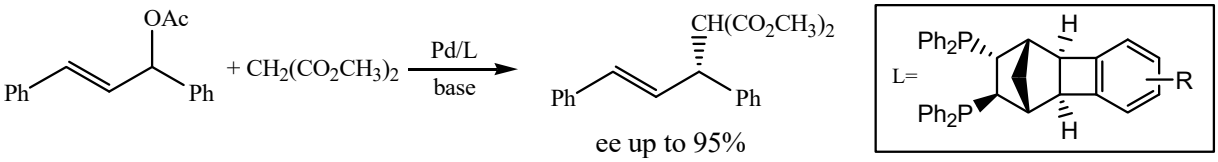
The asymmetric allylic alkylation is an important tool for the synthesis of optically pure organic compounds. This reaction is generally promoted by soluble palladium complexes generated in situ by adding chiral ligands to a solution of π-allylpalladium chloride. A successful ligand design is very important in this process.

Previously, we reported an entirely new method for the synthesis of bidentate phosphine ligands base on the Norphos motif [1]. Norphos is one of the highly efficient chiral biphosphine ligand for the rhodium-catalyzed asymmetric hydrogenation and Diels-Alder cycloaddition reaction [2].

In this poster we wish to present Norphos and our Norphos derivatives and investigate the effectivness and usefulness of these ligands in the palladium-catalyzed asymmetric allylic alkylation reactions.



References

[1] K.Szwaczko, O. M. Demchuk, B. Mirosław, D. Strzelecka, K. M. Pietrusiewicz, *Tetrahedron Letters* 57, **2016**, 3491.

[2] H. Brunner, et al. *Chem. Ber*., 1981, *114,* 1137; H. Brunner, et al., *Synthesis,* 2008, 405

Synthesis of C(3)-functionalized benzo[*e*][1,2,4]triazines

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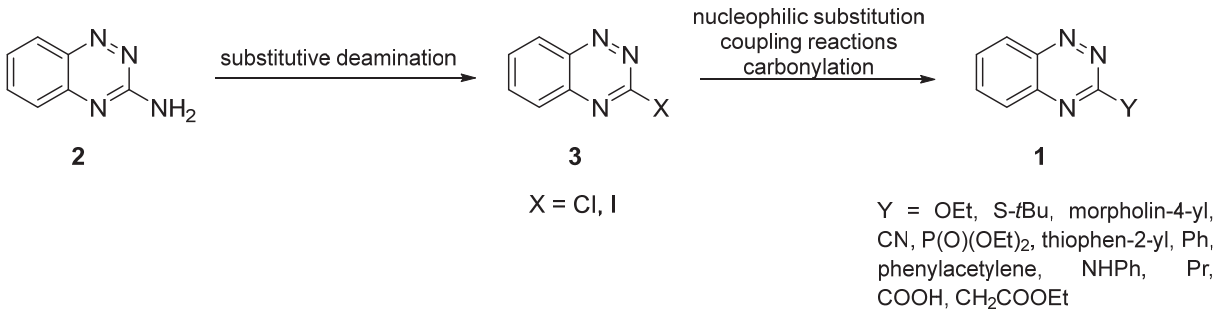
In recent years, benzo[*e*][1,2,4]triazines are becoming increasingly important building blocks for pharmacophores and organic materials. Therefore, new methods for synthesis of this heterocyclic skeleton and access to a variety of functional derivatives are continuously being developed.[1] For pharmacological applications particularly important is the functional substituent at the C(3) position of the benzo[*e*][1,2,4]triazine which typically is an amine, aromatic or aliphatic group. Unfortunately, each class of these compounds requires a separate multi-step synthesis. The goal of our project was to develop a general precursor for the synthesis of a wide variety of C(3)–functionalized benzo[*e*][1,2,4]triazines **1** using a common and readily available precursor. For this purpose, 3-aminobenzo[*e*][1,2,3]triazine **2** has been selected and transformed into 3-Cl and 3-I derivatives **3**. Their reactions with nucleophiles (X = Cl) and Pd-catalyzed (X = I) reactions give rise to a broad range of C(3)–functionalized benzo[*e*][1,2,4]triazines **1**.



