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VI NORTH CAUCASUS ORGANIC CHEMISTRY SYMPOSIUM

BOOK OF ABSTRACTS

УДК 547
ББК 24.2

VI СЕВЕРО-КАВКАЗСКИЙ СИМПОЗИУМ ПО ОРГАНИЧЕСКОЙ ХИМИИ
(СТАВРОПОЛЬ, 18-22 АПРЕЛЯ 2022 г.) - СТАВРОПОЛЬ: СКФУ, 2022. - 273 с.

ISBN 978-5-9296-1160-5

The book of abstracts of the VI North Caucasus Organic Chemistry Symposium held from 18 to 22 April 2022 at the Faculty of Chemistry and Pharmacy of the North-Caucasus Federal University. Includes lectures of plenary, key-note and invited speakers, as well as oral reports and poster session. The present publication is aimed at popularization of scientific research activity in the field of organic chemistry and to discuss modern chemical problems on the international level. The digest is intended for scientists, students, postgraduates, and a wide range of readers interested in current chemistry problems.

Подписано в печать 11.04.2022 г.
Формат 60*84/8
Усл.печ.л. 31,62
Бумага мелованная
Тираж 220 экз.

Отпечатано в Издательско-полиграфическом комплексе ФГАОУ ВО "Северо-Кавказский федеральный университет".
Адрес 355029, г. Ставрополь, пр-т Кулакова, 2

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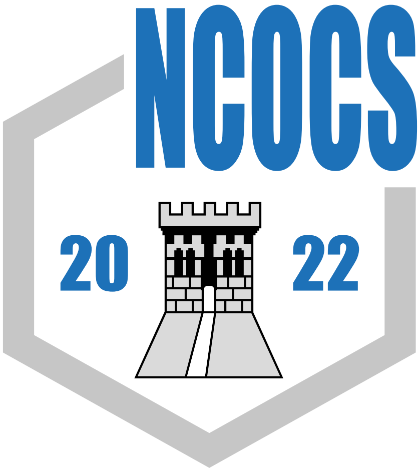


VI NORTH CAUCASUS ORGANIC CHEMISTRY SYMPOSIUM

BOOK OF ABSTRACTS

18-22 APRIL 2022

Dear Colleagues,

We are very pleased to welcome you all here in the south of Russia at the VI North Caucasus Organic Chemistry Symposium 2022. This conference is the continuation of the series of regionally-held international meetings on organic and heterocyclic chemistry organized by Prof. Alexander V. Aksenov and North-Caucasus Federal University every few years since 2009.

The current conference will feature traditional plenary and keynote lectures given by prominent domestic and foreign chemists as well as oral and poster presentations of the graduate students and early career scientists. The topics will include (but not limited to) new organic synthetic tools, methods and conceptions in regards to the development of practically useful paths to the important or perspective biologically active compounds.

While many of the renown invited guests and participants from the abroad were not able to visit us, the list of the symposium attendees is very strong featuring some leading players in the field of organic chemistry both local and international. We sincerely believe that the upcoming conference would be a place for vivid scientific discussion and ideas exchange offering everyone and especially for young chemists the opportunity to present their research and foster fruitful networking.

With best regards,

Chairman of the Organizing committee,
Prof. Alexander V. Aksenov

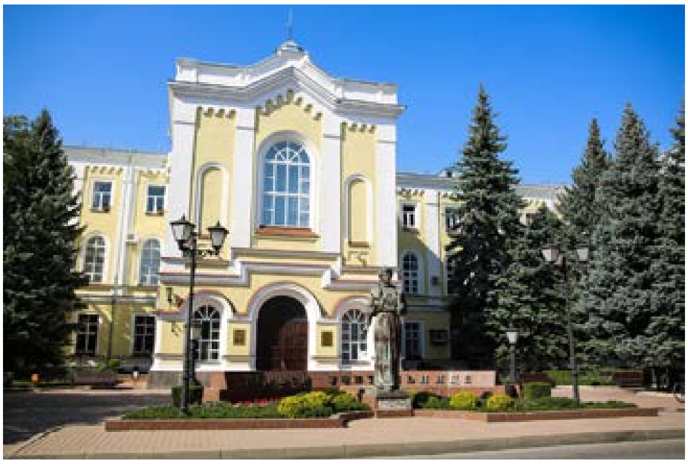
North-Caucasus Federal University is one of ten federal universities in Russia, unique academic institutions created as a new category of higher educational establishment in the framework of the national Education project implementation. The University is located on Stavropol Territory, one of Russia's most picturesque regions. Gold-yellow wheat, fruit gardens, the incredible local cuisine are characteristic of the Stavropol Territory that is called the Gate to the Caucasus. Numerous cultures and confessions have coexisted here for centuries, and today the city is home to over 100 ethnic groups, each of them maintaining the essence of its traditions and customs.

NCFU provides training for qualified staff in areas designated as priorities within the socio-economic development of the District and acts as the leading expert platform for intercultural dialogue in the ethnically diverse region, as well as neighboring countries.

It is committed to the principle of integration of scientific, educational, economic and social processes and is working to strengthen the Russian state and society. It is one of the country's leading universities.

Today the large, integrated scientific and educational staff represents a combination of youth and experience. It remains true to its traditions in training future specialists and is open to innovation and exploring new scientific contacts. It is a center for scientific activity and innovation playing a key role in the life of the North-Caucasus Federal District. The North-Caucasus Federal University comprises 8 Institutes and 7 Faculties:

- Institute of Humanities;
- Institute of Digital Development;
- Institute of Engineering;
- Institute of Law;
- Institute of Earth Sciences;
- Institute of Economics and Management;
- Faculty of Chemistry and Pharmacy;
- Faculty of Psychology and Pedagogy;
- Faculty of Physics and Technology;
- Faculty of Food Engineering and Biotechnology;
- Faculty of Medicine and Biology;
- Faculty of Mathematics and Computer Sciences named after Prof. Nikolay Chervyakov;
- Faculty of Physical Education and Sport;
- Pyatigorsk Institute (Branch of NCFU);
- Nevinnomyssk Technological Institute (Branch of NCFU)



Today the NCFU employs 1053 highly competent teachers most of them holding high scientific degrees (Doctors of Science –189; 746 Candidates of Science of the entire teaching staff body). The University can boast of 27 scientific schools and 47 areas of research. Besides, the University offers training within 160 subject areas for undergraduate, master, postgraduate courses and medical residency studies and 55 bilingual programs. More than 25 thousand people study at the university, representing 86 nationalities and ethnic groups from 52 regions of Russia and 51 countries of the world. North-Caucasus Federal University benefits from the history of successful international cooperation under the auspices of 100 bilateral agreements with universities and centers of science and education in 38 countries. The University regularly hosts international conferences, seminars and masterclasses with participation of experts from leading overseas scientific and educational organizations.

The University has advanced chemistry establishments that allow both students and staff to have the opportunity to work in the modern laboratories using the state-of-art equipment. This research activity is mostly held in cooperation with European and North-American institutions and its results are regularly published in well-known peer-reviewed chemistry journals Faculty of Chemistry and Pharmacy is a hosting party and organizer for Russian and International conferences on a regular basis.

Today the North-Caucasus Federal University is a unique center of science and professional training for competitive employees with high standards of personal culture and creative thinking; the University has great potential for development and offers wide-ranging opportunities for intellectual and professional growth, laying the foundation for success in the ever-changing world.

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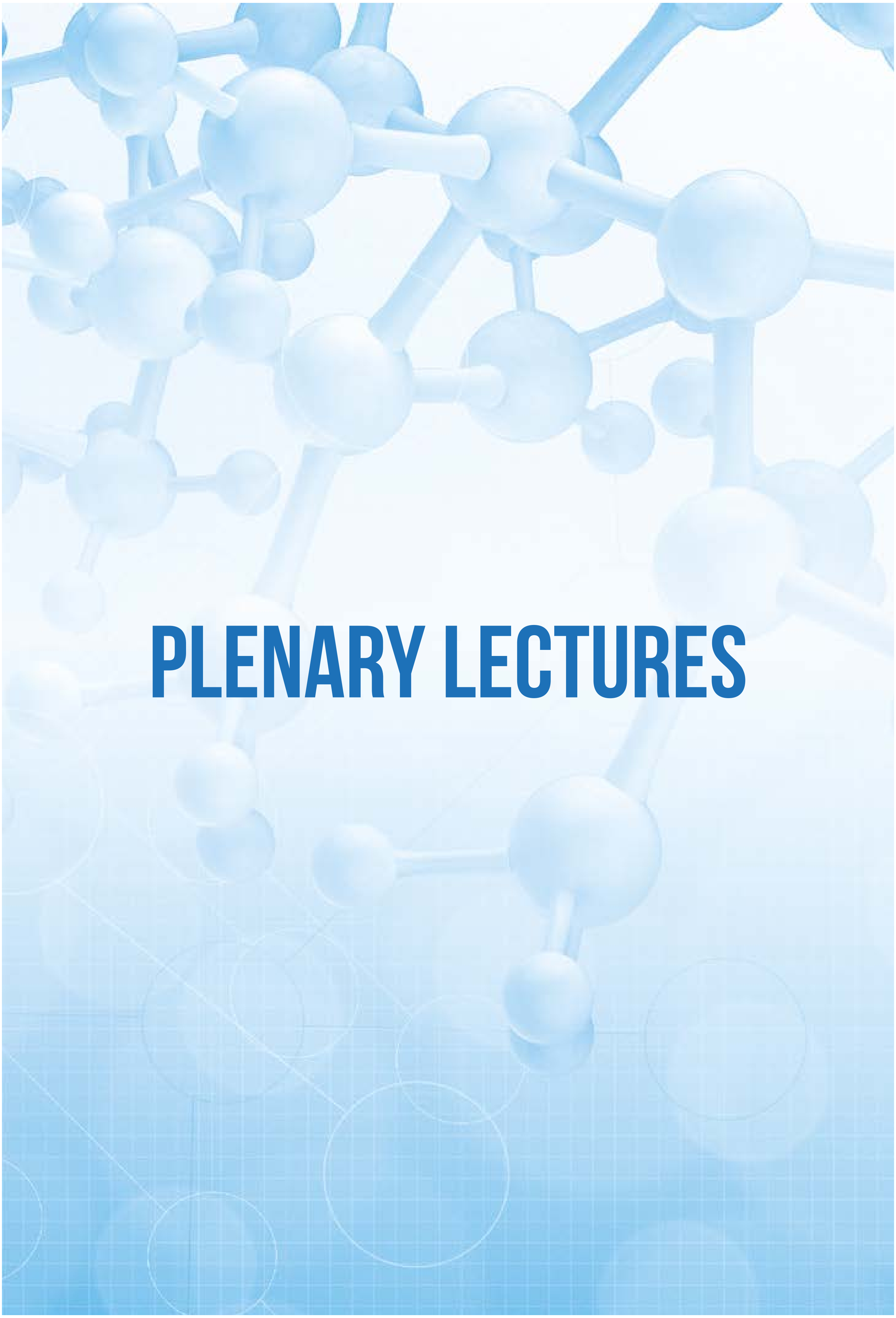

PLENARY LECTURES

КАТАЛИЗ В СОВРЕМЕННОМ ОРГАНИЧЕСКОМ СИНТЕЗЕ

Белецкая И.П.

Московский Государственный Университет имени М.В. Ломоносова, Химический факультет,
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Цель доклада – показать роль различных видов катализа в современной органической химии для создания хемо-, регио- и энантиоселективных процессов. Будут рассмотрены примеры катализа комплексами переходных и непереходных металлов, связь гомогенного и гетерогенного катализа, нанокатализ, асимметрический катализ и органокатализ.

Работа подготовлена при финансовой поддержке РНФ, проект 19-13-00223.

АЛЬТЕРНАТИВНЫЕ ПУТИ ПОИСКА И СОЗДАНИЯ ИННОВАЦИОННЫХ ЛЕКАРСТВЕННЫХ СРЕДСТВ

Спасов А.А.

Волгоградский государственный медицинский университет

STUDYING CATALYSIS WITH MACHINE INTELLIGENCE

Valentine P. Ananikov

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Developing a new generation of efficient catalysts and seeking mechanistic understanding have substantially contributed to revealing the nature of catalytically active sites. The dynamic nature and relationship between homogeneous and heterogeneous catalysis are now well established for C-C cross-coupling reactions [1]. Recently, the involvement of a dynamic "cocktail"-type catalysis was experimentally evidenced for such different reactions as C-N cross-coupling (Figure 1) and hydrosilylation of alkenes and alkynes [2]. Catalysis pathways beyond common assumptions were revealed for C-H functionalization and S-H bond addition reactions [3].

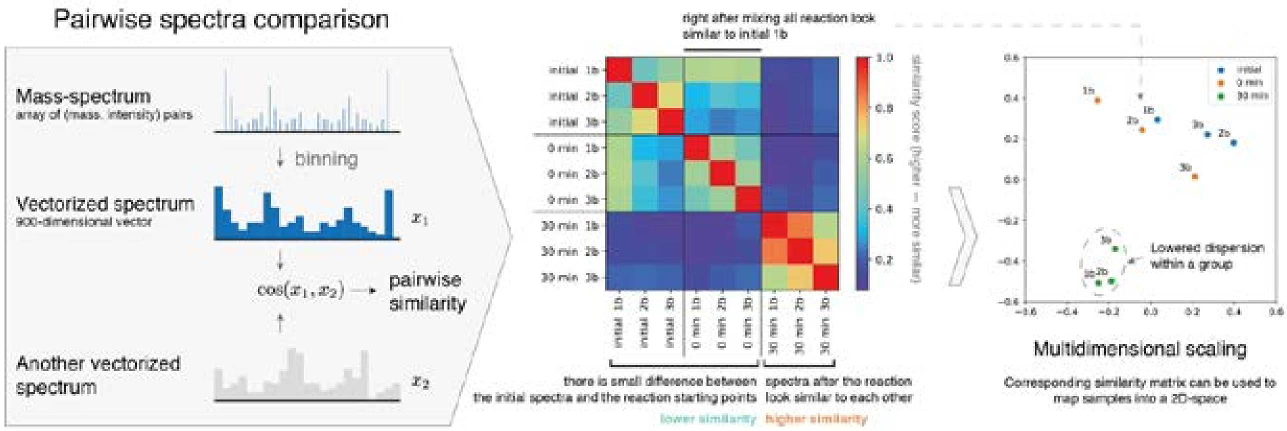

Figure 1. Automated analysis of reaction mixtures of Buchwald-Hartwig reaction [2a].

The non-innocent nature of carbon groups and involvement of carbene centers were shown for catalytic acetylene trimerization [4]. Using machine learning techniques to analyze the experiments in catalysis, reported highly active catalytic centers with TON ~ 10^9 and led to the discovery of a concept of totally defined catalysis [5], which will be discussed in details.

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Acknowledgement: The author thanks Scientific Schools grant NSh-5199.2022.1.3.

NEW DESIGNS IN GOLD(I) CATALYSIS

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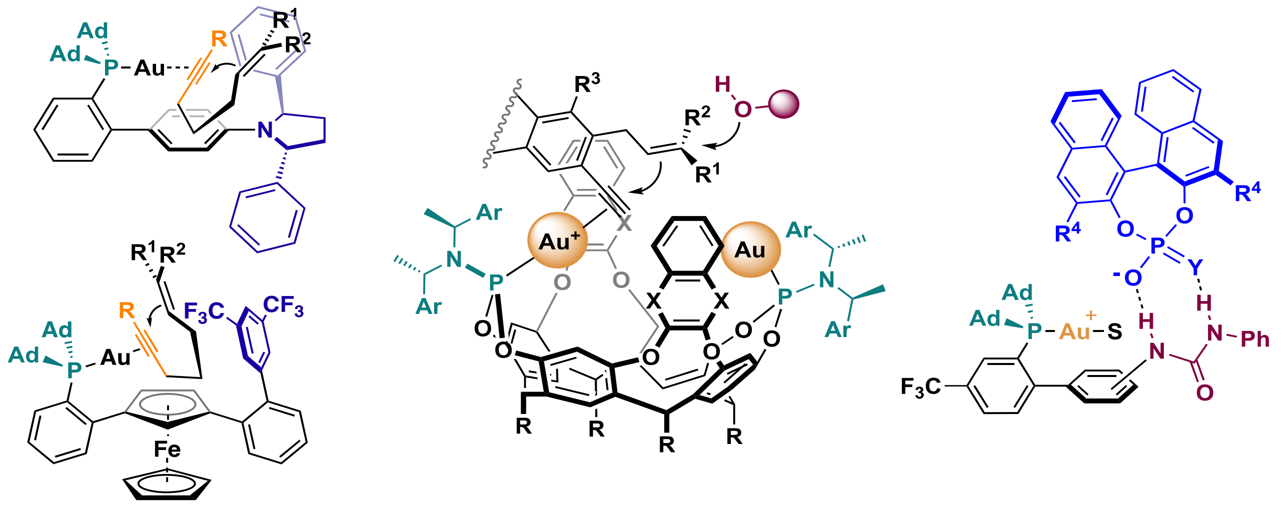
Gold(I) catalysts selectively activate alkynes under very mild conditions. However, the linear coordination displayed by gold(I) complexes places the chiral ligand far away from the substrate, resulting in the inefficient transfer of chiral information. In this lecture, recent results on the design of new chiral ligands and the application of the corresponding complexes in gold(I) catalysis for the asymmetric folding of unsaturated alkyne-containing substrates will be presented.[1-4]



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KEYNOTE LECTURES

DESIGN OF NOVEL CHEMICAL TRANSFORMATIONS UTILIZING NITROOLEFINS, AND THEIR APPLICATION TO ACCESS BIOLOGICALLY ACTIVE MATERIALS

A. V. Aksenov[a], D. A. Aksenov[a], N. A. Aksenov[a], I. V. Aksenova[a], M. Rubin[a,b]

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Development of synthetic approaches towards alkaloid analogs containing indolyl fragment is one of the central topics of modern synthetic and medicinal chemistry. We have recently reported on investigations of assuring antitumor properties for 2-aryl-2-(3-indolyl)acetohydroxamic acids, which demonstrated significant cytotoxicity against glioma, melanoma, esophagus cancer and many other cancer cell lines inherently resistant to induction of apoptosis and poorly responding to the treatment with proapoptotic medicines. Expanding the search, we stumbled upon the need for elaboration of novel approaches towards analogous structures non-accessible by standard methods. To this end, during the first stage of the project, an efficient method for activation of 3-(2-nitroethyl)-1H-indoles towards spirocyclization and subsequent rearrangement into 2-(1H-indol-2-yl)acetonitriles was developed. These compounds serve as key precursors for the entire project.

It was proposed that the mechanism of this activation involves stabilization of reactive tautomeric nitronate species in a form of phosphorylated mixed anhydride, formed upon interaction of poorly reactive nitroalkane with phosphoryl chloride in the presence of a base.

Biological activity of these novel 2-(1H-indol-2-yl)acetonitriles was investigated. It was found, that a number of these compounds showed micromolar activity (about 10 μм) against seven cancer cell lines: A549, A549, U373n, HS683, HeLa, HS683, and B16F10.

Reactivity of 2-(1H-indol-2-yl)acetonitriles and their immediate precursors 4’H-spiro[indole-3,5’-isoxazoles] in the presence of various nucleophiles under various conditions was investigated. Preparation of alkaloid-like structures employing this approach should be specially mentioned.

Funding: This work was supported by grants from the Russian Science Foundation (Grant number 21-73-20051).

ENERGY OF CHEMICAL BONDS AS A DRIVING FORCE FOR ORGANIC REACTIONS: MOLECULAR SPRINGS, STEREOELECTRONIC FRUSTRATION, AND ELECTRON UPCONVERSION

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Molecules store energy and, as bonds are formed and broken, every chemical process can either store or release energy. This talk will discuss practical ways for incorporating this common knowledge into reaction design and in searching for new physical phenomena.

After outlining the interplay of kinetics with thermodynamics and the special role of weak bonds in catalysis, I will discuss how much energy can one store in common functional groups and introduce the familiar textbook functionalities that accumulate more energy than an excited state.

I will show that the key to in controlling the flow of energy in chemical reactions is in using unique stereoelectronic features of each functionality and in coupling unfavorable and favorable elementary steps in a chain of chemical transformations.

In the final part, I will introduce the phenomenon of electron upconversion, a counterintuitive way to transform weak reductants into strong reductants in a thermodynamically favorable fashion. Such processes enable electrocatalytic transformations where a single electron can drive multiple catalytic cycles.

METACYCLOPHANES: DESIGN OF FUNCTIONAL SUPRAMOLECULAR ARCHITECTURES BY SELF-ASSEMBLY

Antipin I.[a,b], **Solovieva S.**[a,b], **Ovsyannikov A.**[a,b], **Burilov V.**[a] **and Ziganshina A.**[b]

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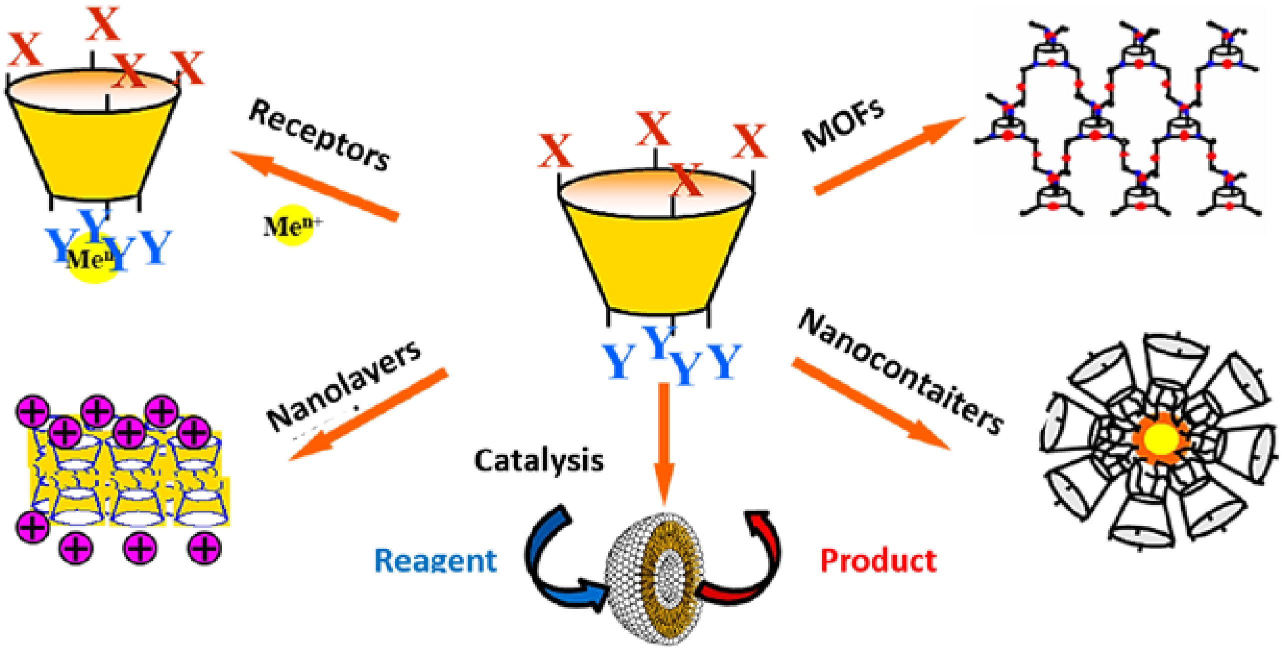
Metacyclophanes derivatives are of great interest for the design of a wide range of functional supramolecular architectures and materials.



Such compounds can be considered as molecular platform for the design of nanomaterials by self-assembly. In the report a particular attention will be paid to the application of metacyclophane derivatives for the design of various supramolecular systems, devices and smart materials: colloidal nanoparticles, catalytic systems, metal-coordinated networks, Langmuir-Blodgett nanolayers, molecular magnets, etc. [1].

The authors thank the Russian Science Foundation (19-73-20035) for financial support.

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FLUORINATED ALKENES AND ACETYLENES IN THE SYNTHESIS OF PRACTICALLY IMPORTANT COMPOUNDS

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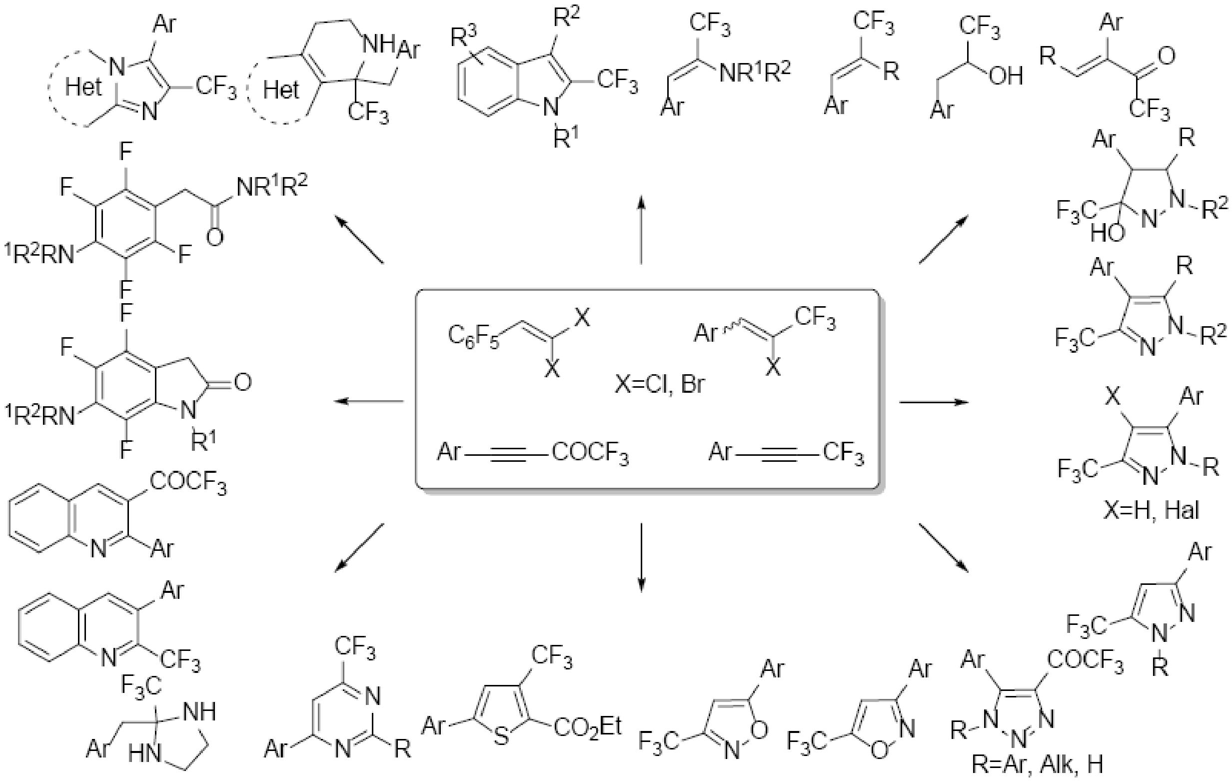
Organofluorine chemistry is one of the most rapidly developing areas of modern organic chemistry. Many fluorine containing compounds exhibit high biological activity. Currently 25-30% of drugs contain fluorine. Fluorine containing compounds also play an important role in agrochemistry and chemistry of materials. At the same time, direct introduction of fluorine or fluorine-containing substituents do not always have the proper selectivity and efficiency. The lecture discusses the use of fluorine containing alkenes and acetylenes in the synthesis of various heterocycles.



CONJUGATION IN ORGANIC MOLECULES

S.A. Ponomarenko[a,b] , **O.V. Borchshev**[a], **Yu.N. Luponosov**[a], **S.A. Pisarev** [b], **N.M. Surin**[a]

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The active development of organic electronics and photonics leads to the search for new highly efficient functional organic materials possessing semiconducting, light emitting or light harvesting properties. A large number of works are devoted to the synthesis and study of novel πconjugated molecules for use in organic field-effect transistors, light-emitting diodes, solar cells, plastic scintillators, spectral shifters and other devices. A wide variety of molecular structures of organic molecules leads to different conjugation pathways within the molecule, which influence their HOMO and LUMO levels, bandgap, and hence their optical and semiconducting properties. Liner-, cross- and omniconjugation introduced by J.C. Hummelen in 2004 not only lead to understanding the difference in optical properties of many conjugated molecules of various structure, but also allows to designing novel organic molecules with linear π-conjugated pathways between all the substituents [1].

In this presentation, several classes of organic molecules with different conjugation patterns, peculiarities in their synthesis, properties and application in organic electronic and photonic devices will be compared (Fig. 1). Branched molecules based on 1,3,5-substituted benzene initially considered by Hummelen as non-conjugated were later accepted as meta-conjugated molecules. Branched oligoarylsilanes were found to be non-conjugated as a whole molecule, leading to molecular antenna properties with ultrafast intramolecular energy transfer between their branches [2]. Donor-acceptor molecules based on triphenylamine were found to be fully conjugated with internal energy transfer leading to low bandgaps [3]. Changing molecular structure of such molecules allows tuning their optical properties for various optoelectronics devices, even for such exotic as full-colour artificial retinas [4].

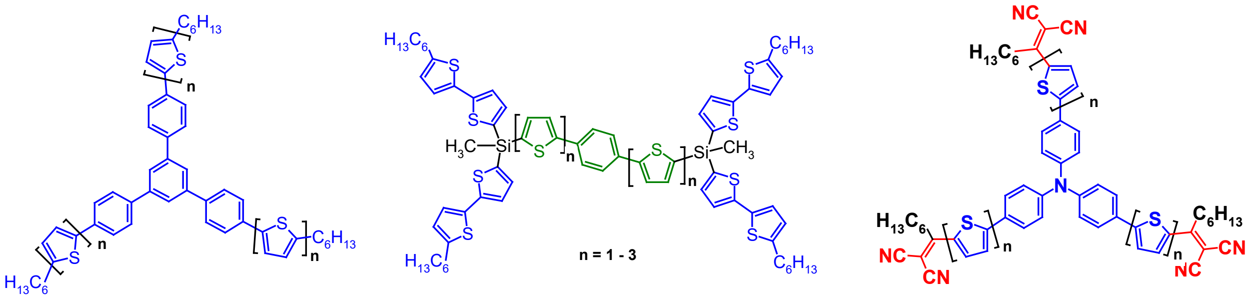

Figure 1. Examples of π-conjugated molecules with different conjugation patterns.

This work was financially supported by the Russian Science Foundation (grant 19-73-30028).

PEROXYL, N-OXYL, AND SULFONYL RADICALS IN OXIDATIVE COUPLING

Alexander O. Terent'ev, Igor B. Krylov, Olga M. Mulina, Stanislav A. Paveliev

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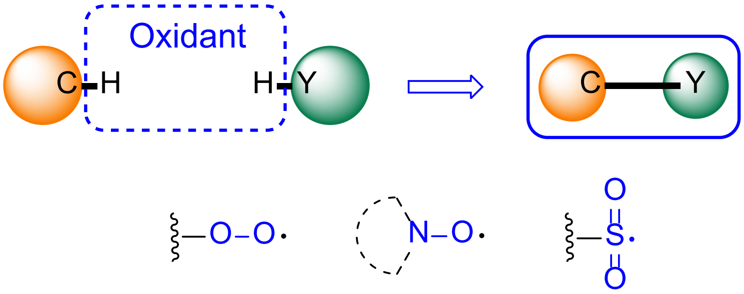
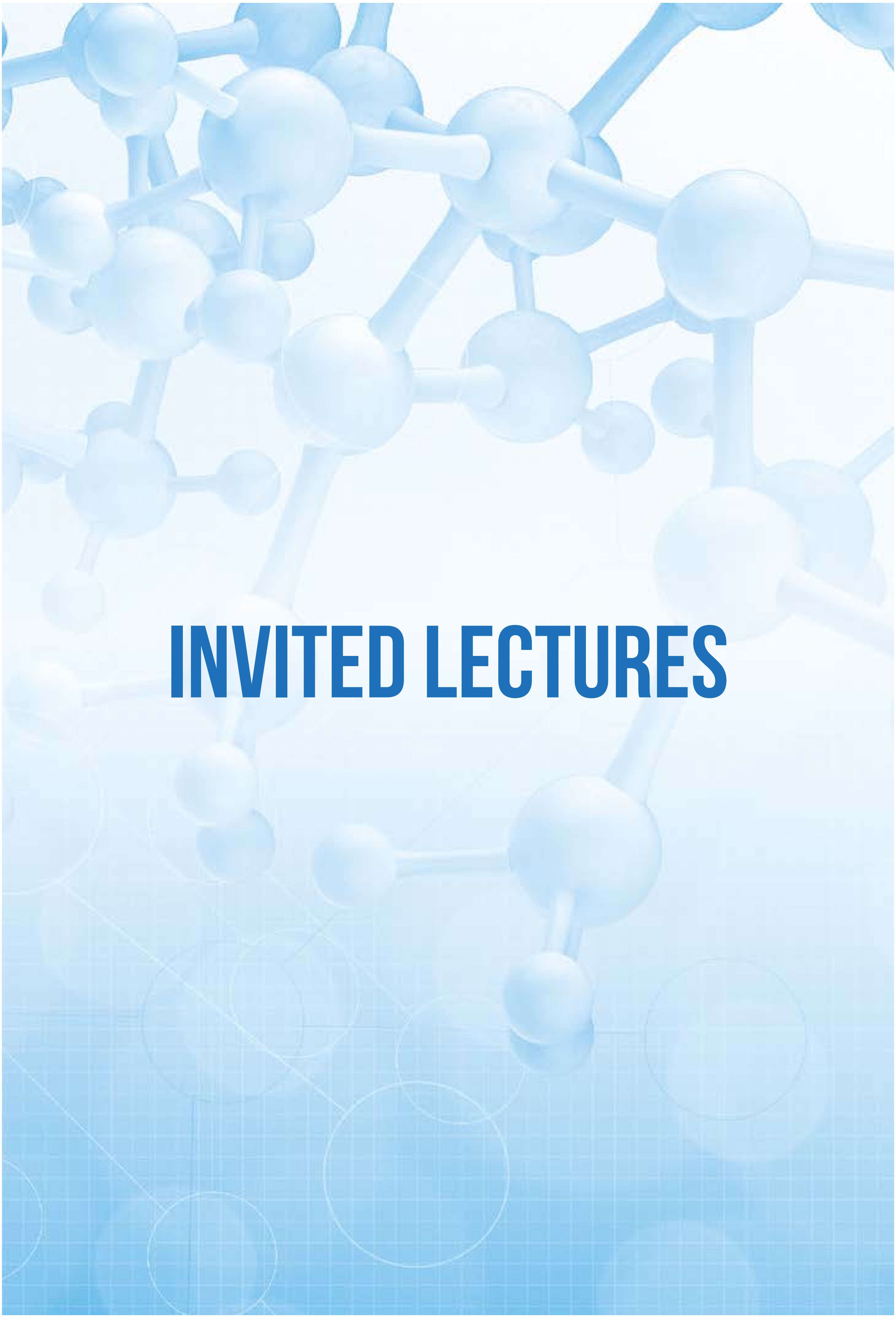
The search for efficient processes of oxidative coupling with the formation of carbon-carbon, carbon-heteroatom, and heteroatom-heteroatom bonds is one of the priority tasks of modern organic synthesis due to high atom-economy and environmental friendliness. This is ensured by the absence of the need to introduce leaving groups into the initial reagents, thereby reducing the number of synthetic steps and wastes.



We are grateful for the support of the Russian Science Foundation (Grant No. 21-43-04417)



INVITED LECTURES

NEW SYNTHESIS OF QUINOLES FROM 2-AZIDOSTYRYLFURANS

Abaev V. T.[a,b], **Chalikidi P. N.**[a] **and Magkoev T. T.** [a]

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b) North-Caucasus Federal University
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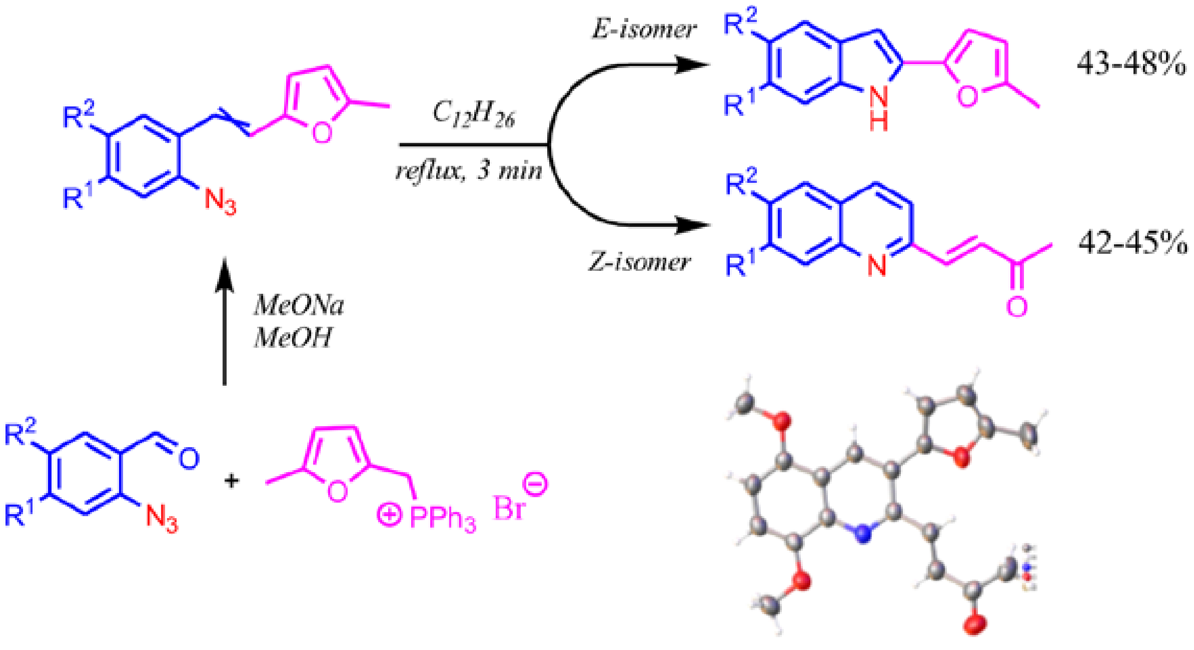
The intramolecular opening of the furan cycle by the nitrene generated from the azide function is a key step in the synthesis of the indole chalcones. Lengthening the linker between the furan cycle and the azide function by one carbon atom with the aim to synthesize the pyridine cycle leads to 2-azidostyrylfurans. However, these substrates are precursors of indoles in the classical Sandberg reaction, giving rise to indoles even in the case of double substitution at the end of vinyl bond.



R^1, R^2 = H, MeO, NO_2

X-Ray crystal structure of (E)-4-(5,8-dimethoxy-3-(5-methylfuran-2-yl)quinolin-2-yl)but-3-en-2-one.

We discovered that the corresponding 2-azidostyene bearing furan ring along with anticipated indole can also afford quinolone derivative under thermolysis. This new type of reactivity was characteristic for Z-isomer while pure E-isomer gave the corresponding indole exclusively.

CASCADE TRANSFORMATIONS IN SYNTHESIS OF HETEROCYCLES

Aksenov N.A.,[a] **Aksenov A.V.,**[a] **Aksenov D.A.,**[a] **Prityko L.A.,**[a] **Aksenova D.S.,**[a] **Rubin M.**[b]

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[b] Department of chemistry, University of Kansas, 66045, USA, Lawrence, Irving Hill Road, 1567
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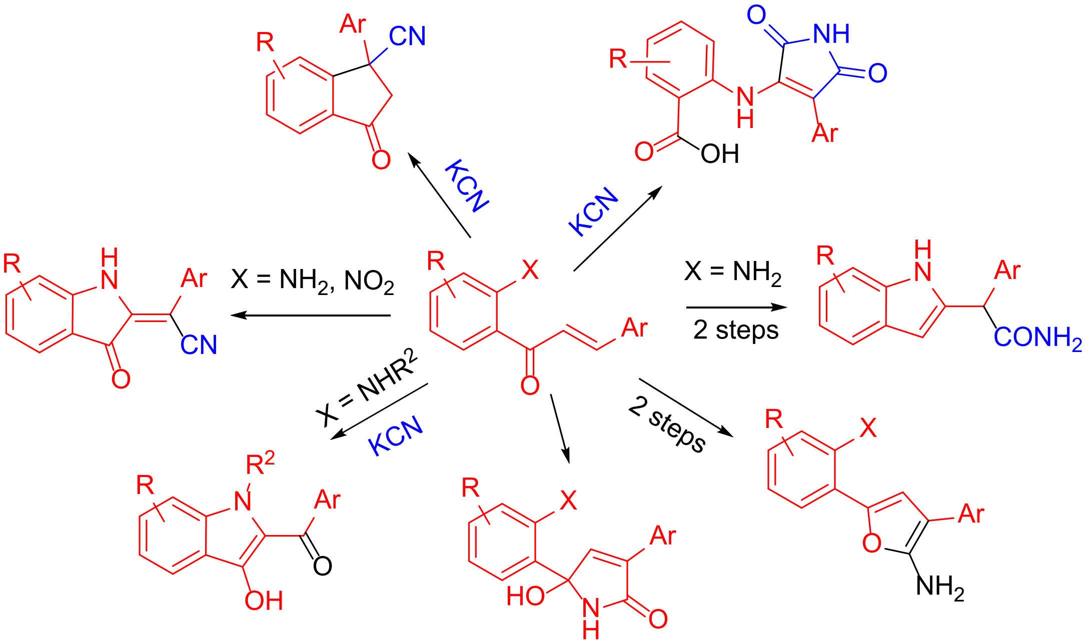
The last time presented to mankind quite a few new problems. Efficient and environmentally friendly synthesis methods, characterized with high yields, a small number of stages, and the use of available reagents, began to take the first place. Cascade transformations allow is able to solve all of the above problems at once, excluding the intermediate isolation of reaction products, reducing the process time, which is reflected in lower resource consumption and less influence of the human factor.

In the course of our recent studies, we have shown efficient cascade and one-pot transformations based on the reactions of aliphatic nitro compounds in the PPA medium. This made it possible to obtain a number of compounds with high anticancer activity against MDR cells.

No less interesting was the direction devoted to the chemistry of 3-cyanoketones. These derivatives contain a high density of functional groups, which allows implement a bunch of unexpected transformations with the formation of previously unknown and difficult to obtain compounds with promising properties.



The study was supported by the Russian Science Foundation (grant № 21-73-10029, https://rscf.ru/project/21-73-10029/)

SPIN LABELS AND SPIN PROBES. APPLICATION IN STRUCTURAL BIOLOGY

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Distance distribution information obtained by pulsed dipolar EPR spectroscopy provides an important contribution to many studies in structural biology. Increasingly, such information is used in integrative structural modeling, where it delivers unique restraints on the width of conformational ensembles. In order to ensure reliability of the structural models and of biological conclusions, recently quality standards for sample preparation and characterization, for measurements of distributed dipole–dipole couplings between paramagnetic labels, for conversion of the primary time-domain data into distance distributions, for interpreting these distributions, and for reporting results was defined [1]. Application of pulsed dipolar EPR spectroscopy is only possible when the spin labels based on nitroxides, triarylmethyl (TAM) radicals, copper of gadolinium complexes are used. During the last years several new approaches for the application of pulsed dipolar EPR spectroscopy were developed: highly stable nitroxide spin labels for in cell measurements [2], TAM spin labels with narrow linewidths which increase the sensitivity [3], photochemical spin labels based on fullerene [4], and high-field ENDOR spectroscopy in the W-band for pairs of triarylmethyl and fluorine labels [5].

This presentation is the review of the synthesis of spin probes [2,3] and their application to study complexes of ribosomes mimicking the process of translation [6], penetration of intrinsically disordered protein into cancer cells [7], and distance measurements of membrane proteins in E coli using Finland and OX063 trityl labels [8] and studding protein aggregates [9].

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Acknowledgement: This work was supported by Russian Science Foundation № 21-14-00219.

ADVANCES OF REACTIONS OF HETEROCYCLIC AZIDES WITH ACETYLENES AND ENAMINES

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In this review, for the first time, the features of the synthesis and reactions of heterocyclic azides with acetylene derivatives, alkenes, enamines, dicarbonyl compounds and acetonitrile derivatives have been collected and demonstrated mainly over the past 15 years. The use of these reactions in biological chemistry for research in living systems, in organic synthesis for the production of mono-, bi- and tricyclic compounds, and ensembles of various heterocycles, including 1,2,3-triazole derivatives, non-aromatic 1,2,3-triazolines and other azoles and azines, amidines, diazo compounds, supramolecular compounds, ligands, complex compounds, bioconjugates and biologically active compounds, in the chemistry of materials for the production of phosphors and sensors on metals.

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This work was supported by the Russian Science Foundation grant №18-13-00161(продление).

DESIGN AND SYNTHESIS OF NEW REAGENTS FOR BIOCONJUGATION AND BIOIMAGING

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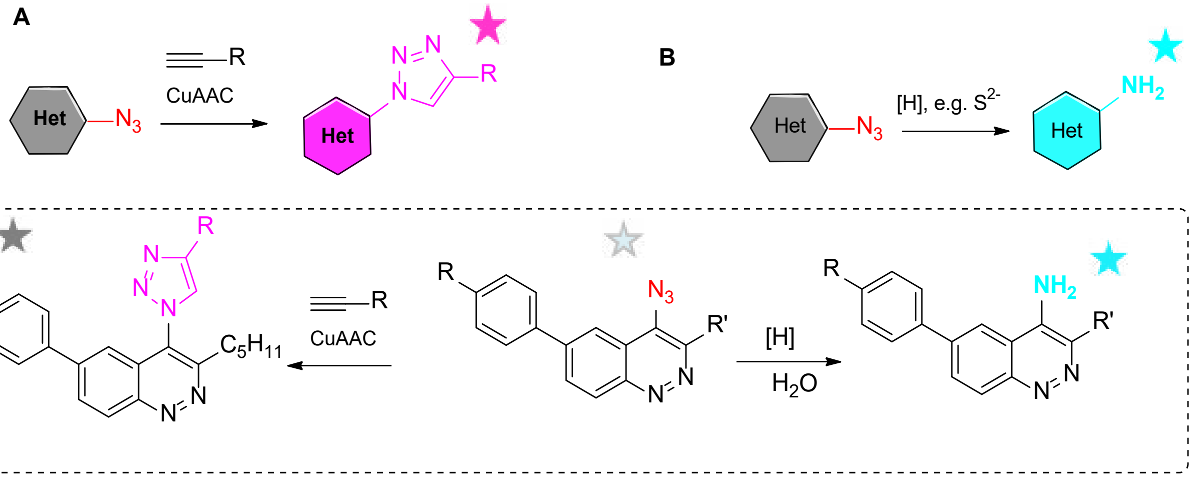
Bioimaging allows visualizing biological processes in living cells, tissues, as well as in living organisms in real-time. Visualization is carried out using fluorescent dyes, which must be securely “sewn” to the selected biological molecules.

To create fundamentally new effective SPAAC reagents for bioconjugation, we proposed heterocyclononyns, which have an optimal balance between stability and reactivity towards azide cycloaddition. Their unique properties are due to steric and stereoelectronic effects created by both heterocycle and heteroatom [1].

The design of derivatives of 4,5-diarylethynyl- and 5-aryl-4-arylethynyl-1H-1,2,3-triazoles that are promising for use as fluorescent labels [2] and new fluorogenic pairs based on reduction of 4-azidocinnolines to cinnoline-4-amines for the development of new fluorogenic probes will be also discussed.



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This work was supported by Russian Science Foundation (RSF) (project No. 21-13-00218). The research was carried out using the equipment of the SPbSU Resource Centres: Centre for Magnetic Resonance, Centre for Chemical Analysis and Materials Research.

SPIRO DERIVATIVES OF INDOLINONES AND IMIDAZOLONES: APPROACHES TO THE SYNTHESIS VIA 1,3-DIPOLAR CYCLOADDITION

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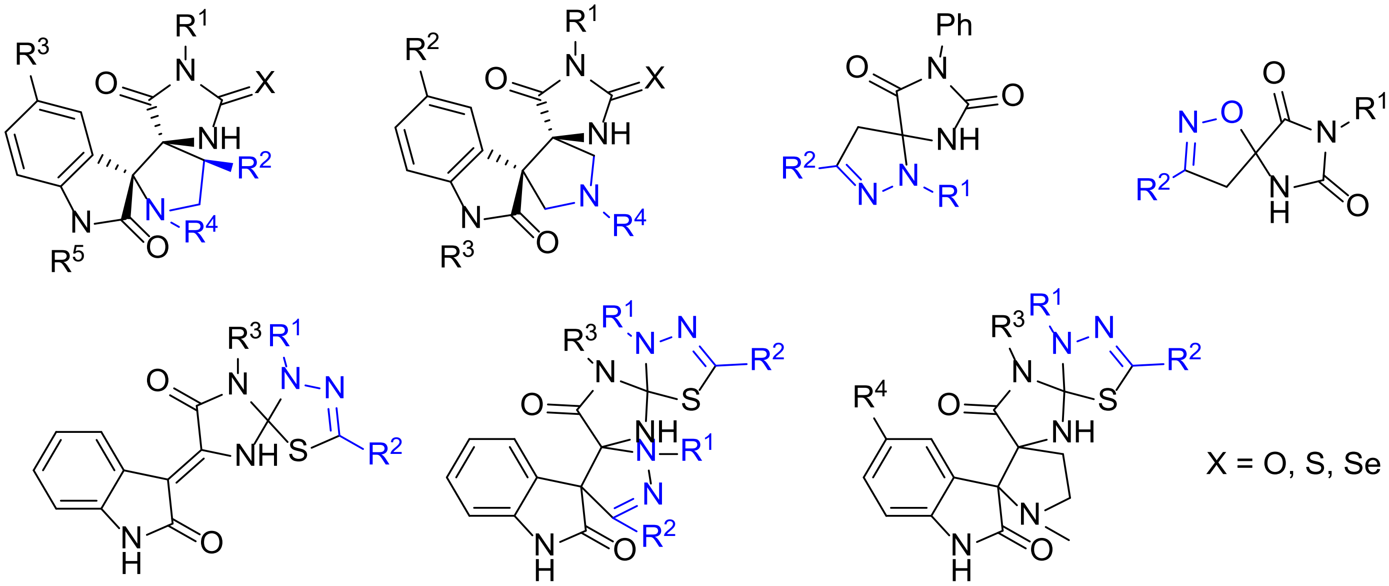
Spiro- and dispiro-conjugated heterocycles containing pharmacophore indolinone 2-chalcogenimidazolones fragments demonstrated high antitumor activity, which is usually associated with their limited conformational mobility, allowing them to maintain the spatial position of important substituents required for interaction with biotargets, and the ability of the indolinone fragment to act as inhibitors of BECN1, AKT1 kinase, and p53-MDM2 protein-protein interaction [1, 2].