References

[1] E. Obijalska, M. K. Kowalski, *Chem. Heterocyclic Comp.*, **2017**, *53*, 846-848 and references therein.

P-136

Synthesis of new chiral thiourea derivatives based on 2-azabicycloalkanes

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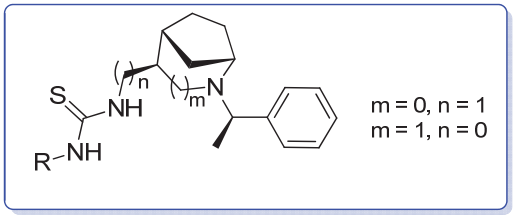
Chiral catalysts containing both acidic and basic (nucleophilic) structural units are gaining importance in the development of asymmetric synthesis [1]. Thiourea derivatives play an important role in catalyst design and modification. Recently, bifunctional organocatalysts that possess a thiourea moiety and an amino group on a chiral scaffold have been successfully applied in different asymmetric transformations, such as aldol reaction, Morita-Baylis-Hillman reaction, Mannich reaction, Henry reaction, and Michael addition [2,3].

We have designed and synthesized thiourea derivatives based on chiral frameworks of 2-azabicycloalkanes [4] and *Cinchona* alkaloids.



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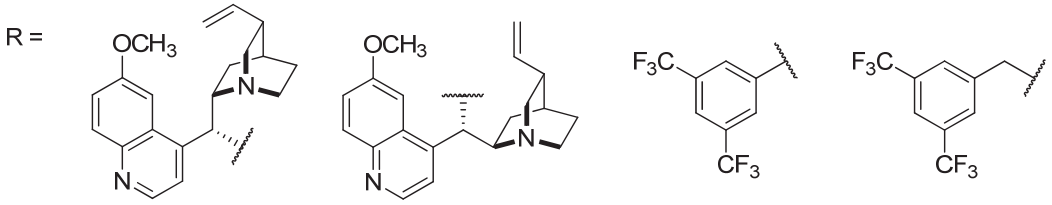

The new compounds were tested as organocatalysts in the asymmetric Michael addition reaction of nitromethane to *trans*-chalcone giving products with good yields and high enantioselectivity (up to 90%).

References

[1] *Asymmetric Synthesis - The Essentials.* (Christmann, M., Bräse, S., Eds.), 2nd Ed., Wiley-VCH, Weinheim **2007**.

[2] Takemoto, Y. *Chem. Pharm. Bull.* **2010**, *58*, 593-601.

[3] Serdyuk, O. V., Heckel, C. M., Tsogoeva, S. B. *Org. Biomol. Chem*. **2013**, *11*, 7051-7071.

[4] Wojaczyńska, E., Wojaczyński, J., Kleniewska, K., Dorsz, M., Olszewski., T. K. *Org. Biomol. Chem.* **2015**, *13*, 6116-6148.

Cytotoxic and fungicidal activities of colchicine derivatives and their semi empirical and molecular modeling studies

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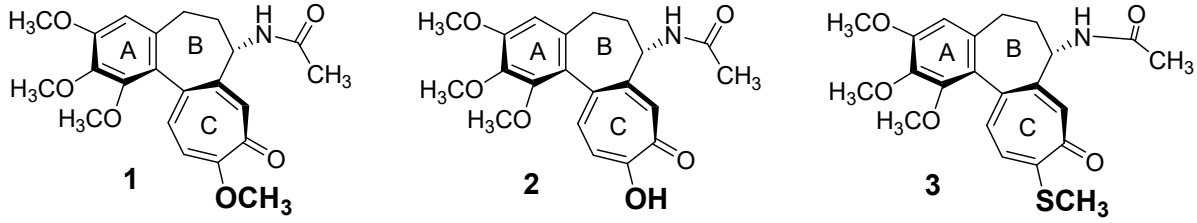
Colchicine **1** is a tropolone alkaloid naturally occurring in plants of *Liliaceae* family especially in meadow saffron (*Colchicum autumnale*). It possesses antimitotic, antifibrotic, anti-inflamatory activity and can efficiently relieve the symptoms of gout attack. Moreover, colchicine is a potent anti-mitotic agent and shows carcinogenic activity [1]. Synthesis of colchicine derivative has been made to decrease its toxicity and increase its therapeutic properties [2-4]. Colchiceine **2** and 10-methylthiocolchicine **3** are well known semisynthetic derivatives of colchicine. Compound **3**
is less toxic and has good therapeutic index.



Scheme 1. Structure of colchicine **1,** colchiceine **2** and 10-methylthiocolchicine **3** molecules.

Based on the above, a series of new colchicine derivatives were synthesized. Its cytotoxic activity was tested mainly against SKOV-3 ovarian cancer cell culture model. Structures of active compounds were also calculated by semiempirical methods DFT/PM5/PM7 and molecular modeling to be able to explain their biological activity.

References

[1] Kurek J., Boczoń Wł., Murias M., Myszkowski K., Borowiak T., Wolska I., *Let. Drug Des.& Disc*., **2014**, *11*, 3, 279–289.
[2] Kurek J., Boczoń Wł., Przybylski P., Brzeziński B., *J. Mol. Struct*., **2007**, *846*, 13-27.
[3] Kurek J., Barczyński P, *Croat. Chim. Acta*. **2016**, 98, 3.
[4] Kurek J., Kwaśniewska-Sip P., Myszkowski K. Cofta G., Murias M., Barczyński P., Jasiewicz B., Kurczab R., MedChemComm, **2018, *9,*** 1708 – 1714.

Optical control of physicochemical properties of azobenzene-thiourea-2-azabicycloalkane systems

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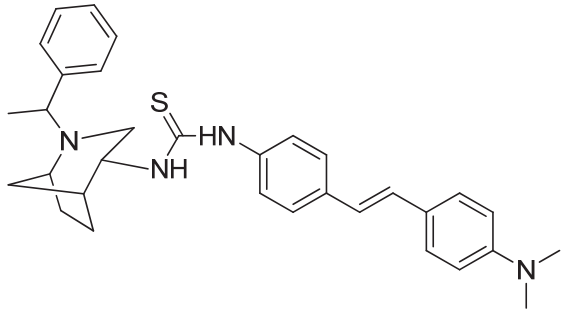
Photochromic materials have been used in optical information processing for several decades. Due to the possibility of modifying the molecular structure, materials containing azobenzene group turned out to be particularly interesting. Derivatives of 2-azabicycloalkanes are widely used in research on biological activity as well as in stereoselective synthesis [1]. In our research, we focused on 2-azabicycloalkanes substituted with thiourea as scaffolds for azobenzene derivatives. The final products were synthesized in the coupling reaction of the corresponding amine based on a bicyclic skeleton and the azo compound with the isothiocyanate moiety.

The effect of structure and configuration of a rigid bicyclic fragment, the presence of thiourea moiety and the azobenzene fragment on physicochemical properties of the obtained systems will be discussed.



References

[1] Wojaczyńska, E., Wojaczyński, J., Kleniewska, K., Dorsz, M., Olszewski, T. K. *Org. Biomol. Chem.* **2015**, *13*, 6116-6148..

P-139

Chiral N-oxides; preparation and catalytic applications

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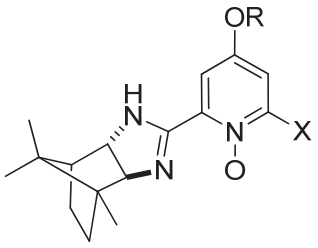
The development of Lewis basic organocatalysts for several types of asymmetric reactions has received much attention over the past decade.[1] A particular focus has been in the development of chiral catalysts based on N-heterocycles. Among others, N-oxides are powerful electron donors and, when possessing rigid chiral skeleton, they can provide good efficiency in asymmetric reactions. It has been shown, that whilst the amines are generally superior to the N-oxides for acylation, the N-oxides are superior for sulfonylation and silylation.[2] Several chiral pyridine N-oxides have been introduced to effect the desymmetrization of meso-epoxides.[3]

We present the synthesis of new Lewis bases that feature a pyridine N-oxide fragment attached to a chiral imidazole functionalyzed backbone. The enantiomeric pure compounds were tested in asymmetric reaction of benzaldehyde with allylchlorosilanes or in opening the meso-epoxides.