We have shown the possibility to use 1,3-dipolar cycloaddition reactions of nitrogen-containing 1,3-dipoles of various structural types (azomethine ylides, nitrile oxides, nitrilimines) for the regio- and stereoselective synthesis of shown in the scheme below five-membered nitrogen-containing heterocycles, spiro-linked with imidazolone and indolinone fragments [3,4].



The proposed synthetic procedures make it possible to introduce into reactions both low-reactive dipoles and dipolarophiles, and highly reactive low-stable 1,3-dipoles.

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PROGRESS IN THE CHEMISTRY OF FUNCTIONALLY SUBSTITUTED FRAMEWORK PHOSPHONATES

Burilov A.R.[a], **Sadykova Yu.M.**[a], **Zalaltdinova A.V.**[a], **Smailov A.K.**[b], **Sennikova V.V.**[a], **Pudovik M.A.**[a], **Gazizov A.S.**[a]

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The chemistry of organophosphorus framework compounds has recently achieved significant progress, both in synthetic and applied aspects. To date, significant data have been accumulated in the literature on the synthesis of framework compounds, the cyclic backbone of which is formed from various types of endocyclic P–E bonds (E are oxygen, nitrogen, and carbon atoms). Practical interest in such rigidly structured structures is determined by the possibility of using them as complexing agents, ligands in metal complex catalysis, organocatalysts, and, importantly, drugs with a wide spectrum of action. Previously, we presented the results of a new cascade reaction of 2-ethoxyvinyldichlorophosphonate with various phenols, which makes it possible to obtain unknown symmetrical, asymmetric, regioisomeric framework phosphonates. The general method we proposed for their preparation did not allow the synthesis of framework phosphonates containing terminal functional groups (aldehyde, halogenmethyl, carboxyl, sulfamide, etc.). This report presents the latest data from studies of the reactions of 2-ethoxyvinyldichlorophosphonate with various phenols containing aldehyde, halogenmethyl, carboxyl, and sulfamide groups in the 4 position of the aromatic ring. The role of trifluoroacetic acid has been demonstrated, and a new mechanism for this unique cascade reaction has been proposed, which makes it possible to purposefully obtain new classes of framework phosphonates of a symmetric, asymmetric type containing terminal functional groups.

The reported study was funded by RFBR according to the research project № 20-03-00118-a.

NOVEL ROUTES TO HETEROATOM-FUNCTIONALIZED NHC-PROLIGANDS AND COMPLEXES M/NHC

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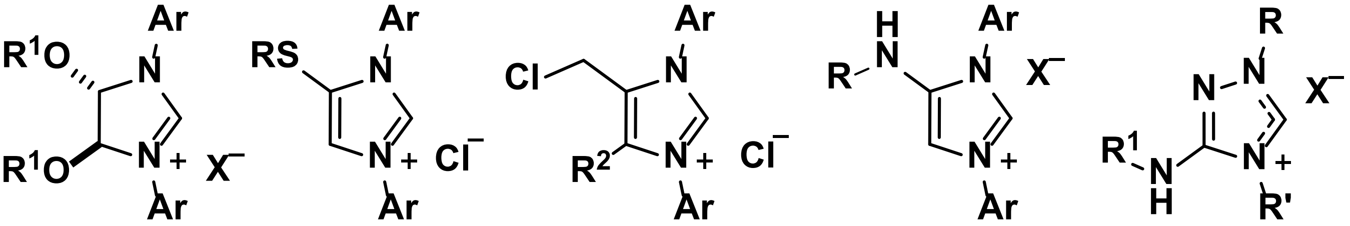
Azolium salts containing quite acidic C-H bonds are widely applied as precursors for N-heterocyclic carbenes (NHCs). Fine tuning of electronic, steric and other parameters of NHCs can often be provided via introducing heteroatomic substituents and functional groups in the heterocycle core.

Herein we discuss novel routes to diverse azolium salts, precursors of heteroatom-functionalized NHCs, and complexes of transition metals with the functionalized NHCs [1-3].



Effects of heteroatomic substituents in some of new Pd/NHC and Ni/NHC complexes on their catalytic properties are also considered.

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This work was supported by the Russian Science Foundation, grant 19-03-20058

STRAIGHTFORWARD ACCESS TO HIGH-PERFORMANCE ORGANOMETALLIC CATALYSTS BY FLUORIDE ACTIVATION

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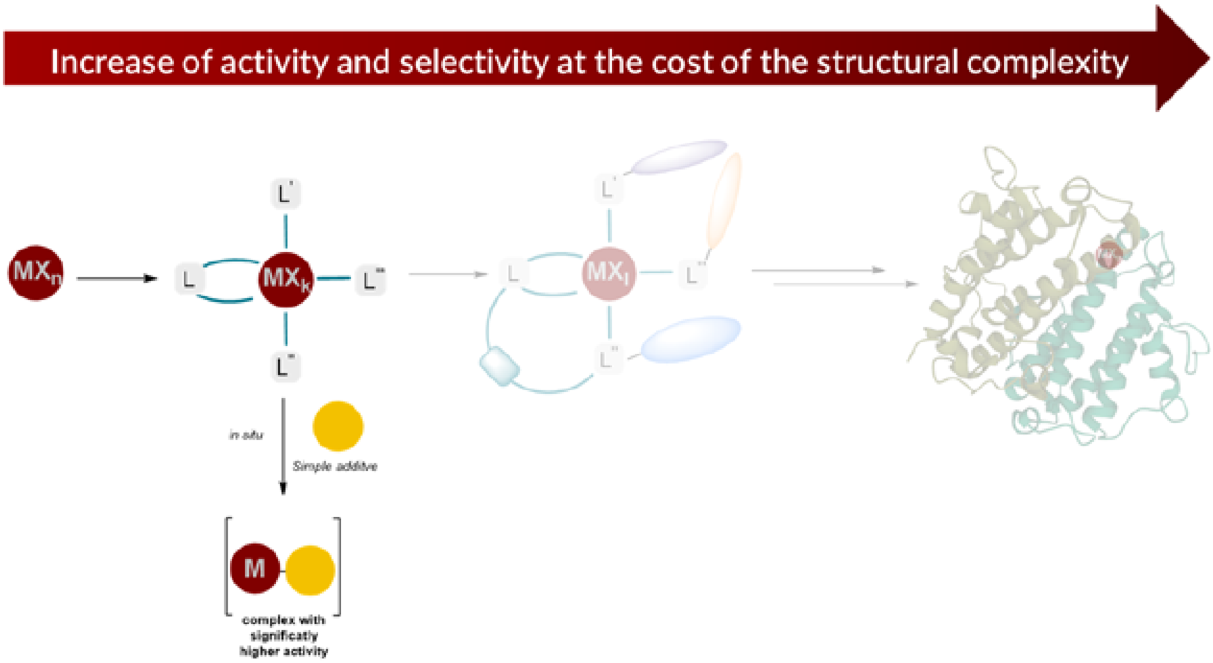
Catalysis plays a key role in a wide variety of chemical transformations in both academic and industrial settings. The development of active and selective catalytic systems is therefore an important research topic; however, the increasing structural complexity of emerging catalysts, together with the poor stability and difficult isolation of the most active catalytic species, emphasize the need for alternative strategies based on the in situ activation of well-established and relatively simple systems. The addition of active fluoride additive might provide an effective means for improving the performance of some existing catalysts. We demonstrated the effectiveness of this approach on four transformations. [1]



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The work was financially supported by the Russian Science Foundation (grant 21-13-00157).

AZOLO[1,5-a]PYRIMIDINES: SYNTHESIS AND REGIOSELECTIVITY OF TRANSFORMATIONS

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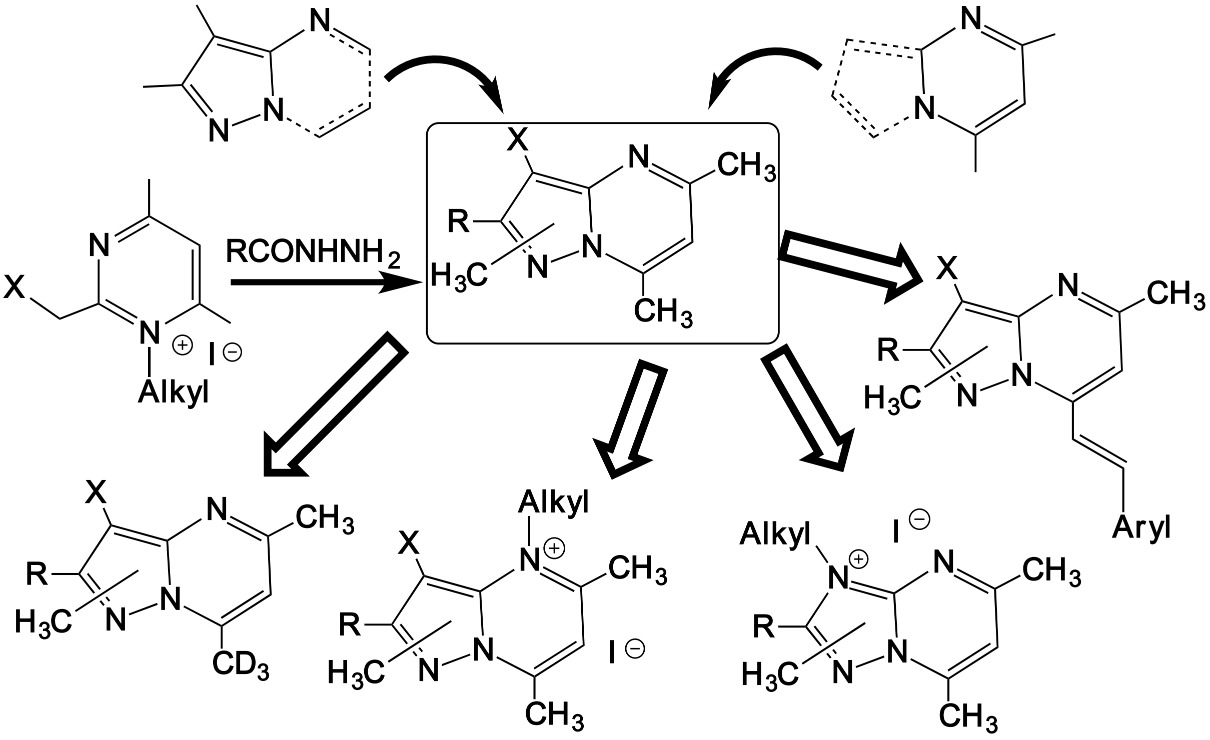
Various (traditional and unusual) routes for the synthesis of azolo[1,5-a]pyrimidines containing a bridging nitrogen atom will be presented. On the example of the reactions of deuteration and condensation with aromatic aldehydes, the regioselectivity of transformations is shown, which depends on the location of the methyl groups in the bicyclic system.

Depending on the type of azole connected to a pyrimidine ring, the regioselectivity of alkylation of azolo[1,5-a]pyrimidine was noted.



This work was carried out with the financial support of the State Committee on Science of the Republic of Armenia and the Russian Foundation for Basic Research (project 20RF-138 / 20-53-05010 Arm_a /), as well as within the framework of the grant of the Ministry of Education and Science of the Russian Federation for scientific research of the Russian-Armenian University.

HETEROCYCLIZATION REACTIONS OF MALONTHIOAMIDES

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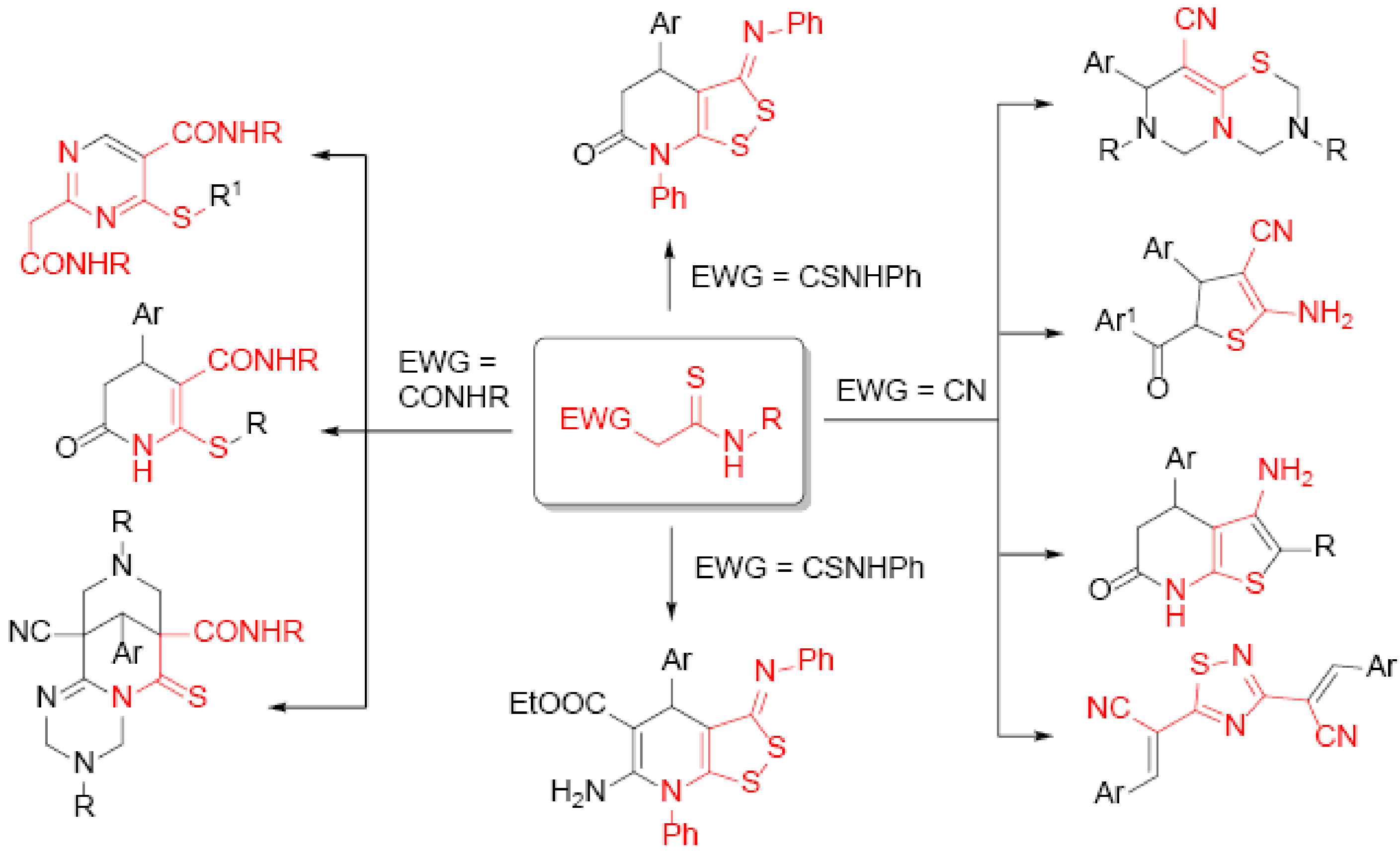
Malonthioamides are multifunctional reagents with several nucleophilic and electrophilic centers. They easily react with a wide range of electro- and nucleophilic agents to give a variety of cyclization products. We have studied the oxidation and reduction reactions of methylene active thioamides and developed the simple and efficient methods for the synthesis of the new compounds of 1,2,4-thiadiazole and oxirane-2-carboxamide series. The reactions of methylene active thioamides with a number of 1,3-dielectrophilic reagents have been studied comprehensively. Cascade methods for the preparation of polyheterocyclic ensembles based on cyanothioacetamide, N-(un)substituted malonthioamides and malondithiodianilide have been developed.



This work was financially supported by the Administration of the Krasnodar Region and the Russian Scientific Foundation (project N 22-23-00458).

FLUORESCENT TURN-ON PROBES FOR DNA/RNA BASED ON MONO- AND BI(STYRYL) DYES

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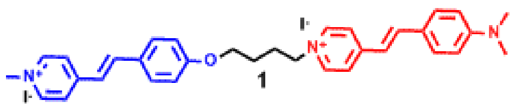
Cyanine dyes, in particular styryl dyes, exhibit remarkably high affinity towards nucleic acids along with a significant change of their photophysical properties upon DNA binding. These properties are used for DNA detection and quantification in a variety of methods and techniques such as the polymerase chain reaction, DNA fragment sizing, DNA staining, DNA damage detection, flow cytometry, and evaluation of biological activity. In this respect, DNA/RNA-binding properties of mono- and bis-styryl dyes were investigated in the presence of ct- DNA and cl-RNA. To access the factors that influence the nuclea association in the series of these ligands, the structure of the molecules was varied by either changing size of the heterocyclic moiety or altering the position of the styryl substituents. The major binding mode for the monostyryl dyes is intercalation, for bisstyryl dyes the interaction with DNA through the minor groove binding was found.



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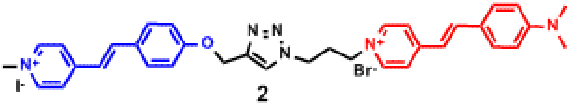
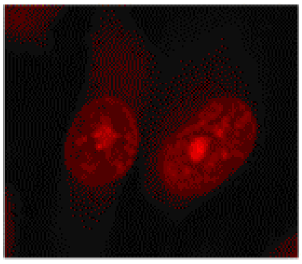
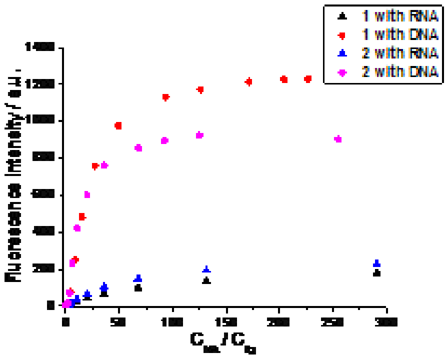
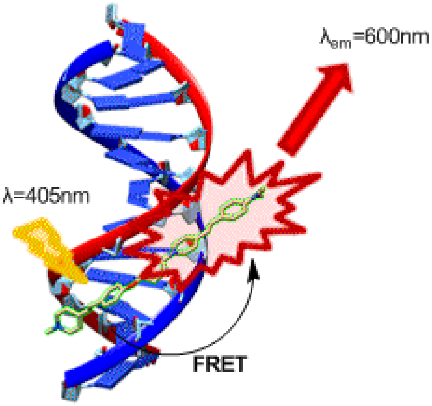


2

Fixed A549 cells + dye 1







Recently, we showed that asymmetric bi(styryl) dyes are fluorescence turn-on probes for intracellular DNA/RNA distribution. These fluorogenic dyes possess the properties of highly soluble in water, cell permeable, high photoresistance and not toxic to cells thus being promising dyes for biological and biochemical non-toxic applications.

This work was supported by RSF project № 21-73- 20158.

POLYNITROGEN HETEROCYCLES: SYNTHESIS AND APPLICATION

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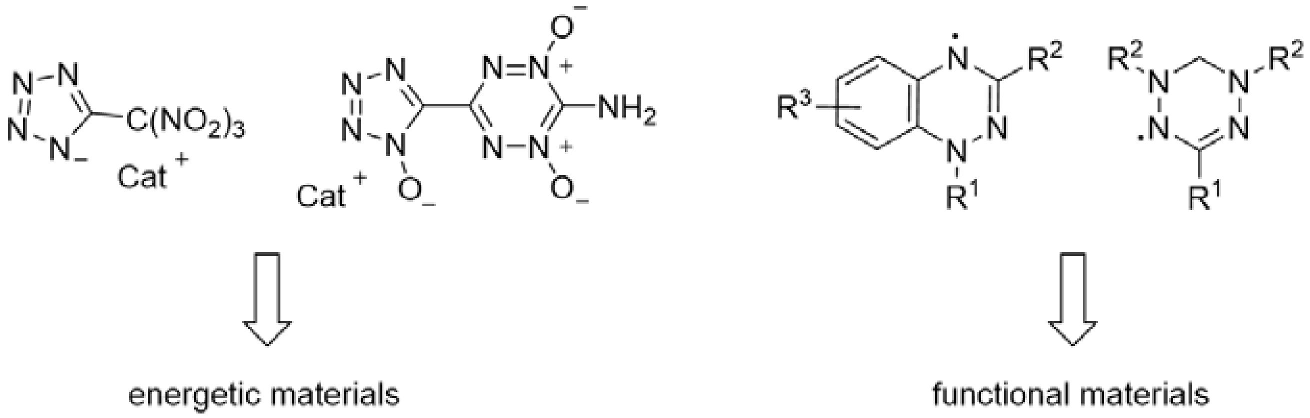
Polynitrogen heterocycles are of paramount importance in the design and preparation of novel organic materials. As a rule, polynitrogen heterocycles exhibit an optimal set of functional properties enabling their application potential in non-linear optics and/or energetic materials science. Herein, we present recent achievements of our research group in the synthesis of structurally diverse polynitrogen heterocyclic compounds incorporating tetrazole, tetrazine or 1,2,4-triazine ring. An estimation of crucial physicochemical parameters along with an application potential of the synthesized compounds as energetic or functional materials will also be discussed.



This work was supported by the Russian Science Foundation (project 21-73-10109).

REARRANGEMENT OF 4-ARYLBENZO[d]OXAZOLE DERIVATIVES. A NEW STRATEGY FOR THE SYNTHESIS OF PHENANTHRIDINES AND THEIR HETEROANALOGUES

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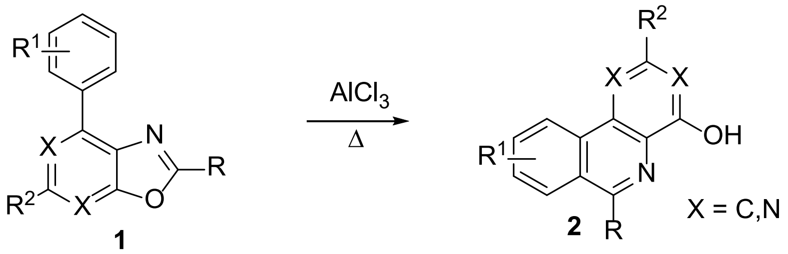
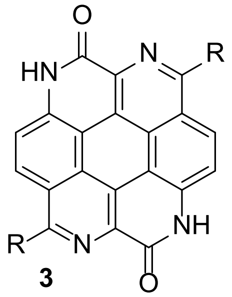
A new rearrangement of fused oxazoles **1** treated with aluminum chloride into synthetically hard-to-reach polycyclic derivatives of isoquinoline **2** was discovered. The rearrangements of 4-phenylbenzo[d]oxazole, 7-phenyloxazolo[5,4-b]pyridine, 7-phenyloxazolo[5,4-d]pyrimidine, 4-phenyloxazolo[4,5-c]pyridine and their fused derivatives were studied. This strategy was used to synthesize tetraazacoronene **3**.





The proposed reaction mechanism and key elementary reaction acts were studied in detail using quantum chemical calculations. The photophysical properties of the synthesized compounds were studied by UV-VIS spectroscopy and spectrofluorimetry. The obtained luminophores were used as dyes for enzyme immunoassay and for staining histochemical sections.

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This work was supported by the Russian Science Foundation (Grant no. 19-13-00273).

ACID-CATALYZED REACTIONS OF AMINOACETAL DERIVATIVES: ONE-POT ACCESS TO NITROGEN HETEROCYCLES

Gazizov A.S., Smolobochkin A.V., Rizbayeva T.S., Kuznetsova E.A., BurilovA.R., Pudovik M.A.

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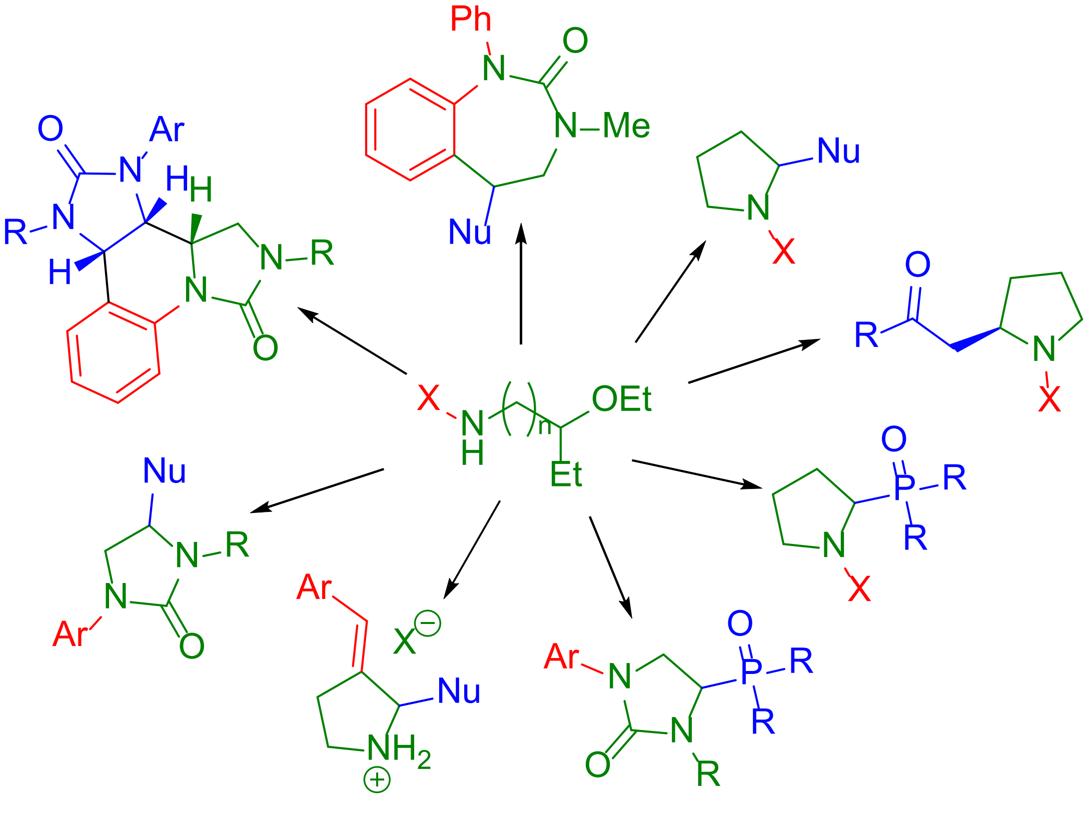
Nitrogen heterocycles play an essential role in both medicinal and organic chemistry due to their usefulness as versatile synthetic intermediates and biological importance. More than 75% of drugs currently available in the market are nitrogen-containing heterocyclic moieties and the number of novel *N*-heterocycles with promising applications is ever-growing. Thus, it is of no surprise that a lot of efforts are devoted to the development of novel approaches to these compounds.

Herein we summarize the results of our studies of acid-catalyzed cascade reactions of nitrogen-containing acetals various *C*- and *P*-nucleophiles and demonstrate their considerable potential in the synthesis of various classes of new heterocyclic compounds [1-3].



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This work was supported by the Russian Science Foundation, grant number 21-73-20020

N-NITROHETEROCYCLES: EASILY ACCESSIBLE, BENCH-STABLE AND BROADLY APPLICABLE REAGENTS FOR CATALYTIC NITRATION

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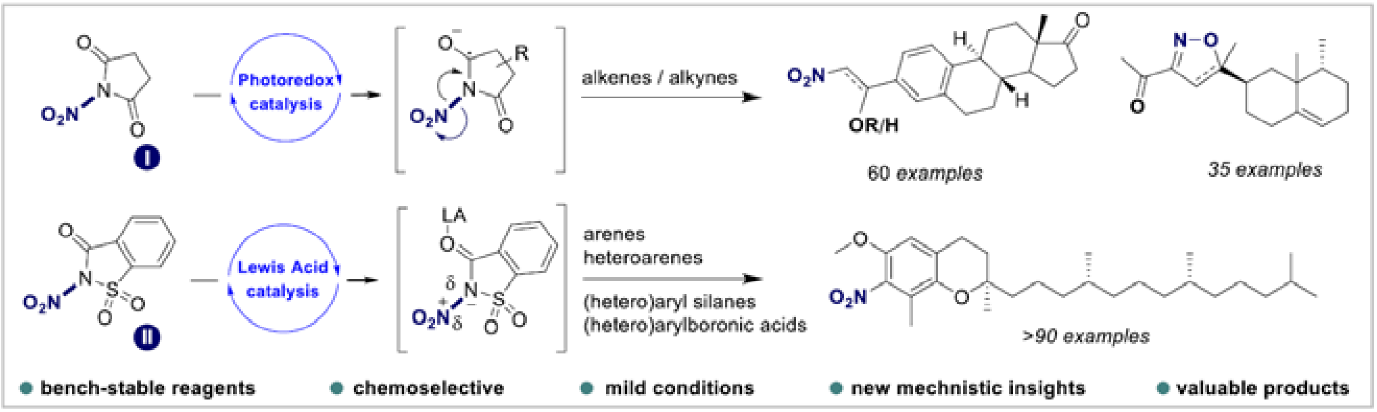
Nitro compounds are essential constituents of drugs and intermediates in the synthesis of biorelevant molecules, agrochemicals and materials. The most frequently exploited synthetic method for the nitration of various carbon−hydrogen bonds involves the use of a mixture of concentrated nitric and sulphuric acid. This methodology is limited in its application in the synthesis of complex molecules, since such harsh conditions do not tolerate acidsensitive functionalities, and results in numerous by-products. Herein, we report the design, synthesis and applications of one of the first, bench-stable non-metal based, organic nitrating reagents, which can be prepared from cheap, commercially available chemicals in one-step on a large scale [1,3]. These reagents act as a controllable source of both the nitronium ion using Lewis acid catalysis and the nitryl radical species using photoand electrochemical activation strategies. In the first case, broad range of Lewis acids were found to be efficient catalysts to promote nitration through the direct or *ipso*-substitution reaction of aromatic and heteroaromatic compounds. Due to the reagent's excellent reactivity and the very mild and neutral conditions of methods, reactions exhibit an unprecedentedly broad substrate scope, and were successfully used for the nitration of various pharmaceuticals, agrochemicals and materials. Detailed mechanistic studies strongly support an electrophilic reaction pathway, which was found to proceed through a unique and highly ordered transition state. Furthermore, a single-electron reduction enables the formation of NO_2 radicals in a controlled and selective fashion under visible-light photocatalytic as well as electrochemical conditions, allowing access to a broad range of nitrated molecules such as nitroolefins, **β**-nitrohydrines, isoxazole derivatives, etc. [2].



Scheme: Novel class of nitrating reagents and their use in organic synthesis (selected examples of applications).

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MULTICOMPONENT ASSEMBLY OF TRISUBSTITUTED IMIDAZOLES AND THEIR PHOTOCHEMICAL CYCLIZATION INTO FUSED POLYHETEROCYCLIC SCAFFOLDS

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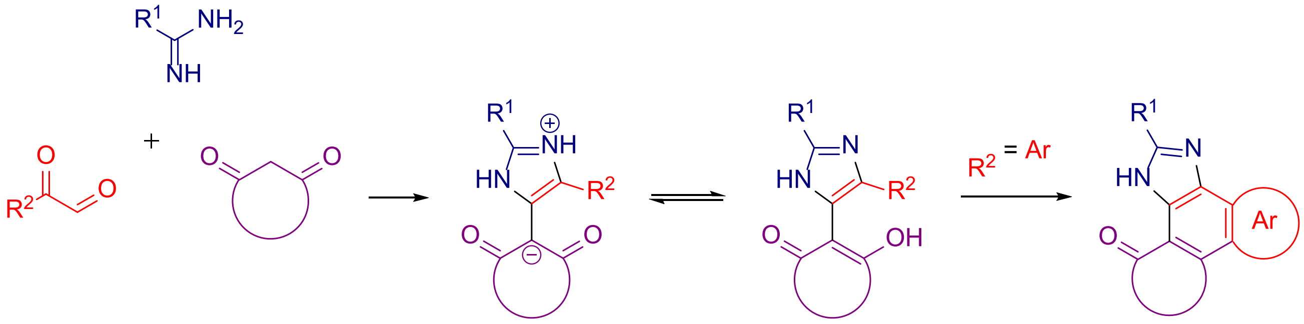
A straightforward route to a large and diverse library of trisubstituted imidazoles was established via three-component reaction of 2-oxoaldehydes, 1,3-dicarbonyl compounds and acyclic nitrogen bis-nucleophiles. The obtained products were subsequently explored in a photochemical cyclization yielding a variety of imidazole-fused polycyclic compounds.



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We are grateful to the Russian Foundation for Basic Research (grant 20-53-56002) and the Iranian National Science Foundation (grant 98029575) for the financial support.

SYNTHESIS AND BIOLOGICAL ACTIVITY OF NOVEL PURINE CONJUGATES

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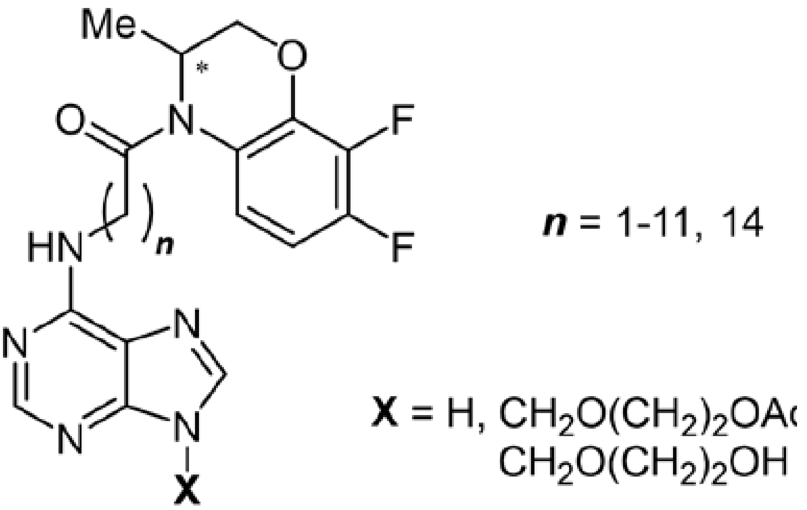
Purine derivatives play an important role in the biochemical processes in living organisms. Therefore, it seems promising to synthesize and study the biological activity of novel purine derivatives. As a result of our studies of various purine conjugates (or related compounds) with heterocyclic amines linked by an omega-amino acid fragment, we found a compound (***n*** = 5, **X** = H) exhibiting significant activity against herpes simplex virus type 1 (HSV-1).



The purpose of this study was to synthesize structural analogs of the lead compound and study their antiviral and antitumor activity.

As a result of the research, we found a series of compounds with high anti-herpesvirus activity against both the reference HSV-1/L2 strain and the acyclovir-resistant HSV-1/L2/R strain, as well as a number of compounds with high cytotoxic activity against human tumor cell lines. Some structure–activity relationships of the obtained compounds were revealed.

The work was financially supported by the Russian Science Foundation (project no. 19-13-00231).

NATURAL AND SEMI-SYNTHETIC PHENOLIC ANTIOXIDANTS AND BIOLOGICALLY ACTIVE SUBSTANCES

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Both alkylphenols and terpenophenols (meroterpenoids), a special class of semi-synthetic and natural compounds, can serve as the basis for the synthesis of new antioxidants and biologically active compounds. The development of polyfunctional stabilizers or hybrid structures capable of inhibiting oxidative processes by various mechanisms is the most promising direction in the improvement of phenolic antioxidants[1].

A series of previously undescribed polyfunctional derivatives, analogues of natural chalcones, coumarins containing terpene fragment, has been synthesized on the basis of isobornylphenols[2-4]. Studies of the antioxidant effect of new molecules have been carried out. Compounds with biocidal activity, which differ in the degree of activity and the width of the spectrum of action, have been identified, patterns of "structure-property" have been detected and leader compounds have been identified.

The wood greenery of spruce is a source of highly active phenolic compounds that are promising for the creation of natural environmentally friendly plant protection products. Natural phenolic compounds are capable of neutralizing free radical processes, performing a protective and stabilizing function in plant cells and growth-stimulating activity in plants[5]. We have studied the qualitative and quantitative composition of phenolic compounds of the emulsion extract of wood greenery of spruce.

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This work was financially supported by the Russian Science Foundation (Project No. 21-73-20091).

REARRANGEMENTS OF QUINOXALIN-2-ONES TO BENZIMIDAZOLE(ONE)S

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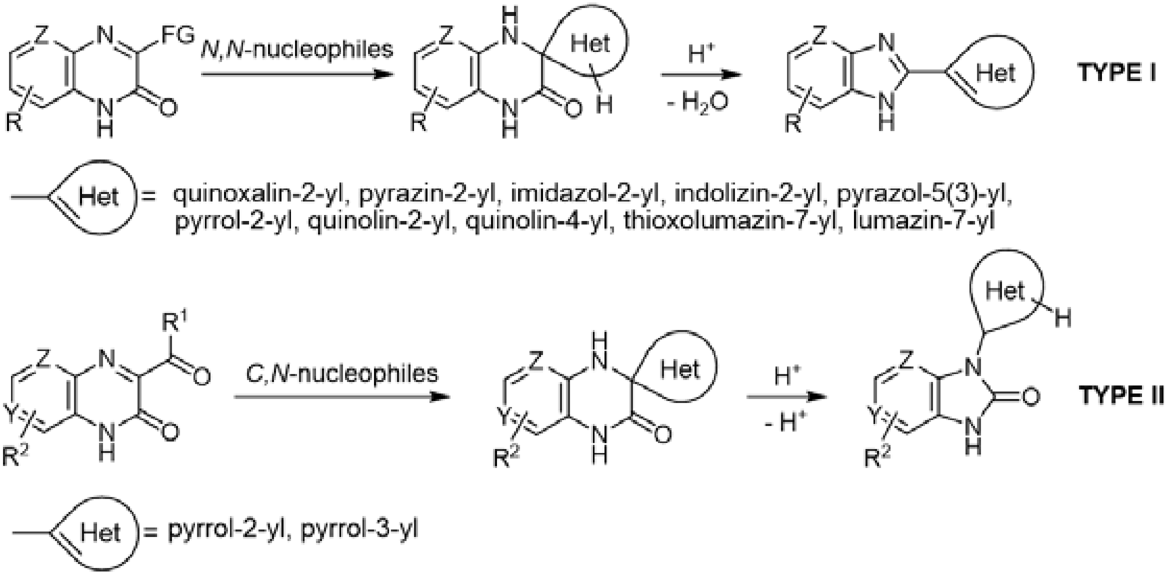
Two types of acid-catalyzed rearrangements of quinoxalin-2(1H)-one derivatives are discussed, which proceed when exposed to various *N,N*[1-6]and *C,N*-nucleophilic[6-9] reagents via the spiro-compounds with (TYPE I) or without (TYPE II) a mobile hydrogen atom in the spiro-forming fragment. Rearrangement of TYPE I leads to 1-hetarylbenzimidazoles, and rearrangement of TYPE II leads to 2-hetarylbenzimidazolones.



Depending on the nature of the substituent in position 3 and the nature of the nucleophilic reagent, the rearrangements under consideration make it possible to synthesize various types of biheterocyclic structures with benzimidazole and benzimidazolone systems.

The possibility of synthesizing a wide variety of 3-substituted derivatives of quinoxalin-2(1*H*)-it and the availability of a number of nucleophilic reagents indicate the broad possibilities of TYPE I and TYPE II rearrangements. Rearrangements are also applicable for aza-analogues of quinoxalin-2(1*H*)-ones, which significantly expands their synthetic potential.

This work was financially supported in part by the Russian Science Foundation (18-13-00315-n).

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POLYCARBONYL COMPOUNDS IN THE SYNTHESIS OF HETEROCYCLES: NEW DATA

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Nucleophilic and pericyclic transformations of polycarbonyl compounds, dioxoheterocycles and heterocumulenes, including cascade and multicomponent heterocyclizations and recyclizations, Diels-Alder reactions and dipolar cycloaddition reactions have been studied. New approaches to the construction of heterocyclic systems similar to biologically systems have been developed.

Cascade nucleophilic recyclizations and heterocyclizations of polycarbonyl compounds and dioxoheterocycles (substituted furan-2,3-diones, 1H-pyrrole-2,3-diones, and hetareno[e]pyrrole-2,3-diones) represent new directions in the construction of previously inaccessible and inaccessible carbonyl derivatives of heterocycles, fused, bridged and various spiro-bis-heterocyclic systems.

Multicomponent reactions of 1H-pyrrole-2,3-diones, including hetareno[e]pyrrole-2,3-diones - a method of nucleophilic “superstructure” of the pyrroledione ring with various types of spiro-heterocycles.

The toxicity, antimicrobial, anti-inflammatory, analgesic, antihypoxic, psychotropic and other types of biological activity of the representatives of the synthesized compounds have been studied. Most of the studied compounds are derivatives of acylpyruvic acids, structurally close to the natural metabolites of a living organism, which justifies the search for biologically active substances among the synthesis products.

The report presents the results of more than 40 published articles and more than 10 patents of the Russian Federation for synthesis methods and physiological activity for 2019-2022.

This work was supported financially by the Russian Ministry of Education and Science (Project No. FSNF-2020-0008).

RHODIUM(III)-CATALYZED C-H ACTIVATION/ ANNULATION OF (HETERO)ARENES WITH ACETYLENE-CONTAINING AMINO ACID DERIVATIVES

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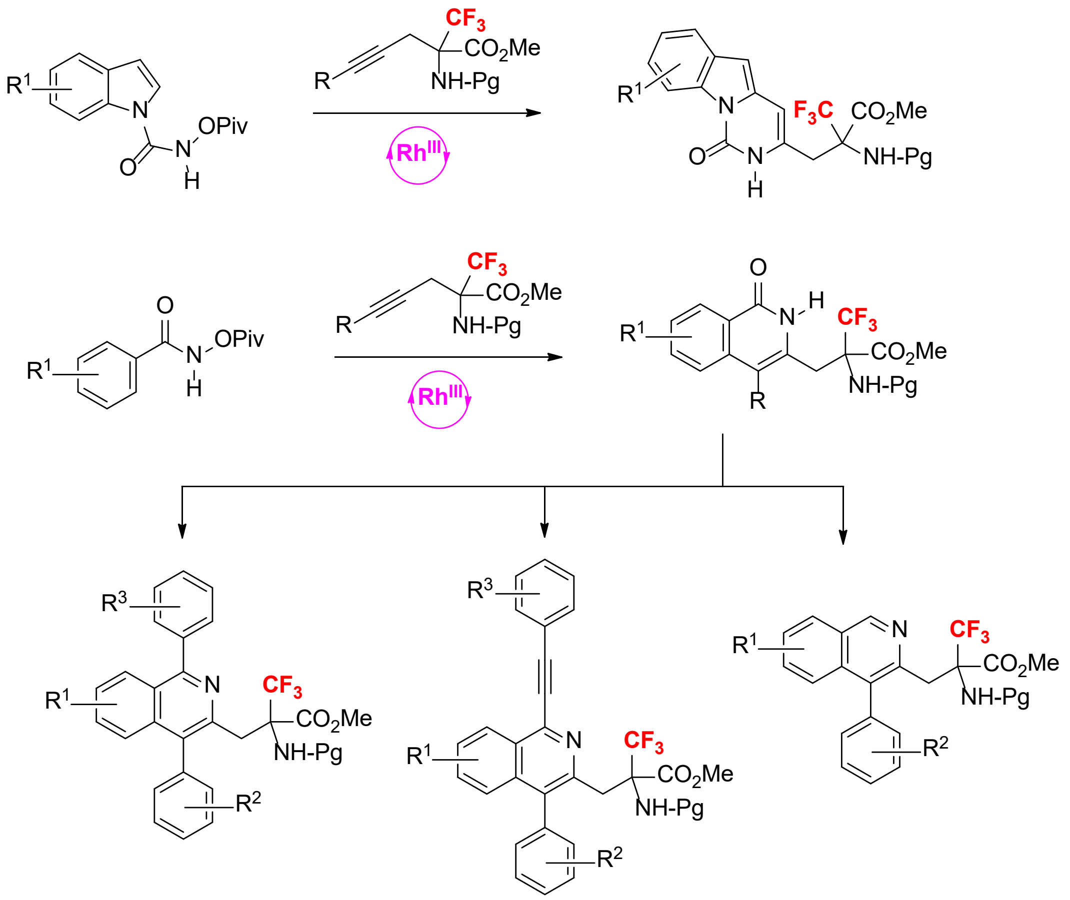
An efficient and highly selective method for the preparation of various hetaryl-containing α-CF_3-α-amino acid derivatives has been developed based on rhodium(III)-catalyzed C-H activation/annulation of (het)aryl hydroxamates with functionalized acetylenes.[1,2]



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This work was financially supported by the Russian Science Foundation (grant RSF No 21-13-00328).

3-NITRO-4*H*-CHROMENES AND 3-NITROBENZOFURANS: PREPARATION AND CHEMICAL TRANSFORMATIONS

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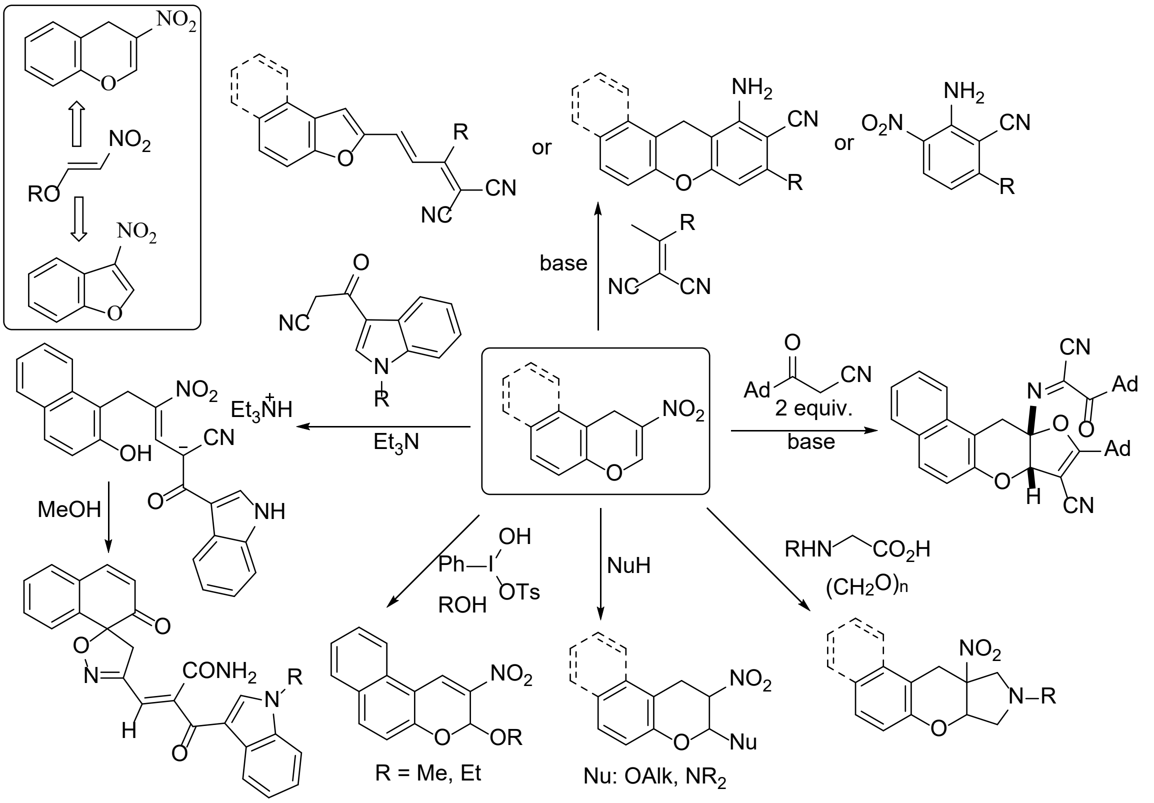
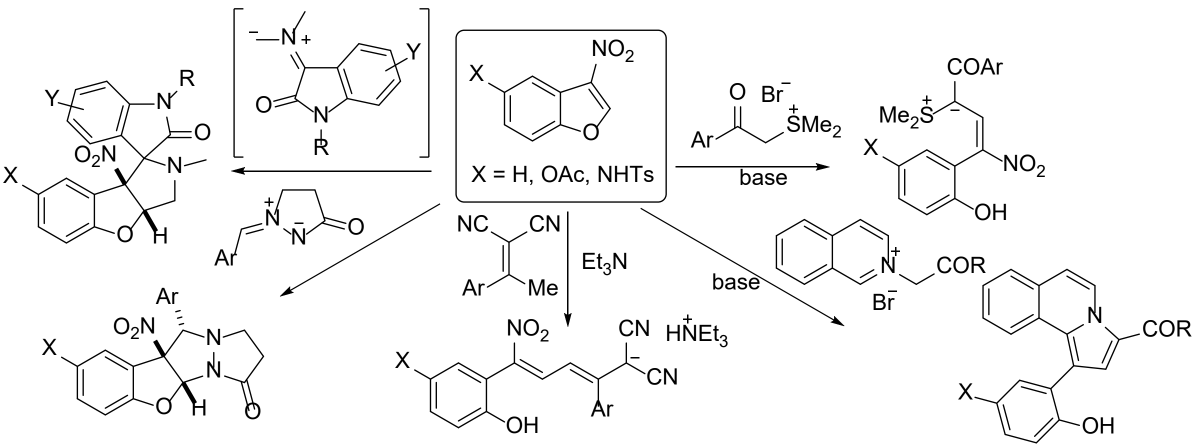
When a nitro group is introduced into the β-position of 4*H*-chromene or benzofuran, umpolung of these heterocycles occurs. The nucleophilic nature of the pyran/furan ring, because of the presence of a vinyl ether fragment, changes to an electrophilic character due to conjugation with an acceptor group. This is especially true for 2-unsubstituted heterocycles, since the presence of a substituent (usually a donor group) in this position, for electronic and sterical reasons, sharply reduces the susceptibility to conjugated addition reactions. We have shown that such heterocycles, which are structural analogues of cyclic β-nitrovinyl ethers, react with different nucleophiles under Michael reaction conditions and enter into [3+2]-cycloaddition reactions with various 1,3-dipoles. Wherein, in the case of 3-nitrobenzofurans, dearomatization of the furan ring occurs.