References

[1] Denmark, S. E., Bentner, G. L., *Angew. Chem. Int. Ed*. **2008**, *47*, 1560-1638.
[2] Murray, J., Spivey, A. C., *Adv. Synth. Catal*. **2015**, *357*, 3825 – 3830.
[3] Gnanamani, E., Someshwar, N., Sanjeevi, J., Ramanathan, C. R., *Adv. Synth. Catal*. **2014**, *356*, 2219-2223.

P-140

MW assisted synthesis and activity of new long-chain arylpiperazines with stiffened carbon linker as D_2 receptor ligands

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The proper level of serotonin is one of the most important factors affecting the state of mental health. Too high level of this neurotransmitter is associated with manic behavior, while reduced serotonin level leads to depression [1]. Due to this, the search for new drugs for central nervous system disorders, including psychiatric disorders largely relies on the search for active ligands of serotonin receptors [2]. The group of long-chain arylpiperazines [3] can be included among the active ligands of the mentioned receptors. There are reports in the literature about the increase in ligand activity by stiffening the flexible carbon chain present in the structure of the molecule [4].

The aim of the conducted research was the synthesis and evaluation of the activity of new long-chain arylpiperazine having a stiffened carbon chain, containing a part of 1,2,4-triazolo[4,3-a]pyridin-3(2H)-one or salicylamide. Compounds were tested for their affinity for selected serotonin and dopamine receptors. Interesting results have been obtained describing the dependence of Structure-Activity (SAR).

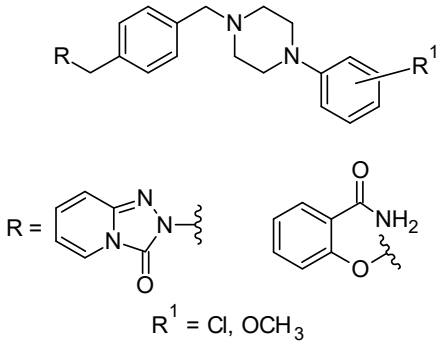

Figure 1. General structure of ligands.

References

[1] M.Z. Wróbel et al. *Biul. Wydz. Farm*. WUM, **2015**, 5, 28-39.

[2] X. Zhang, J.S. Tian, H. Liu, X.M. Qin, *China Jour. of Chin. Mat. Med.*, **2017**, 42(1), 29-33.

[3] A. Rague, K. Tidgewell, *Min. Rev. in Med. Chem*., **2018**, 18(7), 552-560.

[4] P. Kowalski, K. Mitka, J.Jaśkowska, B. Duszyńska, A.J. Bojarski, *Arch. Pharm.,* **2013**, 346(5), 339-348.

P-141

Reduction of bis sulfoxides with phenylsilane

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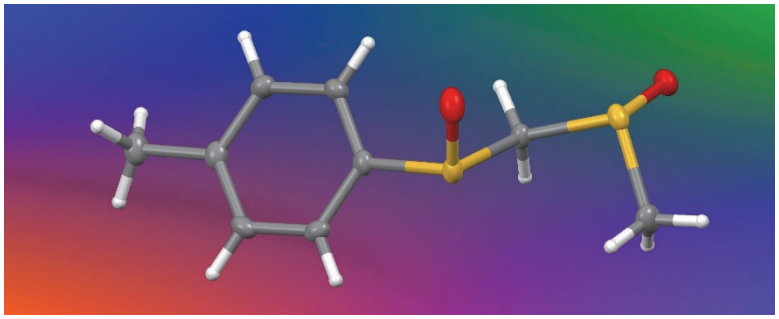
Our recent investigations were connected with the reduction using silanes in the presence of KOH[1]. They appeared that results of these reactions strongly depended on the relative position of particular substituents. This reaction is for carboxylic acid esters a regiospecific method of its desulfinylation[2]. In our further investigations 1-methyl-4-methylsulfinyl)methylsulfinylbenzene was employed having in mind that sulfinyl moiety is also an EWG substituent.