This work was supported by the Russian Science Foundation (grant 19-73-10109).

SYNTHESIS, STRUCTURE, AFFINITY TO BENZODIAZEPINE RECEPTORS, AND PHARMACOLOGICAL PROPERTIES OF 3-ARYLIDENE-, HETERYLYDENE-1,4-BENZODIAZEPINES

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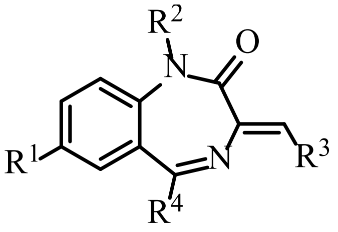
Derivatives of 1,4-benzodiazepine have been widely used in medical practice since the 1960s, mainly as psychotropic, anticonvulsant, hypnotic, anxiolytic, and other types of drugs. Currently, more than 50 original compounds are used in medical practice as pharmaceutical substances. Basically, they are ligands of central or peripheral benzodiazepine receptors. Also, among these compounds are ligands of CCK_1 and CCK_2 receptors, antagonists of bradykinin.

As a result, they have the properties of anorexigenic and orexigenic (affecting food intake) [1-3], or analgesic and anti-inflammatory drugs [4, 5].

A number of derivatives of 3-arylidene-, heterylidene-1,4-benzodiazepines of general formula **I** were synthesized, their structure, affinity to benzodiazepine receptors, and pharmacological properties were investigated.



I

R^1 = H, Br; R^2 = H, Alkyl; R^3 = Ar, HetAr;
R^4 = Ar, HetAr, VinilAr, VinilHetAr

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BLUE LIGHT-PROMOTED CROSS-COUPLING OF DIAZO ESTERS WITH ISOCYANIDES: SYNTHESIS OF FUNCTIONALIZED KETENIMINES

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Ketenimines are reactive compounds which are widely used in organic synthesis [1]. There are a number of reliable methods for the synthesis of ketenimines, which include the Wittig and aza-Wittig reactions, alkylation of nitrile anions, dehydrochlorination of imidoyl chlorides, dehydration of amides, etc. One of the attractive and perspective ways to access functionalized ketenimines is an addition of isocyanides to carbenes derived from diazocarbonyl compounds. In recent years, the coupling of isocyanides with diazo compounds has undergone a revival due to the application of transition metal catalysis. In particular, palladium catalysis has been the most actively studied [2]. Several examples of the application of rhodium [3] and cobalt catalysis [4] have also been published. Despite the impressive progress in the metal-catalyzed synthesis of ketenimines, the development of a mild metal-free synthesis continues to be important, since removing trace amounts of toxic transition metals from pharmaceuticals remains a long-standing problem.

In this work, a metal-free scalable synthesis of functionalized ketenimines from alkyl α-(aryl/heteroaryl)-α-diazoacetates and alkyl isocyanides induced by blue light irradiation has been developed [5] (Fig. 1). The reaction proceeds at room temperature without any photocatalyst and provides ketenimines in moderate to good yields. DFT calculations and experimental study showed that aryl(alkoxycarbonyl)carbenes in both singlet and triplet states can react with isocyanides, but only the reaction of the former leads to the smooth formation of ketenimines. The obtained ketenimines were used for the synthesis of functionalized amidines under mild metal-free conditions.

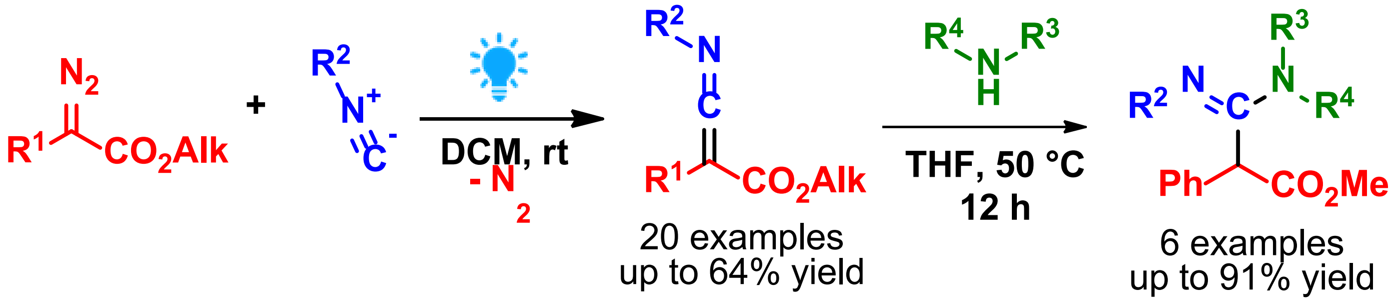

Figure 1. Metal-free synthesis of ketenimines and amidines.

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Acknowledgements. This work was supported by the Russian Science Foundation (project No 19-73-10090). This research used resources of the Magnetic Resonance Research Centre, Chemical Analysis and Materials Research Centre and Computing Centre of the Research Park of St. Petersburg State University.

FROM ACETYLENE GAS TOWARD A MOLECULAR COMPLEXITY AND DIVERSITY

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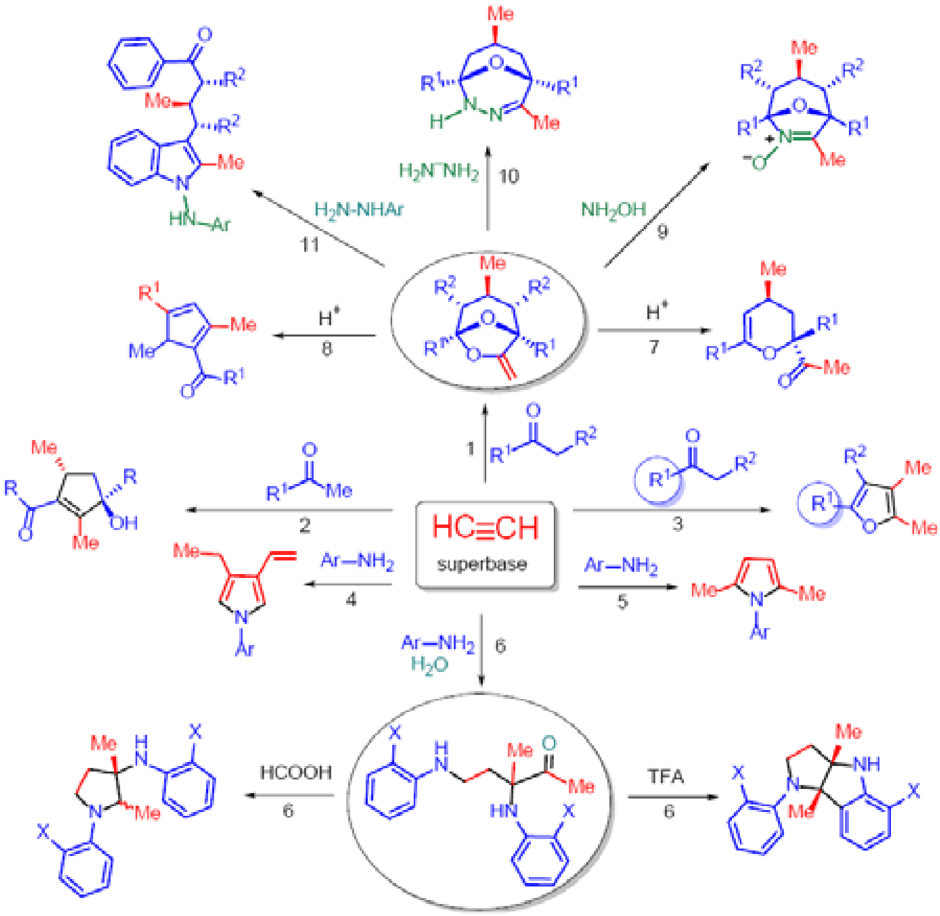
Cascade multi-component syntheses of complex functionalized structures with the simultaneous participation of several acetylene molecules and the simplest nucleophiles in superbase media are discussed.



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This work was financially supported by a grant from the Russian Science Foundation (project no. 19-13-00052).

DEVELOPMENT OF ANTITUMOR LIGANDS OF THE NON-CANONICAL STRUCTURES OF NUCLEIC ACIDS

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The non-canonical structures of nucleic acids were founded in some disease-related genes. Thus, four-stranded guanidine-rich (G-quadruplexe, G4) or cytosine-rich quadruplex (I-motif) elements of the secondary structure of nucleic acids have been discovered in the telomeric regions of DNA, promoter regions of oncogenes and in untranslated mRNA sequences. Low-molecular weight compounds which can bind with non-canonical structures inhibited or dysregulated of important biological process including gene transcription or the cell proliferation. Ligands which can stabilize G-quadruplexes or I-motifs considered as promising candidates for the anticancer drug development.

Based on linear heteroareneanthracenediones we have designed and prepared series ligands with high affinity for different G4s of DNA or RNA. Firstly, an original bisguanidine derivative of anthra[2,3-b]thiophene-5,10-dione, which has a high affinity for telomeric quadruplex and G4 from promoters of oncogenes was discovered [1]. The side chains optimization, via a replacement of guanidine groups with the chloroacetamidine groups, lead to G4-ligands with significant improved penetration in tumor cells [2]. Strong stabilization of G4 hras-2 (form hRAS promoter) with selected ligands caused a decreasing of the accumulation of the p21hRAS protein (the product of translation of hRAS oncogene) in T24 bladder cancer cells and induced apoptosis in tumor cells. The introduction in the heterocyclic moiety of an additional side chain with guanidine group lead to discovery of «tri-armed» G4-ligands which have a higher affinity for telomeric G4 and a significantly higher selectivity [3]. As part of the screening of G4 RNA ligands, it was found that derivative of 4,11-diaminoanthrafurandione has a high affinity for the G4 from 5′-untranslated region of the KRAS oncogene mRNA [4].

Based of tetra(4-pyridinyl)porphyrin scaffold we have obtained photoactivated G4-ligands which capable efficiently penetrating into tumor cells [5]. These cationic porphyrins in nanomolar concentrations after irradiation (660 nm) cause ROS-induced degradation of G4s in untranslated region of KRAS mRNA that lead to block KRAS synthesis in tumor cells. The effectiveness of these ligands as a new antitumor photosensitizer was confirmed in the model of pancreatic cancer xenografts Panc-1.

Finally, we have developed an original method for the introduction of aminoalkylamino-groups into poliketide antibiotic heliomycin [6]. This modification of the heliomycin can modulate their affinity to different DNA secondary structures, including G4s and I-motifs. Moreover, we identified one derivative (7-deoxy-7-(2-aminoethyl)amino-10-*O*-methylheliomycin) demonstrated strong affinity, stabilization potential and good selectivity towards i-motif-forming DNA sequences over duplex and G4s.

Thus, some promising directions in the development of ligands of non-canonical structures of nucleic acids have been developed.

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NEW HETARYL AND ENAMINO DERIVATIVES OF 4-PYRONE WITH USEFUL PROPERTIES

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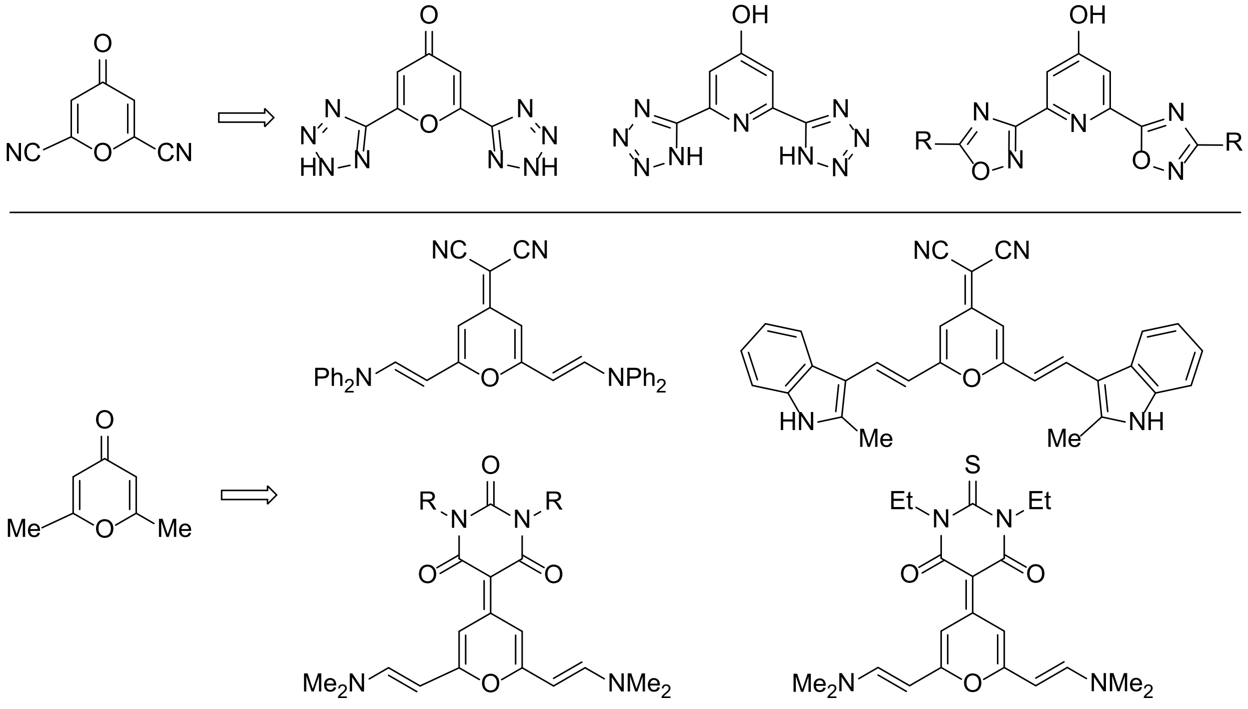
Despite their natural origin, diverse biological activity and high reactivity of substituted 4-pyrones, many representatives of this class of oxygen-containing heterocycles are still among the little-studied molecules. This is especially true of 2,6-(bis)hetaryl-4-pyrones, including 2,6-(bis)hetaryl-4-pyridinols as useful ligands, which can be easily obtained from 4-pyrones, and enamino derivatives of 4-methylene-4*H*-pyranes with interesting optical properties. The report will consider the most important chemical properties of 2,6-dicyano-4-pyrone and 2,6-dimethyl-4-pyrone [1,2].



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This work was supported by the Russian Science Foundation (grant no. 18-03-00186).

BORON(III) AND PHOSPHORUS(V) DERIVATIVES OF PORPHYRAZINOIDS

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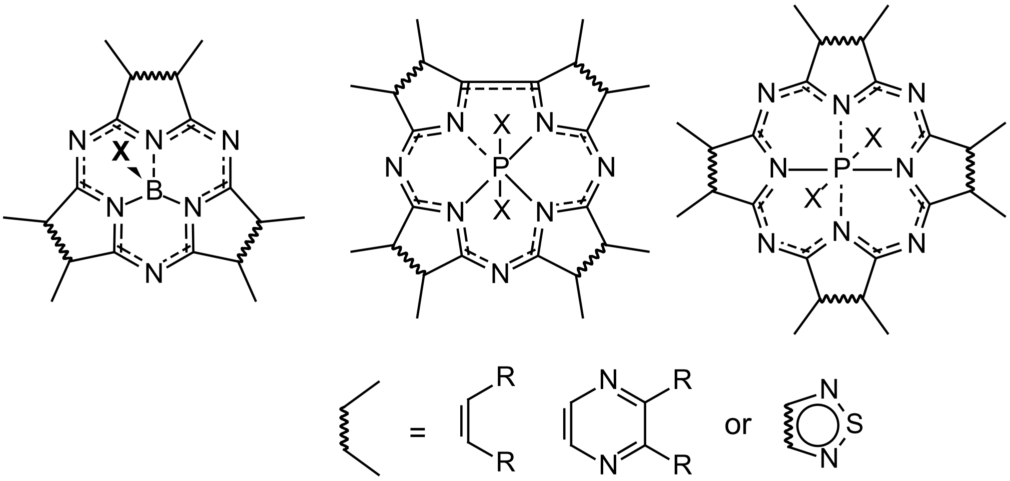
Porphyrazines with fused electron-deficient heterocycles (pyridine, pyrazine, 1,2,5-thia(selena)diazole) due to their enhanced electron affinity widely studied as perspective functional materials for application in organic electronics as n-type semiconductors, in bioimaging as pH-sensitive fluorophores and in other fields. We present our recent results on preparation of novel porphyrazines, their derivatives with fused heterocycles and ring contracted analogues - corrolazines and subporphyrazines containing boron(III), or phosphorus(V)) as a central atom and discuss their spectral-luminescence, photophysical, electrochemical and other properties [1-7].



This study was supported by Russian Foundation and Basic Research (grant 20-53-26004) and Russian Science Foundation (grant 13-17-01522)

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NEW DIAMONDOID STRUCTURES DOPED WITH MULTIPLE HETEROATOMS AND METALS

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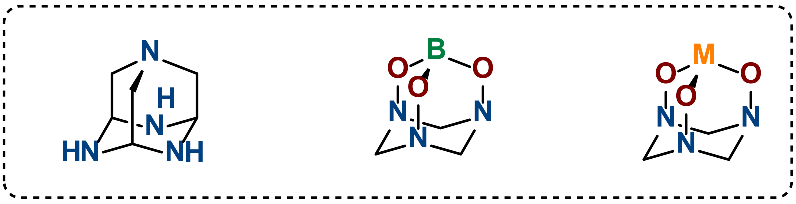
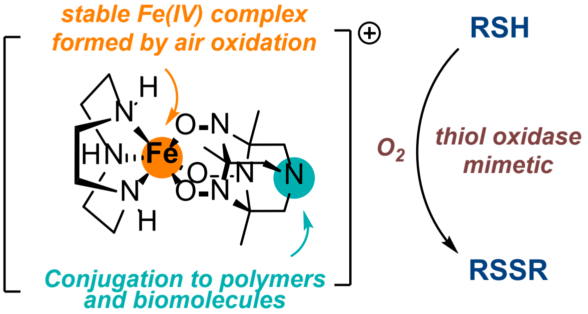
Diamondoid molecules, such as adamantane and diamantane derivatives, find applications in the design of pharmaceticals, ligands, polymers, high-energy materials and supramolecular structures [1]. The replacement of carbon atoms by heteroatoms opens up vast opportunities for tuning the properties of diamondoid scaffold allowing the design of substances and materials with pre-defined characteristics. Accordingly, the synthesis of new types of diamondoids doped with heteroatoms and metals is an urgent task from both applied and fundamental points of view.

The talk will outline our research group's recent achievements in the synthesis of novel hetero/metalloadamantane and diamantane frameworks, some of which are shown below [2–4]. Applications in catalysis and bioconjugate chemistry will be also discussed.





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This work was supported by the Russian Foundation for Basic Research (grant 20-03-00510).

ENERGETIC TRIAZOLES AND TETRAZOLES

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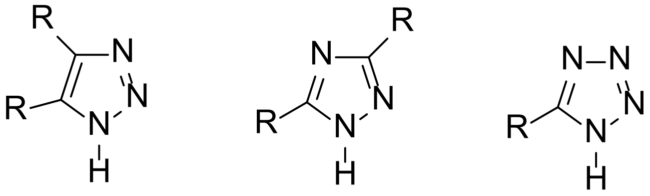
Polynitrogen aromatic five-membered heterocycles, isomeric triazoles and tetrazoles, are well-known accumulators of chemical energy [1]. They have a number of practically valuable properties that determine the possibility of their use as energy-rich substances, biologically active compounds, sensors, etc. These compounds can act as acids and bases, hydrogen bond donors and acceptors, as well as effective ligands in coordination with metal ions. The introduction of various fragments into the structure of these heterocycles, their combination in the form of salts with organic and inorganic ions, and bonding with metals makes it possible to obtain compounds with desired and very diverse properties.



A number of energy-rich triazoles and tetrazoles are very stable and safe substances to handle. The decomposition of such compounds usually proceeds with the evolving of molecular nitrogen and the release of a significant amount of energy.

The report discusses published data on the synthesis, properties and practical application of such compounds, as well as the ways for the development of this field of chemistry of heterocyclic compounds.

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The work was supported by the Russian Foundation for Basic Research, projects 20-53-00039-Bel_a and 20-53-05010 Arm_a.

DONOR–ACCEPTOR CYCLOPROPANE OPENING WITH NITROGEN-CONTAINING NUCLEOPHILES AS AN APPROACH TO THE SYNTHESIS OF AZAHETEROCYCLES

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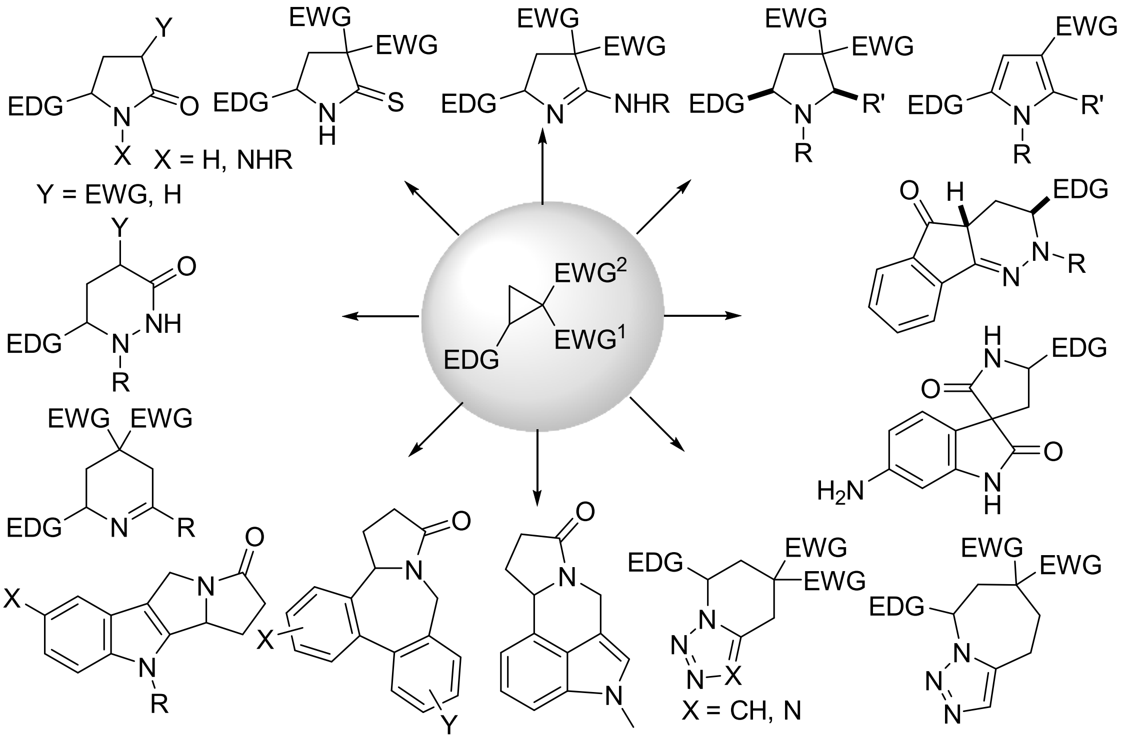
Cyclopropanes bearing donor and acceptor substituents at the vicinal positions (donor–acceptor, or D–A, cyclopropanes) demonstrate high reactivity towards diverse nucleophiles, the formed products being capable for transforming to diverse heterocyclic compounds either *in situ*, or after modification of a functional group in the primary products. For example, in reactions with diverse amines, D–A cyclopropanes served as 1,4-dielectrophiles, providing pyrrolidine-2-ones *via* three-membered ring opening and cyclization. Hydrazines reacted with D–A cyclopropanes as either 1,1- or 1,2-dinucleophiles affording 1-aminopyrrolidones of tetrahydropyridazin-3-ones respectively. Reactions of D–A cyclopropanes with ambident thiocyanide ion produced pyrrolidine-2-thiones (*via N*-attack) or 2-amino4,5-dihydrothiophenes (*S*-attack) depending on the reaction conditions and nature of donor group in cyclopropanes. 1,3-Substituted 5-aminopyrazoles behave also as ambident nucleophiles towards D–A cyclopropanes reacting by either C(4) or exocyclic nitrogen atom; the cyclization of the C-alkylated products yielded pyrazolo[3,4-*b*]azepine derivatives. Oppositely, 1,3-dialkyl-6-amino-uracils was found to be alkylated with D–A cyclopropanes at the C(5) atom exclusively; the following cyclization gave rise to the corresponding pyrimido[4,5-*b*]azepines. Products of D–A cyclopropane ring opening with azide ion were transformed into a broad variety of azaheterocycles. Most of the synthesized heterocycles are of considerable interest for medicinal chemistry and pharmacology.



This work was supported by the Russian Science Foundation (grant 21-13-00395)

TRIFLUOROMETHYL SUBSTITUTED CARBOCATIONS IN ORGANIC SYNTHESIS

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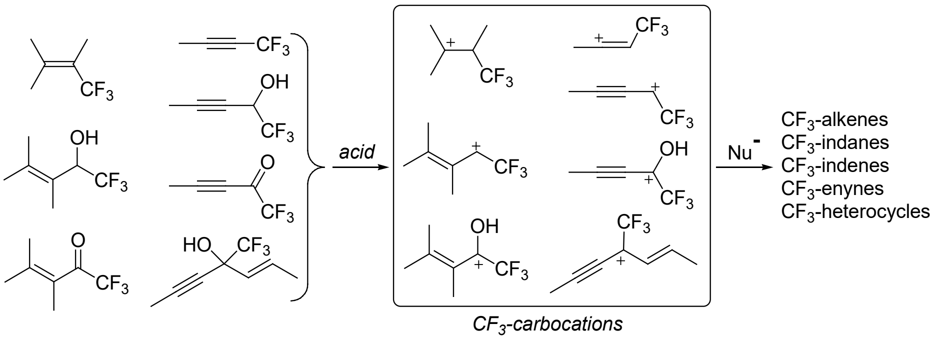
Under the action of Brønsted or Lewis acids, the corresponding CF_3 carbocations can be generated from CF_3-substituted organic compounds (alkenes, alkynes, unsaturated allyl and propargyl alcohols, carbonyl derivatives). These cationic species are highly reactive intermediates. Their transformations lead to the preparation of a variety of fluorinated substances, including carbo- and hetero-cyclic structures [1-3]. Many of the synthesized CF_3-substituted compounds possess unique biologically active properties.



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This work was carried out with the financial support of the Russian Scientific Foundation, grant no. 21-13-00006.

BISPIDINES IN CATALYSIS

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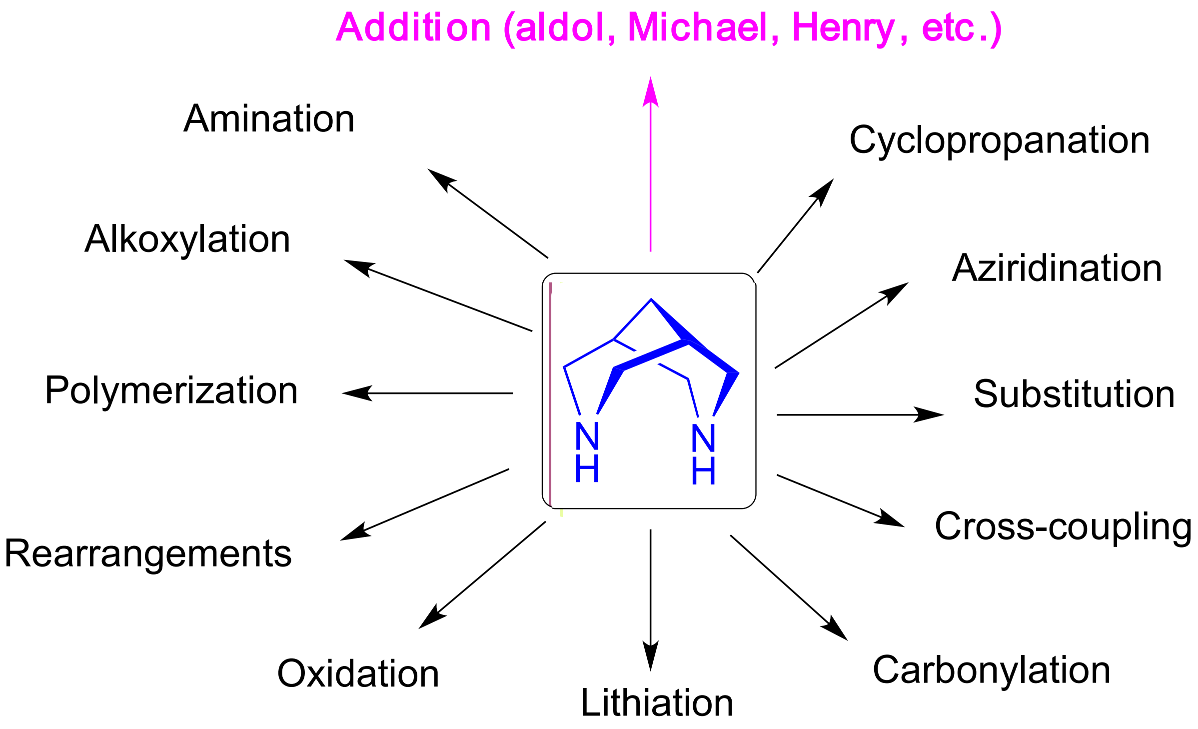
3,7-Diazabicyclo[3.3.1]nonane scaffold (*aka* "bispidine") found its application in various fields of medicinal chemistry and catalysis (see a chapter on review[1]) including both metal-mediated processes, organocatalysis and supramolecular catalysis. In this report the review of the recent developments in bispidine catalytic chemistry is presented together with our own results on application of chiral bispidine-terpene conjugates to Michael addition, addition of diethylzinc to chalcones[2] and Henry reaction[3].



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This work is financially supported by the Russian Science Foundation (grant 19-73-20090).

NEW SYNTHETIC METHODS AND REAGENTS IN ORGANOPHOSPHORUS AND ORGANOMETALLIC CHEMISTRY

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The search for new ecologically friendly and resource saving methods for preparation of various coordination and organoelement compounds and materials bearing practically useful chemical and physical properties are key priority of modern synthetic chemistry. A combination of the electrochemical techniques with classical chemical synthesis can be considered as a powerful tool for preparation of various catalysts, biologically active molecules, ligands for transition metal complexes and new types of mono- and polynuclear complexes and clusters. Moreover, the discovery of new high reactive reagents and new methods for preparation of organophosphorus and organometallic compounds are of high fundamental and practical interest.[1,2]

It this lecture the recent results obtained in the field of application of the electrochemical techniques and new high reactive reagents towards preparation of various types of organoelement and coordination compounds are discussed. Special attention will be paid to the use of the electrochemically generated high reactive phosphine oxide H_3PO[3,4] and organonickel sigma-complexes, including some pincer-type species,[5] served as efficient catalysts for various organic coupling processes and the catalytic reduction of carbon dioxide,[6] activation of P-P bonds in polyphosphorus ligands by organic reagents and the preparation of new metal-free catalysts for hydrogen evolution reaction.[7]

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This work is financially supported by the grant of the President of the Russian Federation for supporting of the Leading Scientific Schools (project no. 4078.2022.1.3) and the Ministry of Science and Higher Education of the Russian Federation (project 0671-2020-0061).

PREPARATION AND APPLICATION OF NOVEL ORGANOHYPERVALENT HALOGEN COMPOUNDS

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Organohypervalent iodine compounds are very common reagents, widely used in chemistry area and biology [V. V. Zhdankin, *Hypervalent Iodine Chemistry: Preparation, Structure and Synthetic Application of Polyvalent Iodine Compounds*, John Wiley & Sons Ltd, 2014]. However, organic hypervalent compounds of other halogens such as bromine, chlorine, and fluorine remain essentially unknown and no significant progress in this area has been reported in recent literature [G. Cavallo, J. S. Murray, P. Politzer, T. Pilati, M. Ursini and G. Resnati, *IUCrJ*, 2017, **4**, 411-419; Halogen bonding in hypervalent iodine and bromine derivatives: halonium salts]. The main reason for the lack of success is that bromine, chlorine, and fluorine have higher electronegativity than iodine and therefore, these elements have higher oxidation potential than iodine.

Aryl compounds are very useful in various synthons, bioactive compounds, or synthetic resins. The proposed diarylhalonium reagents can be utilized as powerful electrophilic aryl transfer reagent for various nucleophiles or substances resulting in the formation of respective carbon-carbon or carbon-heteroatom compounds. Among the other hypervalent halogen(III) compounds, the chemistry of cyclic halonium compounds is potentially important research area.

Acknowledgements. This work was supported by a research grant from the Russian Science Foundation (RSF-21-73-20031).

ASYMMETRIC ORGANOCATALYSIS: FROM PROSPECTIVE METHODOLOGY TO SUSTAINABLE CATALYSTS AND PROCESSES

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In 2021 the Nobel Prize in chemistry was awarded to professors B. List and D.W.C. MacMillan "for the development of asymmetric organocatalysis", a method that uses small organic molecules as catalysts instead of enzymes or metals. This innovation in molecular construction has led to organocatalysts that are convenient in handling and environmentally friendly (green chemistry). They enable facile preparation of massive libraries of enantiomerically enriched compounds for drug design under simple experimental conditions [1].

However, in spite of impressive results attained by various research groups all over the world, asymmetric organocatalysis has not still found wide application in pharmaceutical industry. Available organocatalysts, such as proline, commonly exhibit insufficient activity (up to 30 mol% loading is needed). More efficient catalysts are rather expensive. A week point of organocatalysts is their lability which may lead to fast deactivation over catalytic transformations. Finally, a chromatography undesirable in chemical technology is usually needed for separation of organocatalysts from products during workup. Therefore, available, active, robust and readily recyclable catalysts with high level of stereocontrol are still demanded.

In this presentation novel applications of C_2 or C_1 symmetric chiral heterocyclic amines recently developed in our laboratory as simple and sustainable organocatalysts for asymmetric synthesis are considered [2–6]. In the presence of these catalysts asymmetric aldol, Michael and cascade reactions can be effectively carried out in aqueous / alcoholic media or under neat conditions affording natural product analogs and active pharmaceutical ingredients in high yield with excellent enantioselectively. Moreover, the catalysts can be readily recovered without chromatography and multiply reused in the catalytic reactions, an important feature for practical applications.

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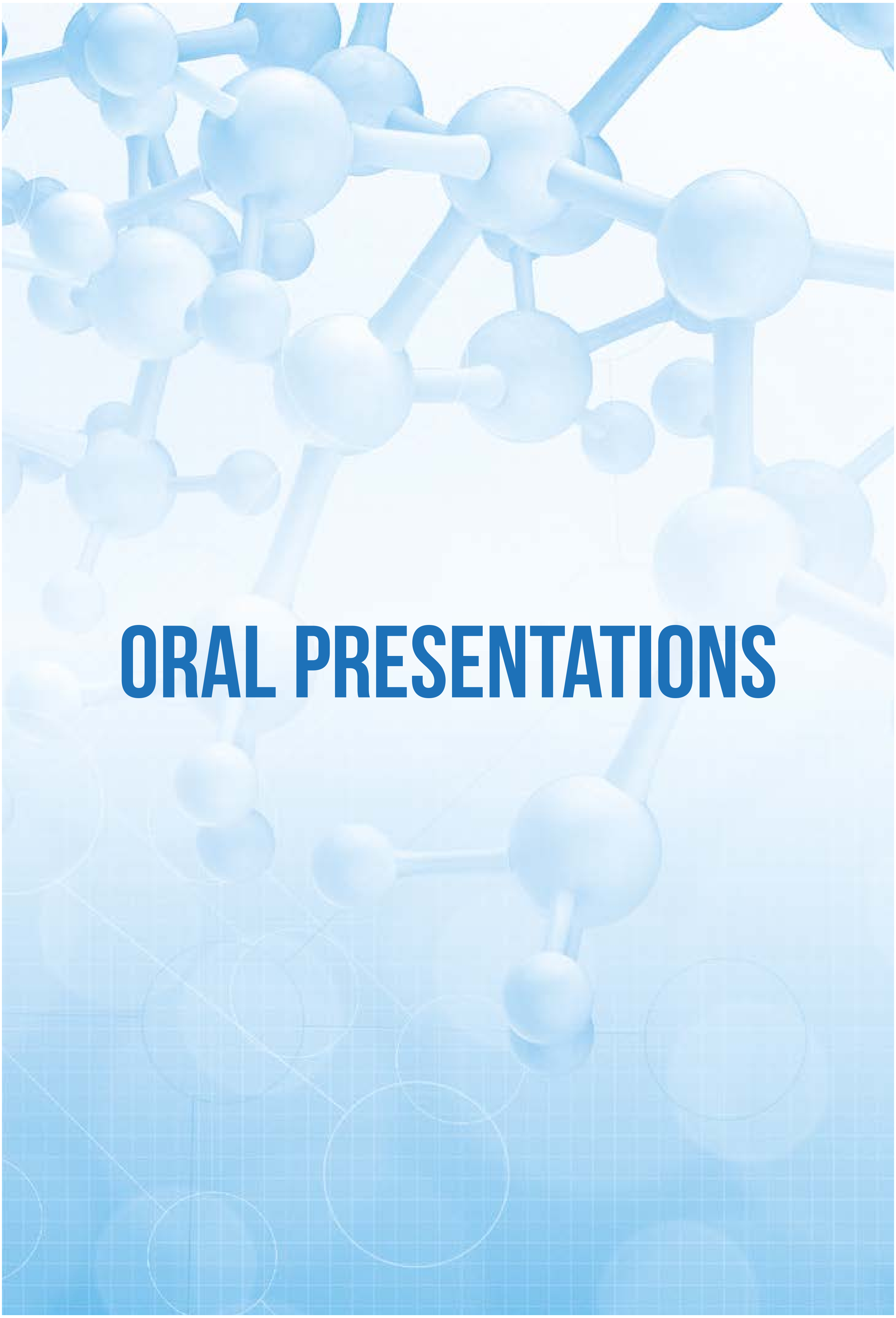

ORAL PRESENTATIONS

REDUCTIVE ADDITION WITHOUT AN EXTERNAL HYDROGEN SOURCE

Afanasyev O.I., Fatkulin A.R., Biriukov K.O., Tsygankov A.A., Ostrovskii V.S., Chusov D.A.

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A concept for atom-efficient reductive addition was developed (figure 1). Carbon monoxide, a multi-tonnage byproduct in steel manufacture, is an efficient reducing agent in reactions between hydrogen-containing nucleophiles (amines, amides, OH- and CH-acids) and carbonyl compounds. Developed approach represents an easy, efficient and ecologically friendly way to secondary and tertiary amines (even sterically hindered amines), substituted amides, nitriles, and esters.[1]

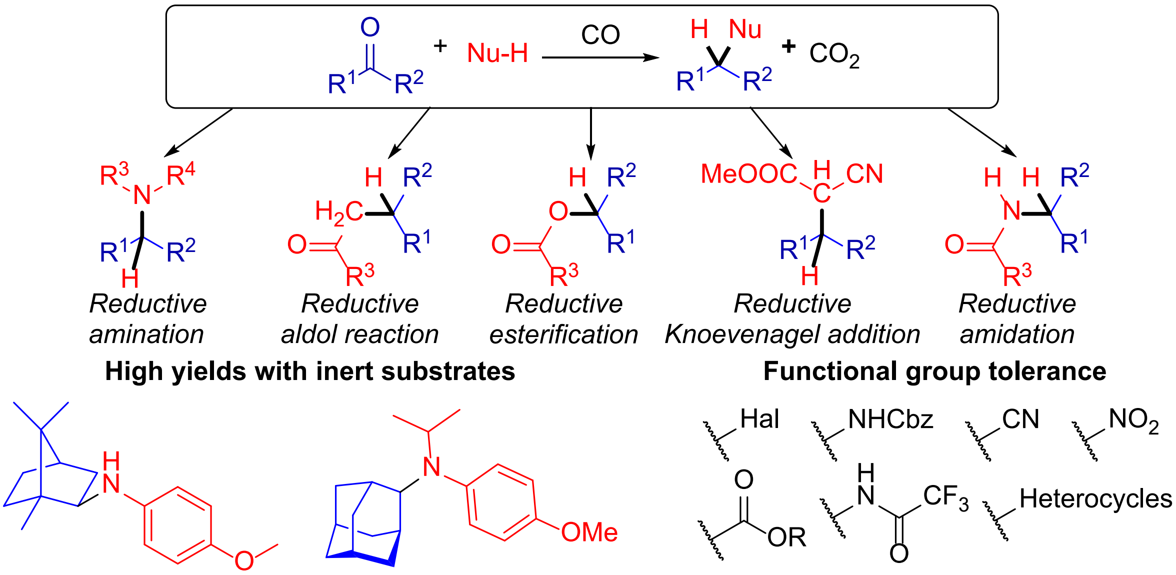

Figure 1. Reductive addition without an external hydrogen source

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The work was financially supported by the Russian Science Foundation (grant 20-73-00010).

OBTAINING HIGH BIOLOGICAL ACTIVITY INDOLYLACETAMIDES VIA USING OXAZOLINE PROTECTION AS A NEW WAY

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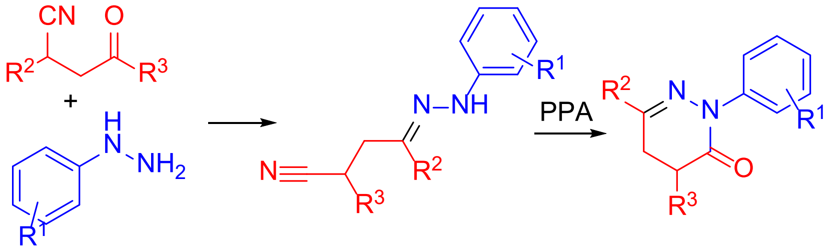
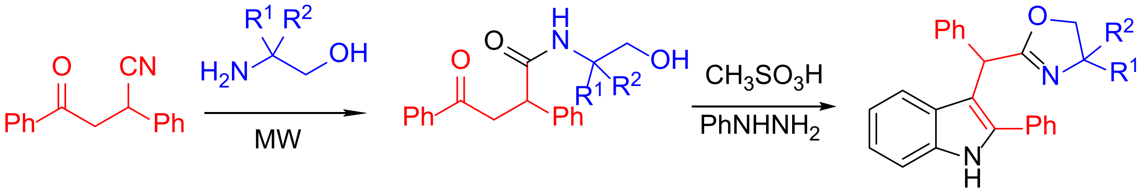
There are many protective groups for carbonyl-, amino-, hydroxy-groups, but there aren’t any protective groups for amides. We have previously synthesized 2-aryl-2-(3-indolyl)acetamides having high anti-cancer activity. Attempts to implement the Fischer reaction with the 4-oxo-butanitrile, led to intramolecular cyclization, with the formation of pyridazine-one as the main product.



We have assumed that we could avoid of intramolecular cyclization via change of nitrile group of 4-oxo-2,4-diphenylbutanitrile into a cyclic analog or by converting into a substituted amide group. The introduction of a protective group based on aminoethanol made it possible to obtain cyclic analogues of indolylacetamides.



This work was supported by the Russian Science Foundation № 21-73-00044, https://rscf.ru/project/21-73-00044/»

TRANSFORMATION OF 3-(2-NITROETHYL)-1*H*-INDOLES INTO 2-(1*H*-INDOL-2-YL)ACETONITRILES

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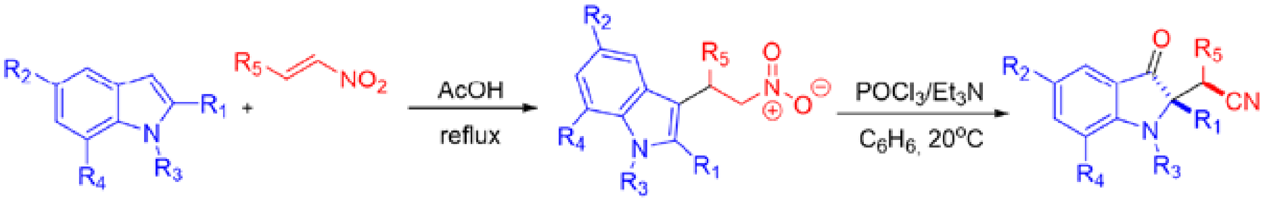
The great interest in our research group is the development of new synthetic approaches for heterocyclic compounds with a 4'*H*-spiro[indole-3,5'-isoxazole] core and their derivatives. Formal [4+1] cycloadducts of indoles and nitrostyrenes was further developed to include an unusual oxazoline ring cleavage and subsequent Beckman cascade rearrangement.[1] Remarkably, this compound possesses a pharmacophoric indolinone core with two contiguous stereogenic centers with one of them being quaternary.

But the recently discovered [4+1]-spirocyclization of nitroalkenes to indoles provided a convenient new approach to 2-(1*H*-indol-2-yl)acetonitriles. Our scientific group has developed an efficient protocol for the activation of 3-(2-nitroethyl)-1*H*-indoles towards spirocyclization and subsequent rearrangement to 2-(1*H*-indol-2-yl)acetonitriles. This methodology was employed to synthesize a small, focused library of nitriles.



Investigation of biological activity of these new 2-(1*H*-indol-2-yl)acetonitriles is currently under way in our laboratories.

This work was supported by the Russian Science Foundation (grant № 21-73-20051)

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STERIC EFFECTS IN ORGANOLITHIUMS: SELECTIVE METALATION AND SYNTHESIS OF NITROGEN HETEROCYCLES

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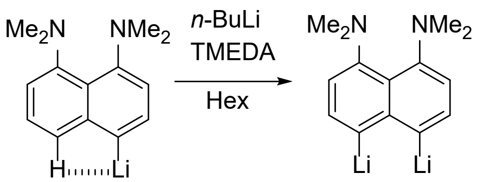
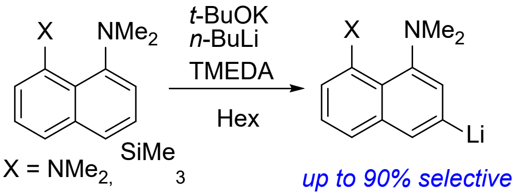
In our work we present the application of steric effects for the non-trivial functionalization of aromatic and heteroaromatic amines with organolithiums. We have found that non-covalent Li···H interaction facilitates second metalation of 4-lithio-1,8-bis(dimethylamino)naphthalene opening a simple way to the hard-to-reach *peri*-disubstituted naphthalene proton sponges with up with 100% selectivity and up to 90% yield. It was demonstrated that presence of bulky substituent in close proximity to NMe_2 and OMe groups in dimethylaniline, anisole and 1-dimethylaminonaphthalene stabilises conformation with an unshared electron pairs turned towards bulky substituent. This forced conformation supresses DOM-effect, thus facilitating *meta*-metalation.

Selective second *peri*-metallation:



100% selective

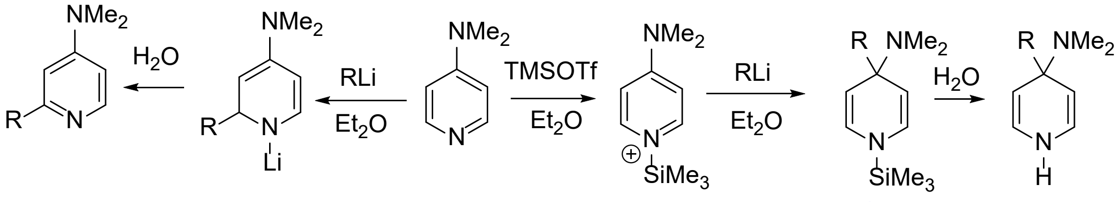
Facilitated *meta*-metallation:



up to 90% selective

We have demonstrated that *N*-silylation “flips” the reactivity of 4-dimethylaminopyridine towards organolithiums leading to the formation of 4,4-disubstituted dihydropyridines: bulky $SiMe_3$ group sterically hinders the addition to the positions 2(6), facilitating nucleophilic attack to the position 4.