The outcome of these studies, including the synthesis of chosen sulfoxide and transformations leading to dialkyl sulfoxides will be presented.

References

[1] Nolan, S. P. et al.*Chem. Commun.,* **2013**, *49*, 9758—9760.
[2] Midura, W. H.; Rzewnicka, A. Krysiak, J. A. *Beilstein Journal of Organic Chemistry* **2017,** *13,* 1513–1517.

Use of functionalizated chiral cycloproppyl sulfoxide in the synthesis of precursor of aminocyclopropanephosphonic acids

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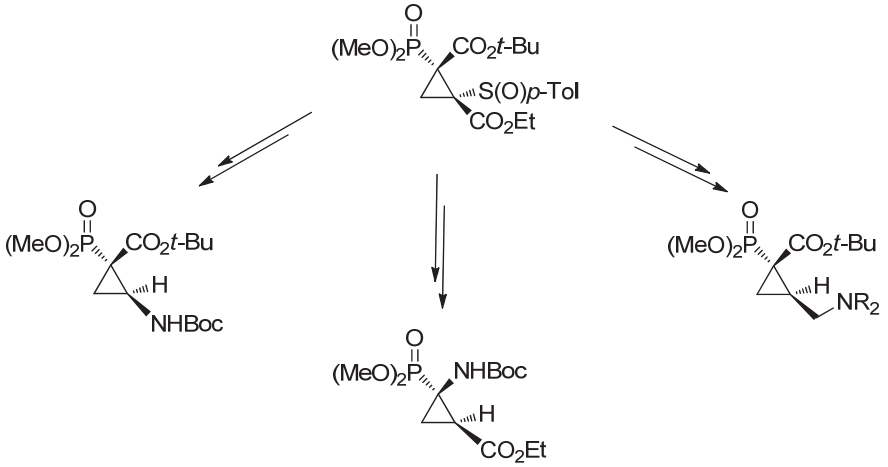
Aminocyclopropanephosphonic acids, defined as analogues of amino acids in which the carboxylic group is replaced by a phosphonic acid moiety acids have attracted considerable attention due to their interesting synthetic studies and their useful biological activities.[1]

As a part of our continuing interest in the synthesis of phosphonic analogues of biologically active compounds, we concentrated our studies on aminocyclopropanephosphonic acids.

Our general approach to this type of structure is based on an asymmetric cyclopropanation of vinylphosphonates using enantiomerically pure (*S*)-dimethylsulfonium (*p*-tolylsulfinyl)-methylide.[2] Based on this concept the synthesis of enantiopure aminocyclopropanephosphonic acids was developed.[3] The highly stereoselective acylation of cyclopropane ring under control of the chiral sulfinyl group provided to substituted cyclopropylphosphonate, which are the useful intermediate in the synthesis of precursors of aminocyclopropanephosphonic acid.



References

[1] For a recent review see (a) A. Mucha, P. Kafarski, Ł. Berlicki, *J. Med. Chem.* **2011**, *54*, 5955-5980; (b) F. Orsini, G. Sello, M. Sisti, *Curr. Med. Chem.* **2010**, *17*, 264-289; (c) M. Ordonez, H. Rojas-Cabrera, C. Cativiela, *Tetrahedron* **2009**, *65*, 17-49; (d) Ł. Berlicki, P. Kafarski, *Curr. Org. Chem*. **2005**, *9*, 1829–1850.

[2] (a) W. H. Midura, *Synlett,* **2006**, 733-736; (b) W. H. Midura, A. Sobczak, P. Paluch, *Tetrahedron Letters* **2013**, *54*, 223-226

[3] (a) W. H. Midura, A. Rzewnicka, *Tetrahedron: Asymmetry*, **2013,** *24*, 937-941; (b) W. H. Midura, A. Rzewnicka, *Synlett*, **2014**, *25*, 2213-2216.