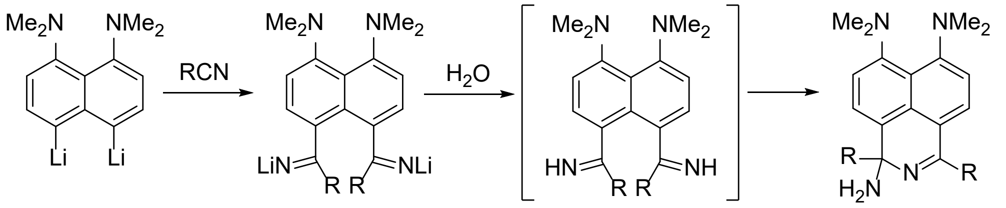
"Flipped" reactivity:



100% selective

We have found that the interaction between *peri*-dilithionapthalenes and nitriles leads to the formation of benzo[*de*]isoquinolines. Reaction starts with the formation of *peri*-diimides, which upon hydrolysis undergo intramolecular nucleophilic cyclisation facilitated by the proximity of imino groups.

Sterically forced cyclization



up to 100% selective

This work was supported by the Russian Science Foundation (project 21-73-10040)

TWO-STAGE ASSEMBLY OF CARBOLINE ALKALOIDS BY AN UNUSUAL REACTION OF NITROALKENES

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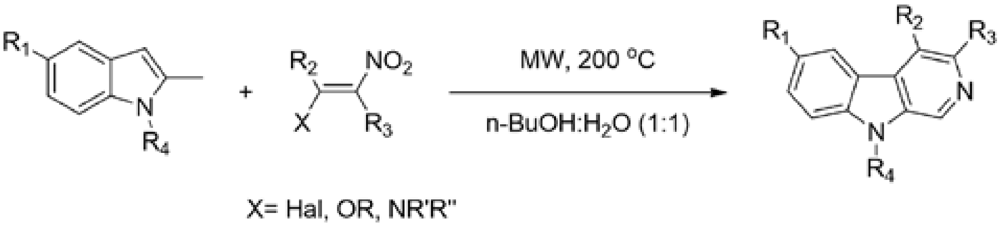
beta-Carboline alkaloids are a large group of natural and synthetic indole alkaloids that demonstrated a broad spectrum of pharmacological properties including sedative, anxiolytic, hypnotic, anticonvulsant, antitumor, antiviral, antiparasitic as well as antimicrobial activities.



The work is based on the use of an unusual cyclization of 2-alkyl-3-nitrovinylindoles, that can be prepared by reaction of indole with substituted nitroalkene, to carbolines.

New derivatives of β-carboline was synthesis with good yield.

This work was financed by the Russian Science Foundation (grant № 22-23-00159)

AEROBIC [M]-/ORGANO-CATALYZED OXIDATION OF C–H- AND Si–H-GROUPS

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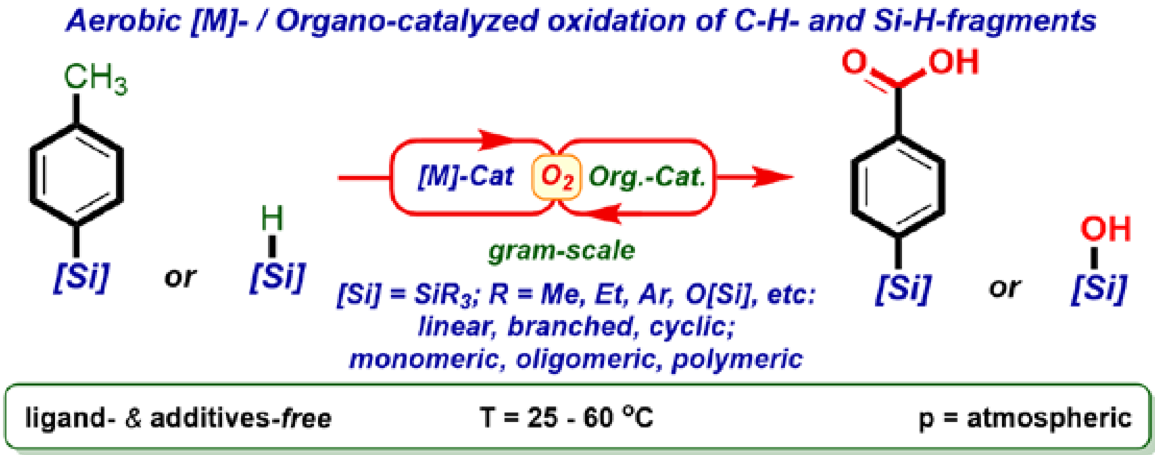
Synthesis of organosilicon products with a "polar" functional group within organic substituents is one of the most fundamentally and practically important challenges in today's chemistry of silicones. Incorporation of a "polar" function into organosilicon compounds opens quite unique opportunities for their subsequent modification and preparation of new copolymers, MOFs, HOFs and other hybrid materials. In addition, modification by incorporation of functional groups would also allow other problems to be solved, namely, the low mechanical strength and "incompatibility" of silicones with organic polymers. Most methods for obtaining functionalized organosilicon compounds have a number of disadvantages: time-consumption; harsh reaction conditions; stoichiometric amounts of toxic and expensive reagents (some of which are not commercially available) that form waste; low selectivity and tolerance to functional groups, etc. Many of these factors provoke the destruction of the organosilicon core of the molecule, in particular Si–C-, Si–O- and other bonds, which significantly complicates the synthesis of organosilicon compounds of a given architecture and their subsequent isolation. [1,2]

To solve these problems the aerobic oxidation of hydride (Si–H-groups) or *p*-tolyl-siloxanes (C–H-groups) was suggested (Scheme 1). This approach is based on "green", commercially available, simple, and inexpensive reagents and employs mild reaction conditions: TM / organic catalyst – catalytic system, O_2 as the oxidant, process temperature from 30 to 60 °C, atmospheric pressure.[3-5]



Scheme 1

All the organosilicon products were obtained and isolated in gram amounts (up to 5 g) and characterized using complex of physico-chemical methods (1D- and 2D-NMR, IR, ESI-HRMS, GPC, X-ray). The synthesized products can serve as building blocks for MOFs, HOFs, COFs, hybrid or well-defined siloxane polymers. [3-7]

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This work was supported by a grant of the Russian Science Foundation (RSF grant 19-73-10172)

SUBSTITUTED 2-(1-HYDROXY-4-NITRONAPTHALEN-2-YL) CYCLOPENTA[*b*]PYRIDINES: SYNTHESIS AND PROPERTIES

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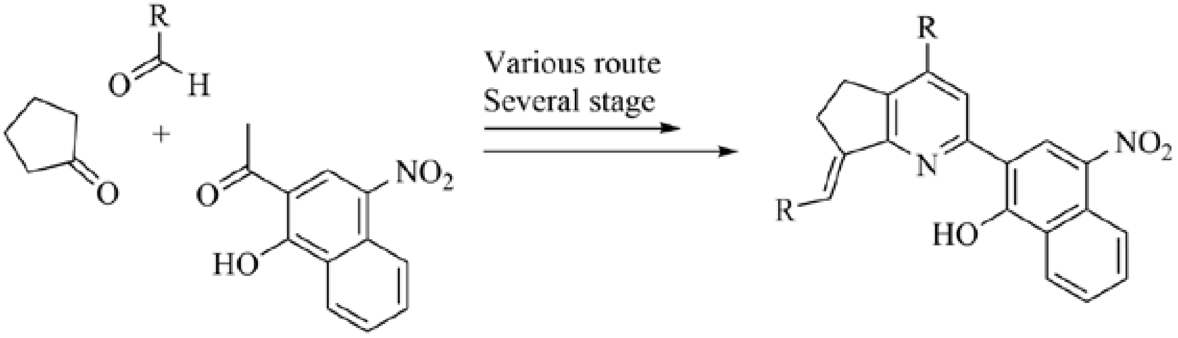
The nitro group is found in azo dyes, explosives, and countless molecules in photochemical research due to its unique characteristics such as strong electron withdrawing ability and facile conversion to a reduced substituent. Recently, a fluorescent benzothiazole derivative having a nitrophenol substituent in its structure has been reported[1].

In continuation of our early research on the preparation of luminescent 2-(ortho-hydroxyaryl)cyclopenta[*b*]pyridines[2], we have considered the synthesis and properties of substituted 2-(1-hydroxy-4-nitronaphthalen-2-yl)-6,7-dihydro-5*H*-cyclopenta[*b*]pyridines. Taking into account the chemical behavior of 1-hydroxy-4-nitro-2-acetonaphtone in the Ortoleva-King reaction and the impossibility of obtaining a brominated product at the acetyl group and pyridinium salt based on the bromoacetyl derivative, a different approach to the synthesis of target systems was required without using Kröhnke pyridine synthesis. Substituted 2-(1-hydroxy-4-nitronapthalen-2-yl)cyclopenta[*b*]pyridines were synthesized via Chichibabin pyridine synthesis protocol. Several ways to obtain target systems were considered. The presence of a 4-nitro-1-naphthol ring at position 2 of cyclopenta[*b*]pyridines promotes the appearance of enol-imino keto-amine tautomerism of the resulting systems. For the obtained compounds, the photochemical properties were considered.



These structures are of interest as ESIPT fluorophores, N-, O- bidentate ligands, and fluorescent labels for solvent polarity.

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The reported study was funded by Russian Foundation for Basic Research according to the research project № 20-33-90088

TETRAHYDRODIPYRROLO[1,2-*a*:1’,2’-*c*] IMIDAZOLES *via* [3+2]-CYCLOADDITION OF ACYLETHYNYLPYRROLES WITH 1-PYRROLINES

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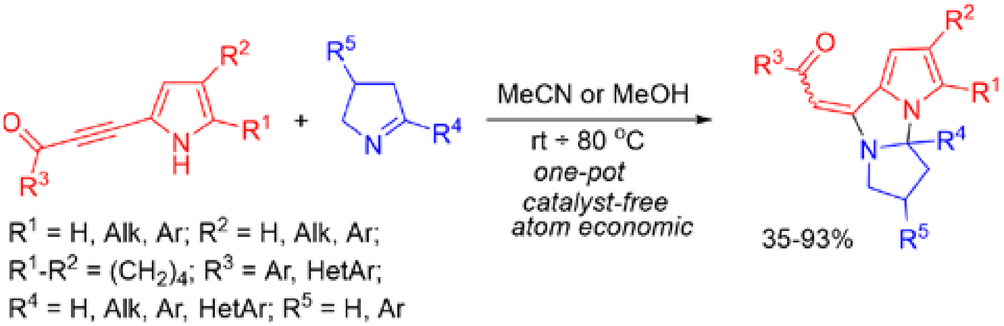
Acylethynylpyrroles, readily available *via* Al_2O_3-promoted cross-coupling of pyrroles with acylbromoacetylenes,[1] now became a rewarding platform for the synthesis of numerous heterocyclic systems and functionalized enaminones.[2]

New horizons of chemical employment of acylethynylpyrroles are uncovered upon reaction with 1-pyrrolines. It is found, that they undergo a facile (rt÷80 °C, MeCN or MeOH, 24-72 h) catalyst-free [3+2]-cycloaddition to 1-pyrrolines to afford acylmethylenetetrahydrodipyrrolo[1,2-*a*:1’,2’-*c*]imidazoles in up to 93% yields and 90% *E*-stereoselectivity of the olefin moiety.



The method demonstrates wide coverage of substituted acylethynylpyrroles and 1-pyrrolines with the potential of expanding the substrate scope.

The reaction mechanism is a concerted process including nucleophilic attack of the pyrroline nitrogen at the triple bond and simultaneous addition of the pyrrole nitrogen to the positively charged C2 of the same ring that is electrophilically assisted by proton transfer to the emerging carbanionic site in the acetylenic counterpart.

The synthesized compounds represent rare fused heterocyclic systems with three 5-membered nitrogen heterocycles – the core of fungal metabolite quinadoline B and prospective precursors for drug design.

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This work was financially supported by the Russian Science Foundation (grant No 21-73-10134).

REACTIONS OF ACETYLENES WITH IMINES IN SUPERBASE SYSTEMS

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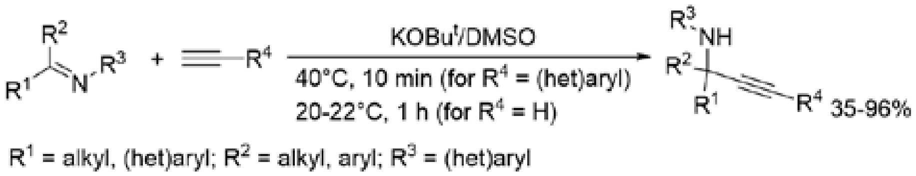
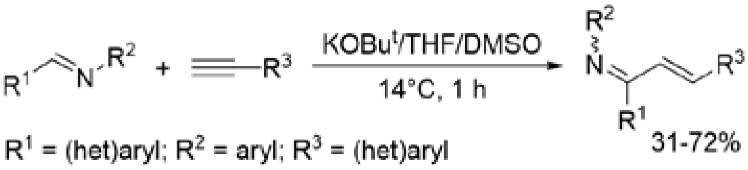
Main features and synthetic potential of the reactions of acetylenes with imines in superbase systems are discussed:

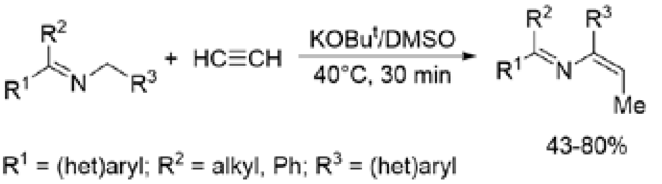
1. reaction of acetylenes with ketimines (*aza*-Favorsky reaction), one-pot synthesis of terminal and internal propargylamines [1, 2];



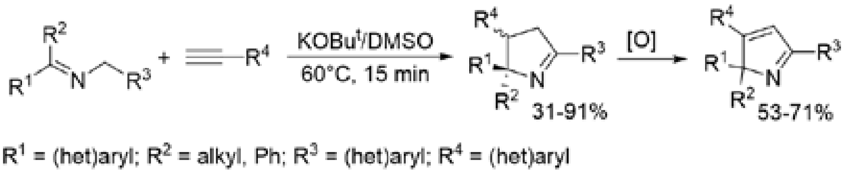
2. reaction of acetylenes with aldimines, one-pot synthesis of 1-azadienes [3];



3. reaction of acetylene with *N*-benzylketimines, one-pot stereoselective synthesis of (*E*,*Z*)-2-azadienes [4];



4. reaction of (het)arylacetylenes with *N*-benzylketimines, one-pot synthesis of 2,3,5-triaryl-1-pyrrolines and -2H-pyrroles [5].



This work was supported by the Russian Science Foundation (grant no. 19-13-00052).

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NEW ORGANIC LUMINOPHORES: ONLY BEAUTIFUL CHEMISTRY OR NEW PERSPECTIVES IN ORGANIC PHOTONICS AND ELECTRONICS?

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During the last years, the number of light-harvesting luminescent dendritic molecules has increased rapidly. One of the most interesting features of these molecules is a possibility of incorporation of different chromophores within one molecule that can lead to an intramolecular directional energy transfer from their peripheries to the center. Recently we have developed a new class of highly efficient luminescent materials with unique properties - nanostructured organosilicon luminophores (NOLs).[1,2,3,4,5] These are branched molecules, where two types of organic chromophores are connected to each other via silicon atoms, which brake the conjugation between them and fix them specifically in the space.[6,7,8] NOLs possess several advantages: absorption in a wide optical spectral region; 5–10 times higher absorption cross-sections than those of the best low molar weight organic luminophores; very high photoluminescence quantum yield; luminescence spectra in the defined wavelength region; short luminescence lifetime. Photoluminescence study of the NOLs has shown an intramolecular energy transfer with the efficiency up to 99% and luminescence quantum yield up to 95% in various spectral regions. Optical and thermal properties of the NOLs were compared with the properties of the model linear oligomers.[9] It should be noted that combination of different chromophores in NOLs allows tuning their emission wavelengths in a wide spectral region, which open possibilities for their wide application as spectral shifters – convertors of the emission with the energy of high frequency photons (140–400 nm) into emission in the spectral range (400–700 nm).[10]

We applied NOLs as organic luminophores for manufacturing scintillation and wavelength shifting polymer fibers.[11] A blue and a green emitting prototype fibre were produced and characterised in terms of attenuation length, ionisation light yield, decay time and tolerance to x-ray irradiation. Both the blue and the green prototype fibres show a very short decay time constant and mark to our knowledge new records. The GPF-19-1 prototype fibre is about a factor 6 faster than the SCSF-3HF fibre produced by Kuraray and about two times faster than the green BCF-20 fibre produced by Saint-Gobain Crystals.

The new NOLs used in various devices of organic photonics and electronics, such as spectral shifting fibers[9], organic light-emitting diodes (OLEDs)[12], CIGS photovoltaic devices[13]. NOLs are commercialized by a startup Limited Liability Company «Luminescent Innovative Technologies» (LumInnoTech LLC). All the details can be found on www.luminnotech.com

This work was performed in the framework of leading science school NSh-3843.2022.1.3.

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SYNTHESIS AND PROPERTIES OF 1,3-DISUBSTITUTED UREAS AND ITS ISOSTERIC ANALOGS CONTAINING POLYCYCLIC MOIETY

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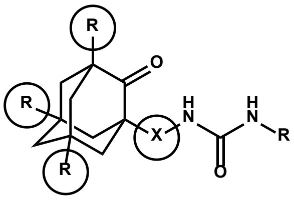
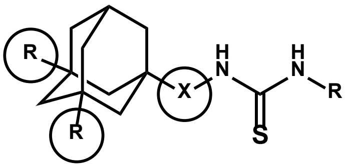
Human soluble epoxide hydrolase (sEH) is a promising target for the treatment of inflammatory processes, pain, kidney diseases, hypertension, and cancer. The high lipophilicity of one of the urea-containing fragments of the sEH inhibitor molecule is an important requirement for achieving high inhibitory activity, which is manifested by the introduction of adamantyl fragments. However, high lipophilicity makes such molecules more likely targets for metabolic enzymes (cytochromes P450), as well as their insignificant water solubility. To reduce the side effects of such inhibitors, their molecular design is implemented, which consists in the introduction of substituents **R** at the nodal and bridge positions of adamantane, including H-bond acceptors (oxo, halogen) and bridging groups **X** (figures I and II); isosteric replacement with a thiourea group (FIG. II).



I

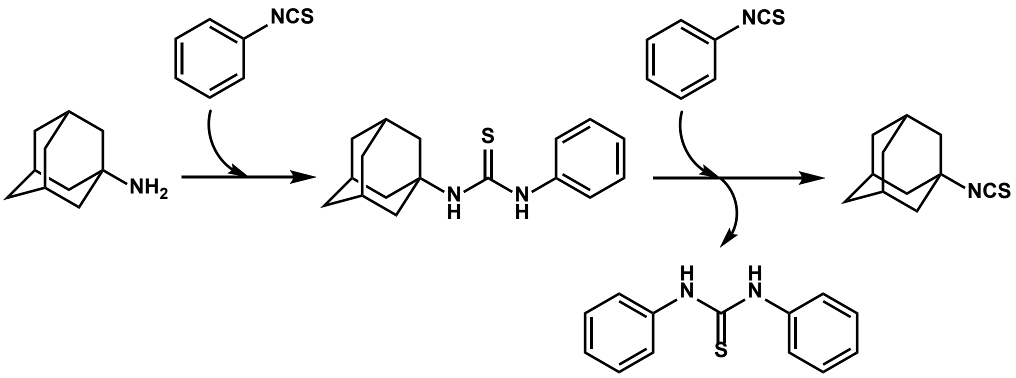


II

Dependencies of the "structure-properties" and "structure-activity" types were found. The effect of bulk factors of the lipophilic group on the inhibition of various hydrolases: human hsEH, mouse msEH, and rat rsEH was established.

Adamantylated urea dimers, which have inhibitory activity in the subnanomolar range of concentrations due to the formation of additional hydrogen bonds in the active center of the enzyme, were studied as inhibitors of soluble epoxide hydrolase. A quantitative dependence of the time of metabolism of ureas in liver microsomes on the number of methyl groups R at the nodal positions of adamantane was established.

An unusual course of the reaction between adamantyl-containing amines and PhNCS (excess) in weakly polar media was established, leading to the formation of adamantyl-containing isothiocyanates in high yield.



For the first time, adamantyl-containing isothiocyanates were studied as antitumor agents (they showed high activity on mda-mb-231 breast cancer cells). The activity of the obtained compounds is up to 25 times higher than that of aromatic analogues.

The work was financially supported by the Russian Science Foundation (project no. 19-73-10002).

ПУТИ МОДИФИКАЦИИ БЕРБЕРИНА

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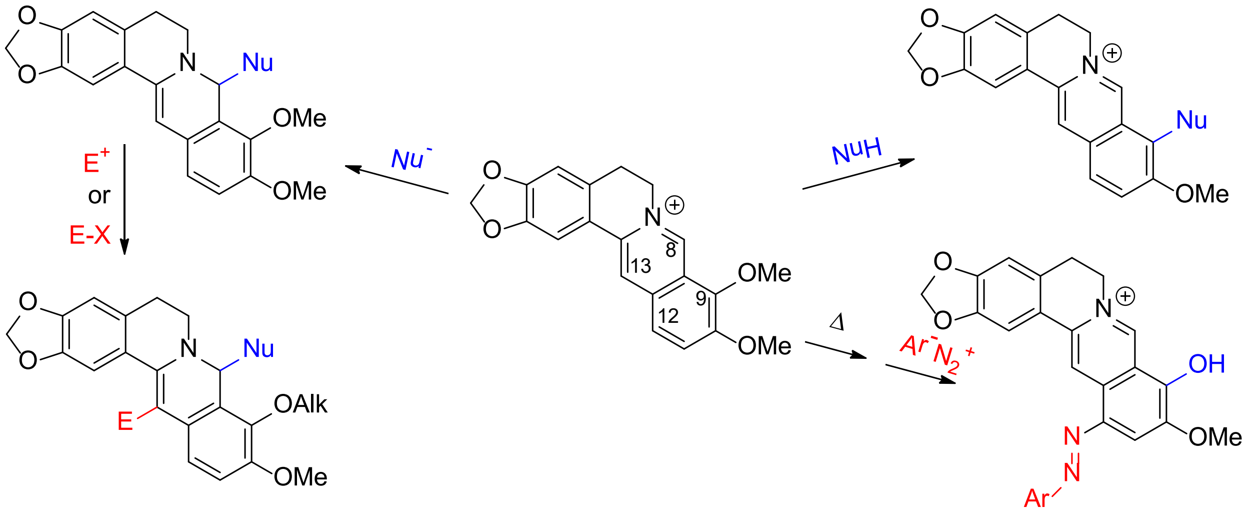
Алкалоид берберин обладает широким спектром противораковой, антибактериальной, противовирусной, противовоспалительной и антинейродегенеративной и другими типами биологической активности. Модифицируя берберин можно существенно увеличить его фармакологическую активность и, как следствие, снизить действующую концентрацию. Путями функционализации алкалоида является его модификация по 8-, 9-, 12- и 13-положениям. Причем модификация по положениям 9 и 12 приводит к образованию катионных форм берберина, в то время как модификация по положению 8 приводит к образованию электронейтральных (восстановленных) форм. Ведение заместителей в 13 положение 8-замещенных берберинов может приводить как к образованию катионных форм 13-замещенных берберинов, так и электронейтральных 8,13-дизамещенных берберинов.



Введение катионных электрофилов в 12 положение возможно только через стадию образования берберрубина, содержащего OH-группу в 9 положении, а значит выступающего в качестве фенола. Последнее обстоятельство делает 12-щамещенные берберины перспективными системами для взаимодействия с нейтральными электрофилами по OH-группе в 9 положении.

Очевидно, что 9- и 12-замещенные берберины далее можно переводить в электронейтральные 8-замещенные и далее дополнительно замещать по 13 положению. Таким образом, берберин – это универсальный скаффолд для получения потенциальных мультифункциональных биологически активных веществ, способный нести на себе фармакофорные группы различной природы. Варьирование физико-химических (полярность/липофильность) свойств берберинов можно осуществлять в очень широких пределах из-за большого числа точек диверсификации.

SYNTHESIS OF FIVE-MEMBERED NITROGEN HETEROCYCLES VIA TRANSFORMATIONS OF MONOSUBSTITUTED FUROXANS

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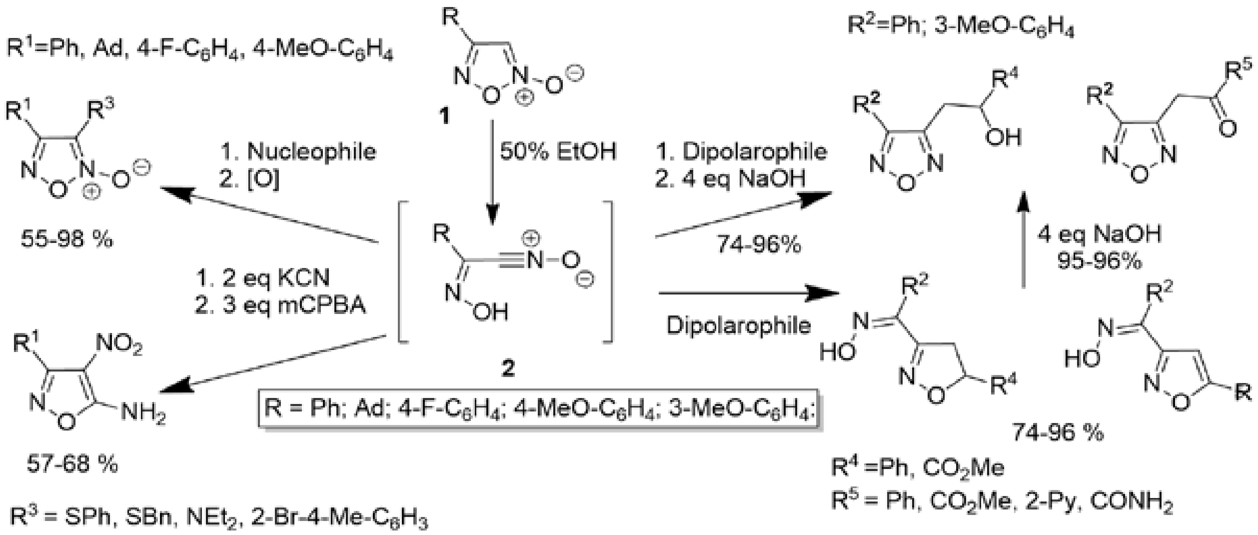
Small molecules, which are usually referred to as compounds with low molecular masses (< 900 Da) have always been of interest in chemistry and biology due to their strong ability to exert powerful effects on living systems. However, the synthesis of such substances often requires long synthetic routes and is of low regioselectivity. Nowadays, interest in development of new nitrogen heterocyclic compounds is constantly increasing.

It is known, that monosubstituted furoxans **1** are capable of the ring cleavage under mild conditions generating nitrile oxides **2**. Herein, we decided to use this phenomenon to perform tandem ring opening/addition sequence and to prepare a series of structurally diverse five-membered nitrogen heterocycles. Our method enabled a one-pot preparation of a wide range of heterocyclic compounds under mild conditions in high yields.



This work was supported by the Russian Foundation For Basic Research (grant 20-33-90205).

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DESIGN OF NEW BIOLOGICALLY ACTIVE COMPOUNDS CONTAINING A BENZOFUROXAN FRAGMENT WITH A WIDE SPECTRUM OF ACTION

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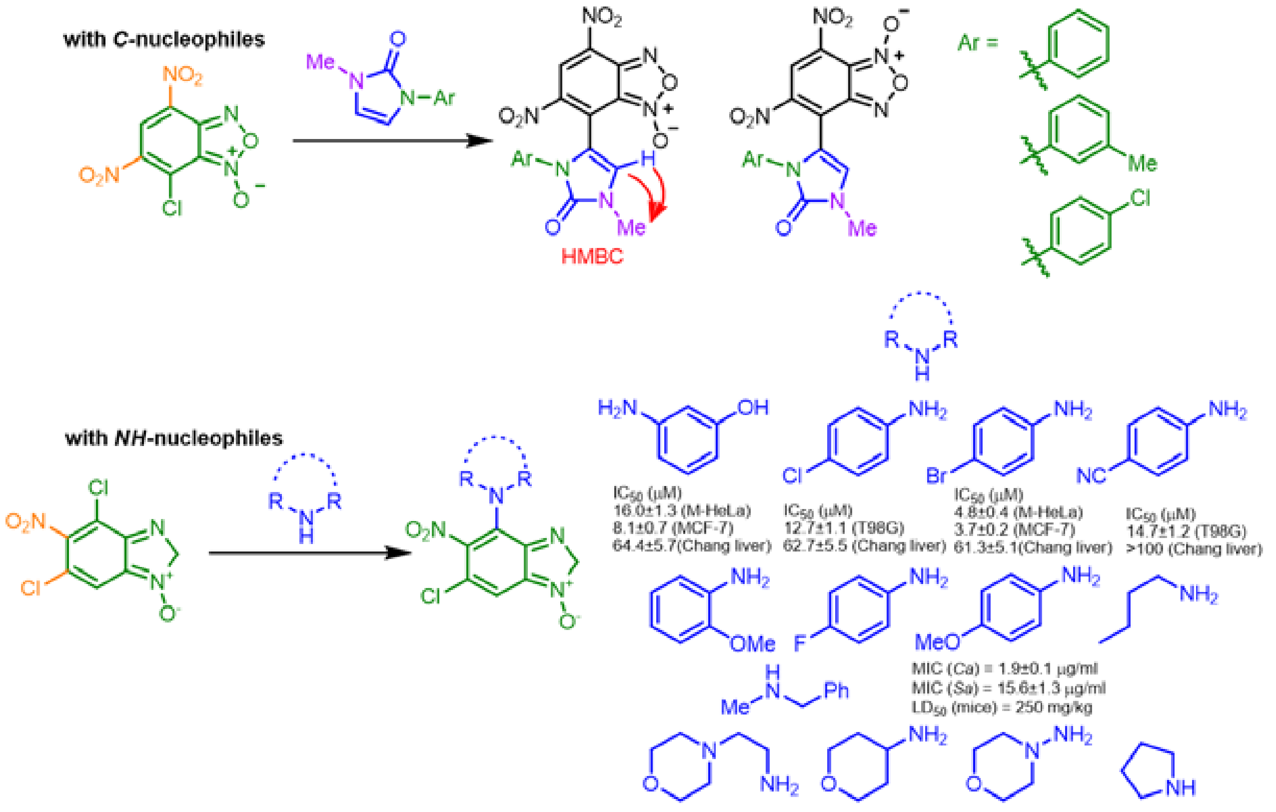
As a result of studying the reactions of substituted benzofuroxans with *NH*- and *C*-nucleophiles, in particular, imidazolin-2-ones, approaches to the creation of new multifunctional compounds on the benzofuroxan platform containing various pharmacophore fragments have been developed and implemented. It was found that the interaction of 7-chloro-4,6-dinitrobenzofuroxan and imidazolin-2-ones proceeds regioselectively with the formation of a single C4 regioisomer. The most significant results of biological activity were obtained for derivatives of aromatic amine compounds showing selective cytotoxicity against the cervical carcinoma cell line (M-HeLa), human breast adenocarcinoma cell (MCF-7), and the glioblastoma cell line (T98G), which was comparable to the reference drug Doxorubicin and significantly outperformed Tamoxifen in its anticancer effect. Among the synthesized compounds containing benzofuroxan fragment, substances with high fungicidal and bactericidal activities were also found. At the same time, the absence of hemolytic activity, genotoxicity and low toxicity of the studied compounds make them promising platform for the creation of drugs based on them.



This work was supported by the Russian Science Foundation (grant no. 21-73-20020).

NOVEL BISPIDINE-MONOTERPENE CONJUGATES — SYNTHESIS AND APPLICATION AS LIGANDS FOR THE CATALYTIC ETHYLATION OF CHALCONES

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Okhina A.A.[2,3], **Rogachev A.D.**[2,3], **Munkuev A.A.**[2], **Kalinin M.A.**[1], **Volcho K.P.**[2],
Salakhutdinov N.F.[2], **Vatsadze S.Z.**[1]

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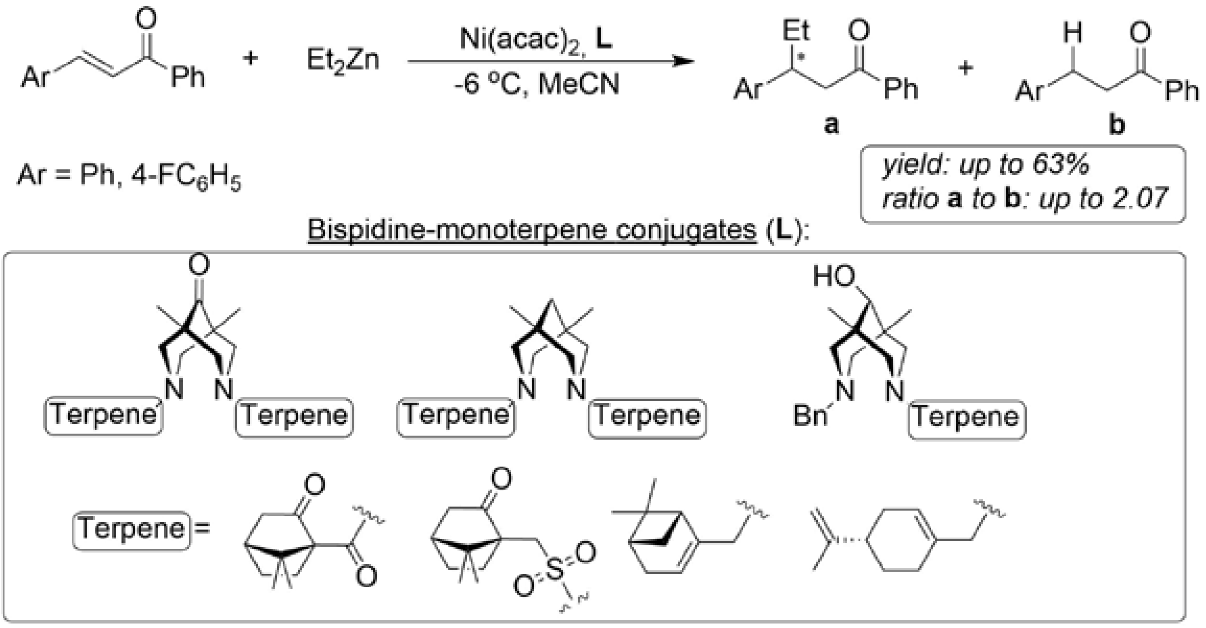
In the present work[1] a number of new chiral bispidines containing monoterpenoid fragments have been synthesized and investigated as ligands in the Ni(II)-catalyzed addition of diethylzinc to chalcones. It was demonstrated that such conjugates could be successfully used as ligands in similar catalytic conversions. For the first time, significant formation of hydrogenation products of the chalcone C=C–bond was observed for such systems.



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This work was financially supported by the RSF (grant 19-73-20090).

DICARBOCYANINES WITH HYDROPHOBIC SUBSTITUENTS AS AN EFFECTIVE TOOL FOR IMAGING-GUIDED DRUG DELIVERY IN BIOSYSTEMS

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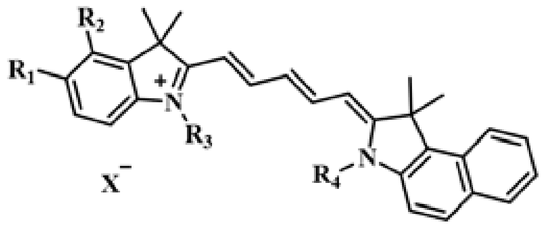
Previously, the effective use of carbocyanine dyes for the visualization of "small molecules" by using non-covalent interactions was studied. We demonstrated the possibility of determining aminoglycosides using the strategy of enhancing the fluorescence of carbocyanines in surfactant solutions at premicellar concentrations [1, 2].

In continuation of these studies, a convenient method for monitoring the delivery of large hydrophilic molecules into cells based on the use of chitosan nanocontainers has been developed. A series of pentamethine carbocyanines containing hydrophobic substituents has been synthesized. Carbocyanine **1** turned out to be the most promising for solving this problem. Using this dye, a method for imaging-guided drug delivery to cells was developed and an approach was proposed for visualizing drug release in the organism.



1: $R_1, R_2 = (\text{-CH=CH-})_2$, $R_3, R_4 = (CH_2)_{10}COOH$ (X = Br)
2: $R_1, R_2 = (\text{-CH=CH-})_2$, $R_3, R_4 = (CH_2)_5CH_3$ (X = I)
3: $R_1, R_2 = (\text{-CH=CH-})_2$, $R_3 = (CH_2)_4SO_3^-$, $R_4 = (CH_2)_5CH_3$ (X -)
4: $R_1, R_2 = (\text{-CH=CH-})_2$, $R_3, R_4 = (CH_2)_9CH_3$ (X = I)
5: $R_1, R_2 = (\text{-CH=CH-})_2$, $R_3, R_4 = (CH_2)_4COOH$ (X = Br)
6: R_1=COOH, R_2=H, $R_3, R_4 = CH_3$ (X = I)
7: R_1=COOH, R_2=H, $R_3 = CH_3$, $R_4 = (CH_2)_5CH_3$ (X = I)
8: R_1=COOH, R_2=H, $R_3 = CH_3$, $R_4 = (CH_2)_{10}COOH$ (X = I)
Cy5.5: $R_1, R_2 = (\text{-CH=CH-})_2$, $R_3 = CH_3$, $R_4 = (CH_2)_5COOH$ (X = Br)

This work was supported by the Russian Foundation for Basic Research (grant no. 20-03-00334).

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FURAN RING OPENING – RING CLOSURE REACTIONS IN THE SYNTHESIS OF DELTA-CARBOLINES

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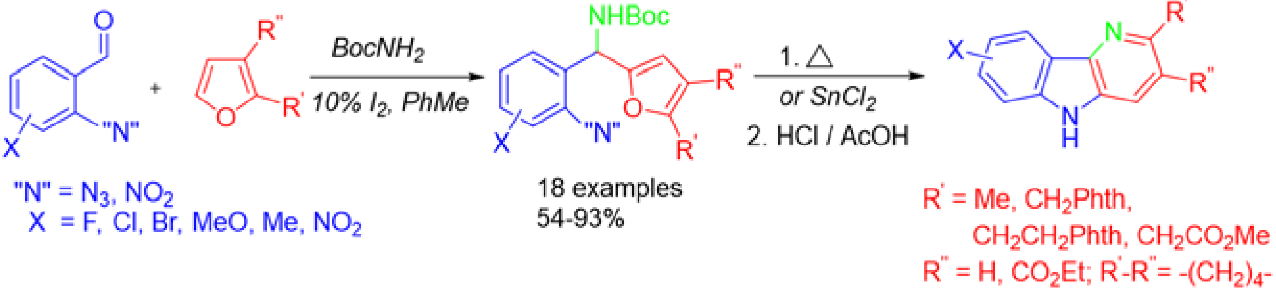
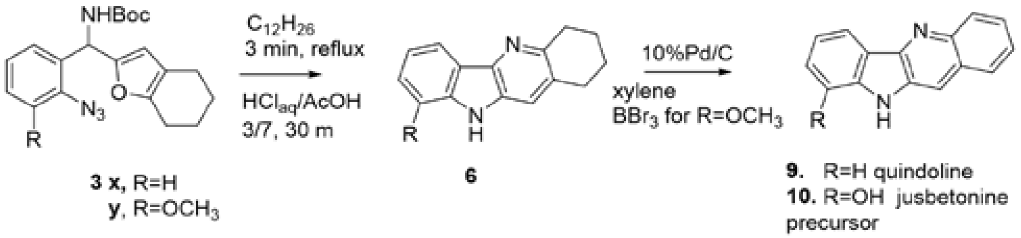
Delta-carbolines belong to a relatively scarcely studied subclass of carbolines, i.e. pyridoindoles. Nevertheless, these substances show interesting biological properties, they are also effective as the materials for the solar panel industry.

We have developed a flexible convergent pathway to delta-carbolines, which is based on ortho-substituted benzaldehydes and alkylfurans. The first step comprises amidoalkylation of furan [1] with a 2-azidobenzaldehyde using molecular iodine as a mild electrophilic catalyst; the 5-(2-azidoaryl)methyl-2-alkylfurans are transformed to delta-carbolines via further reactions. The second step is the azide thermolysis – furan ring opening reaction [2], and the last step is acid-catalysed cyclisation of the intermediate 2-(3-oxobuten-1-yl)-3-acylaminoindoles (not shown here) to the desired delta-carbolines. Alternatively, if starting from a 2-nitrobenzaldehyde, the indole ring closure can be achieved by the reduction of nitro group.



Using this strategy, we have successfully obtained some natural bioactive substances, namely quindoline and jusbetonine aglycone.



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This work was supported by the Russian Foundation for Basic Research (grant N: 19-03-01027).

REACTIONS OF THIOAMIDES WITH SULFONYL AZIDES AND ELECTROPHILES

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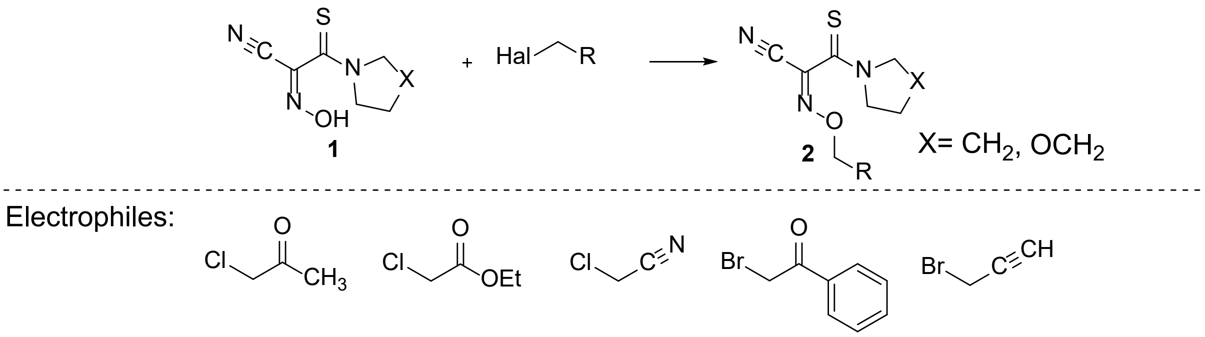
Thioamides are of interest for medicinal chemistry as compounds with various biological activities[1] and for organic chemistry as building blocks[2]. Among the class of thioamides, 2-cyanothioacetamide has found wide application in the synthesis of a huge variety of sulfur- and nitrogen-containing heterocycles[2]. In our previously works[3,4] high yield solvent-base-controlled, transition metal-free synthesis of 4,5-functionalized 1,2,3-thiadiazoles and 1,2,3-triazoles from 2-cyanothioacetamides and sulfonyl azides was described. Under diazo transfer conditions in the presence of a base in an aprotic solvent 2-cyanothioacetamides produce 5-amino-4-cyano-1,2,3-thiadiazoles exclusively. The use of alkoxide/alcohol system completely switches the reaction course due to the change of one of the reaction centers in the 2-cyanothioacetamide resulting in the formation of 5-sulfonamido-1,2,3-triazole-4-carbothioamide sodium salts as the only products.

In continues of our research, we had prepared new 2-hydroxyimino-2-cyanothioacetamides **1** and used them for the synthesis of a wide range of polyfunctional compounds **2**.



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This work was supported by the Russian Science Foundation grant Nº 21-73-00047, https://rscf.ru/project/21-73-00047/

NEW APPROACH TO FUNCTIONALIZED 1-PYRROLINES VIA ANNULATION OF 2-ALKYL-2*H*-AZIRINES WITH DIAZO COMPOUNDS

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1-Pyrrolines are one of the most studied pyrrole derivatives [1]. Compounds, containing the structural moiety of 1-pyrroline, are attractive targets of medicinal chemistry due to their various bioactivity. Thus, some 1-pyrroline derivatives exhibit antidiabetic, antiviral, and antibacterial activities. A wide range of effective and inexpensive approaches to the synthesis of 1-pyrrolines have been developed. However, most of them are not general and applicable only for the synthesis of 1-pyrrolines with a limited substitution pattern. Only few methods allow access to 1-pyrrolines with functional groups at the C3 and C4 positions. Due to the increasing demand of medicinal chemistry, there is a need for the development of novel general synthetic ways to 1-pyrrolines.

In this work, we have developed a novel one-pot approach to the synthesis of 1-pyrroline derivatives **4** via the base-catalyzed anionic 1,5-cyclization of 4-alkyl-2-azabuta-1,3-dienes **3**. Such 2-azabutadienes **3** can be obtained by the Rh(II)-catalyzed reaction of diazo compound **1** with 2-alkyl-2*H*-azirine **2** [2] (Fig.1). It is remarkable that anionic 1,5-electrocyclizations are rare [3], and the proposed method is the first example of 1-pyrroline synthesis using 2*H*-azirines and diazo compounds. This one-pot route makes it possible to obtain 1-pyrrolines **4** containing aryl, alkyl, vinyl, ethynyl, ester and hydroxyl groups at positions 2–4 of the pyrroline system in good and excellent yields. The highest yields were obtained for pyrrolines **4** containing two ester groups at the C2 and substituents R^2 and R^3, differed from hydrogen. Importantly, 3,4-disubstituted pyrrolines **4** were obtained as 3,4-*trans*-pyrrolines (Fig.1). An additional advantage of the developed method is an opportunity of using 4-alkylisoxazoles **5** as precursors of 2*H*-azirine-2-carboxylates **4** [4].

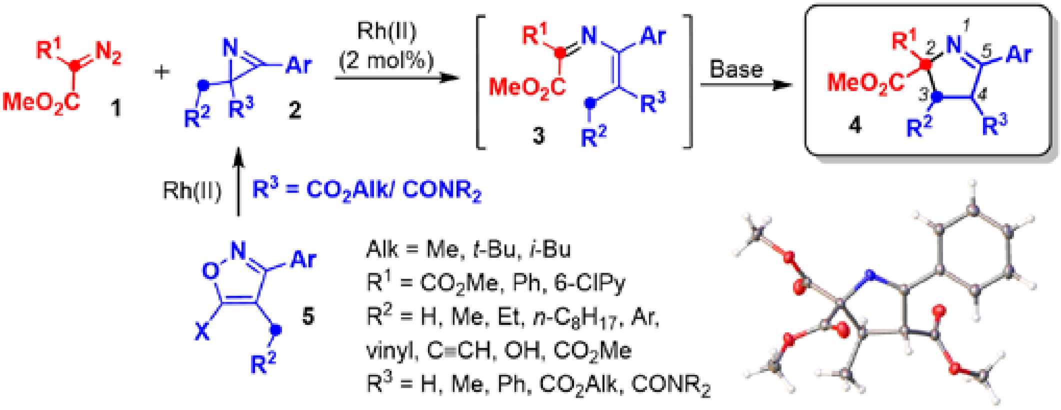

Figure 1. One-pot synthesis of 1-pyrroline derivatives

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Acknowledgements. This work was supported by the Russian Science Foundation (project No 19-73-10090). This research used resources of the Magnetic Resonance Research Centre, Chemical Analysis and Materials Research Centre and Centre for X-ray Diffraction Studies of the Research Park of St. Petersburg State University.

DESIGN AND SYNTHESIS OF POTENTIAL INHIBITORS OF PI3K SIGNALING PATHWAY

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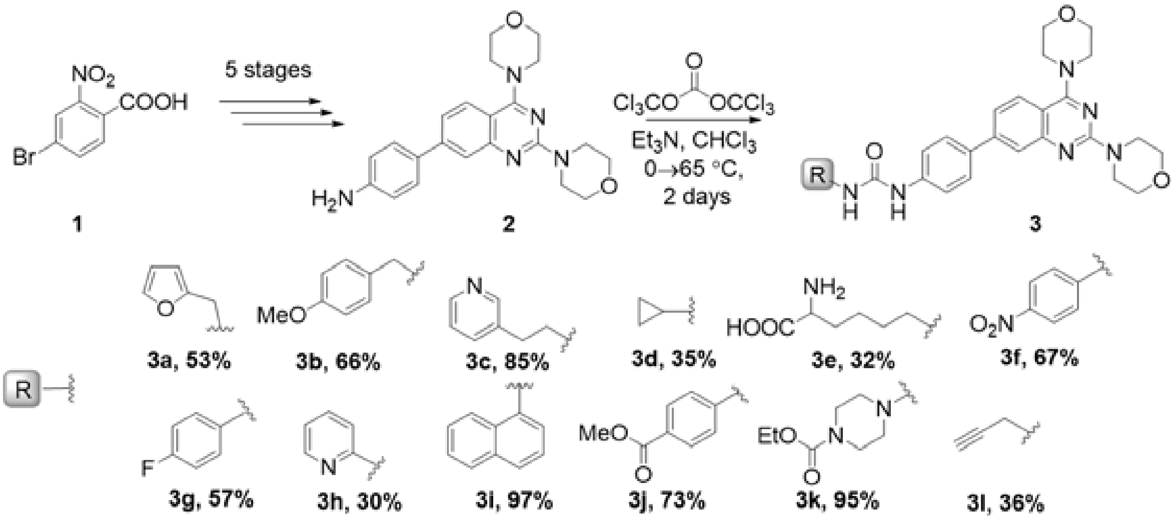
The regulation of PI3K-AKT-mTOR signaling pathway is frequently disturbed in cancer cells. This cascade influences in significant processes supporting proliferation, survival, metabolism of cancer cells. It acts on processes associated with tumor microenvironment that reduces an invasion, angiogenesis and etc.

In this work a number of dimorpholinoquinazoline-based potential inhibitors of PI3K was synthesized. They contain a variable part permitting to increase a selectivity of inhibitor towards PI3Kα-isoform. The cytotoxicity of gained substances was measured using MTT-assays in MCF7 and MDA-MB-231 cell lines. All compounds show cytotoxic activity in low-to-moderate micromolar range.



Cytotoxic activity of compounds 3a-l, IC_{50}, µM

Compound	3a	3b	3c	3d	3e	3f
MCF-7	6.6	**1.1**	**0.16**	5.2	9.5	6.5
MDA-MB-231	6.7	**1.7**	**10.4**	10.5	23.8	8.8
Compound	**3g**	**3h**	**3i**	**3j**	**3k**	**3l**
MCF-7	4.9	13.1	6.1	3.8	11.3	>50
MDA-MB-231	13.5	13.9	11.1	4.1	17.1	>50

This work was supported by grant of Ministry of Education and Science (project 13.1902.21.0004) and carried out at the Research Laboratory of the Chemistry of Natural Compounds and Their Synthetic Analogues, created as part of the State Assignment at the REC "Technoplatforma2035", (project FSWR-2021-014).

ORGANONICKEL SIGMA COMPLEXES OF [NiBr(R)(bpy)] TYPE AS UNIVERSAL REAGENTS IN ORGANIC AND ORGANOELEMENT CHEMISTRY

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Organonickel sigma-complexes of type [NiBr(R)(bpy)], where R – aryl, alkyl; bpy is 2,2'-bipyridine, have outstanding catalytic performance in various organic transformations like olefin oligo- and polymerization, catalytic and electrocatalytic C–C, P–C and N–C coupling reactions. They have been also widely applied as transmetalating agents for synthesis of variety organic and organoelement compounds (primary and secondary phosphines, imines, etc.) and particularly used in activation of small molecules, namely, N_2 (Figure 1).[1] Moreover, we have elaborated an electrochemical approach to the synthesis of [NiBr(R)(bpy)] complexes by oxidative addition of *in situ* electrochemically generated nickel(0) complexes with bpy to organic bromides.[2]

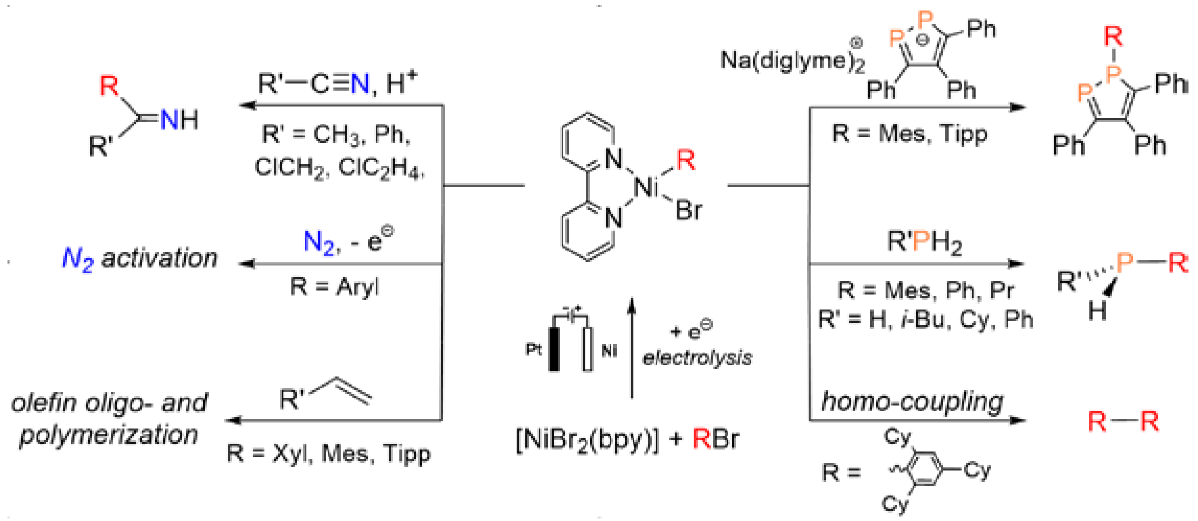

Figure 1. Organonickel sigma-complexes of [NiBr(R)(bpy)] type in some organic transformations.

References
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This work is financially supported by the Russian Science Foundation (project 21-73-00136).

IMIDAZOTHIAZOLOTRIAZINE DERIVATIVES AS PROMISING ANTIPROLIFERATIVE AGENTS

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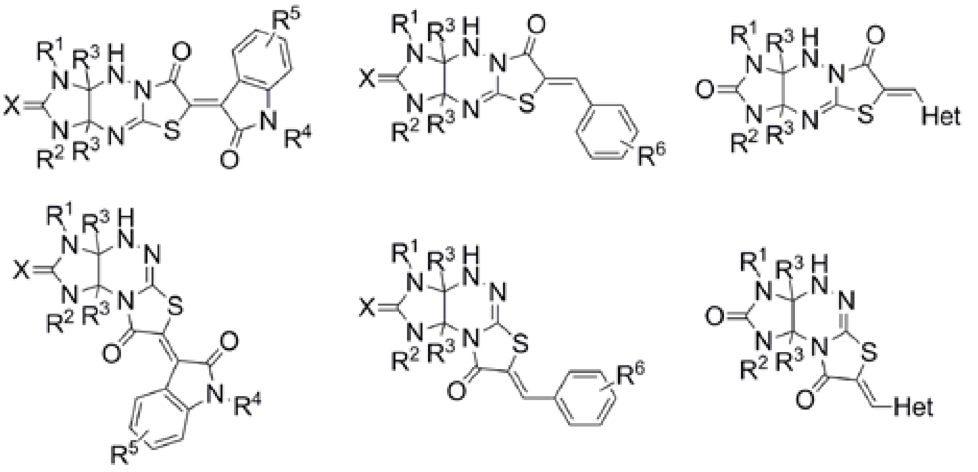
The structure-based design of imidazothiazolotriazine derivatives with oxindole, aromatic or heteroaromatic moieties as potential antiproliferative agents was realised. Two isomeric series of each type of derivatives were synthesized by aldol condensation of imidazo[4,5-e]thiazolo[3,2-b]-1,2,4-triazines and isatins followed by skeletal rearrangement of thiazolotriazine fragment (Fig. 1). Synthesized compounds were evaluated as antiproliferative agents against a panel of approximately 60 cancer cell lines derived from nine neoplastic diseases (leukemia, melanoma, lung, colon, CNS, ovarian, renal, prostate and breast cancers) using the sulforhodamine B method.



X = O, S; R^1 = Alk; R^2 = Alk, Ph; R^3 = H, Ph; R^4 = Alk, allyl, propargyl; R^5 = Hal, Me;
R^6 = Hal, MeO, NO_2; Het = 2-furyl, 2-thienyl, 2(3)-pyridyl, 3-indolyl, 1,2-dimethyimidazol-5-yl

Figure 1. Types of imidazothiazolotriazine derivatives under study

From the structure–activity relationship point of view, we found some regularities: (i) all N-phenyl- or 3a,9a-diphenyl-substituted imidazothiazolotriazines were practically inactive; (ii) 2-oxo derivatives were more potent than 2-thioxoimidazothiazolotriazines; (iii) 1,3-diethyl substituted derivatives showed more potent antiproliferative activity than those with methyl substituents; (iv) imidazo[4,5-*e*]thiazolo[2,3-*c*]-1,2,4-triazine derivatives (angular) are more active compared to imidazo[4,5-*e*]thiazolo[3,2-*b*]-1,2,4-triazines (linear). Lead compounds of each type of imidazothiazolotriazine derivatives were revealed.

This work was financially supported by Russian Foundation for Basic Research (project No. 20-03-00765).

PHOSPHORUS-CONTAINING STERICALLY HINDERED PHENOLS IN THE SYNTHESIS OF COMPOUNDS WITH ANTIOXIDANT, ANTIMICROBIAL AND ANTITUMOR ACTIVITY

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Khasanshina L.R.[a], **Vyshtakalyuk A.B.**[a], **Voloshina A.D.**[a], **Burilov A.R.**

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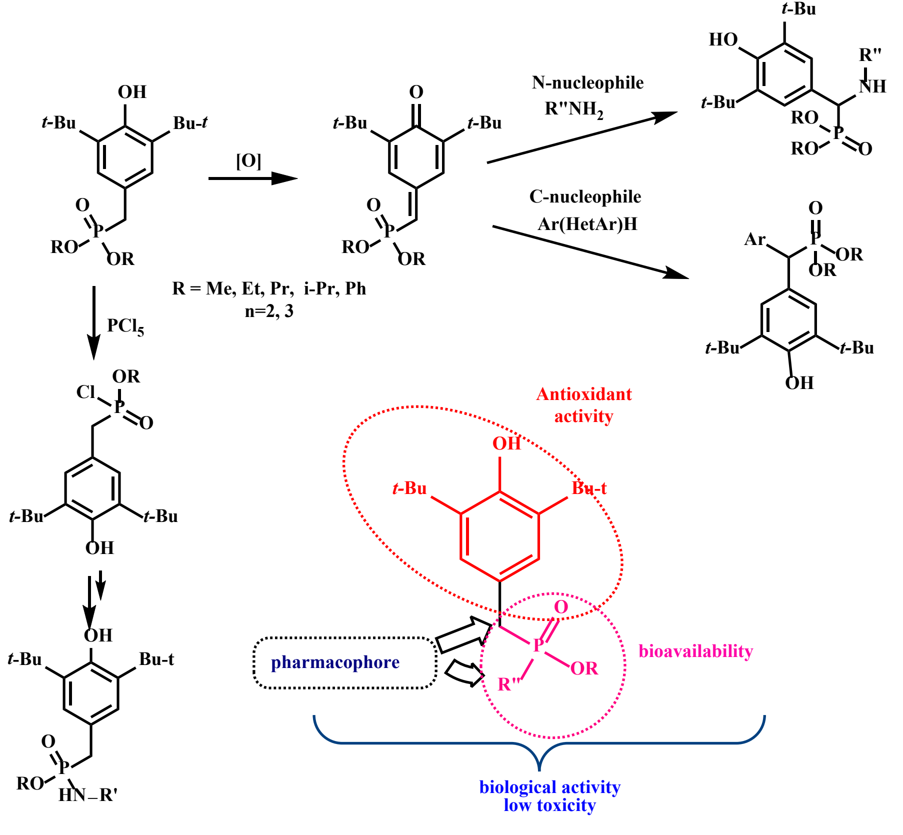
One of the modern trends of medicinal chemistry is to construct multifunctional drugs. Presented in this work strategy for constructing compounds exhibiting antioxidant, antimicrobial or antitumor activities is based on a combination of sterically hindered phenolic, phosphoryl groups and pharmacophore fragments in a single molecule. The introduction of a phosphorus-containing fragment into the molecules of biologically active substances is one of the important trends in the design of potential biologically active compounds, since this not only makes it possible to expect the emergence of new types of biological activity, but also ensures a fairly efficient transport of such molecules through cell membranes. A convenient platform in the synthesis of new sterically hindered phenol derivatives is the use of phosphorus-containing 2,6-di-*tert*-butyl-4-methylene-2,5-cyclohexadienones and 3,5-di-*tert*-butyl-4-hydroxybenzylchlorophosphonate.



As a result of the reaction of benzylchlorophosphonate with amines, phosphorylated methylenequinones with N-nucleophiles (aliphatic amines, hydrazines), and C-nucleophiles (phenolic derivatives, *meta*-phenylenediamine, 2,6-diaminopyridine) we have synthesized a library of compounds. The biological activity of the obtained compounds was studied, among them the lead- compounds with antioxidant, antimicrobial, antitumor activity and low toxicity were found.

This work was supported by the Russian Science Foundation (grant no. 22-23-20015), https://rscf.ru/en/project/22-23-20015/

[M]-/ORGANO-CATALYSED AEROBIC OXIDATION AS THE GREEN WAY FOR THE PREPARATION OF WIDE RANGE OF PRODUCTS WITH SI–OH-GROUPS

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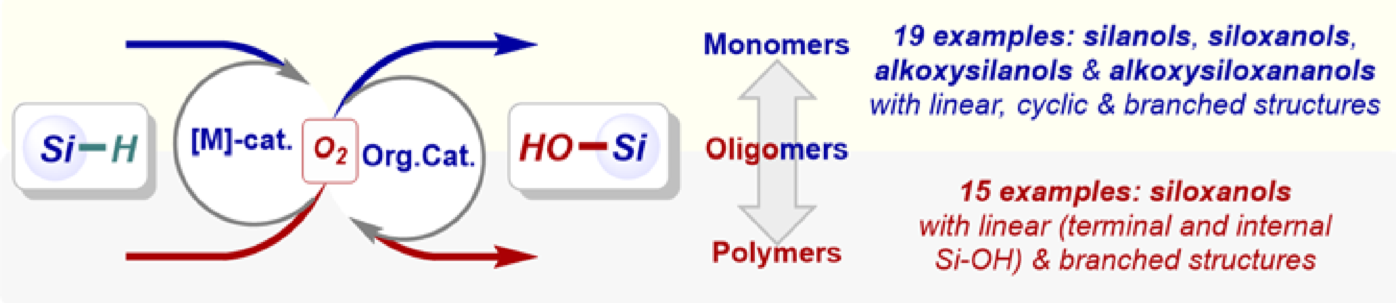
Compounds with a Si–OH group are widely used both in organic and medicinal chemistry as well as in organometallic, polymer and materials chemistry. However, their potential is not yet fully recognized. This is partially due to the difficulties in synthesizing them and the limitations of the synthetic techniques used. The Si–OH-group is unstable under reaction conditions in the presence of acidic or basic admixtures, metal ions, at elevated temperatures, etc. and even under storage in glass vessels.

We proposed an aerobic oxidation of Si–H-derivatives as an efficient method for the Si–OH-derivatives production.[1,2,3] The oxidation using molecular oxygen becomes possible with the use of a combination of transition metal and organic catalysts. Developed catalytic system makes it possible to oxidize a Si–H-group to a Si–OH-group in a wide range of monomeric organo-, siloxy-, alkoxy- and alkoxysiloxy- hydride silanes with linear, cyclic and branched structures. Moreover, oligomer and polymer polyhydride siloxanes with terminal and internal Si–H-groups were efficiently oxidized using this approach.



Scheme 1.

Supramolecular structure in the crystal state of some Si–OH-compounds was studied.[3] Synthesized siloxanols were used in further synthesis of well-defined structures, such as dumbbell-shaped and graft polymers.[3,4]

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This work was supported by a grant of the Russian Science Foundation (RSF grant 19-73-10172)

SYNTHESIS AND INVESTIGATION OF PHOTOPHYSICAL PROPERTIES OF 4-ARYLETHYNYL-1*H*-1,2,3-TRIAZOLES

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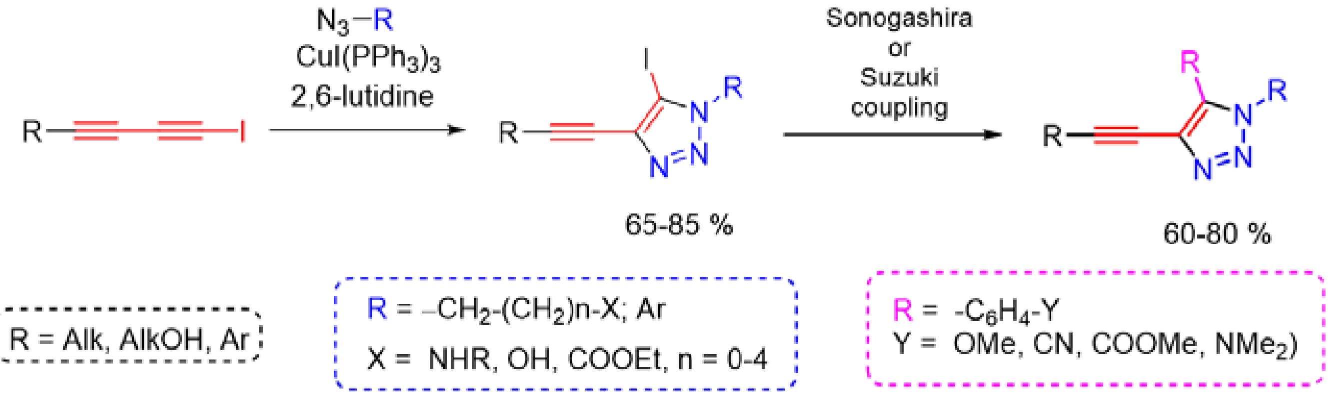
In the past decade, bioorthogonal reactions have been widely used for visualization, detection, diagnosis, and drug delivery. Special attention is paid to the development and use of optical methods for visualizing tumors at the whole organism level and at the cellular level. Therefore, an urgent task is to expand the chemical spectrum of compounds that can be used for the design of new fluorescent tags, taking into account the nature of the objects under study [1].

1,2,3-Triazoles are known to be attractive low molecular weight fluorophores. Our studies showed that 4,5-diethynyl-1,2,3-triazoles derived from 1-iodobuta-1,3-diynes possess significant fluorescent properties, which allows us to offer them as promising fluorescent labels [2]. The aim of this work was design, synthesis and investigation of photophysical properties of new 4-arylethynyl-1*H*-1,2,3-triazoles. The cycloaddition reactions of 1-iodobuta-1,3-diynes with azides were carried out under solvent-free conditions. The cycloaddition proceeds proceed with high regioselectivity giving products in good yields. The following of Sonogashira or Suzuki-Miyaura couplings were gave 1,4,5-trisubstituted triazoles with good to high yields.



Next, we investigated fluorescent properties for synthesized compounds. The promising photophysical properties were demonstrate for all compounds (ΦF up to 60%, Stokes shifts up to 200 nm).

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This work was supported by Russian Science Foundation (RSF) (project No. 19-73-10077). The research was carried out using the equipment of the SPbSU Resource Centres: Centre for Magnetic Resonance, Centre for Chemical Analysis and Materials Research.

ADDUCTS OF 2-PYRIDYLSELENYL HALIDES AND NITRILES AS NOVEL SUPRAMOLECULAR BUILDING BLOCKS

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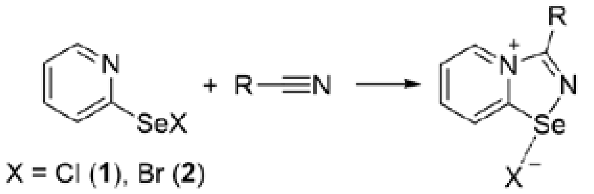
Supramolecular chemistry of chalcogenadiazoles attract attention due to its promising applications in materials chemistry (in the design of molecular materials with conductive and magnetic properties). [1-3] Chalcogen bonding allows a fine tuning of the self-assembly and, therefore, modulation of physical properties when these compounds are employed. We have recently discovered a novel class of cationic 1,2,4-selenadiazoles which could be conveniently synthesized by reaction of 2-pyridylselenenyl halides with a triple CN bond of nitriles with excellent yields and remarkable high tolerance of functional groups. (Figure 1).



	R	X	Yield
3	Me	Cl	96%
4	Me	Br	93%
5	*p*-BrC$_6$H$_4$	Br	92%
6	Et	Cl	94%
7	Br	Cl	96%
8	CH$_2$Cl	Br	92%
9	CH$_2$Br	Cl	94%
10	CCl$_3$	Cl	95%
11	CMe$_2$OH	Cl	96%
12	*o*-NCC$_6$H$_4$	Br	94%
13	pyrazinyl	Cl	91%
14	pyrazinyl	Br	93%
15	Pr	Cl	78%
16	Pn	Cl	94%
17	Ph$_2$CH	Cl	84%
18	*p*-(*N*-MePy)	Cl	86%
19	Br	Br	75%
20	*o*-(N$_2$)C$_6$H$_4$	(BF$_4$)$_2$	52%

Figure 1. Synthesis of 3–20.

The adducts of 2-pyridylselenyl halides and nitriles represent a novel type of supramolecular building blocks which eagerly engage in a variety of ChB interactions. Various available nitriles were employed for the synthesis of corresponding 1,2,4-selenadiazoles to investigate a substituent impact on the self-assembly in the solid state.

Some of these novel selenadiazoles can form the four-center Se···N chalcogen bonding. Besides, other weak interactions, which in some cases outcompete the formation of 2Se–2N squares were investigated. Moreover, the adducts obtained from α-halogenated nitriles can form robust dimers featuring a specific combination of 2Se–2N square, two Hal···Hal and two Se···Hal non-covalent interactions.

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Acknowledgements. This work was performed under the support of the RFBR (award no. 20-53-00006).

STEREOCHEMICAL ASPECTS IN THE SYNTHESIS OF CHIRAL *closo*- AND *nido*-CARBORANE DERIVATIVES

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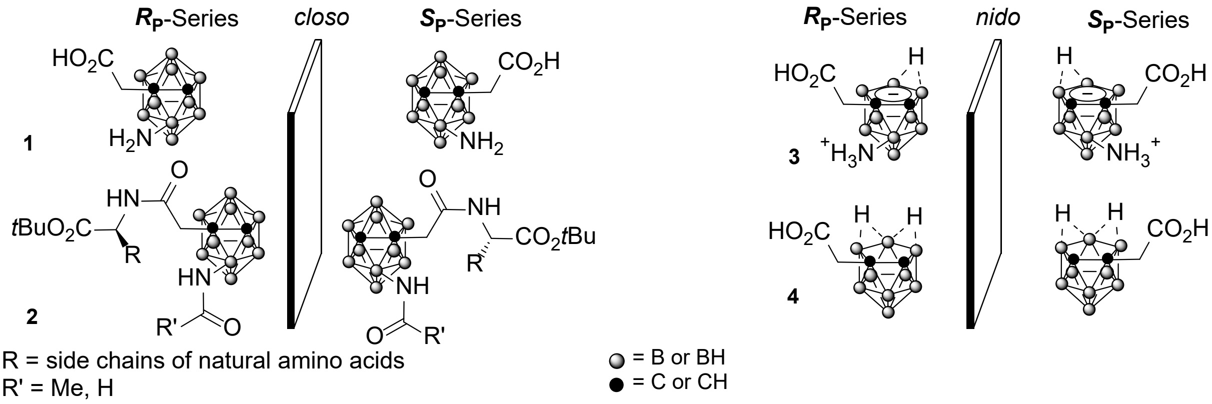
The polyhedral molecules of 1,2-dicarba-*closo*-dodecaborane and 7,8-dicarba-*nido*-undecaborane (carboranes) contain ten or nine boron atoms and represent a basis for a wide range of organoboron compounds. Carboranes find the application both in medicinal chemistry (agents for boron neutron capture therapy, enzyme modulators) and materials science (components of molecular devices and novel materials).

closo-Carborane derivatives with three substituents at one face and *C*-substituted *nido*-carborane derivatives possess a unique property of planar chirality. The presence of planar-chiral *closo*- or *nido*-carborane fragment in molecule leads to the fact that such compounds exist as sets of enantiomers or diastereomers differing in physicochemical properties.



For the first time, we have obtained individual enantiomers of planar chiral *closo*-carborane-based amino acid **1** and its derivatives[1], enantiomerically and diastereomerically pure *pseudo*-dipeptides **2**[2] and assigned their absolute configuration. Further, we developed synthetic approaches to enantiopure (3-ammonio-*nido*-carboran-7-yl)acetic acid (**3**)[3] and related compounds (*e.g.*, acid **4**).

Enantiomerically pure planar-chiral carborane derivatives are of interest as chiral building blocks for preparation of peptidomimetics, chiral ligands and novel materials. Thus, the crystals of compounds **2** demonstrate a high piezoelectric response exceeding that of the most of organic crystals[2].

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The work was financially supported by the Russian Science Foundation (project 21-73-10073).

SYNTHESIS OF BRANCHED UNSATURATED COMPOUNDS BASED ON BROMOCINNAMALDEHYDE

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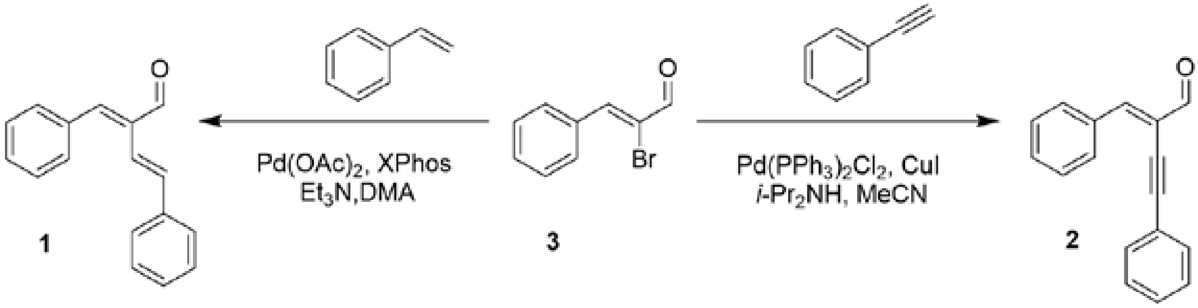
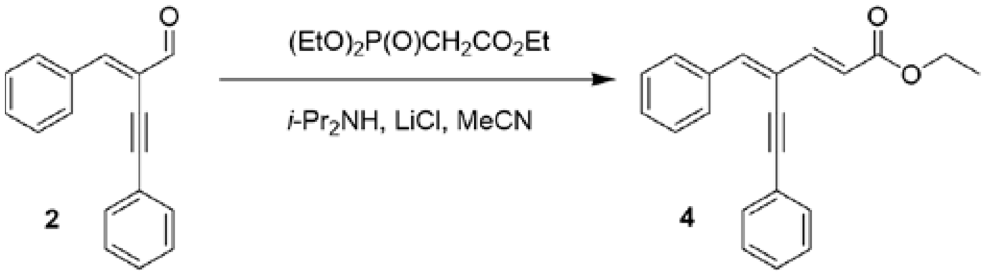
Branched unsaturated compounds are useful diene components in Diels-Alder reactions and key structural motifs of advanced π-conjugated polymers and chromophores.

We developed a stereodirected sinthesis of (2*E*,3*E*)-2-benzylidene-4-phenylbut-3-enal (**1**) and (2*E*)-2-benzylidene-4-phenylbut-3-ynal (**2**) using a Pd-catalyzed coupling of bromocinnamaldehyde (**3**) with styrene (the Heck reaction) and phenylacetylene (the Sonogashira reaction), respectively.



HWE reaction of enyne aldehyde 2 with triethyl phosphonoacetate under standard Masamune-Roush conditions (DBU, LiCl) provided ethyl (2*E*,4*Z*)-4-benzylidene-6-phenylhex-2-en-5-ynoate (4)[1].



The structure and stereochemical purity of compounds 1, 2 and 4 were confirmed by NMR spectroscopy data.

References
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The study was carried out with the financial support of the Russian Foundation for Basic Research within the framework of the scientific project No. 20-33-90106.

REACTIONS OF THIOAMIDES WITH DIAZOCOMPOUNDS AND 1-SULFONYL-1,2,3-TRIAZOLES

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Here, we present a new type of the copper- and rhodium-catalyzed heterocyclization reactions of thioamides with diazocompounds and 1-sulfonyl-1,2,3-triazoles. It was disclosed the aforementioned are resulted in the formation of thioisomunchnones and dihydrothiophenes. The mechanism of thioisomunchnones formation and photophysical properties of the latter were studied.

This work was supported by the Russian Science Foundation grant № 21-73-00047, https://rscf.ru/project/21-73-00047/

PUSH-PULL CHROMOPHORES WITH FUSED HETEROCYCLIC MOIETIES: SYNTHESIS AND COMPARISON OF PHOTOPHYSICAL AND NONLINEAR OPTICAL PROPERTIES

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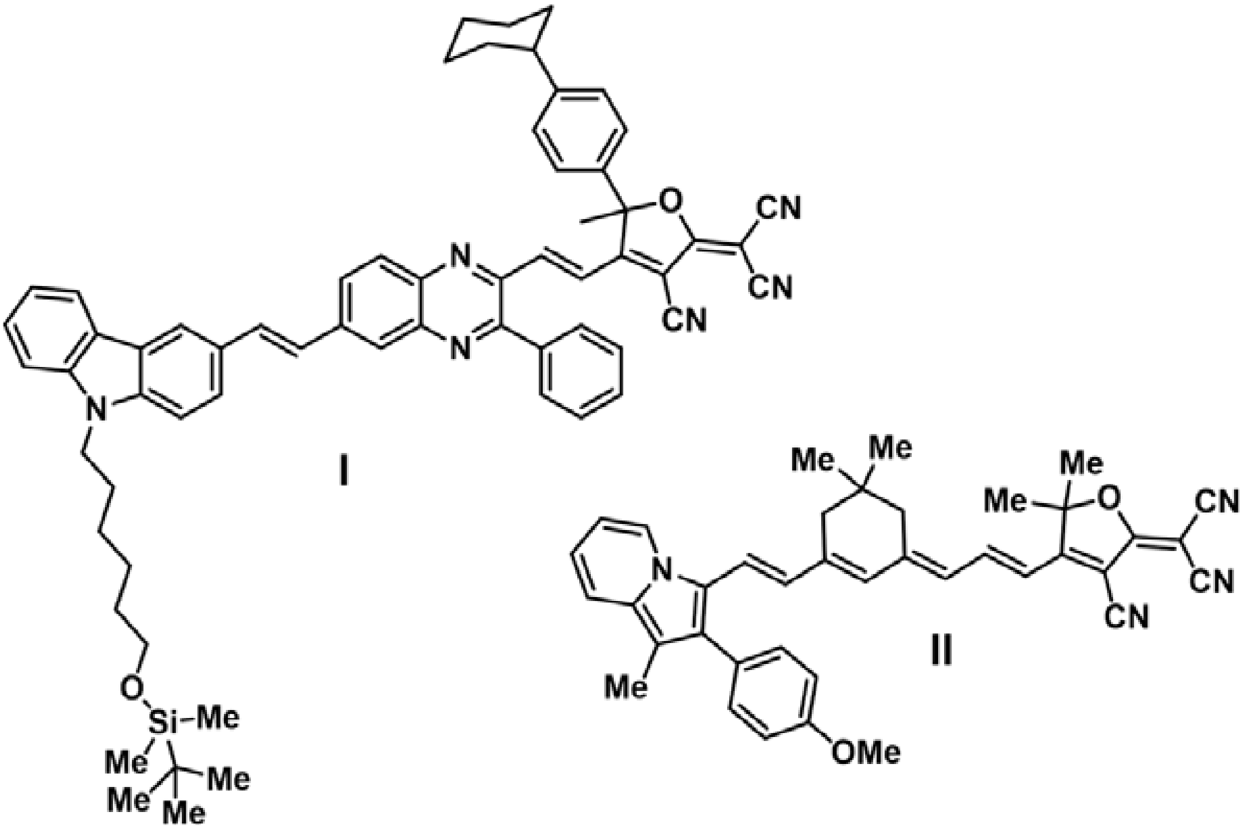
The design of novel push-pull chromophores is very important in the field of organic materials science and engineering, in particular, for the development of high-speed and broadband telecommunication technologies. The report discusses synthetic approaches, photo-physical and nonlinear optical properties of new TCF-based D-π-A chromophores with fused heterocyclic moieties in the terminal position and/or central core of the conjugated bridge. Derivatives of aniline, carbazole, tetrahydroquinoline, indolizine, quinoxaline are considered. The chart below shows two chromophores (**I** and **II**) with large values of the first hyperpolarizability and different absorption maxima in various solvents (from 536 to 950 nm).



I

II

The work was supported by the Russian Science Foundation (grant № 21-13-00206).

SYNTHESIS OF NEW HYDROXAMIC ACIDS BASED ON 4-AMINOQUINAZOLINE-7-CARBOXIC ACID

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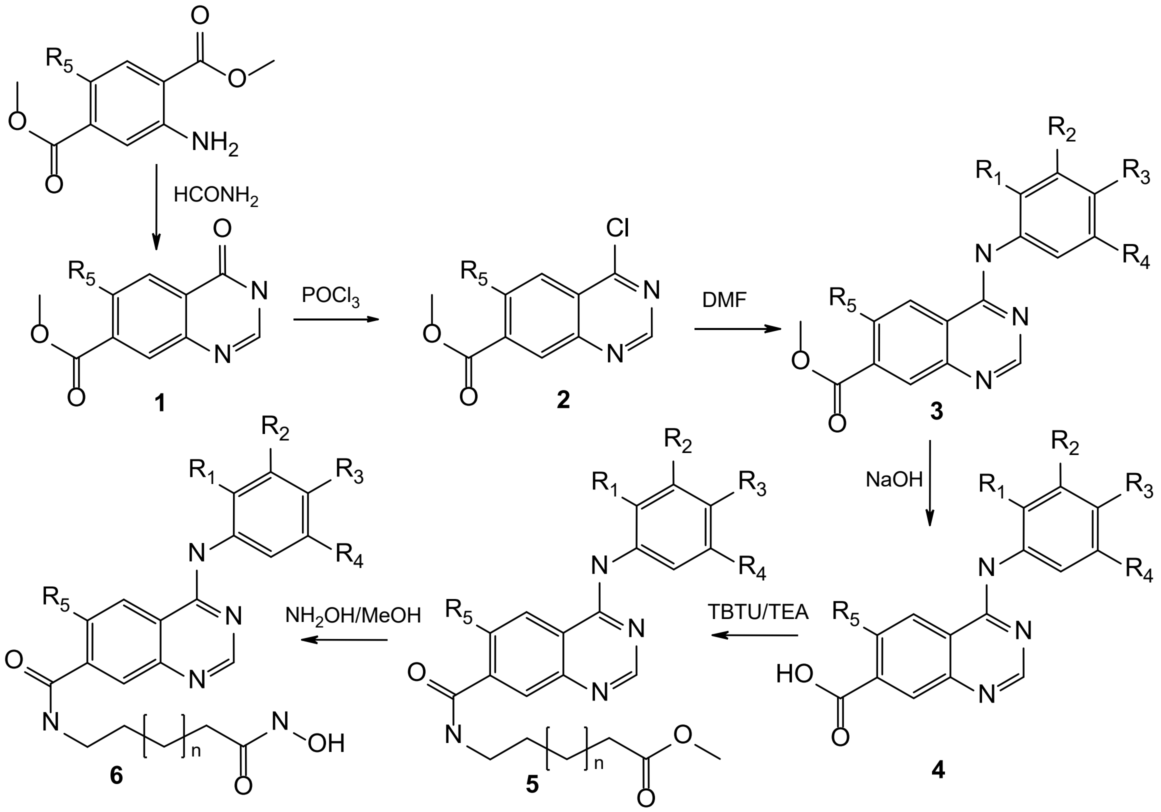
Quinazoline is known to be an important pharmacological moiety. The combination of quinazoline and hydroxamic pharmacophores in one molecule makes it possible to create new promising bioactive group compounds, which are represented by numerous examples[1].

We have synthesized new hydroxamic acids, derivatives of 4-aminoquinazoline-7-carboxylic acid as an example of inhibitors of histone deacetylase inhibitors. Synthesis carried out in six stages according to the scheme:



where R_1, R_2, R_3 R_4 = H, Hal, Me, OMe, R_2, R_3 = -OCH_2CH_2O-; R_5 = H or Hal; n = 3, 4.

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DIRECT C–H ARYLATION OF HETEROCYCLES WITH ARYL HALIDES USING IN SITU GENERATED Ni/NHC CATALYSTS

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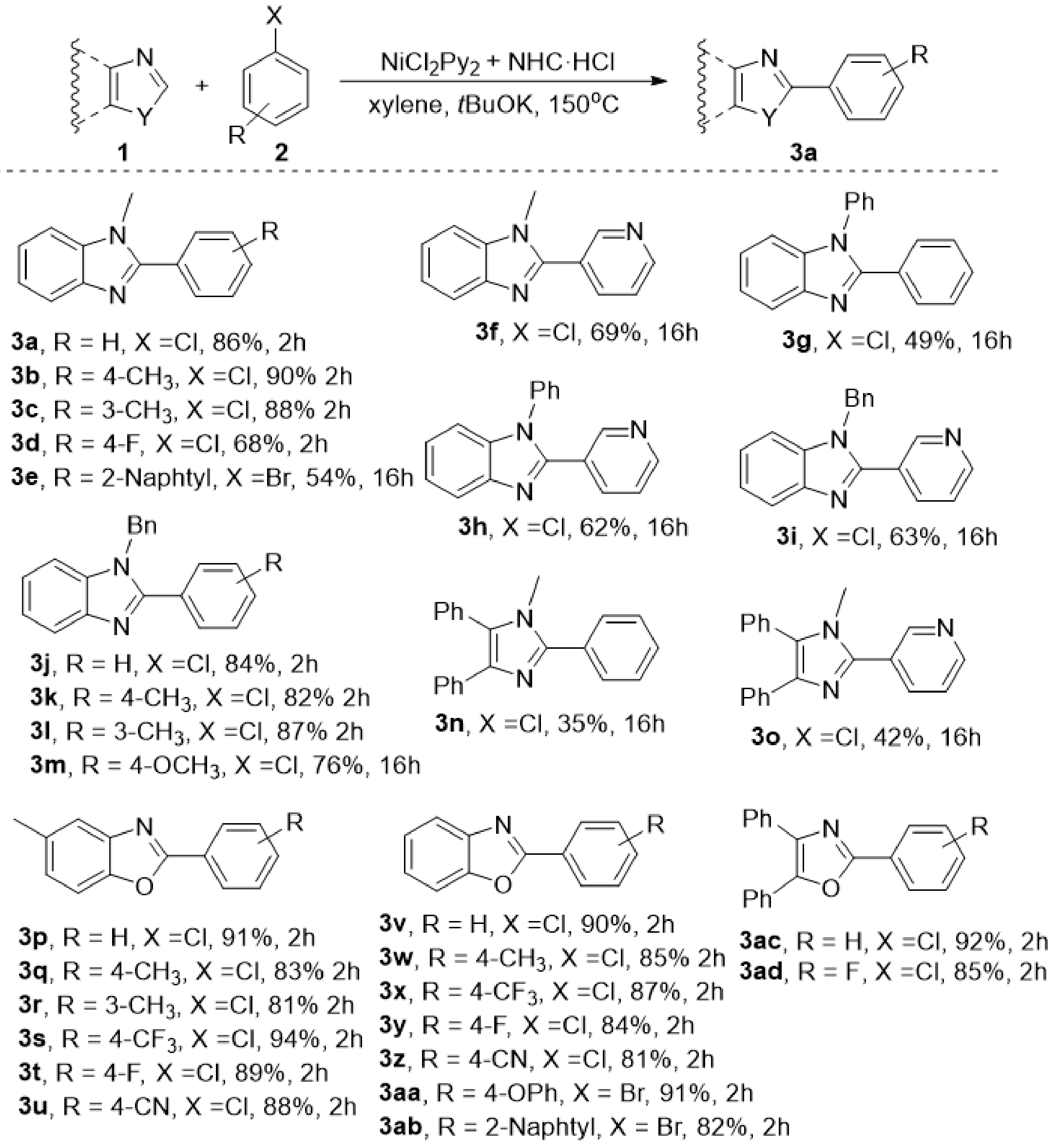
Arylated heterocycles are important structural scaffolds in a number of pharmaceuticals. Nickel, an abundant and relatively cheap metal, represents promising alternative to noble metals in the catalysis of C-H arylation of heterocycles. Herein, we report a facile method for Ni/NHC catalyzed C-H arylation of heteroaromatic compounds with aryl halides relying on the combined use of a phosphine-free catalytic system consisting of $NiCl_2Py_2$ as air-tolerant bench-stable Ni source and stable NHC·HCl salt as NHC-proligand. The *in situ* generated Ni/NHC system was evaluated in the arylation reactions of a wide scope of (benz)oxazoles or (benz)imidazoles by aryl halides.



3a, R = H, X =Cl, 86%, 2h
3b, R = 4-CH_3, X =Cl, 90% 2h
3c, R = 3-CH_3, X =Cl, 88% 2h
3d, R = 4-F, X =Cl, 68%, 2h
3e, R = 2-Naphtyl, X =Br, 54%, 16h

3f, X =Cl, 69%, 16h

3g, X =Cl, 49%, 16h

3h, X =Cl, 62%, 16h

3i, X =Cl, 63%, 16h

3j, R = H, X =Cl, 84%, 2h
3k, R = 4-CH_3, X =Cl, 82% 2h
3l, R = 3-CH_3, X =Cl, 87% 2h
3m, R = 4-OCH_3, X =Cl, 76%, 16h

3n, X =Cl, 35%, 16h

3o, X =Cl, 42%, 16h

3p, R = H, X =Cl, 91%, 2h
3q, R = 4-CH_3, X =Cl, 83% 2h
3r, R = 3-CH_3, X =Cl, 81% 2h
3s, R = 4-CF_3, X =Cl, 94%, 2h
3t, R = 4-F, X =Cl, 89%, 2h
3u, R = 4-CN, X =Cl, 88%, 2h

3v, R = H, X =Cl, 90%, 2h
3w, R = 4-CH_3, X =Cl, 85% 2h
3x, R = 4-CF_3, X =Cl, 87%, 2h
3y, R = 4-F, X =Cl, 84%, 2h
3z, R = 4-CN, X =Cl, 81%, 2h
3aa, R = 4-OPh, X = Br, 91%, 2h
3ab, R = 2-Naphtyl, X = Br, 82%, 2h

3ac, R = H, X =Cl, 92%, 2h
3ad, R = F, X =Cl, 85%, 2h

The present study was supported by Russian Science Foundation, RSF grant 22-23-00308

SILICA-BASED AEROGELS WITH TUNABLE PROPERTIES: THE HIGHLY EFFICIENT BF_3-CATALYZED PREPARATION AND LOOK INSIDE THEIR STRUCTURE

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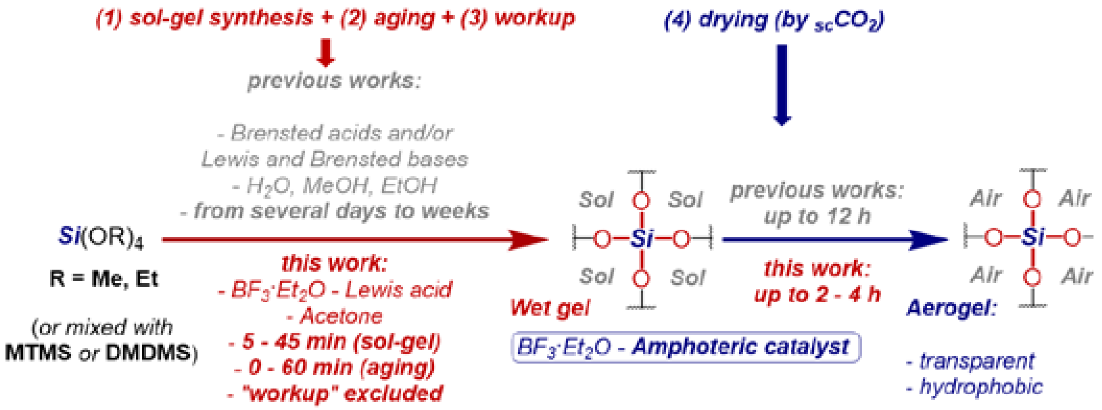
In recent years, there has been an increased interest in porous materials, which is related to their applicability in different areas of science, medicine and technology. Aerogels, silica aerogels in particular, have special abilities: (1) high specific surface area and porosity, with a low density; (2) high insulation and soundproof rates; (3) optical transparency; (4) low permittivity; (5) low Young's modulus; (6) thermostability and other.

There are several successive stages that are carried out when obtaining silica aerogels: (1) sol–gel synthesis - wet gel forming; (2) aging and the formation of a lasting gel; (3) workup - preparing the gel for drying (including replacement one solvent with another, the catalyst and byproducts removal etc.); (4) drying - manufacturing an aerogel from the wet gel.



This work presents a solution to one of the most fundamentally and practically important challenges in the production of silica-based aerogels, time consumption and expensiveness of these processes, with the main focus on the sol–gel process.[1] We suggested a highly efficient BF_3-catalyzed method for the production of aerogels, which allows one to shorten the stage of the formation of a (wet) gel to 5 min, the stage of gel aging to 0, while the stage of gel workup is not required; the duration of these stages, according to the literature, ranges from days to weeks. The process is performed using commercially available, simple, and inexpensive reagents and under mild reaction conditions: $BF_3 \cdot Et_2O$ as the catalyst, acetone as the solvent, room temperature, and at atmospheric pressure. This approach allows one to quickly obtain both classic opaque and transparent silica-based aerogels from $Si(OMe)_4$ or $Si(OEt)_4$ as well as transparent superhydrophobic ones from their mixtures with $MeSi(OMe)_3$ or $Me_2Si(OMe)_2$. In addition, we succeeded in obtaining a series of aerogels with various organic and inorganic additives, in particular, in this way, luminescent and metallasiloxane ones were prepared. Also, the effect of the method for producing silica-based aerogels on their (supra)molecular structure and morphology was thoroughly studied by a set of physicochemical methods of analysis: using scanning electron and light microscopy and X-ray microtomography, the differences between the resulting aerogels at the micro- and nanoscale are shown; using 1D, 2D and 3D NMR[2] experiments: a) the key intermediates involved in the sol-gel process were recorded and the transformation of the $BF_3 \cdot Et_2O$ catalyst over time was studied; b) the kinetics of gel formation over time was studied, and the formation of a huge number of organosilicon intermediates was established, and the importance of stabilizing particles in solution was shown. These findings allow to tune the density, transparency, mechanical strength, hydrophobicity, and other properties depending on the need by choosing the right technique.

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This work was supported by a grant of the Russian Science Foundation (RSF grant 19-73-10172)

THE SYNTHESIS OF NEW SPAAC REAGENTS BASED ON TRIAZOLE-ANNULATED CYCLONONYNES

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Click-chemistry is a unique chemical approach that is growing in popularity among scientists. Bioorthogonal click-reactions are appeared to be the most significant, and the azido group is considered as the most applicable one for bioorthogonal bioconjugation. Both terminal alkynes and cycloalkynes are able to react with organic azides under physiological conditions being involved in Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC) [1,2] or Strain-Promoted Azide-Alkyne Cycloaddition (SPAAC), respectively. SPAAC is preferable over CuAAC due to the absence of toxic affection of Cu(I) and kinetic benefits in the case of some cycloalkyne derivatives [3]but the Cu(I.

Recently, new heterocyclononynes fused to a heterocyclic core have been obtained [4]. However, **BT9O** (Fig. 1) was found to be unstable. We assumed the reason for the kinetic instability of **BT9O** is the rather high ring strain energy (RSE) compared to the RSE values of other cycloalkynes along with the small HOMO−LUMO gap.

The current research aims to check the accuracy of the proposed conjecture and to synthesize new stable heterocyclononynes fused to a heterocyclic core with a higher level of reactivity. DFT calculations (B3LYP-D3/6-31++g(d,p)/SMD) revealed, that triazole has turned out to be the most suitable heterocyclic core which is prone to increase FMO gap, maintaining high SPAAC reactivity. Therefore, the following target structures (**Tr9X**, X = NTs, O) have been chosen for the synthesis (Fig.1).

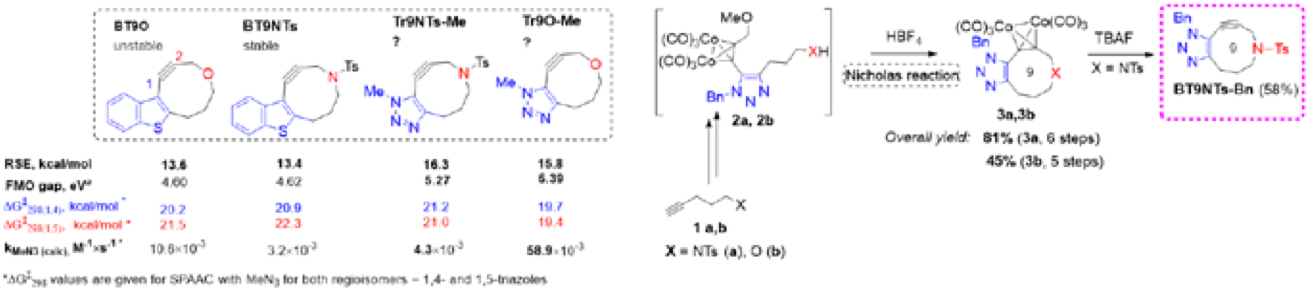

Figure 1. Calculated reactivity parameters for heterocycloalkynes and the synthesis of Tr9X.

The synthesis of the target **Tr9NTs-Bn** was accomplished within 7 steps with viable yields in each step. Thus, the Nicholas reaction followed by Co-decomplexation enabled to obtain triazole-annulated *N*-cyclononyne. Thus, the hypothesis seems to be correct, and heterocyclononynes with higher RSE along with larger FMO gap can be stable. Additionally, Co-complex of **Tr9O-Bn** has been also obtained. Co-deprotection of **Tr9O-Bn** along with the study of SPAAC kinetics essential for the final confirmation of the proposed stability-reactivity relationships theory for heterocyclnonynes is ongoing.

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Acknowledgements. This work was supported by Russian Foundation for Basic Research (project No 20-03-00117) and performed using the equipment of SPbU Recourse centers.