P-143

Synthesis, structure and anticancer activity of novel arene-ruthenium(II) complexes with a pyrazole derivatives

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Arene-ruthenium(II) complexes with different ligands has been recognized as chemo therapeutics agents alternatives to cisplatin and its oxaliplatine analogs. The arene substituent is relatively inert towards displacement and is known to stabilize ruthenium in its +2 oxidation state under physiological conditions [1]. Both the size and hydrophobicity of the coordinated arene substituent as well as the structure of the mono- or bidentate ligands can have an influence on cytotoxic activity of arene-ruthenium(II) complexes [2]. As well know, all substituents enhance pharmacological properties of half-sandwich arene-Ru(II) complexes making them ideal for preparing multifunctional drugs [3]. It is known that melanoma is the most difficult to cure of all skin cancers, due to its high resistance to anticancer drugs. It is already known that arene-ruthenium(II) complexes display anti-melanoma activity, which is possibly based on the interference with *m*TOR and independently from EGFR (epidermal growth factor receptors) inhibition. So far in the literature have described anticancer activity of complexes a pyrazole derivatives with various metal ions e.g. Cu (II), Zn(II), Co(II) and Ni(II) [4-7].

The aim of this study includes the synthesis of newly arene-ruthenium(II) complexes with pyrazole derivatives, also biological examination was determined (anticancer activity of novel compounds on three cell lines HL-60, NALM-6 and WM-115).

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References

[1] G. Sűss-Fink, *Dalton Trans*., **2011,** 39, 1673-1688.
[2] F. Wang, J. Xu, K. Wu, S.K. Weidt, C.L. MacKay, P.R.R. Langridge-Smith, P.J. Sadler; *Dalton Trans.*, **2013**, 42(9) 3188-3195.
[3] G.S. Smith, B. Therrien, *Dalton Trans.,* **2011**, 40, 10793-10800.
[4] E. Budzisz, U. Krajewska, M. Różalski, A. Szuławska, M. Czyż, B. Nawrot, *Eur. J. Pharmacol*., **2004**, 502, 59-65.
[5] E. Budzisz, M. Malecka, I-P. Lorenz, P. Mayer, R. Kwiecień, P. Paneth, U. Krajewska, M. Rozalski, *Inorg. Chem.,* **2006**, 45, 9688-9695.
[6] M. Sobiesiak, I.-P. Lorenz, P. Mayer, M. Wozniczka, A. Kufelnicki, U. Krajewska, M. Rozalski , E. Budzisz *Eur. J. Med. Chem*., **2011**, *46,* 5917-5926.
[7] M. Grazul, E. Besic-Gyenge, C. Maake, M. Ciolkowski, M. Czyz, R. K.O. Sigel, E. Budzisz; *J. Inorg. Biochem*., **2014**, 135, 68-76.

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The first synthesis of enantiomerically pure hydroxymethyl derivatives of 1,3,5-triaza-7-phosphoadamantane (PTA)

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1,3,5-triaza-7-phosphaadamantane (PTA) has recently received great interest of organic chemists and has been a subject of several overviews, eg [1]. As a result of the enzymatic acetylation of racemic P-sulfide hydroxymethyl derivative of PTA, performed under kinetic resolution conditions, both enantiomers of the product were obtained for the first time, whose absolute configurations were determined by crystallographic analysis [2]. The single molecules of each enantiomer are present in the asymmetric units. Both structures were deposited at the Cambridge Crystallographic Data Center: CCDC 1842806 for *R*-enantiomer (Figure 1.) and CCDC 1842807 for *S*-enantiomer.

The results obtained will be presented and discussed.

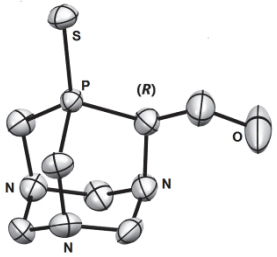

Figure 1.

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References

[1] A. Guerriero, M. Peruzzini, L. Gonsalvi, Coord. *Chem. Rev.* 2018, *355*, 328-361;
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