ADVANCE IN HETEROCYCLIC CHEMISTRY OF ELECTROPHILIC ACTIVATION OF NITROALKANES IN REACTION WITH HYDRAZINE DERIVATIVES

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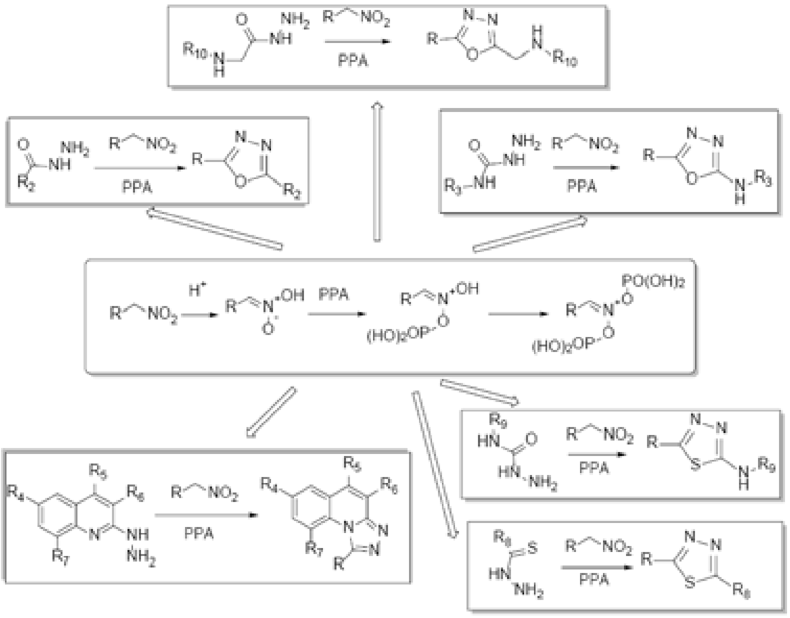
This message presents a summary of the reactions of hydrazine derivatives with electrically activated nitroalkanes in the polyphosphoric acid medium. Over the past years, our scientific group has developed and deepened an approach to the synthesis of various heterocycles through an unusual transformation of nitro compounds and binucleophiles in the PPA. Our group has reported efficient synthesis of 1,3,4-oxadiazoles using a given approach [1], 1,3,4-thiodiazoles [3], with various substituents in 2 and 5, including substituents containing hydrophilic alkylamino grope [5]. As well as about obtaining 1,3,4-triazolo[4,3-*a*]quinolines [2], as well as about the simultaneous annulation of the oxadiazole and triazole ring on the quinoline substrate [4]. Also during our work, we came across the byproduction process of the formation of fursing, through intermediate nitriloxides [6]. Many of the proposed syntheses proceed with good yields and fluently. There is also data on biological research of the library of our substances in the fight against neuroblastoma.



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Acknowledgements. This work was supported by Russian Foundation for Basic Research № 20-33-90026.

TWO DIRECTIONS OF THE 6,7-DIHYDRO-5*H*-1,2,4-TRIAZOLO[3,4-*B*][1,3,4]THIADIAZINE RING CLEAVAGE

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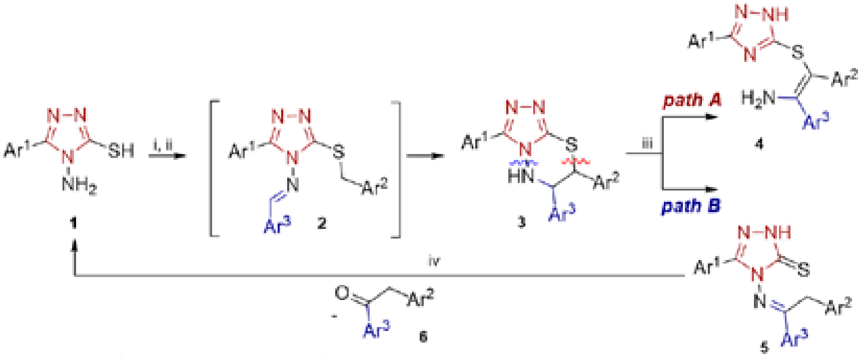
An intramolecular cyclization of 4-amino-4*H*-1,2,4-triazole-3-thiols **1** leads to 6,7-dihydro-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines **3**. The dihydrothiadiazine ring opening reaction of compounds **3** under basic conditions could proceed via two possible pathways: the N–N-bond cleavage (path A), or C–S-bond cleavage (path B), yielding new triazole derivatives **4** and **5** (Scheme 1). Interestingly, the compound **5** was further hydrolysed to produce the starting 4-amino-4*H*-1,2,4-triazole-3-thiol **1** and a new product, namely aryl benzyl ketone **6**.

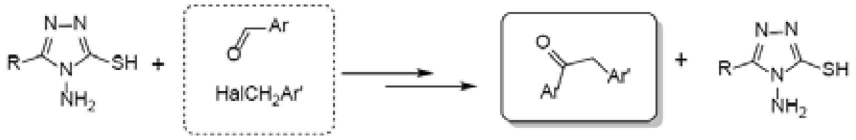
Scheme 1



Reagents: (i) Ar^2CH_2Hal, NaOH, EtOH; (ii) Ar^3CHO, NaOH, EtOH, reflux; (iii) EtONa, DMF, (iv) 40% HCl

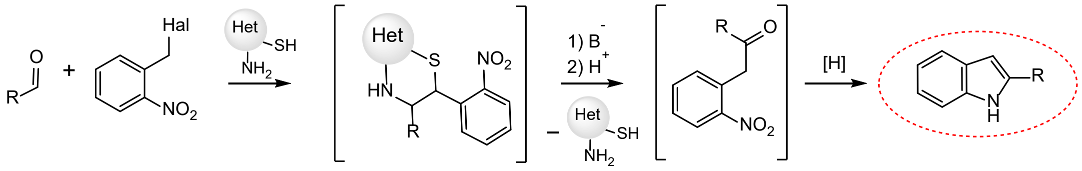
Apparently, the sequence 1→3→5→1 could be utilized for the synthesis of valuable aryl benzyl ketones (deoxybenzoins) from aromatic aldehydes and benzyl halides, herewith 4-amino-4*H*-1,2,4-triazole-3-thiol **1** would serve as a template (Scheme 2).

Scheme 2



One of the applications of the deoxybenzoins synthesis reaction, which we have optimized, is the *one-pot* synthesis of 2-aryl(hetaryl)indoles from the starting benzaldehyde and benzyl halide according to Reissert indole synthesis (Scheme 3).

Scheme 3



The study was financially supported by the Ministry of Science and Higher Education of the Russian Federation (project No. 0852-2020-00-19).

A NEW PATHWAY FOR THE SYNTHESIS OF A OLIGOPEPTIDE AS A VECTOR FOR TARGETED DELIVERY OF RADIONUCLIDES

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Now targeted therapy is one of the major methods of medical treatment for cancer. The creation of new radiopharmaceuticals to treat and diagnose the neuroendocrine tumors expressing somatostatin receptors is a topical task needed to increase their selectiveness and to overcome occurring tumor resistance. The search for new vectors and more efficient conjugates is required for this goal. A new method of conjugate synthesis based on pentapeptides (somatostatin analogs) containing the aryl-substituted thiazolidinecarboxylic acids has been developed. The most optimal ethylenediamine is proposed as a linker, binding the vector with the chelator. Earlier we synthesized the DOTA conjugate DOTA-P2 [1], where the P2 pentapeptide P2 demonstrated earlier unique antiproliferative activity together with a high level of selectiveness of cytotoxic activity on tumor cells and normal cells [2]. A ratio of IC50 (embryonal human fibroblasts) to IC50 (HCT-116) was 6,5.

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2-TRIHALOMETHYL-SUBSTITUTED 3-NITRO-2*H*-CHROMENES IN THE SYNTHESIS OF SPIRO[CHROMENOPYRROLI(ZI)DIN-OXINDOLES] WITH PRONOUNCED ANTITUMOR ACTIVITY

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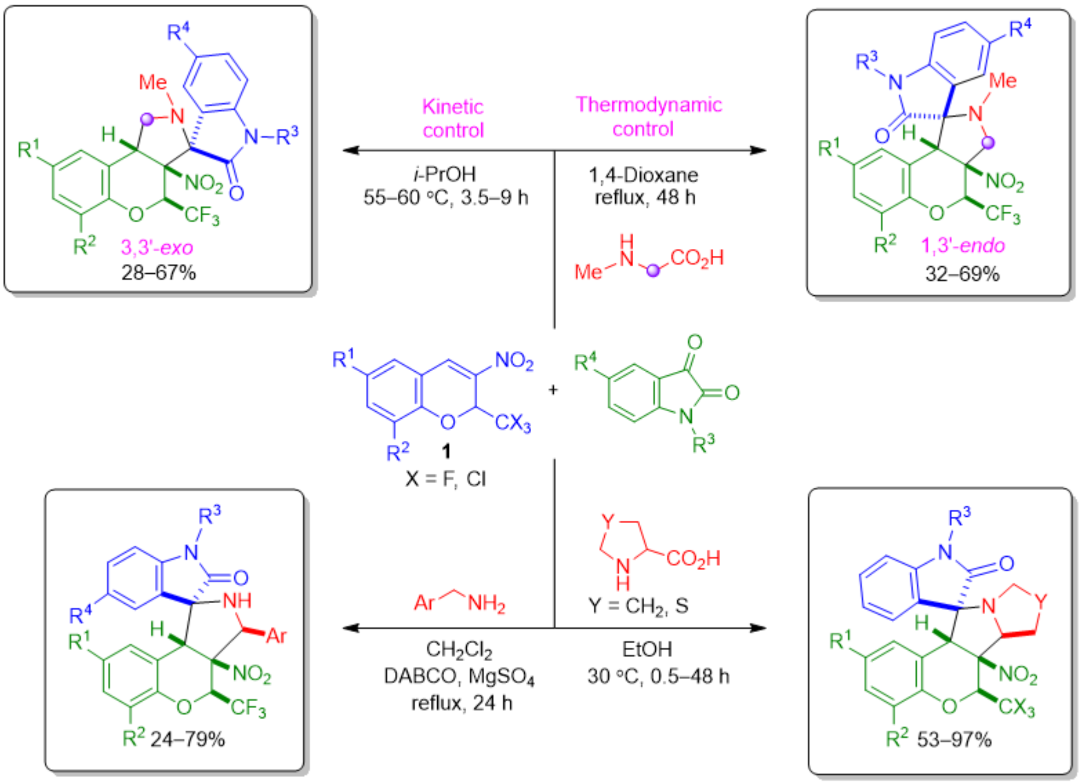
One-pot regio- and stereoselective methods for the synthesis of trifluoro(chloro)methyl-containing spiro[chromenopyrroli(zi)din-oxindoles] based on the three-component reactions of 3-nitro-2-(trihalomethyl)-2*H*-chromenes with isatin-derived azomethine ylides have been developed.



R = H, Me, Bn; R^1 = H, Me, MeO, Cl, Br, NO$_2$; R^2 = H, EtO, Cl, Br, NO$_2$; R^3 = H, Me, Et, Bn; R^4 = H, Me, Br;
Ar = Ph, 2-ClC$_6$H$_4$, 2-BrC$_6$H$_4$, 3-CF$_3$C$_6$H$_4$, 4-ClC$_6$H$_4$, 4-FC$_6$H$_4$, 4-MeC$_6$H$_4$, 4-MeOC$_6$H$_4$

The resulting compounds showed cytotoxic activity against human cervical carcinoma HeLa and human rhabdomyosarcoma RD cells in the micromolar concentration range. Some compounds have demonstrated high selectivity for healthy human dermal fibroblast cells and are potential drag candidates.

This work was carried out with the financial support of the Russian Foundation for Basic Research (project 20-03-00716) and within the framework of the State Assignment of the Ministry of Science and Higher Education of the Russian Federation (project FEUZ-2020-0052).

SYNTHESIS AND PHOTOPHYSICAL PROPERTIES OF FUSED DERIVATIVES OF THIOPHENE AND THIAZOLE

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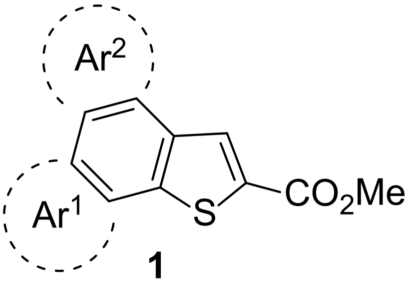
Fused derivatives of thiophene and 1,3-thiazole have unique electronic and photophysical properties. They are widely used in organic electronics, as materials for LEDs, thin-film transistors, and solar cells.[1-3] New derivatives of 4H-thieno[3,2-b]pyrroles (2), benzo[b]thiophene (2), and 2,7-diarylbenzobis(thiazoles) (3) were obtained using microwave and photochemical synthesis as well as other environmentally friendly methods.[4]



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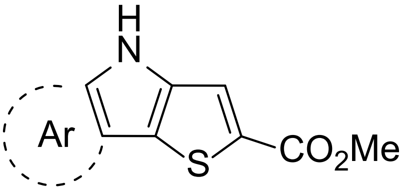

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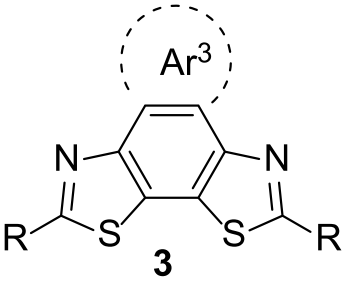

3

The photophysical and (spectro)electrochemical properties of synthesized compounds **2**, **3** were studied in detail.

This work was supported by the Russian Science Foundation (Grant № 20-73-10043).

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THE VARIETY OF MEROCYANINE FORMS OF NEW CATIONIC SPIROPYRAN

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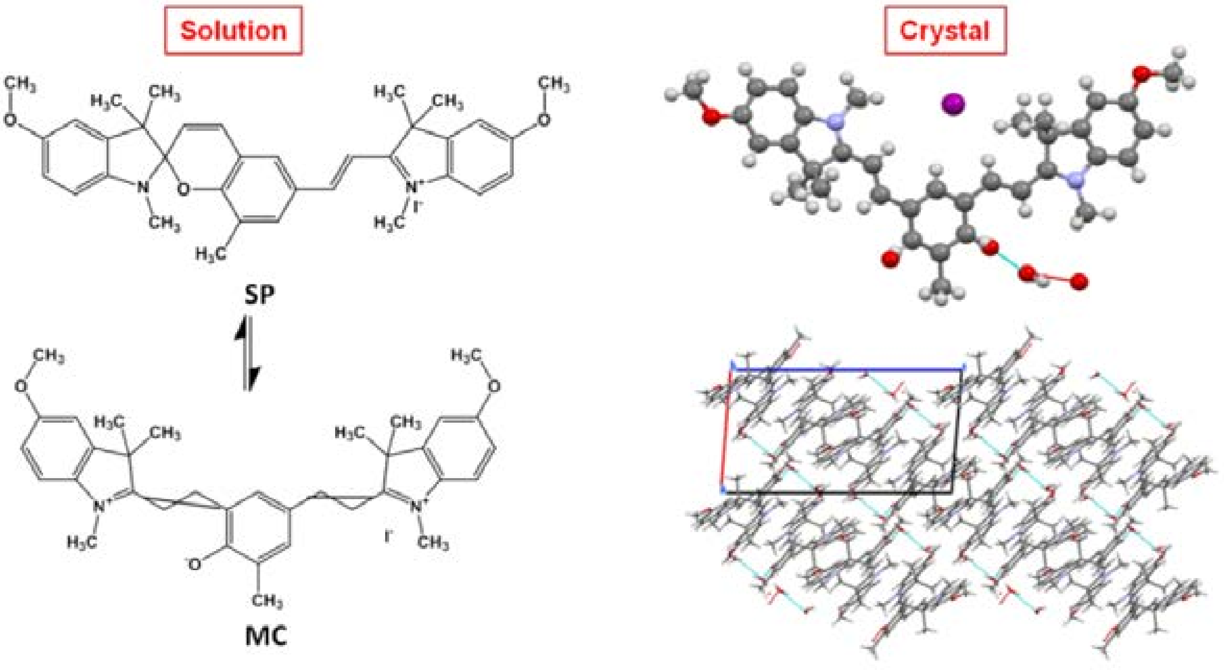
Spiropyrans are well-knowncompoundsthat are ofgreat interest in many fields of humans' life. First of allnumericala lot ofpromising smart materials for sensing and electronics have been developed based on them [1]. Special attention is attracted by cationic derivatives due to the possibility to create smart materials with functional anion [2] and to additionally control the properties using different counterions [3].Perspective properties were demonstrated by spiropyrans containing a conjugated cationic substituent in the 2H-chromene moiety [4].It should be noted that the properties of the compounds vary depending on the structure of the predominant merocyanine (MC) isomer.

New cationic spiropyran **1**shows increased stability of MC in solution and in the crystalline state. According to NMR analysis data compound **1**forms the SP:MC mixture (2:1) in the DMSO solution. In single crystals it exists as two unsymmetrical MC forms – TTC-TTT and TTT-TTC.



This indicates a previously unmentioned increased tendency of the cationic moiety to isomerize. Thus, compound **1**can be considered as the first representative of a three-position molecular switch among spiropyrans with a conjugated cationic fragment.

The research was supported by the Strategic Academic Leadership Program of the Southern Federal University ("Priority 2030"); Demidov O.P. would like to acknowledge the North Caucasian Federal University for financial support in the framework of the project to support the projects of scientific groups and individual scientists.

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INVESTIGATION OF THE SPECIFIC PROCESS OF ACID-CATALYZED REACTION OF SUBSTITUTED QUINALDINES WITH 4,6-DI (*TERT*-BUTYL)-3-NITRO-1,2-BENZOQUINONE

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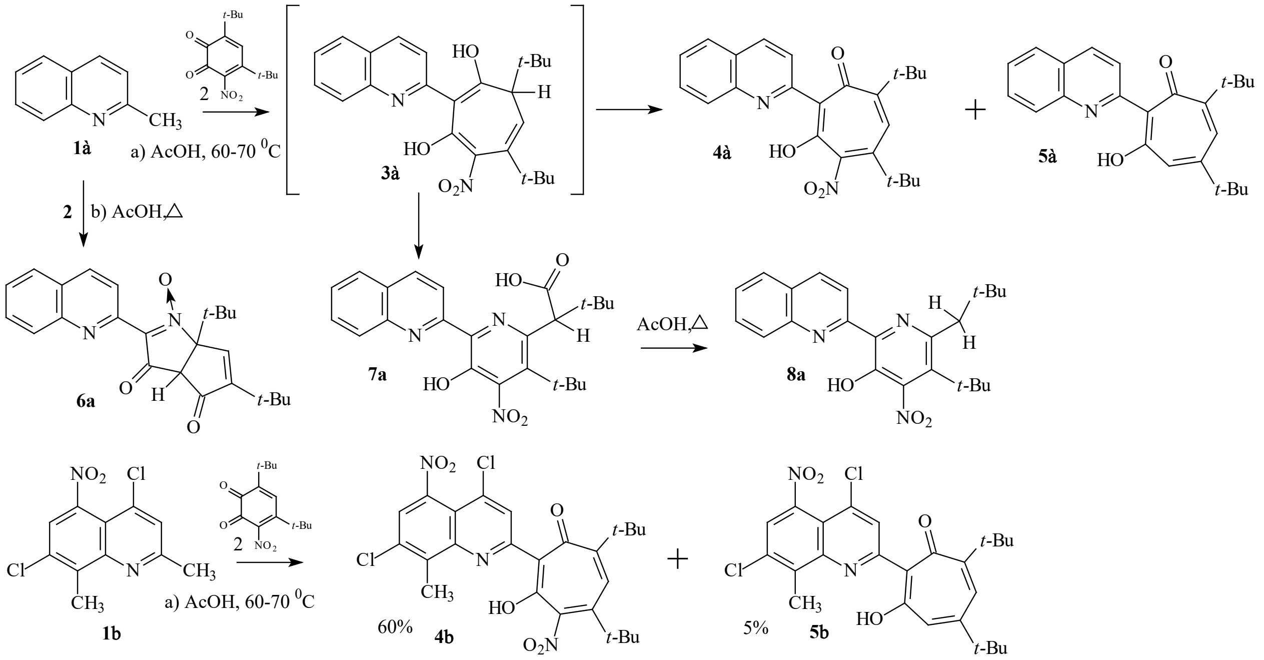
In the current paper, we report unusual transformations of 2-methylquinolines **1a**, **b** derivatives when interacting with 4,6-di(t*ert*-butyl)-3-nitro-1,2-benzoquinone **2**, that produce 2-(2-quinolyl)-1,3-tropolones **4**,**5**, 2-azabicyclic substituted **6** and pyridinquinolines **7** and **8** derivatives. In the case of substituents in the initial heterocycle **1b** the development of the reaction proceeds primarily with the formation of 2-(2-quinolyl)-4-nitro-1,3-tropolone **4b** and trace amounts of **5b**.



Reaction mechanisms are proposed for new compounds **3-8** presented in the scheme. The structure of the obtained compounds **3-8** was investigated by ^{1}H, ^{13}C NMR, IR spectroscopy, mass spectrometry and X-ray diffraction analysis. The interest in compounds **4** and **5** — 1,3-tropolones — is resulted from the presence in this group of substances of the previously studied high biological activity, which in many respects exceeds the activity of pharmacological preparations used nowadays in the market.

This research was supported by the Ministry of Science and Higher Education of the Russian Federation (State assignment in the field of scientific activity, project no. 0852-2020-0031).

SYNTHESIS AND PHOTOPHYSICAL PROPERTIES OF PHOTOCLEAVABLE PORPHYRIN/TRANS-COMBRETASTATIN CONJUGATES FOR COMBINED TUMOR THERAPY

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The multidrug resistance of tumors and significant general toxicity are the main problems of modern chemotherapy [1]. The first problem can be solved using combination therapy approaches. In this work new combined photoactive conjugates **1a-b** consisting of a synthetic tetra(*meso*-aryl)porphyrin photosensitizer (Ps), a photocleavable linker, a therapeutic agent (*trans*-combretastatin A-4 **2**), and carbohydrates were synthetized [2]. The *o*-nitrobenzyl linker was chosen as the photocleavable linker. It binds the chemotherapeutic drug in an inactive form and releases it upon light irradiation (Fig. 1). During irradiation, the low-active *trans*-combretastatin **2** is also isomerized to *cis*-combretastatin **3**, which is cytotoxic at nanomolar concentrations [3].

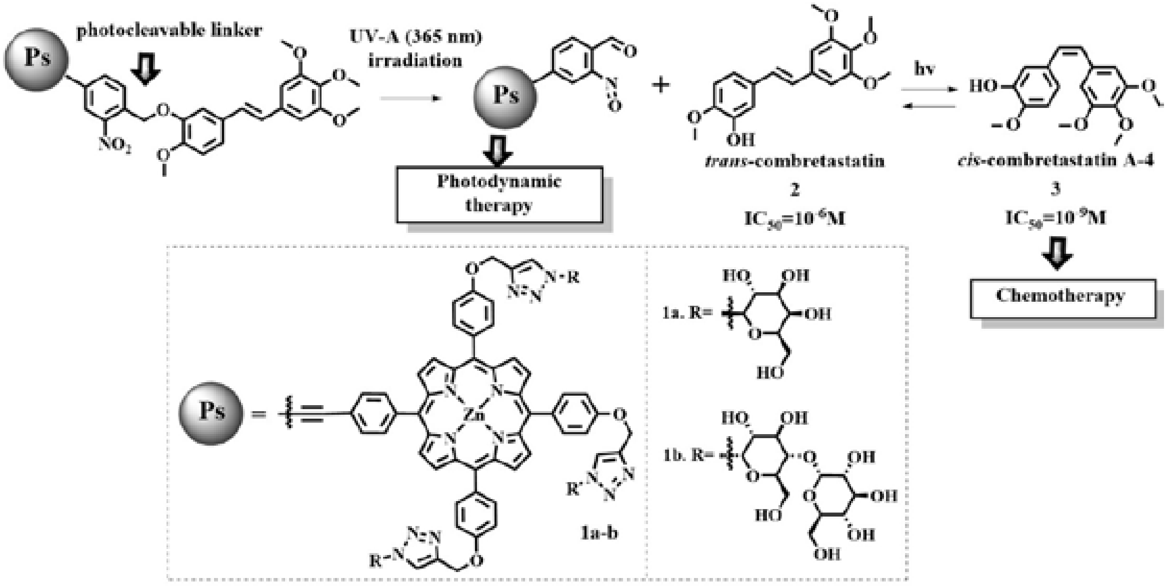

Figure 1. The conception of photocleavable conjugates.

We hypothesized that, through the action of light, we would be able to control the cytotoxicity of conjugates during tumor therapy. However, when the conjugates **1a-b** are irradiated with light at a wavelength of 365 nm (the absorption maximum of the *o*-nitrobenzyl linker), they do not undergo any changes, which is confirmed by HPLC and UV-visible spectroscopy. It has been shown that the desired *cis*-combretastatin **3** is converted to the phenanthrene derivative upon prolonged light exposure. Computational studies have shown that the presence of a triple bond between the porphyrin and the linker fragment does not contribute to the photocleavage process.

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This work was supported by the Russian Science Foundation under Grant No. 21-73-10230.

ACID-CATALYSIS REACTION OF 1-(2,2-DIMETHOXYETHYL)UREAS – A NEW METHOD FOR THE SYNTHESIS OF CYCLIC AND POLYCYCLIC UREAS

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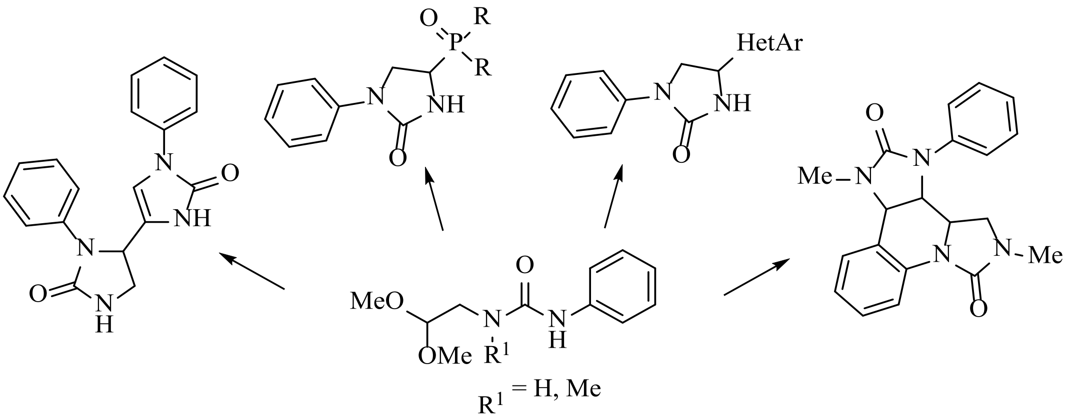
Aza-heterocycles are valuable artificial and natural substances including pharmaceutical compounds, therapeutic agents, and natural products. Among them, imidazolidin-2-one derivatives are of a particular interest due to their well-known biological activity.

In this work we have collected the results of our research aimed at developing new one-step approaches to the synthesis of substituted imidazolidin-2-ones based on acid-catalyzed reactions of 1-(2,2-dimethoxyethyl)ureas with aromatic, heterocyclic, and phosphorus-containing nucleophiles.



This work was supported by the Russian Science Foundation (grant 21-73-20020).

“CHIRAL-AT-METAL” COBALT(III) COMPLEXES AS NON-CLASSICAL ORGANOCATALYSTS FOR FIXATION OF CO_2 INTO CYCLIC CARBONATES

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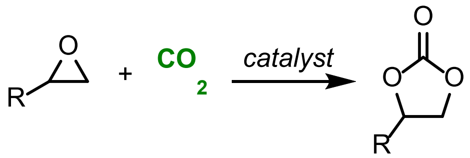
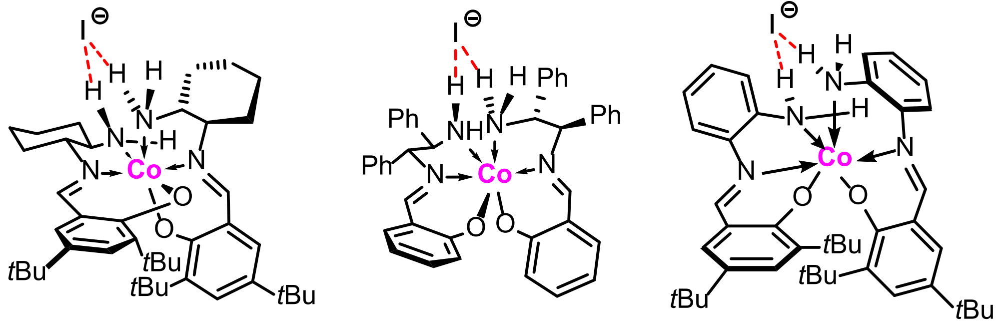
The excess of carbon dioxide (CO_2) in the atmosphere causes a greenhouse effect, and therefore its transformation into valuable organic materials is one of the top priorities of chemistry. In particular, the reaction of epoxides with CO_2 with the formation of practically important cyclic carbonates attracts much attention, since the resulting products are in a great demand in industry.

Herein, we have developed new homogeneous catalytic systems based on chiral octahedral Co(III) complexes derived from Schiff’s bases of chiral diamines and salicylic aldehydes for the fixation of CO_2 into cyclic carbonates under mild and ambient (1 atm CO_2, RT) conditions [1-4]. The obtained complexes operate as bifunctional catalysts activating the epoxides via hydrogen-bonding [5].





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This work was supported by the Russian Science Foundation, project No. 20-13-00155.

SPIROPYRANS POSSESSING PHOTOCHROMIC PROPERTIES IN THE SOLID PHASE

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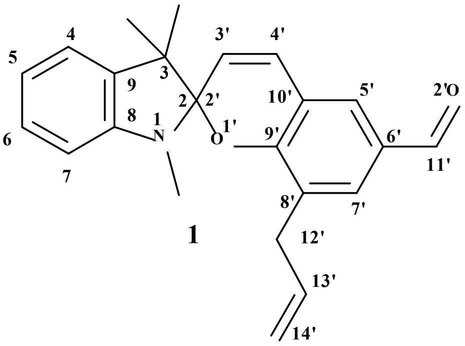
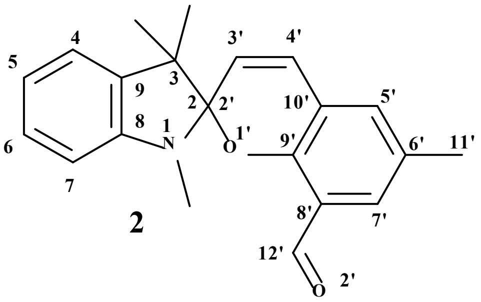
Spiropyrans are one of the most promising and well-studied classes of organic photochromic compounds due to strong changes in the absorption spectra, fluorescence properties, and the dipole moment of the molecule induced by electromagnetic radiation[1].



1



2

The structure of target indoline spiropyrans containing a formyl group in positions 6' **1** and 8' **2** of the 2H-chromene part exhibit photochromic properties in the solid phase, has been investigated. The structure were studied using multinuclear NMR spectroscopy including 2D techniques. The molecular structure of spiropyrans **1** and **2** was established by X-ray diffraction analysis. Intermolecular interactions, Hirshfeld surfaces and voids in the crystals were investigated using the CrystalExplorer17[2] software package. Further studies of photochromism and mechanochromism of these spiropyrans in the crystalline state are shown to be promising. Spiropyrans **1**,**2** show photochromic properties in thin solid films obtained during vacuum thermal deposition onto cooling glass or quartz plates. After irradiation by UV light λ_{max} 365 nm photoinduced form of spiropyran **1** (λ_{max} 567 nm) and **2** (λ_{max} 615 nm) was generated. Photocoloration reaction was found thermally and photochemically reversible.

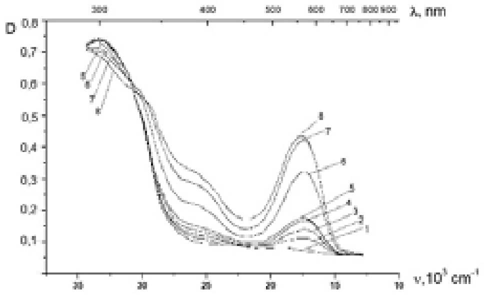


Fig.1 Changing of absorption spectra of thin solid film of spiropyran **1**

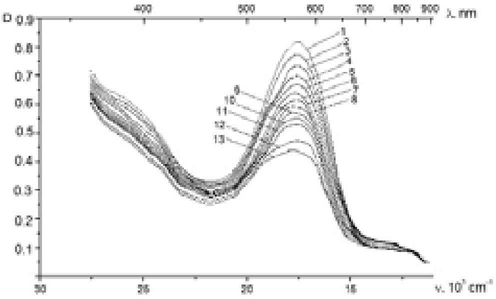


Fig.1 Changing of absorption spectra of thin solid film of the spiropyran **1 p**hotoinuced form

Spiropyrans **1**,**2** show photochromic properties in thin solid films obtained during vacuum thermal deposition onto cooling glass or quartz plates. After irradiation by UV light λ_{max} 365 nm photoinduced form of spiropyran **1** (λ_{max} 567 nm) and **2** (λ_{max} 615 nm) was generated. Photocoloration reaction was found thermally and photochemically reversible.

This work was supported by RFBR, Grant 20-03-00214. The X-ray diffraction study was performed by V.V.Tkachev within the framework of the state assignment (registration number AAAA-A19-119092390076-7).

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DEVELOPMENT OF π-CONJUGATED DONOR-ACCEPTOR OLIGOMERS FOR ORGANIC PHOTOVOLTAICS

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Organic solar cells (OSCs) have attracted considerable scientific and technological interest compared to conventional PV technologies based on traditional inorganic semiconductors, since printed, inexpensive, and mechanically flexible OSC can be fabricated on plastic substrates at low temperatures using inexpensive solution-process methodologies. Donor-acceptor (D-A) π-conjugated oligomers are one of the most promising molecular architectures for usage in OSCs, since their optoelectronic and physicochemical properties can be finely tuned. Nowadays, non-fullerene acceptors (NFA) having a condensed heteroarylene chemical structure are a major focus of the research in that field. Due to the intensive development of NFA, the search for new suitable donor materials (especially small molecules) for them has become an urgent task.

In this work, we report on the design, synthesis and comprehensive investigation of the series of D-A oligomers as new donor (p-type semiconductors) and acceptor (n-type semiconductors) materials for bulk-heterojunction organic solar cells [1-6]. The report will include the synthesis and study of the optical, electrochemical and thermal properties of new D-A molecules that have various condensed fragments as an electron-donor fragment, for example, such as benzodithiophene, benzotriindole and acridine derivatives, thiophene or thienothiophene units as a conjugated spacer, and various derivatives of dicyanovinyl, cyanoacetate and cyanoindanone groups as terminal electron-withdrawing fragments. The developed novel non-fullerene acceptors demonstrate their high efficiency in the photovoltaic devices. The work results showed that the performance of non-fullerene OSCs are very sensitive to the type of electron-withdrawing groups of the donor molecule.

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The work was supported by the Russian Science Foundation (grant number 19-73-10198)

SYNTHESIS OF NEW 5-AMINOAZOLO[1,5-A]PYRIMIDIN-7-ONES AS PRECURSORS OF ANTITUMOR COMPOUNDS

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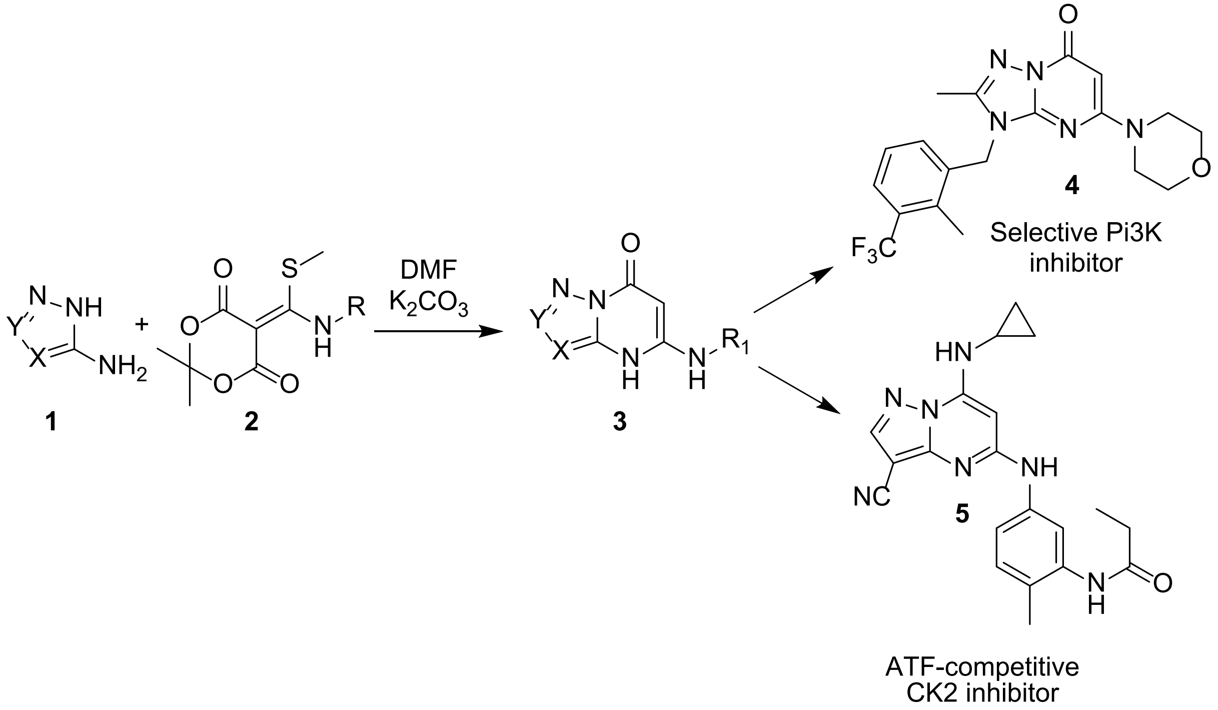
Cancer is one of the world's leading causes of death, with an estimated 10 million deaths in 2020. However, many types of cancer are curable with early diagnosis and treatment. Establishment of alternative ways to treat tumor diseases allows the use of new effective and low-toxic drugs in the early stages of the disease. One of the actual directions is the inhibition of biological targets responsible for the growth, proliferation, and survival of tumor cells. For example, CK2 and Pi3K receptors are targets for such treatment.



We have developed a method for the synthesis of compounds of the azolo[1,5-a]pyrimidin-7-ones 3 series, which consists in the cyclocondensation of aminoazoles **1** with a modified derivative of Meldrum's acid **2** by heating in DMF in the presence of potassium carbonate. The synthesis of inhibitors **4** and **5** is usually also based on the cyclocondensation of aminoazoles **1**, but with malonic ester, therefore the synthesis of the desired compounds mainly proceeds in 5 or more stages. The approach we have developed makes it possible to reduce the number of chemical steps to two.

The work was supported by the Ministry of Science and Higher Education of the Russian Federation, State Contract № FEUZ-2020-0058 (H687.42B.223/20).

FIRST EXAMPLE OF SYNTHESISOF QUINOLINE DERIVATIVE FROM FURAN CORE

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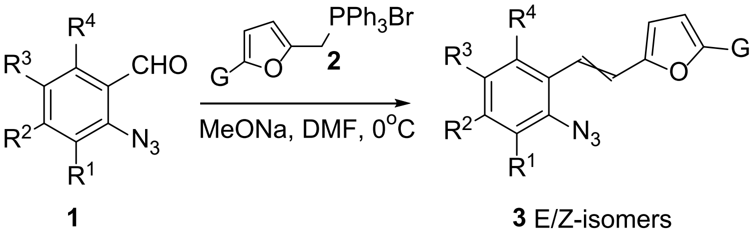
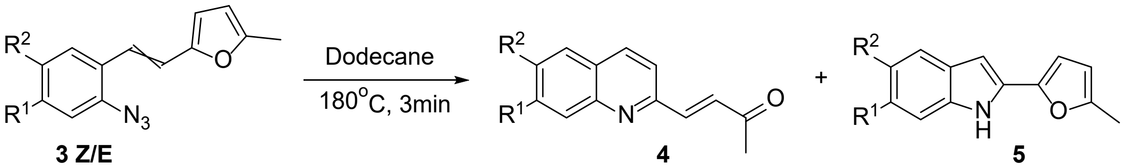
Previously, we reported an efficient methodology for one-pot synthesis of triphenylphosphonium salts from (het)arylmethyl alcohols, which above all enabled convenient access to furfurylphosphonium salts.[1] The Wittig olefination of substituted 2-azidobenzaldehydes**1** with furfurylphosphonium salts**2** delivers a mixture of corresponding *E*/*Z*-olefins**3**(Scheme 1).

Scheme 1



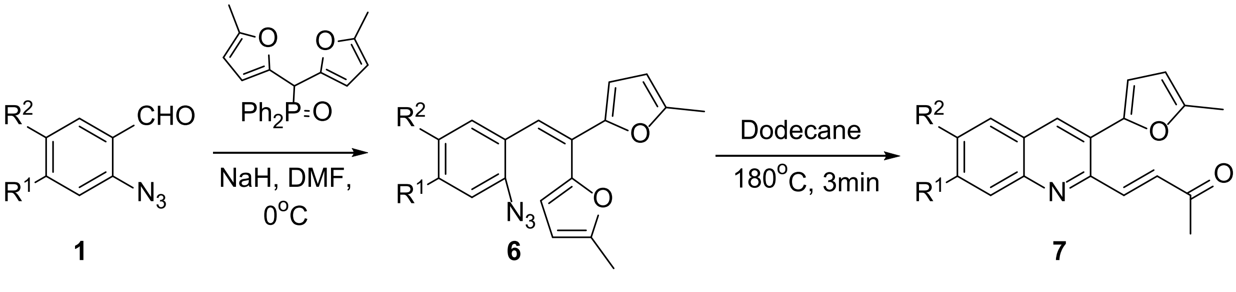
Subsequent thermolysis of the isomeric mixture of olefins **3** furnished two heterocyclic compounds. Interestingly, separate experiment with the *Z*-isomer provided quinoline**4**, which is accounted for by nitrene attack on the furan ring, followed by oxidative cleavage of the latter. In case of the *E*-isomer, the Sundberg reaction proceeded resulting in the corresponding indole **5** (Scheme 2).

Scheme 2



Furthermore, the second furan moiety may be introduced into the starting olefin molecule via the Horner-Wittig reaction of 2-azidobenzaldehydes **1** with difurylphosphinoxide. Thermolysis of the obtained olefin **6** gives exclusively quinoline-type chalcone products**7** (Scheme 3).

Scheme 3



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This work was supported by the Russian Science (Grant No. 22-23-00612)

SYNTHESIS OF NITROGENOUS HETEROCYCLIC COMPOUNDS USING THE ELECTROPHILIC ACTIVATION OF NITRO COMPOUNDS UNDER THE ACTION OF STRONG PHOSPHORYLATING REAGENTS

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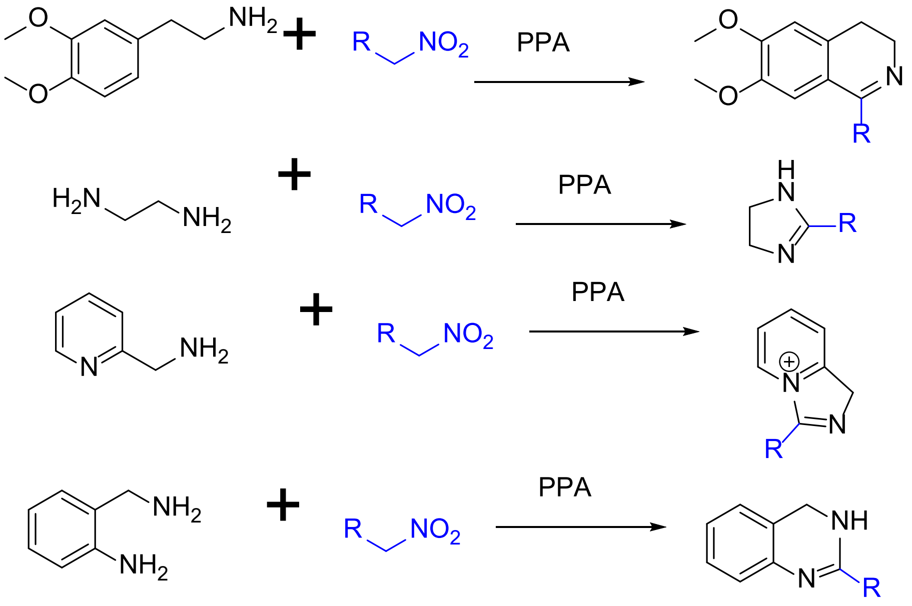
The constant search for methods for assembling new structures that make it possible to effectively develop large libraries of compounds for screening biological activity remains an urgent task. From this point of view, interest in nitrogenous heterocyclic compounds, such as isoquinolines, imidazolines, imidazopyridines, quinazolines, does not weaken. Such structural fragments are included in a number of currently widely used drugs.

In recent years, our group has gained experience in the development of new acid-mediated multi-step cascade transformations of nitroalkenes and nitroalkanes aimed at applications in science and medicinal chemistry. This report will cover the following transformations:



The work was supported by the Russian Foundation for Basic Research (project № 20-33-90027 postgraduate students) as well as by Ministry of Education and Science of the Russian Federation (grant #0795-2020-0031).

SUPRAMOLECULAR [2+2] CROSS-PHOTOCYCLOADDITION OF DIARYLETHYLENES

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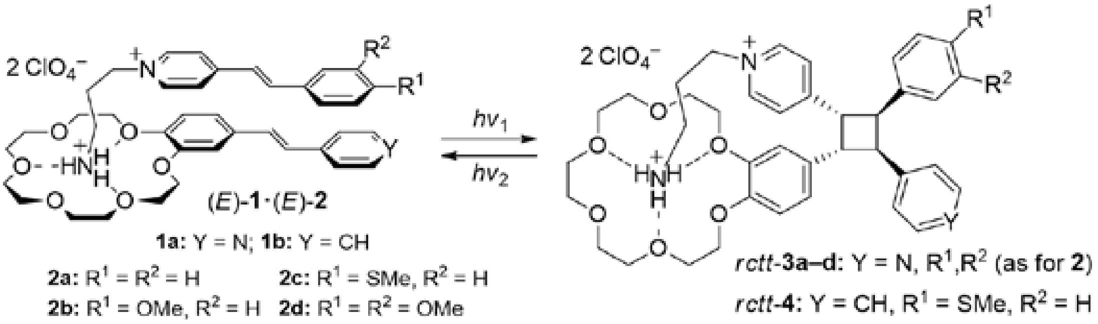
The [2+2] photocycloaddition (PCA) reaction of unsaturated compounds is an important photoreaction used in synthetic organic chemistry [1]. Cross-PCA, which takes place between different olefins, markedly expands the synthetic potential of the reaction. In the case where unsaturated electron donor and electron acceptor are used as the starting reactants, it is very difficult to predict the possibility and efficiency of cross-PCA. Herewith, the appearance of side photoprocesses, such as photoinduced charge transfer (PET) and energy transfer, which will result in low yield of the cyclobutane derivative, is possible. The introduction of a crown ether moiety into the structure of one olefin and an ammonioalkyl moiety into the structure of other olefin makes it possible to combine unsaturated compounds into pairs and carry out the cross-PCA reaction even in the presence of competing photoprocesses.

The influence of donor substituents in the benzene ring of the styryl dye (*E*)-**2a-d** on the quantum yield of the cross-PCA reaction in pseudodimeric complexes of these dyes with (18-crown-6)styrylpyridine (*E*)-**1a** was studied. It was shown that the photoreaction proceeds stereospecifically with the formation of a single *rctt* isomer of the corresponding cyclobutane derivative **3a–d**.



It was shown that when the styrylpyridine moiety in the crown ether component is replaced by the stilbene moiety (*E*)-**1b**, PET from the donor (stilbene) to the acceptor (styryl dye) takes place in approximately half of the conformers of the (*E*)-**1b**·(*E*)-**2b** complex, which leads to a 5-fold drop in the quantum yield of cross-PCA.

The results of the present study markedly expand the boundary conditions for conducting the cross-PCA reactions of diarylethylenes using the supramolecular assembly. They will also be useful for the development of methods for the synthesis of macrocyclic cyclobutanes as a new type of photoswitchable host molecules.

The work was supported by the Russian Science Foundation (projects no. 19-13-00020 and no. 22-13-00064).

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SULFUR-CENTERED RADICALS IN ORGANIC SYNTHESIS

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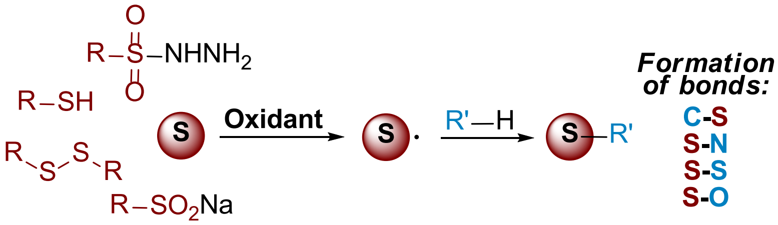
Radical species are often found as intermediates in abiotic and biotic oxidation reactions, and are also involved in atmospheric chemistry of organic compounds. Radical reactions usually demonstrate high tolerance to a wide range of functional groups but suffer from low selectivity.

We have developed approaches to the functionalization of multiple bonds using sulfur-centered radicals of various nature using both classical chemical oxidants and methods of electro- and photochemistry. Available and easy-to-use precursors were used as sources of these species: thiols, disulfides, derivatives of sulfinic and sulfonic acids.



1,3-PROPANESULTONE RING OPENING IN ALKYLATION OF PYRIDINAMIDES. AMIDE GROUP PROMOTES, INHIBITS OR STAYS UNINVOLVED IN PRODUCT FORMATION DEPENDING ON THE GROUP'S POSITION IN THE RING

Vadim V. Negrebetsky [a] **Eugene P. Kramarova** [a], **Dmitry V. Tarasenko** [a], **Sophia S. Borisevich** [b], **Edward M. Khamitov** [b], **Alexander A. Korlyukov** [a], **Tatiana A. Shmigol** [a] **and Yuri I. Baukov** [a]

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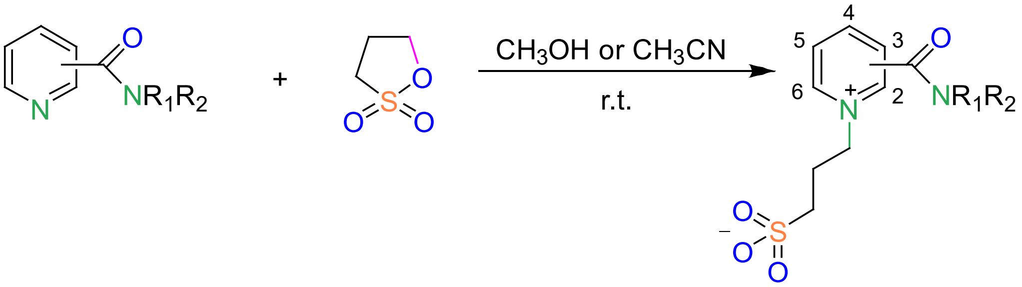
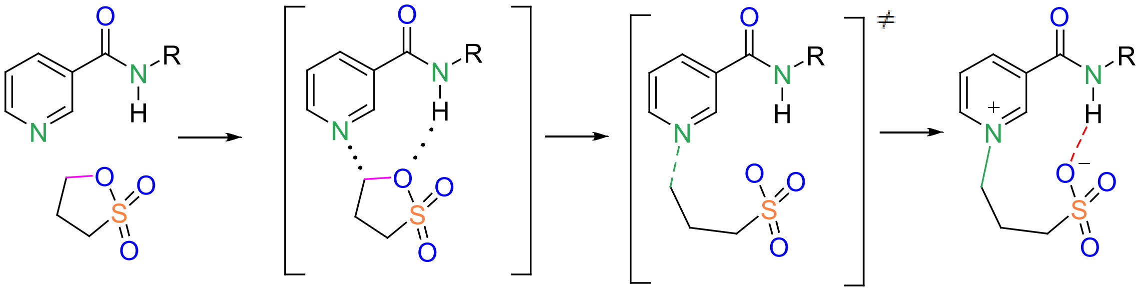
The synthesis of the products of 1,3-propanesultone ring opening during its interaction with amides of pyridinecarboxylic acids has been carried out:



The dependence of the yield of the reaction products on the position (*ortho*-, *meta*-, para-) of the substituent in the heteroaromatic fragment was revealed. The compounds are characterized using elemental analysis, FTIR, ^{1}H, ^{13}C NMR spectra and X-ray crystallography. On the basis of combined spectroscopic, X-Ray and quantum-chemical calculation data, the structure of the transition state "subrate-1,3-propanesultone" in the studied reaction of nucleophilic substitution is proposed.

A mechanism has been proposed that includes the opening of the 1,3-propanesultone ring at the C – O bond, followed by coordination (a distance of slightly more than 2 Å) through the carbon atom to the nitrogen atom of the pyrimidine fragment.



A higher product yield in the case of *meta*-substituted substrates can be caused by the opening of the sultone cycle in the transition state due to the formation of intramolecular H-bonds between sulfo and amide groups. Based on the analysis of ESP maps, the positions of the binding sites of reagents with a potential complexing agent in space were determined.

Acknowledgement: Research of synthetic aspects and quantum-chemical investigation studies were funded by the Russian Foundation of Basic Research, grant number 20-03-00858. Research of the mechanism of reaction by dynamic FT-IR and 2D NMR approaches, in silico studies were funded by the Russian Science Foundation, grant number 21-73-20250.

AZIRINE-ENOL CYCLOADDITION STRATEGY IN THE SYNTHESIS OF *ortho*-FUSED HETEROCYCLES

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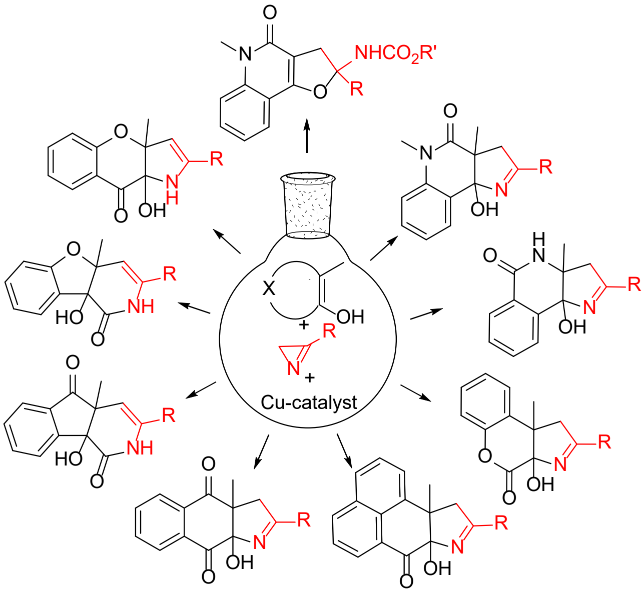
2*H*-Azirines are versatile building blocks for the preparation of various nitrogen-containing heterocycles [1,2]. They also attract increasing attention as biologically active compounds [3]. The most known application of these compounds is the synthesis of pyrrole and azoles derivatives. The synthesis of polycyclic nitrogenous heterocycles has been studied to a much lesser extent. In this work, we analyze our latest results on the use of azirines as annulation agents for heterocyclic enols under copper(I) and copper(II) catalysis. It has been demonstrated that the catalytic opening of the azirine ring in the presence of a heterocyclic enol enables the annulation not only the pyrroline ring to the latter, but also pyrrolidine system, and even nitrogen-free furan system [4,5]. The mechanisms of all reactions are discussed.



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Acknowledgements. This work was supported by the Russian Science Foundation (project № 20-13-00044). This research used recourses of the Magnetic Resonance Research Centre, Chemical Analysis and Materials Research Centre, Computing Centre, Centre for X-ray Diffraction Studies, and Chemistry Educational Centre of St. Petersburg State University.

NOVEL SPIROPYRANS BASED ON β-ESTRADIOL AND ESTRONE AS POTENTIAL PHOTOPHARMACOLOGICAL AGENTS

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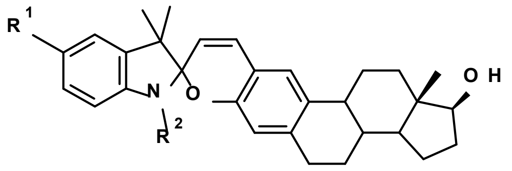
β-Estradiol and estrone are the two main representatives of estrogens, a subclass of female sex hormones produced in the human body, demonstrating a wide spectrum of biological activity, such as anti-inflammatory, antioxidant, anti-atherosclerotic and cardioprotective properties. Many estrogen derivatives including β-estradiol and its metabolites possess antiproliferative effects against various cancer cell lines, including breast tumor cells MCF-7 and MDA-MB 231 [1].

This work is devoted to the preparation and study of new spirocyclic derivatives of β-estradiol and estrone **1-2**. Spiropyrans are one of the most interesting and promising classes of organic photochromic compounds capable of switching between different forms under the action of activating radiation and other external stimuli. The introduction of a switchable function in the form of a spiropyran fragment into a molecule of a bioactive compound can endow it with unique capabilities for regulating biological activity under the influence of various types of exposure, which, together with the increased water solubility of MC forms, makes spiropyrans promising objects for photopharmacology, an actively developing field of biomedicine, which implies the possibility of remote control over biological activity of the drug [2].



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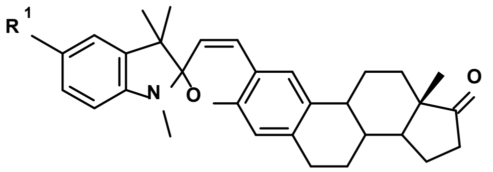

2

R^1 = H, OMe
R^2 =
$-(CH_2)_3SO_3H$

In the course of this study, we obtained 5 new indoline spiropyrans based on β-estradiol and estrone. The structure of compounds was confirmed by NMR, IR and HRMS. Photo- and acidochromic properties of the resulting spiropyrans were studied. The mechanisms of their transformations and the absorption spectra of were investigated by quantum chemical calculations at the DFT level of theory. The study of the cytotoxicity of new derivatives of β-estradiol and estrone revealed that they exhibit different and non-additive properties with respect to their components and can be used in various strategies of anti-cancer treatment.

The study was financially supported by the Russian Science Foundation grant No. 21-73-10300, https://rscf.ru/project/21-73-10300/, and carried out at Southern Federal University.

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SUPRAMOLECULAR ASSEMBLIES OF ETIOPORPHYRIN REGIOISOMERS DEPOSITED ON HOT SUBSTRATES

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We are currently dealing with synthetic petroporphyrins, laboratory analogs of macroheterocyclic components of heavy oils, which have a strictly defined substitution pattern. These molecules tend to aggregate into well-shaped supramolecular objects (rods, fibers) when deposited in vacuum on unheated substrates. The shape of aggregates depends on the region-isomeric form of a molecule. In this work, we studied self-assembly of Cu(II) complexes with etioporphyrin-I, -II and -III deposited in vacuum on hot substrates with particular interest in obtaining highly ordered structures for photovoltaics. After structural characterization, the thin-film samples with either planar or sandwich-type electrodes were subjected to the photoelectric testing. It was found that position isomerism of etioporphyrin ligand strongly affects morphology of hot-deposited films and determines their contrast with reference films grown on unheated substrates. Molecular packing of the least symmetric III-isomer undergoes smaller changes than packing of I- and II-isomers on upon transition from the LT phase. The thermal activation energy of conductivity raises in the series I→II→III isomers from 1.2 to 2.0 eV.

This work in supported by RSF, project #20-13-00285.

STUDY OF FLUORINE EFFECT ON THE Pd/NHC$_F$ COMPLEXES PROPERTIES

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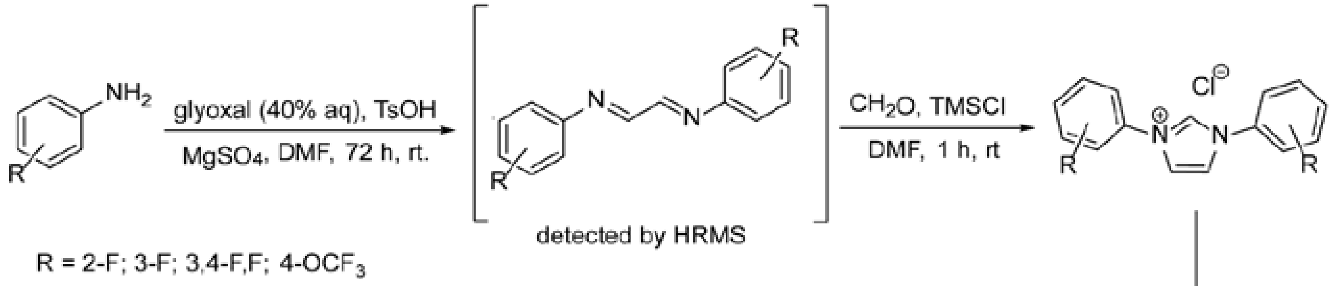
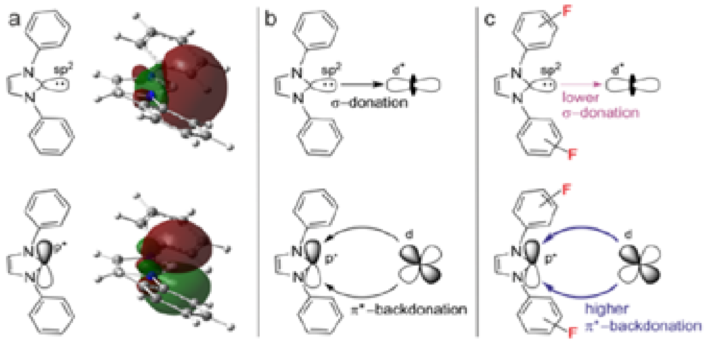
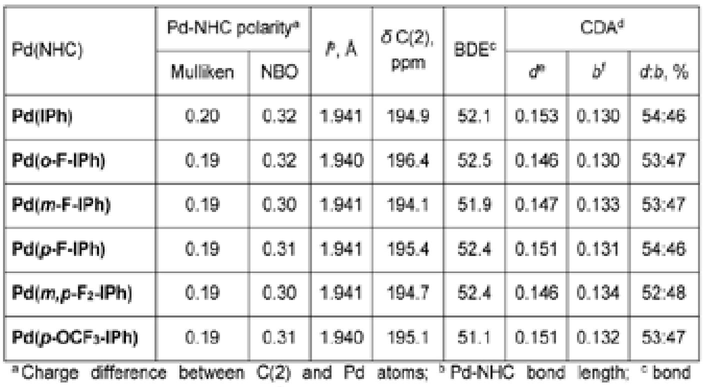
The well-known problem of the synthesis of fluorine-containing (NHC$_F$) and their palladium complexes was solved in the course of this work. For the first time, a series of new NHC$_F$ and Pd/NHC$_F$ complexes were obtained directly from fluorine-containing anilines. Using DFT and XRD calculations, it was shown that the introduction of F atoms into the ligand leads to an insignificant decrease in its σ-donor properties. At the same time, π-donation increases, which practically eliminates the effect of the decrease in σ-donation, so the NHC-Pd binding energy remains almost unchanged. It was also shown that the trans effect of NHC$_F$ ligands weakens, which is expressed in the strengthening of the Pd-Solv bond in the (NHC)Pd(Solv) complexes.



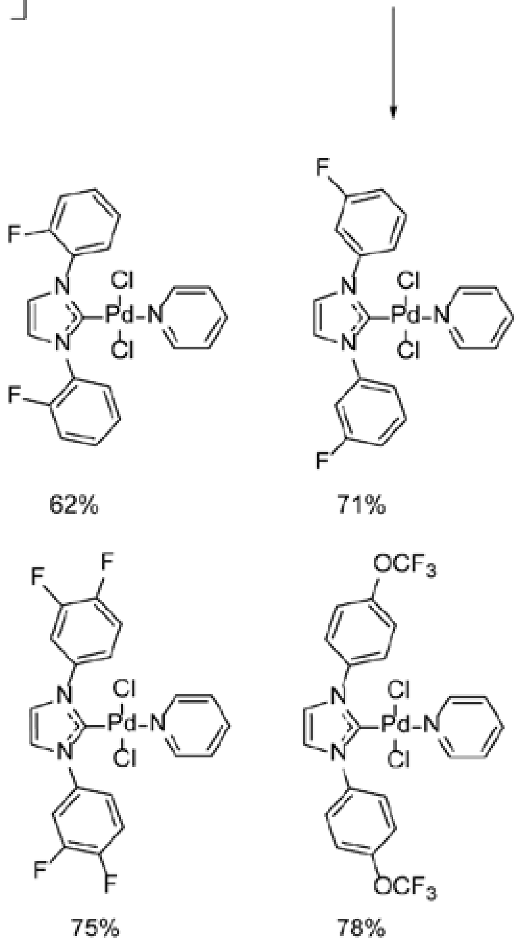


Structural and electronic parameters of Pd-NHC bonds.



Pd(NHC)	Pd-NHC polarity[a]		r[b], Å	δ C(2), ppm	BDE[c]	CDA[d]		
	Mulliken	NBO				d[e]	b[f]	d:b, %
Pd(IPh)	0.20	0.32	1.941	194.9	52.1	0.153	0.130	54:46
Pd(*o*-F-IPh)	0.19	0.32	1.940	196.4	52.5	0.146	0.130	53:47
Pd(*m*-F-IPh)	0.19	0.30	1.941	194.1	51.9	0.147	0.133	53:47
Pd(*p*-F-IPh)	0.19	0.31	1.941	195.4	52.4	0.151	0.131	54:46
Pd(*m*,*p*-F$_2$-IPh)	0.19	0.30	1.941	194.7	52.4	0.146	0.134	52:48
Pd(*p*-OCF$_3$-IPh)	0.19	0.31	1.940	195.1	51.1	0.151	0.132	53:47

[a] Charge difference between C(2) and Pd atoms; [b] Pd-NHC bond length; [c] bond dissociation energy (kcal/mol); [d] charge decomposition analysis; [e] the number of electrons donated from the NHC to the Pd atom; [f] the number of electrons donated from the Pd atom to the NHC.



This work has been supported by the grants the Russian Science Foundation, RSF 20-73-00259.

PHTHALIMIDE-*N*-OXYL RADICAL IN ELECTROCHEMICAL OXIDATIVE COUPLING

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Dzyunov M.M.,[c] **Terent'ev A.O.**[a]

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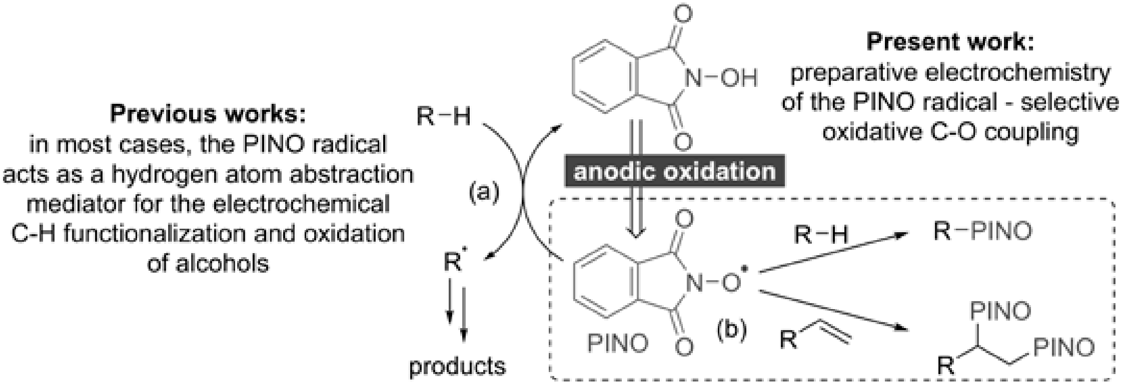
The preparative electrochemistry of O-centered *N*-oxyl radicals remains a poorly studied and complex topic. Imide-*N*-oxyl radicals are widely presented in many processes of C-O coupling and difunctionalization of alkenes, but in electro-organic synthesis they are used to a limited extent as mediators of C-H functionalization and oxidation of alcohols (Scheme 1, a).



Scheme 1. Present work is in the context of the electrochemical applicability of the phthalimide-N-oxyl radical

In this work, phthalimide-*N*-oxyl (PINO) radicals anodically generated from *N*-hydroxyphthalimide are used for radical oxidative coupling in new reactions of C-H functionalization and difunctionalization of alkenes (Scheme 1, b).[1,2]

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The work was supported by Russian Science Foundation (grant no. 21-13-00205).

ALKYL 3-BROMO-3-NITROACRYLATES IN THE SYNTHESIS OF CARBO- AND HETEROCYCLIC STRUCTURES

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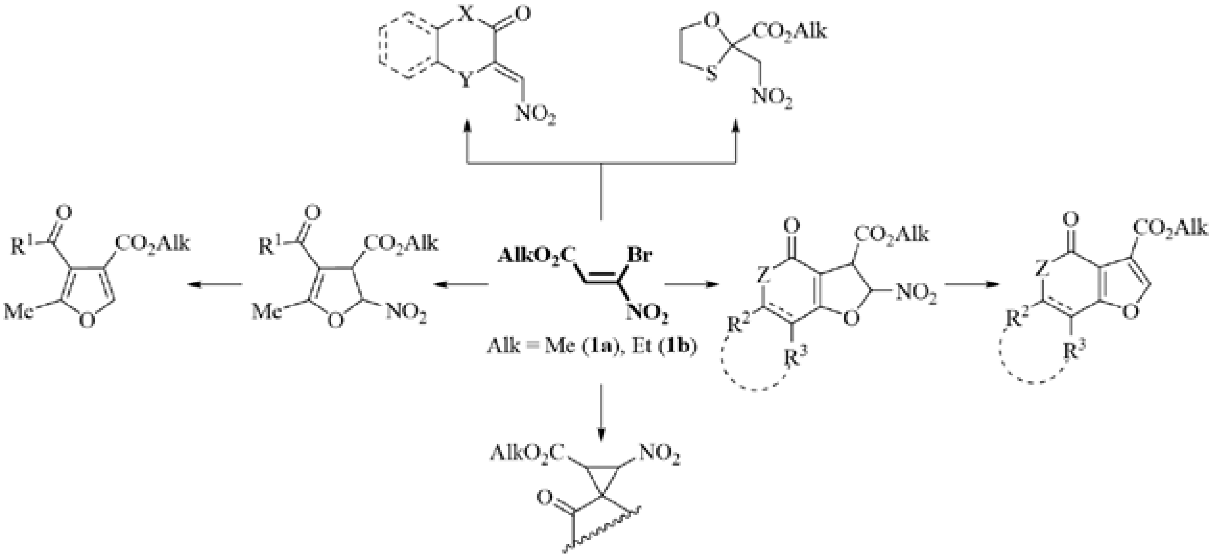
The presence of several electrophilic centers in the molecule of alkyl 3-bromo-3-nitroacrylates creates good conditions for obtaining various carbo- and heterocyclic structures in the reaction with nucleophilic reagents.

We have studied the behavior of alkyl 3-bromo-3-nitroacrylates **1a,b** in reactions with representatives of acyclic and cyclic CH-acids, aliphatic and aromatic 1,4-binucleophilic reagents.



It was shown that the reactions of bromonitroacrylates **1a,b** with representatives of acyclic CH-acids (pentane-2,4-dione, alkyl 3-oxobutanoates) lead to the formation of polysubstituted nitrodihydrofurancarboxylates, which undergo aromatization due to the elimination of HNO_2. Interaction with cyclic CH-acids, in the case of cyclohexane-1,3-dione, 5,5-dimethylcyclohexane-1,3-dione, 4-hydroxy-6-methyl-2*H*-pyran-2-one, 4-hydroxy-2*H*-chromen-2-one proceeds similarly and leads to the production of condensed nitrodihydrofurancarboxylates and the corresponding furancarboxylates. At the same time, reactions with 2,2-dimethyl-1,3-dioxane-4,6-dione and 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one result in the formation of spiro-fused nitrocyclopropanecarboxylates.

Reactions of bromonitroacrylates **1a,b** with 1,4-binucleophiles (ethane-1,2-diamine, propane-1,2-diamine, 2-aminoethan-1-ol, benzene-1,2-diamine, 2-aminophenol, 2-mercaptophenol) lead to the formation of nitromethylidene containing derivatives of piperazinone or 1,4-benzodiazinone, as well as their sulfur- and oxygen-containing heteroanalogues. The interaction of bromonitroacrylates **1a,b** with 2-mercaptoethan-1-ol, depending on the conditions, ends with the synthesis of a mixture of easily separated 1,3-oxathiolane-2-carboxylates and 1,4-oxathian-2-one.

In general, the studied chemical behavior of alkyl 3-bromo-3-nitroacrylates demonstrates a high potential in the synthesis of carbo- and heterocyclic structures.

This work was carried out within the framework of a state assignment with financial support from the Ministry of Education of Russia (project No. FSZN-2020-0026).

ALKYLATED VERDAZYL RADICALS AS STRUCTURAL CORE OF THERAPIC AGENTS AGAINST CANCER

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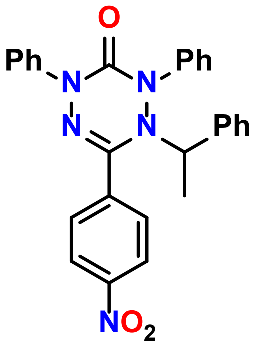
Due to huge impact of oncological diseases on human life the development of new treatment methods against cancer is in demand field of science. Photodynamic therapy (PDT) is relatively new area and only several drugs (Temoporfin, Verteporfin, Motexafin lutetium and other) produced reactive oxygen species (ROS) from triplet form find wide-spread application in clinical practice. Another way for cell killing is active radical generation *via* homolysis of closed-shell molecules into two radical parts. Some classes of organic compounds (e.g. alkoxyamines) could produce radicals *via* external stimuli and work against cancer. Here we presented derivatives of heterocyclic radicals specifically alkylated verdazyls (AlkVZ) and investigation of their cytotoxicity on cancer cell lines MCF-7 under light irradiation.



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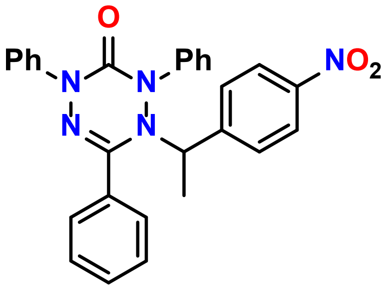

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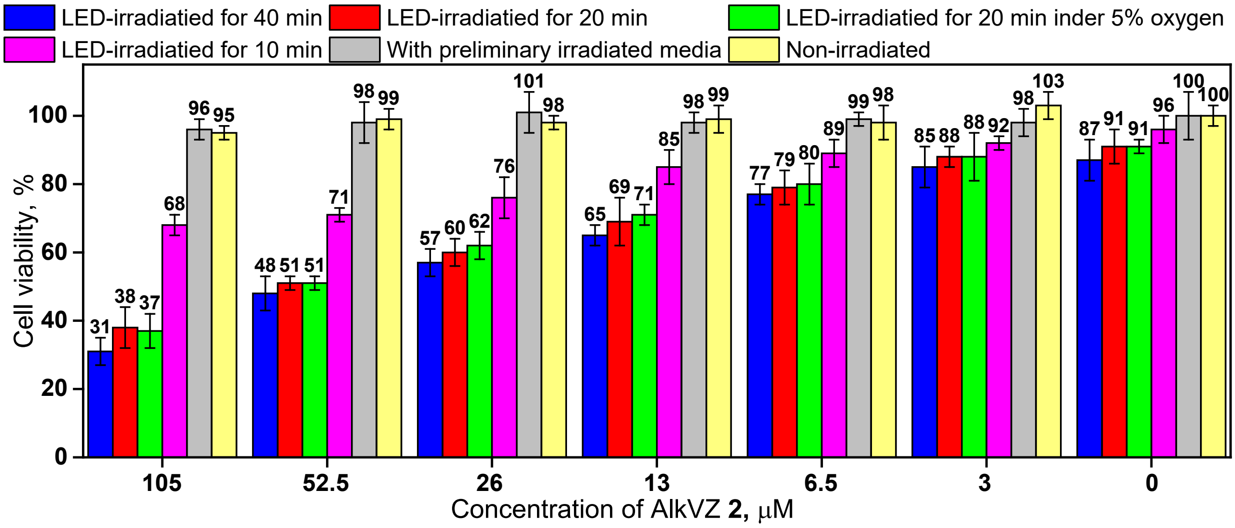

We investigated two alkylated verdazyls **1** and **2** and found that compound **2** has appropriate properties and tested it on breast cancer MCF-7 cells. Results of cell viability (based on MTT test) are reported in Figure. In our experiments we irradiated plates by LED matrix with 395-410 nm diodes. Data from Figure clearly demonstrated good efficiency of AlkVZ **2** in *in vitro* treatment of breast cancer cells MCF-7 even in 105 μM concentration. It is significant that without irradiation (yellow bars) free radicals did not realize from AlkVZ which could allow exclusively selective killing of target cells.

Acknowledgements - This research was supported by the Russian Science Foundation (project 20-73-00236)

A NEW PATHWAY TO OBTAIN 9-*N*-ARYLBERBERINES

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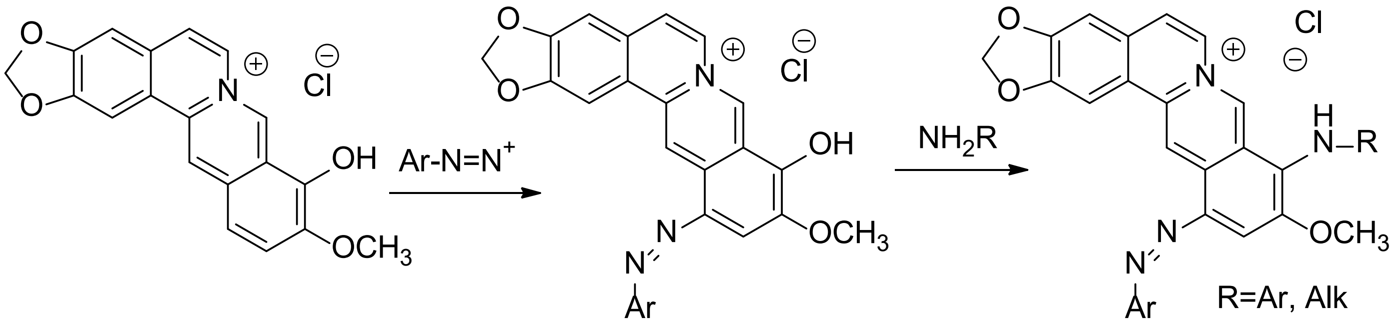
9-*N*-berberines have a high tropism for mitochondria, which determines a wide range of biological activity. For example, 9-*N*-berberines are being investigated as promising compounds for the treatment of diseases associated with impaired mitochondrial function such as cancer, Parkinson's and Alzheimer's diseases.

The list of amines introduced into the position C-9 of the berberine skeleton is limited to primary aliphatic amines. Previously, we developed a method for amination of reduced forms of berberine leading to 9-*N*-arylberberines. But the list of arylamines introduced by this method was limited. We have developed a method for introducing arylamines into 12-substituted berberines. The insertion of substituents in the position C-12 is carried out in berberrubine, which contains a hydroxyl group at the position C-9. This process is an azo coupling reaction at the para position relatively to the phenol hydroxyl group.

Next, 12-substituted berberines are introduced into the substitution reaction of the hydroxyl group at the position C-9. A wide range of diazonium salts can be used as a substituent at the position C-12, and a variety of aromatic and aliphatic amines can be used for substitution at the position C-9.



The insertion of aromatic amines into the position C-9 of the berberine system makes it possible to increase the lipophilicity of berberine derivatives and to vary the affinity for mitochondria over a wide range. In addition, by varying the counterion for aromatic 9-N-berberines, it is possible to change significantly the physicochemical properties of derivatives to achieve the desired solubility and amphiphilicity.

DIARYLIODONIUM SALTS AS TECTONS FOR SUPRAMOLECULAR ASSEMBLIES

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The application of relatively weak non-covalent interactions can be considered an important trend in supramolecular chemistry [1]. Across all types of non-covalent interactions, the directed bonds, such as halogen, pnictogen, tetrel, and others, occupy a special place due to the wide application in the design of materials with enhanced properties [2]. The applicability of supramolecular systems based on non-covalent interaction drives the never-ending quest for the search for novel tectons to build complex functional networks.

As the typical example of hypervalent iodine compounds, iodonium salts are able to form supramolecular assemblies due to the presence of two σ-holes [3]. Such structure features open novel opportunities for the design of materials, including non-covalent organic frameworks.

The report will be dedicated to the recent findings in the field of supramolecular design of novel materials involving iodonium salts as tectons. Starting from the general approach to the preparation of iodonium salts, we will present our results in the targeted preparation of diaryliodonium metallates and their main structural features. Finally, the influence of halogen bonding on the reactivity of iodonium salts and the application of iodonium cations in the design of porous organic frameworks will be demonstrated [4].

The research was supported by the Ministry of Science and Higher Education of Russian Federation in the framework of "Mega-grant" project (No 075-15-2021-585).

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INDOLINE SPIROPYRANS DEMONSTRATING THREE DIFFERENT TYPES OF PHOTOCHROMISM

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Spiropyrans are a well-known class of organic compounds capable of reversible isomerization between two forms [1]. A colorless spiropyran form is usually non-fluorescent in contrast to a brightly colored merocyanine form. The transformation between two forms can occur under the influence of external stimuli [2]. Due to these properties, spiropyrans are widely used in such fields of science as chemosensing, nanoelectronics and bioimaging.

Most indoline spiropyrans exhibit positive photochromism. However, we have shown that by introducing a small set of substituents, depending on the position, three fundamentally different types (**Fig. 1**) of photochromes can be obtained [3].

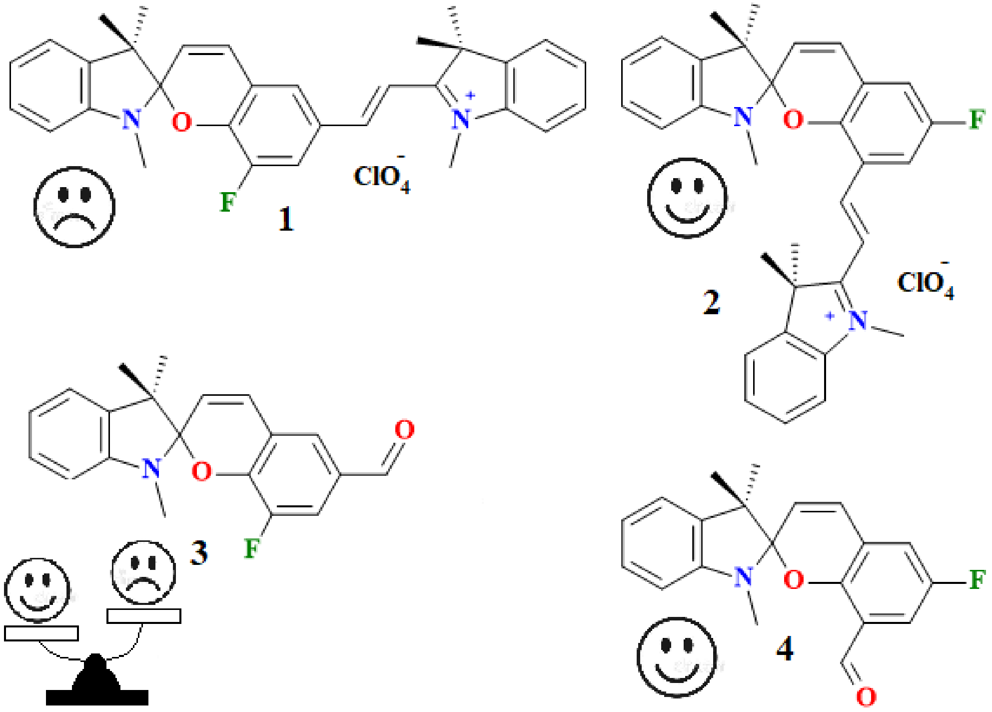

Fig. 1. Structures of spiropyrans and the type of photochromism demonstrated (positive, negative and photochromic "balance")

It is important to note, that salt spiropyrans **1** and **2** are characterized by photoswitchable fluorescence in the range of biological window with maxima at 715 and 791 nm (quantum yields are 0.020 and 0.012) respectively. Such properties allow using of these compounds as fluorescent probes for bioimaging investigations. Compound **3** demonstrates the principal ability to realize a bipolar absorption switch. In contrast to a conventional switch with two switching states, the bipolar absorption switch allows switching between three states. Thus, we have shown that by selecting a substituent and its position in the 2*H*-chromene fragment, molecular switches for various purposes can be obtained. Spectral studies were carried out obtained using the equipment of the Center for Collective Use "Molecular Spectroscopy" of Southern Federal University.

The study was financially supported by the Russian Science Foundation grant No. 21-73-10300, https://rscf.ru/project/21-73-10300/, at Southern Federal University

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SYNTHESIS OF BIFUNCTIONAL IMIDAZOLIUM SALTS BASED ON IMIDAZOLE-4,5-DICARBOXYLIC ACID – THE PERSPECTIVE NHC-LIGANDS

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[b] *A.E. Arbuzov Institute of Organic and Physical Chemistry*
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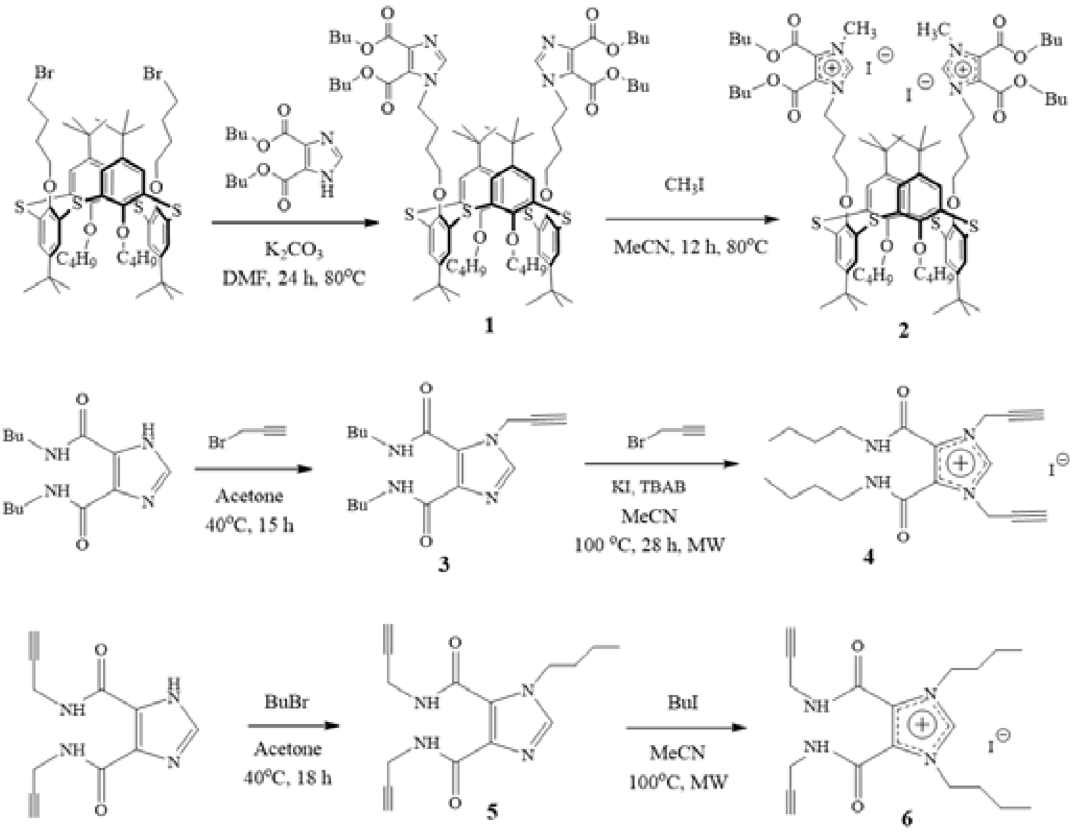
There is a growing interest to amphiphilic catalysts of cross-coupling reactions. Such catalysts allow carrying out cross-coupling reactions in water by forming emulsions. Thiacalixarene platform allows to obtain an amphiphilic catalyst via step-by-step modification of the TCA lower rim with the substituents of different nature. The space separation of the hydrophilic and lipophilic area of the molecule is achieved with the help of the structural features of the TCA derivatives in the *1,3-alternate* stereoisomeric form. Introduction of dibutylimidazole-4,5-dicarboxylate into the TCA platform let us to obtain the amphiphilic NHC-ligand **2**, wich has a further possibility for improving its water solubility by hydrolysis of the ester groups.



Such spatial separation can also be achieved through imidazole-4,5-dicarboxylic acid as the original platform for obtaining bifunctional imidazolium salts. Propargyl groups in the structure of such derivatives allow to introduce hydrophilic fragments via azide-alkine cycloaddition reaction either nearby the carbene centre or at a distance from it. This possibility allows the NHC-ligands **4** and **6** to form aggregates with different structure.

The work was supported by a grant from the Russian Science Foundation № 21-73-00100

CONDENSATION OF TRIOLS AND TETRAOLS WITH CARBONYL COMPOUNDS

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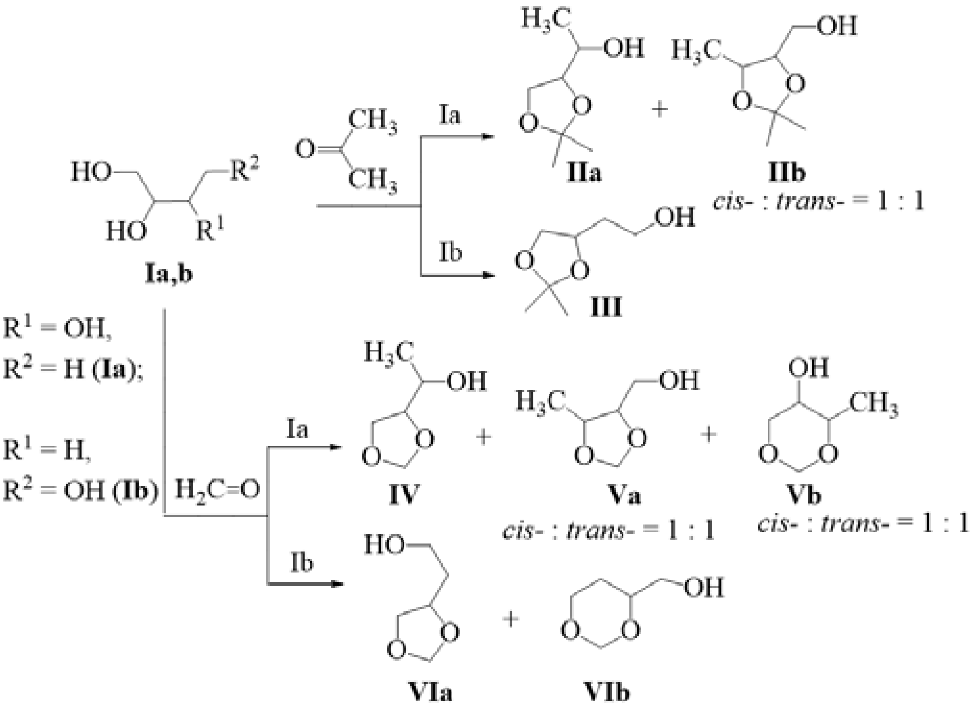
The predominant (more than 95%) formation of 1,3-dioxacycloalkanes during the condensation of glycerol with ketones is well known. This triol and aldehydes form a complex mixture of structural isomer and stereoisomer – substituted 1,3-dioxolanes and 1,3-dioxanes [1, 2].

We found that, as a result of the interaction of 1,2,3- and 1,2,4-butanetriols (**Ia,b**) with acetone, the corresponding 1,3-dioxolanes (**IIa,b** and **III**) also dominate. Structural isomers **IIa** and **IIb** are formed in a ratio of 1 : 1, and compound **IIb** is presented as two stereoisomers.



Diols **Ia,b** react with formaldehyde to form a complex mixture of 5- and 6-members formals where 4-α-hydroxyethyl-1,3-dioxolane **IV** (in the case of **Ia**) and 4-hydroxymethyl 1,3-dioxane **VIa** (in the case of **Ib**) are dominant. 4-Methyl-5-hydroxyethyl-1,3-dioxolane **Va** and 4-methyl-5-hydroxy-1,3-dioxane **Vb** are formed in ratio 1 : 1 and there are as a mixture of cis- and trans-forms, which was proved by NMR spectroscopy.

Acetalization of tetraols (diglycerol and diethriol) leads to bisacetals in high yields. According to NMR spectroscopy, the compounds exist as diastereomers of bisdioxolanes in the ratio erythro- : threo- = 5:4 with the configuration of chiral centers, and the diethriol derivative stereoisomers have diaxial- and axial-equatorial orientations of ethyl-groups is in the ratio 1:1.

This workwas support by the Ministry of Science and Higher Education of the Russian Federation under agreement № 075-15-2020-900 within the framework of the development program for a world-class Research Center.

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CABOZANTINIB-BASED PROTACS: SYNTHESIS AND BIOLOGICAL EVALUATION

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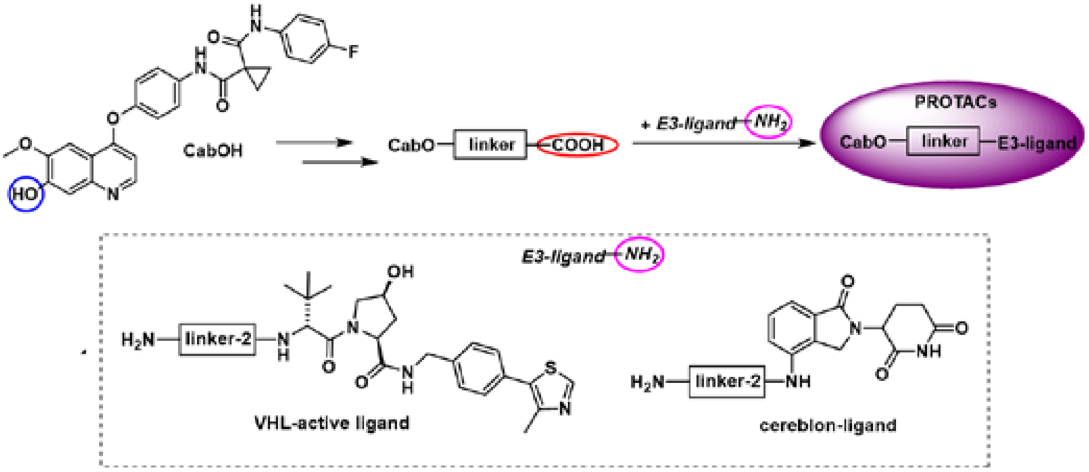
PROTACs (PROteolysis TArgeting Chimeras) are bifunctional molecules containing two ligands. One ligand serves as an “anchor” for pathogenic protein, while the other part of PROTAC binds with ubiquitin E3 ligase, which promotes the binding of the target protein to ubiquitin and its subsequent proteasomal degradation.

We synthesized PROTACs, based on the multikinase inhibitor cabozantinib. It plays role of a ligand for the target pathogenic proteins (Fig.1). The initial step was synthesis of hydroxy- derivative of cabozantinib (CabOH), obtained by previously published method [1]. Then CabOH was successfully modified by insertion of carboxyl group for subsequent conjugation with the second part of PROTAC in amine form. Inhibitors of von Hippel-Lindau protein (VHL) [2-3] and cereblon (CRBN) [4] were used as the second component of PROTACs, binding E3- ubiquitin ligases.



Scheme 1. Cabozantinib-based PROTACs synthesis

For some of the final molecules biological activity was investigated. Containing triazole fragment as a part of linker PROTACs appeared to be active as inhibitors at micromolar concentarations.

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Acknowledgements. This work was supported by the Russian Science Foundation (project No 22-23-00736)

THE REACTIVITY OF ORGANONICKEL SIGMA-COMPLEXES TOWARDS 1,2-DIPHOSPHOLIDE

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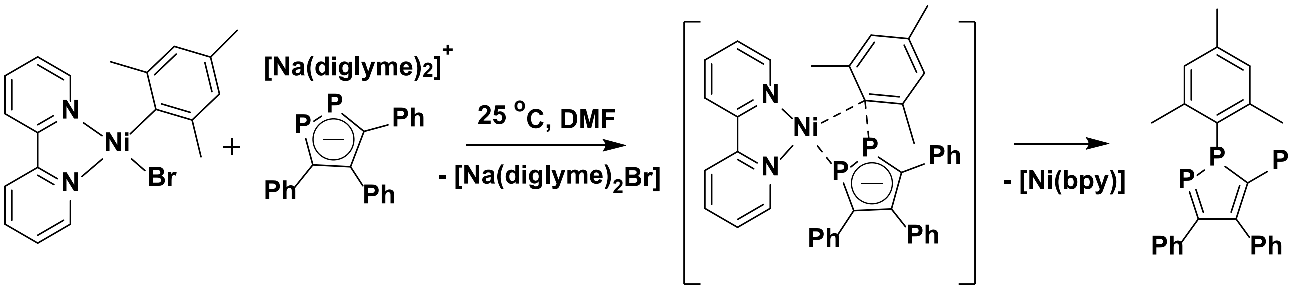
The use of organonickel sigma-complexes in the reactions of C-P bond formation between two conjugation partners is an excellent route for the synthesis of organophosphorus compounds, which are widely used in transition metal catalysis and biochemistry.[1] Moreover, some approaches using organonickel complexes as transmetabolizing agents for organophosphorus compounds are also known.[2] Various phosphorus derivatives bearing element (white, red) phosphorus, P(III) (PH_3; primary, secondary, and tertiary phosphines; phosphine chlorides), and P(V) compounds (dialkyl phosphites; secondary phosphine oxides) are traditionally used as phosphorus bond partners. However, the methods described are usually based on harsh conditions, the use of expensive and flammable reagents, and often associated with a limited range of substrates, low yields, and the formation of various undesirable and sometimes dangerous by-products.[3]

In the present work the reactivity of organonickel sigma-complexes of type [NiBr(Aryl)(bpy)], where Aryl = 2,4,6-trimethylphenyl (Mes), 2,3,5,6-tetramethylphenyl (Tmp), 2,4,6-triisopropylphenyl (Tipp), 2,4,6-tricyclohexylphenyl (Tchp), bpy = 2,2′-bipyridine, towards 1,2-diphospholide was studied. It was found that this interaction leads to the formation of unknown 1-aryl-1,2-diphospholes by formation of new P-C bond by transfer of the aromatic fragment of organonickel sigma-complexes to one of the phosphorus atoms of 1,2-diphospholide.



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This work is financially supported by the grant of the President of the Russian Federation for supporting of the Leading Scientific School (project no. 4078.2022.1.3).

FLUORESCENT PYRROLOCOUMARIN CONGENERS: SYNTHESIS AND PHOTOPHYSICAL PROPERTIES OF PYRANO[3,2-F], [2,3-G], [2,3-F] AND [2,3-E]INDOLES

**A.D. Sharapov, I.A. Khalymbadzha, R.F. Fatykhov, O.N. Chupakhin, M.I. Savchuk,
I.L. Nikonov, D.S. Kopchuk, G.V. Zyryanov, A.S. Novikov**

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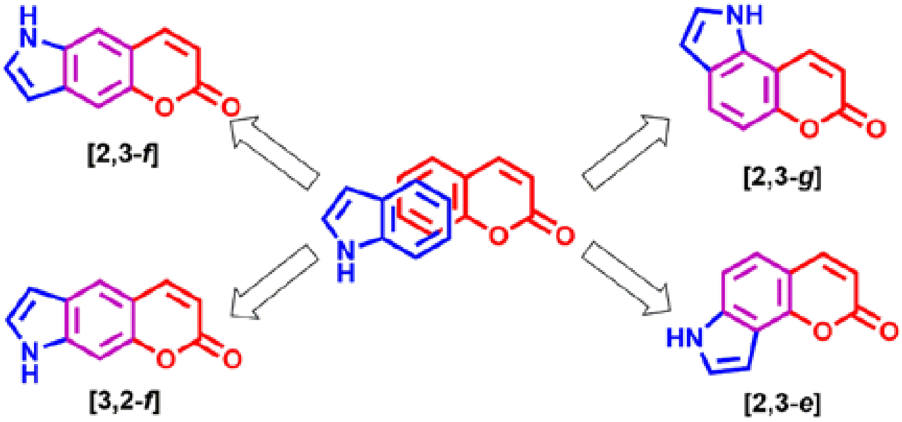
Herein, we report a synthesis of four types of annulated pyranoindole congeners: pyrano[3,2-f]indole, pyrano[2,3-g]indole, pyrano[2,3-f]indole.

We have found that methanesulfonic acid-catalyzed Pechman condensation of 4-, 5- and 6-hydroxyindoles with β-ketoesters provides pyrano[2,3-e]indoles, pyrano[3,2-f]indoles and mixture of pyrano[2,3-g] and [2,3-f]indoles, respectively.



Among the pyranoindoles studied, the most promising were pyrano[3,2-*f*] and [2,3-*g*]indoles. These compounds are characterized by moderate to high quantum yields (30-89%), large (100-200 nm) Stokes shift, absorption maxima at 287-342 nm and emission maxima at 421-537 nm in acetonitrile solution.

In the case of N-alkylation and N-benzylation of pyrano[3,2-f] and [2,3-g]indoles, bathochromic shifts and a decrease in quantum yields were observed in comparison with the parent pyranoindoles. Unfortunately, in the case of annulation of additional benzene ring, we observed a deterioration in the photophysical properties.

More detailed photophysical studies were carried out for the most promising derivatives of pyrano[3,2-*f*] and [2,3-*g*]indoles to demonstrate their positive solvatochromism, and the collected data were analyzed by using Lippert-Mataga equation.

To understand the nature of energy transition processes and molecular orbitals, DFT and TD-DFT quantum calculations were performed.

The work was supported by the Russian Science Foundation, project no 21-73-00214

STUDY OF THE ANTI-CANCER ACTIVITY OF PYRROLECARBOXYLIC ACID DERIVATIVES

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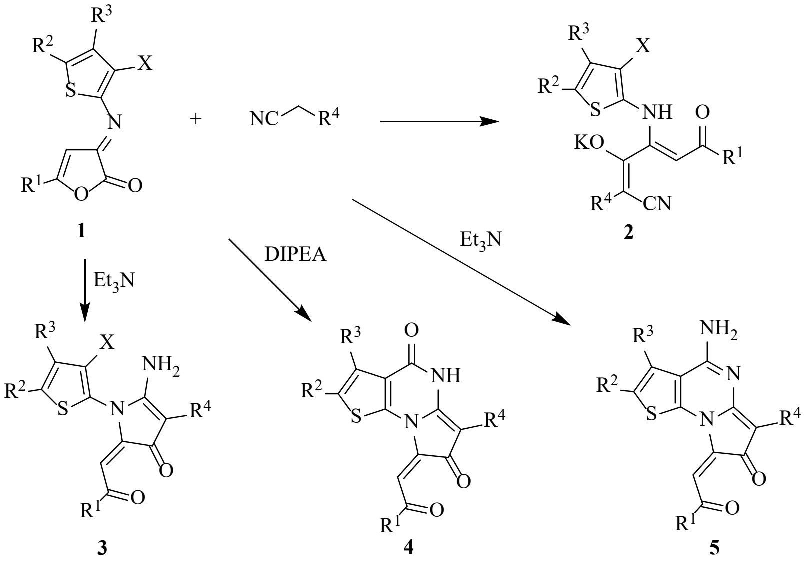
We synthesized substituted 3-imino-3*H*-furan-2-ones 1 and investigated their recyclization reactions. It was found that 1 in the presence of cyanoacetic acid derivatives and different bases gives acyclic compounds 2 and cyclic compounds 3-5. Antitumor activity was studied in the B16 mouse melanoma model.



SYNTHESIS OF BIOTIN DERIVATIVES OF [1] BENZOTHIENO[3,2-B] [1]BENZOTHIOPHENE FOR BIORECOGNITION AND BIOSENSING

Maxim S. Skorotetcky[a], **Elena Yu. Poimanova**[a], **Polina A. Shaposhnik**[a,b], **Daniil S. Anisimov**[a] ,
Oleg V. Borshchev, Elena V. Agina and Sergey A. Ponomarenko[a,b]

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Requirements on the speed and simplicity of testing stimulate the development of modern biosensors. Electrolyte gated organic field-effect transistors (EGOFETs) is a promising platform for ultrasensitive, fast and reliable detection of biological molecules for low-cost, point-of-care bioelectronic sensing [1]. In this work we propose a universal, fast and simple technique based on Doctor Blade and Langmuir-Schaefer methods for functionalization of the semiconducting surface of C8-BTBT-C8 allowing to fabricate large scale biorecognition layer based on the novel functional derivative of BTBT containing biotin fragment as a foundation for further biomodification [2]. For this, commercially available biotin was activated by preparing of N-succinimide ester, and then its alkyne derivative 2 was obtained by the amidification reaction with propargylamine. The synthesis of the azide derivative of BTBT was based on a combination of Friedel-Crafts acylation reactions and the reduction of corresponding ketones. For the subsequent functionalization, a cheap commercially available 6-bromohexanoyl chloride was used. The resulting terminal bromine was converted by nucleophilic substitution with sodium azide into the corresponding organic azide under mild conditions. At the last stage, the obtained precursors were introduced into a 1,3-dipolar cycloaddition reaction in the presence of monovalent copper and a tertiary amine in dioxane to give target compound (BTBT-biotin).

The fabricated devices are very efficient and stably operate in phosphate buffer saline (PBS) solution with high reproducibility of electrical properties in the EGOFET regime. The development of biorecognition properties of the proposed biolayer is based on the streptavidin-biotin interactions between the consecutive layers and can be used to a wide variety of receptors. As a proof-of-concept, we demonstrate the specific response of the BTBT-based biorecognition layer in EGOFETs to a virus of influenza A (H7N1 strain). The elaborated approach to the biorecognition layer formation is appropriate but not limited to aptamer-based receptor molecules and can be further applied for fabricating several biosensors for various analytes on the one substrate and paves the way to an “electronic tongue” creation.

This work was supported by the Russian Science Foundation (Grant 19-73-30028).

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ACID-CATALYZED REACTION OF ACETALS WITH (HET)ARYLAMINES: THE SYNTHESIS OF FUSED PYRIDINE DERIVATIVES

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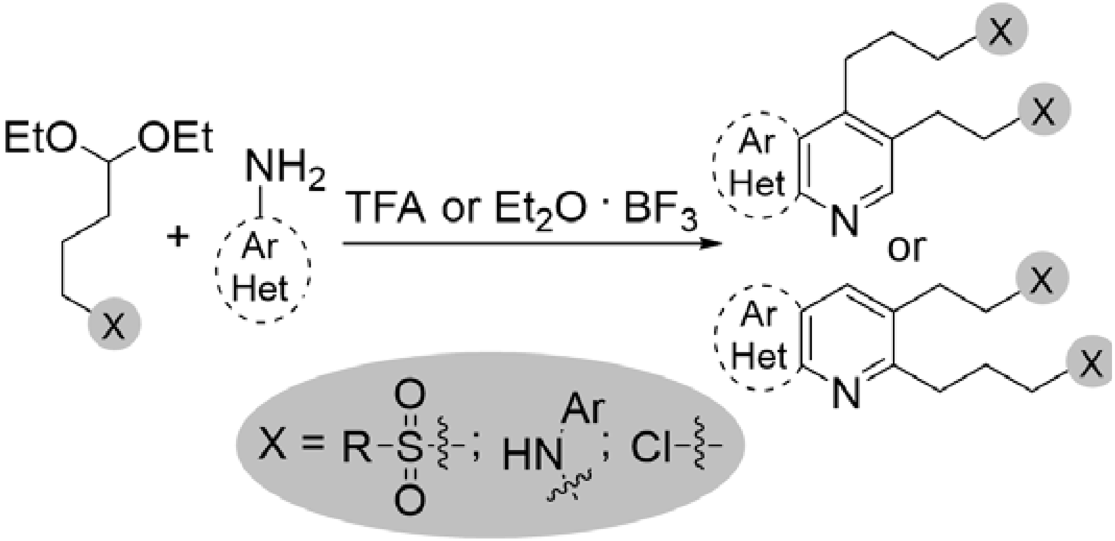
The fused pyridine derivatives play the important role in organic chemistry, primarily due to their pronounced biological activity. This scaffold is often found in pharmaceuticals and bioactive compounds. Thus, the development of novel approaches to these compounds is an urgent task.



Herein we present the methiod of the synthesis of fused pyridines via the reaction of (het)arylamines with 4,4-diethoxybutane-1-amine derivatives. The described approach benefits from simple one-pot procedure, wide reaction scope and provides easy and effective entry to the target compounds.

The work was supported by Russia Science Foundation № 21-73-00074, https://rscf.ru/project/21-73-00074/

SYNTHESIS, PHOTO- AND IONOCHROMIC PROPERTIES OF SPIROPYRANS BASED ON HYDROXYQUINOLINE ALDEHYDE

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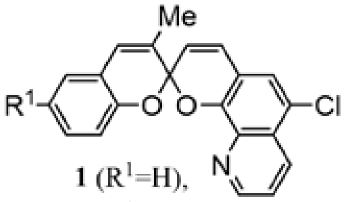
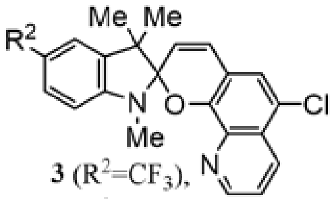
We continued the research towards the synthesis of new photochromic spiropyrans with ionophore fragments as potential chemosensors for heavy metal cations by using 5-chloro-substituted hydroxyquinoline aldehyde to prepare spiropyrans **1-4**. The structure of spiropyran-quinolines has been established by NMR, mass spectroscopy, and X-ray structural analysis. The compound possesses weakly pronounced photochromic properties at room temperature. Interaction with Co^{2+}, Ni^{2+}, Zn^{2+}, Cd^{2+} ions leads to the formation of intensely colored complexes absorbing in the $\lambda > 600$ nm region, which is important for the study of biological objects.



1 (R^1=H),
2 (R^1=OMe)



3 (R^2=CF_3),
4 (R^2=Br)

This work was financially supported by Ministry of Science and Higher Education of the Russian Federation (project No. 0852-2020-00-19).

SYNTHESIS AND BIOLOGICAL ACTIVITY OF NEW DERIVATIVES DITERPENIC ACIDS

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Svetlana Meshcheryakova [b] **and Semen Zlotsky** [a]

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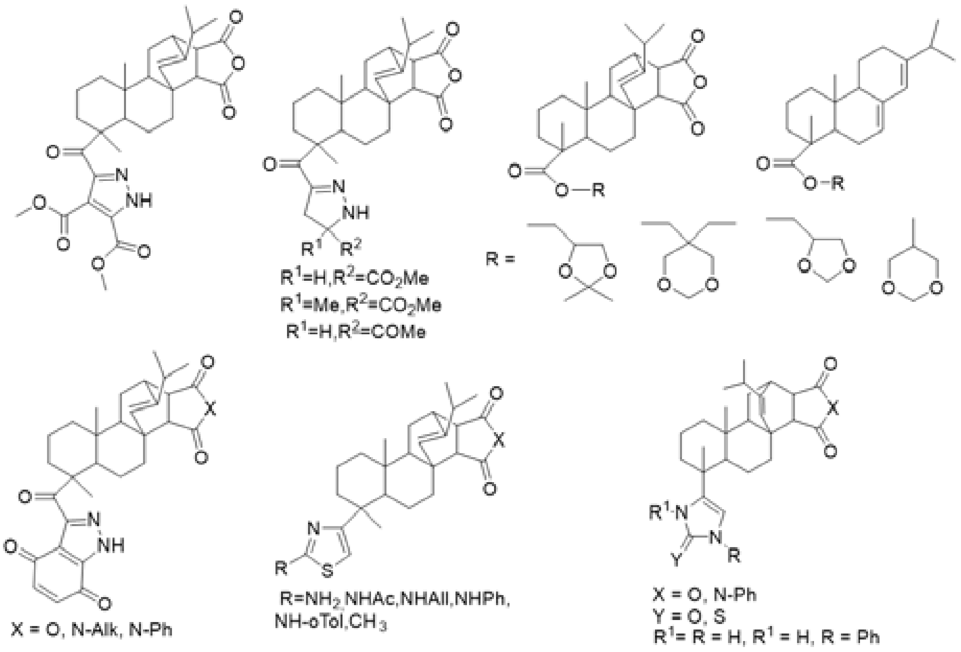
Widespread diterpenic acids, abietic and levopimaric acids, are readily available components of *Pinus sylvestris L.* pine resin, common in Russia, and are used as a basis for obtaining libraries of biologically active derivatives with various types of biological activity [1].

Based on abietic acid (AA) and maleopimaric acid (MPA), we synthesized a number of new heterocyclic amides, esters, pyrazolines, pyrazoles, indazoles, thiazoles, and imidazolinones containing a diterpene fragment. The conditions allowing the preparation of these compounds in high yields are considered.



The cytotoxic activity of new compounds was screened on human cancer cell culture lines and their antimicrobial, antioxidant, anticoagulant, and anti aggregation activities were studied *in vitro*. Leading compounds have been identified.

The work was supported in part by the USPTU 2022 leadership grant No. 15-2-22.

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SYNTHESIS AND PH DEPENDENT DISPROPORTIONATION OF VERDAZYLS

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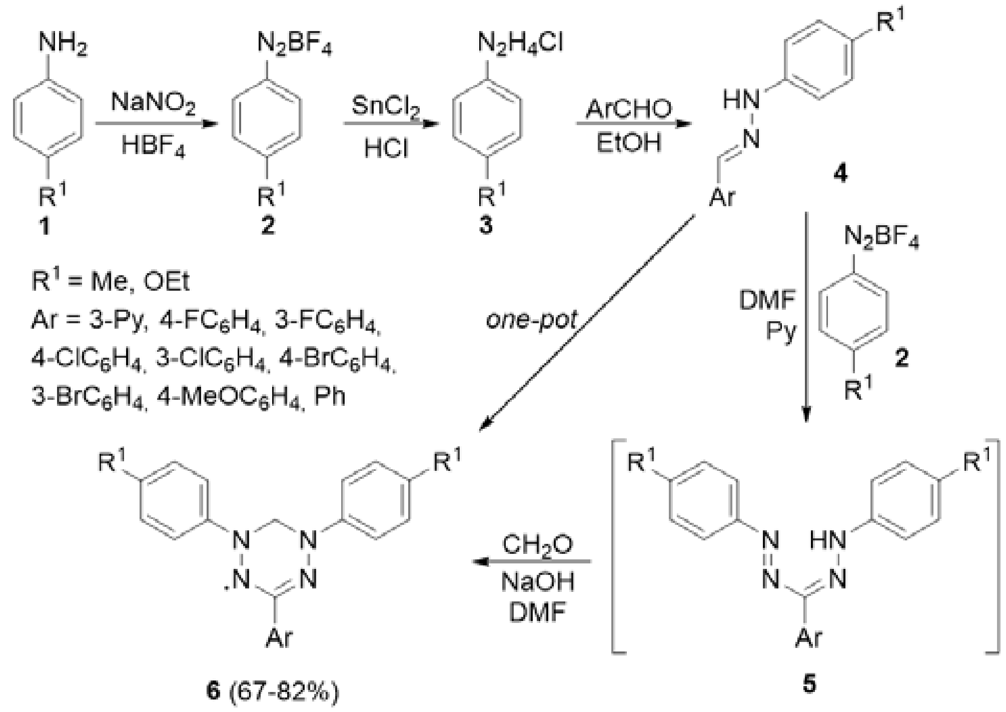
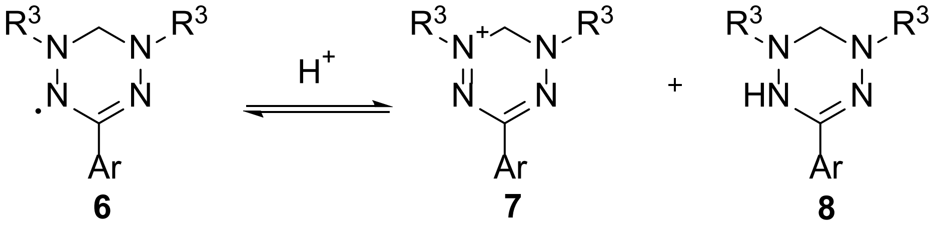
Verdazyl radicals are known as one of the stable organic radicals. Several methods for the synthesis of verdazyls are described, most of them are based on azo coupling of diazonium salts **2** with hydrazones **4**. Thus obtained formazans **5** undergo tandem condensation-reduction protocol to the target verdazyls **6**. It should be noticed, that reaction yields highly depend on substituents and diazonium salts are usually generated *in situ.* Herein, we present an improved one-pot method to the verdazyl construction which does not require isolation of formazans **5** due to the utilization of tailor-made diazonium salts **2**. Our approach allowed us to raise the yields of target verdazyls **6** up to 82% starting from hydrazones **4** (Scheme 1).



Scheme 1. Synthesis of verdazyls 6

Also, the pH dependent disproportionation of verdazyls **6** was studied. It was found that the reaction outlined in Scheme 2 included oxidation of **6** into cation **7** and reduction-protonation sequence into leucoverdazyls **8**. As a result, neither whole reaction, nor Red/Ox steps showed correlation with known Hammet substituent constants. These interconversions were studied using UV/Vis spectroscopy and with cyclic voltammetry.



Scheme 2. pH dependent disproportionation of verdazyls 6

This work was supported by the Russian Foundation for Basic Research and Moscow city Government according to the research project # 21-33-70056.

DIMERIZATION OF SOME TERMINAL ACETYLENE ALCOHOLS

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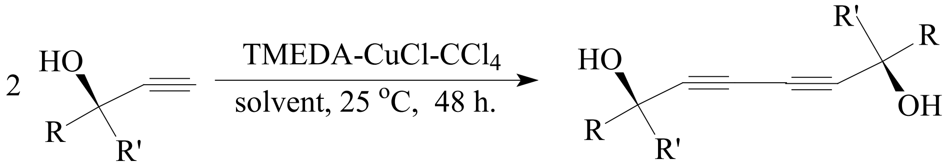
Due to the fact that terminal acetylene alcohols have a number of reaction centers, its high ability to nucleophilic, electrophilic, radical, alkylation, cyclobination and polymerization reactions, the synthesis of biologically active organic substances based on such a series of compounds, a narrow range of scientific research is being conducted to study their physico-chemical properties and applications[1,2].

In this study, for the first time, the reactions of synthesis of 1-(4-(1-hydroxycyclohexyl)-buta-1,3-diynyl)cyclohexanol (**1**), (2R,7S)-2,7-diphenyl-octa-3,5-diyne-2,7-diol (**2**), (7S)-2,7-bis(4-chloro-phenyl)octa-3,5-diyne-2,7-diol (**3**), 1-(1-hydroxy-4-tricyclo[3.3.1.1^{3,7}]decanyl)-buta-1,3-diynyl)-tricyclo-[3.3.1.1^{3,7}]decanol (**4**), 8,13-dimethylicosa-9,11-diyne-8,13-diol (**5**), (5S,10R)-5,10-diethyltetradeca-6,8-diyne-5,10-diol (**6**) based on the dimerization process of some terminal acetylene alcohols 1-ethynyl-1-siklohexanol, 2-phenylbutyn-3-ol-2, 2-(4-)-chlorophenyl)butyn-3-ol-2, 2-ethynyladamantanol-2, 3-methyldekin-1-ol-3 and 3-etilheptyn-1-ol-3 were studied. Methanol, ethanol, isopropanol, tetrahydrofuran, ethylene glycol and acetonitrile were used as solvents in the dimerization of selected terminal acetylene alcohols. The process was carried out in the TMEDA-CuCl-CCl_4 catalytic system for 48 h. at a temperature of 25 °C. The reaction scheme was proposed as follows[3].



Here: RR′= –^{c}Hex (**1**); R= –Me, R′= –Ph (**2**); R= –Me, R′= –^{p}ClPh (**3**);
RR′= –Ad (**4**); R= –Me, R′= –Hep (**5**); R= –Et, R′= –^{n}Bu (**6**),
solvents– MeOH, EtOH, EG, ^{i}PrOH, THF, MeCN

Based on the results of the research was synthesized with **1**– 64,7%, **2**– 48%, **3**– 63,9%, **4**– 70,8%, **5**– 82,0% and **6**– 53,7% yields.

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SYNTHESIS OF NEW POLYCYCLIC DERIVATIVES OF PYRIDOXAL (AZACOUMARINS) EXHIBITING ANTITUMOR ACTIVITY

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Gazizov A.S.[a] **and Burilov A.R.**[a]

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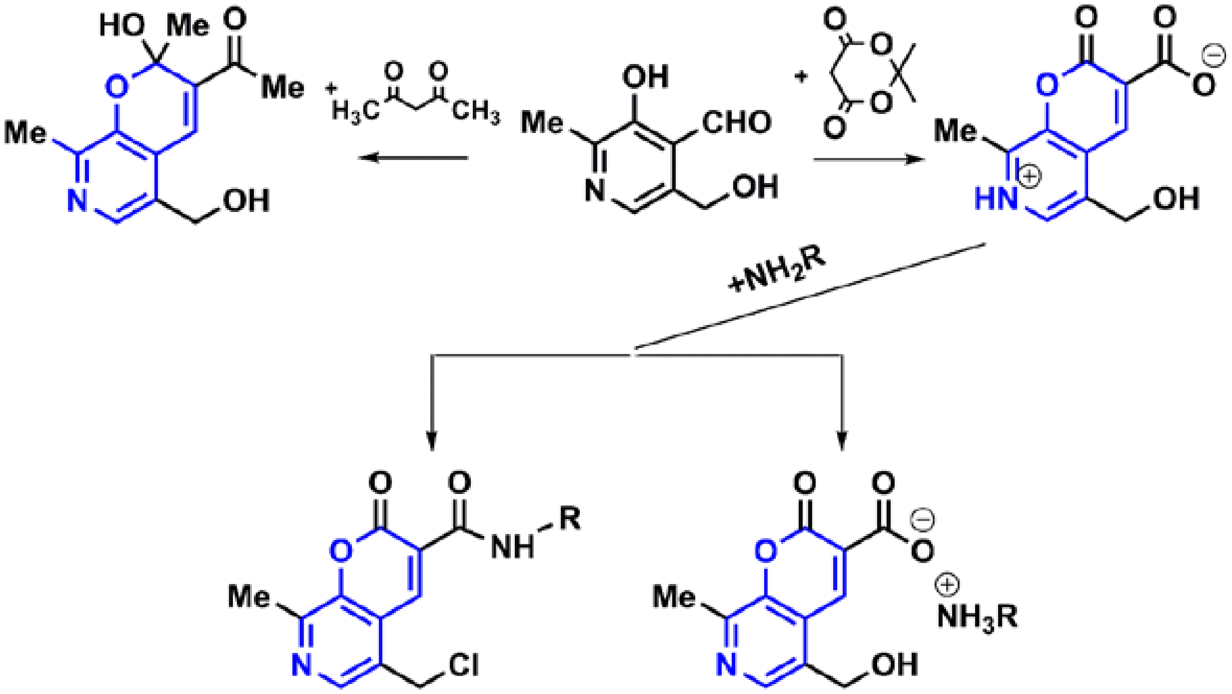
The intruduction of new structural fragments into the molecules of compounds known for their biological activity is a technique that is widely used in modern organic chemistry. The analysis of medicines shows that the bulk of it is made up of cyclic and heterocyclic compounds. Among them, a certain niche is occupied by substances containing coumarin or azacoumarin fragments.

In this report we present data on the synthesis of new 7-azacoumarins based on the Knovenagel condensation of pyridoxal and its derivatives with active methylene compounds (Meldrum's acid, acetylacetone). It has been established that the compounds obtained in these reactions (7-azacoumarins containing a carboxyl group in the third position) are capable of interacting with amines of various structures. It has been shown that, depending on the conditions of these reactions, the formation of two types of products is possible – salts of the acid or its amides.



Also in this study, the biological activity of the obtained compounds was tested and it was shown that they have high antitumor activity against M-HeLa and HuTu 80 cell lines.

This work was financially supported by the Russian Science Foundation (Project No. 21-13-00022); https://rscf.ru/en/project/21-13-00022/.

HETEROCYCLONONYNES AS NEW SPAAC REAGENTS FOR CLICK CHEMISTRY

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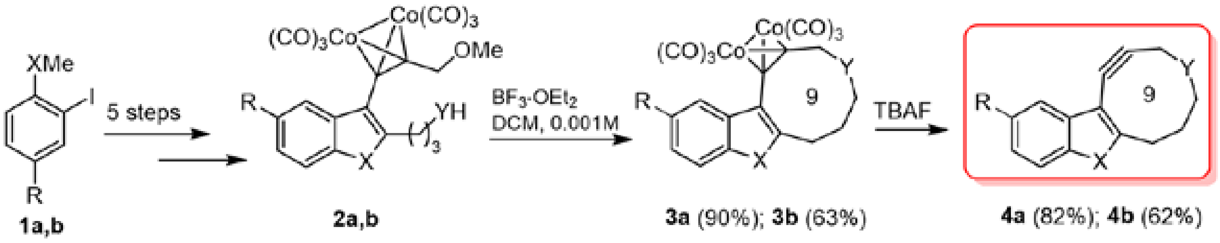
Since the beginning of the 21st century, when Sharpless et al. described a new strategy for organic chemistry, namely, “click” chemistry,[1] and Bertozzi et al. introduced the term “bioorthoganal reactions” for click chemistry in cells,[2] there has been an explosive growth in scientific work and publications dedicated to the practical applications of these innovative chemical approaches.[3] These fast reactions take place in mild environment; they are highly reliable and selective. All these properties allow bioorthogonal click reactions to be used in living organisms. Nowadays, a huge number of scientific effort is focused on the search for new bioorthogonal click reagents. Cycloalkynes are an important family of reagents, used in Strained-Promoted Azide-Alkyne Cycloaddition (SPAAC) bioorthogonal transformation.

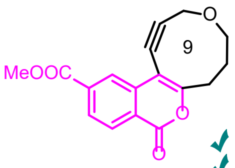
The purpose of this work is to develop new SPAAC reagents based on heterocyclononynes fuse to a heterocyclic core, bearing functional groups either responsible for the fluorescent properties of cycloalkynes, or necessary for further dye attachment. Our synthetic approach is based on the key Nicholas-type cyclization which is tolerant to different functional groups and allows the formation of strained 9-membered cycle.



a series: $X = S$, $R = H$, $Y = N\text{-}(SO_2\text{-}p\text{-}NH_2\text{-}C_6H_4)$; **b** series: $X = COO$, $R = COOMe$, $Y = O$

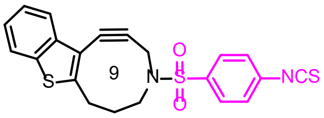
As target structures, we have chosen and synthesized oxacyclononyne fused to an isocoumarin **IC9O-COOMe**, which has its own fluorescence due to the ester group in the isocoumarin fragment and azacyclononyne fused to a benzothiophene **BT9N-NCS**, which has an isothiocyanate group, a usable site for modification with a dye. Modification of **BT9N-NCS** with a dye and investigation of the applicability of new SPAAC reagents in cells are ongoing.

New SPAAC reagents



IC9O-COOMe

✓ Fluorescent itslelf
✓ Active in SPAAC
✓ Overall yield - 7%



BT9N-NCS

✓ Site for modification
✓ Active in SPAAC
✓ Overall yield - 10%

This work was supported by a financial grant from the Russian Foundation for Basic Research (20-03-00117)

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CYCLIC ETHERS IN THE ELECTROCHEMICAL SYNTHESIS OF HETEROCYCLIC COMPOUNDS

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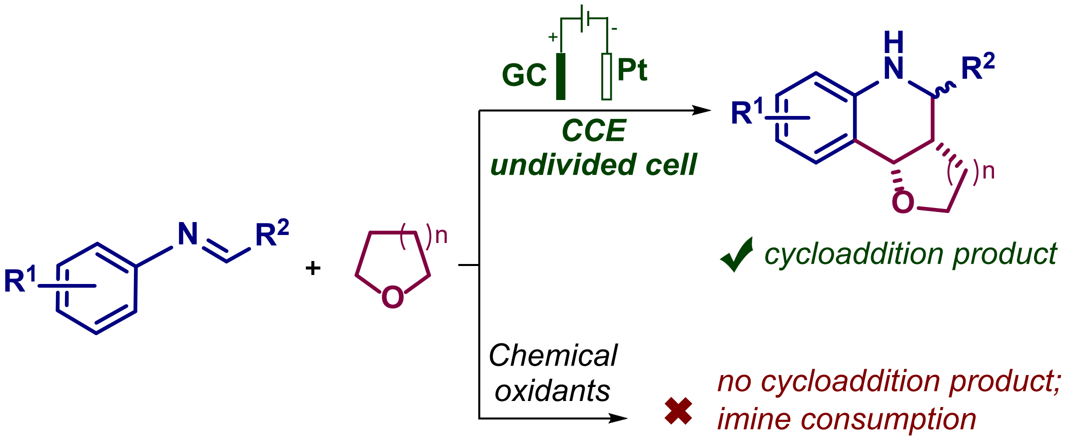
Nowadays, electroorganic synthesis is considered as one of the most actively developing areas of modern organic chemistry. This study develops state-of-the-art synthetic organic electrochemistry - an electrochemical synthesis of heterocyclic structures, which have always been basic scaffolds from pharmaceuticals to organic materials.



Electrochemical synthesis of cyclic ether-annulated tetrahydroquinolines from imines and cyclic ethers in an undivided cell under constant current conditions was developed.[1] The electrosynthesis proceeds *via* the enol ether formation from ethers following the aza-Diels-Alder [4+2] cycloaddition. The non-obviousness of the discovered process is due to the fact that cyclic ethers, common solvents for electrochemistry, are oxidized into enol ethers while the electrochemically labile imines must wait for the formation of a partner for cycloaddition while remaining unconsumed. Synthesized cyclic ether-annulated tetrahydroquinolines exhibit high antifungal activity, which is superior to the commercial fungicide Triadimefon.

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This work was supported by the RSF (project 21-13-00205).

NOVEL EXTRANUCLEAR HETEROSTEROIDS: SYNTHESIS AND APPLICATIONS

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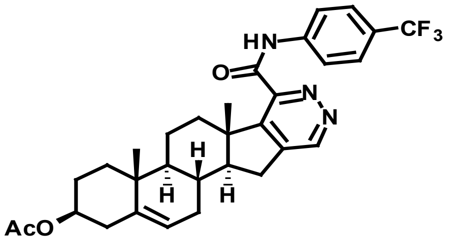
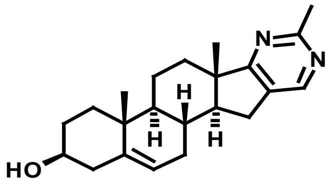
Heterosteroids of the estrane and androstane series containing the aza-substituents are privileged scaffold for drug discovery due to their outstanding biological activity [1]. Thus, synthetic azasteroids encompass a wide range of compounds among which are reductase inhibitors such as finasteride, the high-affinity agonist ligands for the glucocorticoid receptor e.g., cortivazol, GnRH agonists such as danazol, aromatase inhibitors such as formestane and exemestane and neuromuscular junction blocking agents such as pipecuronium.

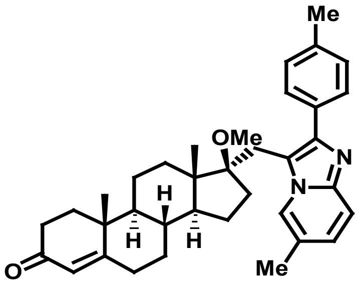
This study was focused on a strategic development toward functionalized extranuclear azasteroids diversity and assessment of their potential as anticancer, antiviral, and neuromodulatory agents [2]. A flexible synthetic approach to unknown pyrazole, 1,3,4-thiadiazole, thiadiazine, and pyridazine derivatives of steroids with selective control of heterocyclization patterns was disclosed. Syntheses of steroidal propargylamines, imidazo[1,2-a]pyridines, 1,2,3-triazoles, *N*-sulfonyl imidates were achieved from ethynyl steroids using copper catalysis. The synthesized compounds were screened for inhibition activities in different cancer cells and were found to be highly promising for development of anticancer agents, in particular, against breast cancer.



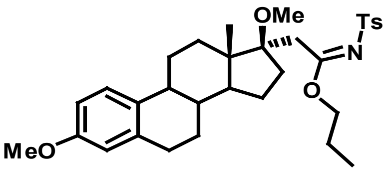
IC_{50} (MCF-7) = 4.9 mkM
not active agaist MDA-MB231



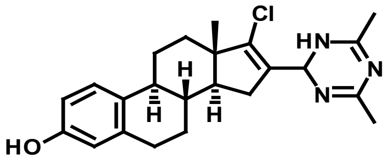
IC_{50} (MCF-7) = 12.0 mkM
not active agaist MDA-MB231, PC-3, 22Rv1



IC_{50} (MCF-7) = 3.2 mkM
IC_{50} (MDA-MB231) = 11.8 mkM



IC_{50} (MCF-7) = 4.3 mkM



IC_{50} (MCF-7) = 7.4 mkM

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UNVEILING THE ROLE OF CHEMICAL STRUCTURE IN PLASMON CATALYSIS USING ALKOXYAMINES AS A CHEMICAL PROBE

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Plasmon active materials have been sparking great attention in the field of modern chemistry as novel efficient catalysts. Application of plasmon energy is the principally new stimuli for the activation of catalytic reactions involving organic molecules by improving selectivity, enhanced reaction rates, and enabling milder reaction conditions [1-3]. However, the mechanism of interaction between plasmon and organic molecules is still in dispute. Nowadays, three main hypotheses have been proposed: (1) acceleration of reactions through plasmonic heating, (2) transfer of «hot» carriers to the organic molecule, followed by the formation of highly reactive species, and (3) intramolecular excitation [4]. None of the mechanisms considers in detail the effect of the chemical structure of organic molecules on plasmon-induced transformations. It is known that alkoxyamines (AAs) are excellent thermal probes for plasmon catalysis because the reaction is 1st order and has a single component [5]. This feature of the system allowed us to study the effect of the organic molecule on the kinetics of the plasmon-induced photoreaction.

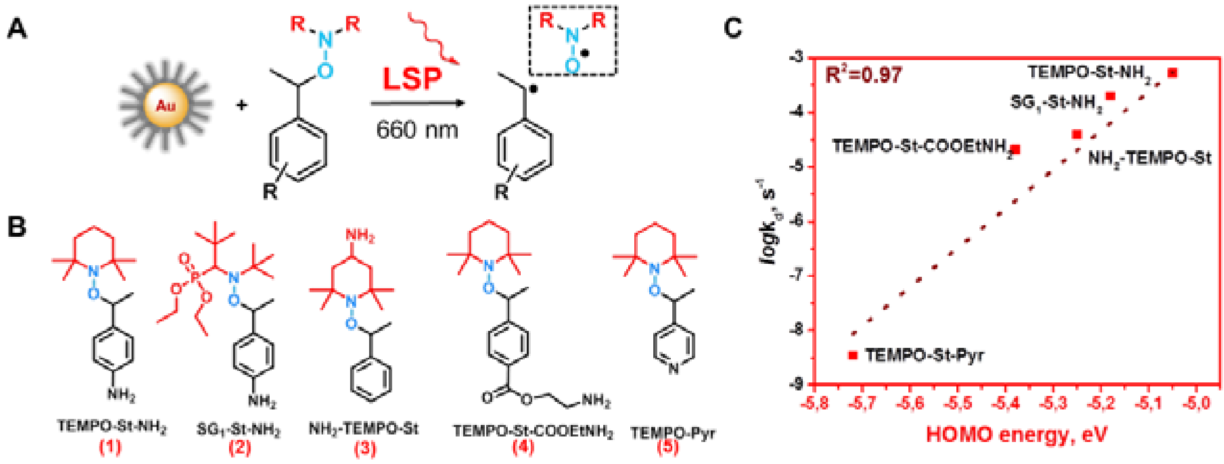

Figure 1. A) The concept of plasmon-induced homolysis of alkoxyamines.
B) The structures of alkoxyamines under study. C) Trends of logk_d (plasmon) vs. E_{HOMO}

The obtained kinetic data revealed the dependence of the plasmonic homolysis rate constant (k_d) with the HOMO energy of AAs, which cannot be described by the kinetic parameters derived from thermal homolysis experiments. The observed trend in k_d indicates that the intramolecular excitation mechanism plays a pivotal role which was supported by DFT calculations, additional spectroscopic characterization, and control experiments.

The obtained results open up the prospects not only for fine-tuning plasmon-assisted reactions, but for carrying out efficient radical generation that allows chemical engineering and medical science to be more efficient, cheaper and safer.

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HALOGEN-LITHIUM EXCHANGE IN 2,4,5,7-TETRABROMO-1,8-BIS(DIMETHYLAMINO) NAPHTHALENE

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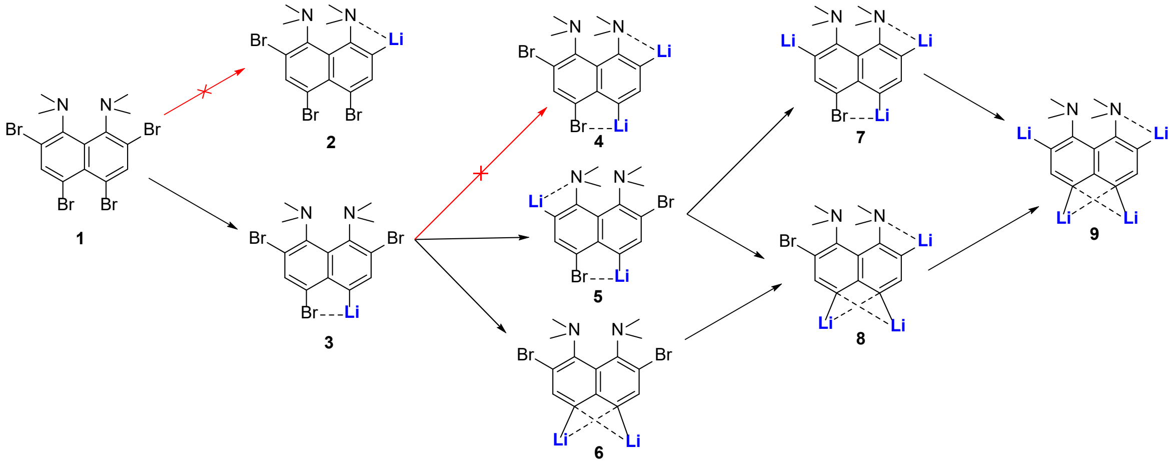
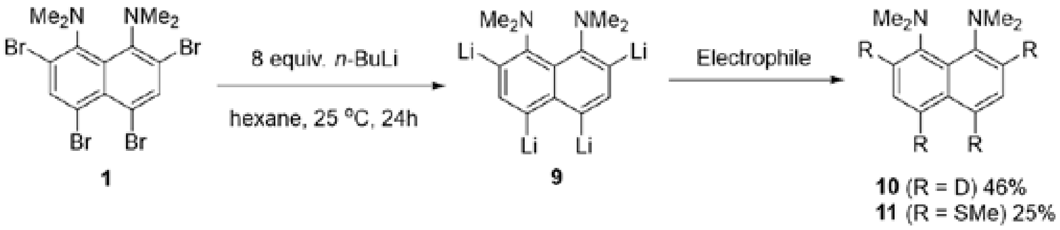
Nowadays organolithium reagents play indispensable role in organic synthesis. Featured by Karl Ziegler, halogen-lithium exchange remains one of the most common ways for the preparation of organolithiums. This phenomenon is well investigated in the benzene series, while multiple halogen-lithium exchanges in the synthesis of naphthyllithiums are much less studied. Thus, the influence of directing groups and the steric strain effects, as well as the possibility of more than two halogen atoms exchange, remain unknown. Here, we present the study on bromine-lithium exchanges in 2,4,5,7-tetrabromo-1,8-bis(dimethylamino)naphthalene **1**, a convenient model compound with different directing situations, a significant steric strain of *peri*-substituents, and the possibility of an exchange of up to four bromine atoms.



Scheme 1

We have shown that step-by-step lithiation proceeds precisely as shown on the Scheme 1. Thus, first exchange occurs in position 4 with formation of **3** due to the significant decrease of a steric strain of the molecule. The second exchange takes place in either position 5 or 7 leading to the formation of the mixture of **5** and **6** due to the more even negative charge distribution in the naphthalene core. As a result, the third exchange leads to the species containing lithium in positions 2,4,7 (**7**) or 2,4,5 (**8**). Using a large excess of n-BuLi in hexane, 2,4,5,7-tetralithio-1,8-bis(dimethylamino)naphthalene **9** was successfully prepared. The latter was used for the synthesis of several tetrasubstituted derivatives of 1,8-bis(dimethylamino)naphthalene by quenching with different electrophiles (Scheme 2).



Scheme 2

This work was supported by the Russian Science Foundation (project 21-73-10040)

HOW TO BUILD RIGID OXYGEN-RICH HETEROCYCLES?

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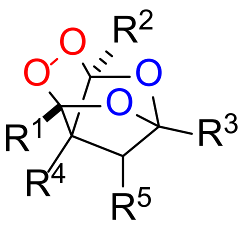
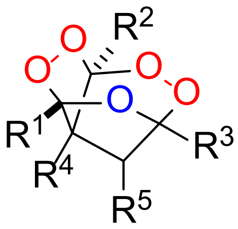
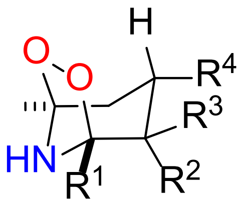
Organic peroxides offer a largely uncharted chemical space for the development of new medicinal agents with antimalarial, anthelmintic, anticancer, fungicidal, antitubercular, and antiviral activities [1]. Natural peroxide Artemisinin, its derivatives and synthetic analogs such as Artesunate and Arterolan (synthetic ozonide) are important antimalarial drugs. It was found that synthetic ozonides are able to inhibit both the α-coronavirus NL63, β-coronavirus OC43, and SARS-CoV-2 [2].

In our studies, we developed approaches to the synthesis of rigid oxygen-rich heterocycles from carbonyl compounds and hydrogen peroxide, and also proposed an approach to the synthesis of bridged aminoperoxides, which contain both an oxidizing agent and a reducing agent [3–5]. It was found that cyclic peroxides exhibit antimalarial activity and high cytotoxicity and selectivity towards cancer cells.







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RECENT ADVANCES IN CHEMISTRY OF PHOSPHACYCLOPENTADIENIDE DERIVATIVES

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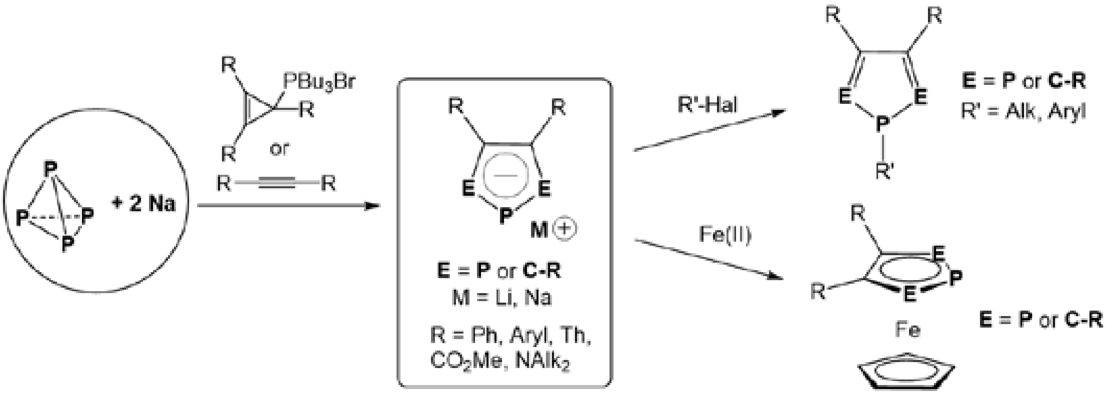
Phosphacyclopentadienide (phospholide) anions and their derivatives are very attractive as building blocks for the construction of versatile organophosphorus molecular materials with useful and interesting catalytic, optical, luminescent, magnetic properties.[1] Therefore, development of convenient methods for directed synthesis of these phosphorus heterocycles and their derivatives through elemental phosphorus P_4 activation (excluding the use of chlorine Cl_2) has a significant interest.[2] This lecture will particularly focus on recent advances on the synthesis of various phosphacyclopentadienide-anions and their chemical behavior toward organic, organoelement substrates and transition metal complexes.



A rational and highly efficient method to access 1-mono-[3], 1,2-di-[4] and 1,2,3-triphospholide[5] anions in individual forms directly from white phosphorus P_4, alkali metals and small molecules (alkynes and cyclopropenylium halides) have been developed. Interaction with various chiral and non-chiral alkyl halides has allowed to formation of novel *P*-heterocycles - 1-mono-, 1,2-di- and 1,2,3-triphospholes. Reaction with Fe(II) complexes was used as a direct way for efficient synthesis of number of phosphaferrocenes.[6] First results on application in material science and homogeneous catalysis of phospholide derivatives (phospholes and their [4+2] cycloadducts) was also presented.[7]

This work was supported by Russian Science Foundation (project no. 21-73-10204)

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CORRELATIONS BETWEEN THE MAJOR AMINO ACIDS IN THE SAMPLES OF THE PIG BLOOD

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Amino acids (AAs) are performing important functions in the body as the major components of protein metabolism [1-4]. It is important to highlight that there are no clear standards for the content of free AAs in the studied animal species [4-6]. In the work [7], the content of various AAs in the blood serum of pigs “of early maturing meat breed” was estimated as 3.521±0.252, which is slightly lower than the usually cited [3-6]. There are practically no works on a detailed study of the correlations between the AAs and biochemical parameters of pig blood, while the study of correlations between the biochemical parameters itself of numerous blood samples of some pig breeds and various another animals is carried out all over the world [3-5, 8].

The main aim of the work was to evaluate the possible correlations between the major AAs and biochemical parameters of the pig blood. 80 animals were divided onto 4 animal groups: 1) 65 fattening days (n=12), 2) 72 fattening days (n=36), 3) 82 fattening days (n=19), 4) 90 fattening days (n=13), respectively. The amino acid contents (of pig blood serum) were measurements by HPLC in accordance with the Russian official document (GOST 34132-2017) [9]. The content of each type of the amino acid were presented in units of g/100 g of dry weight of the blood sample.

The authors obtained first the major correlations between AAs and the total protein or its fractions (TP&F), nitrogen metabolites, carbohydrates, lipids, some enzymes in the pigs’ blood for each of these animal groups (65-90 fattening days). The correlation tendencies of some AAs vs. TP&F-parameters and vs. enzyme levels were the following: groups 1›4›3›2 and 3›4›1›2. High correlation coefficients (r>0.75) between the majority of the studied amino acids in the pig blood samples were obtained. Thus, about 82-90 days (groups 3, 4) can be the optimal for the pig fattening that based on the correlation analysis. These results are useful for fundamental aspects of blood AAs, animal health monitoring, as the reference values for husbandry practice, etc. taking into account an increasing importance of pig farming and a share of pork meat products in human consumption.

This work was supported by the grant from the Russian Science Foundation (project No. 20–16-00032).

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ELECTRONEUTRAL DISUBSTITUTED BERBERINES AS A NEW WAY TO OBTAIN AMPHIPHILIC DRUGS

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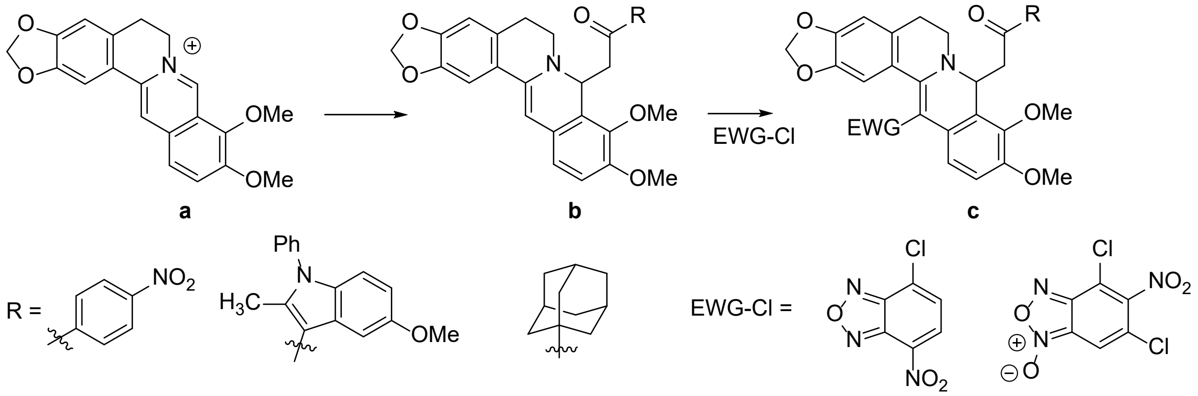
Alkaloids are a natural nitrogen containing organic compounds. They are able to exhibit multiple biological activity in relation to human body. Since ancient times, alkaloids (in particular berberine) have been used by people to treat many diseases in Chinese and Indian medicine. Today berberine (**a**) use as anti-cancer, antibacterial, antiviral drugs. There are many investigations which also demonstrate synergistic activity of berberine for other substances.

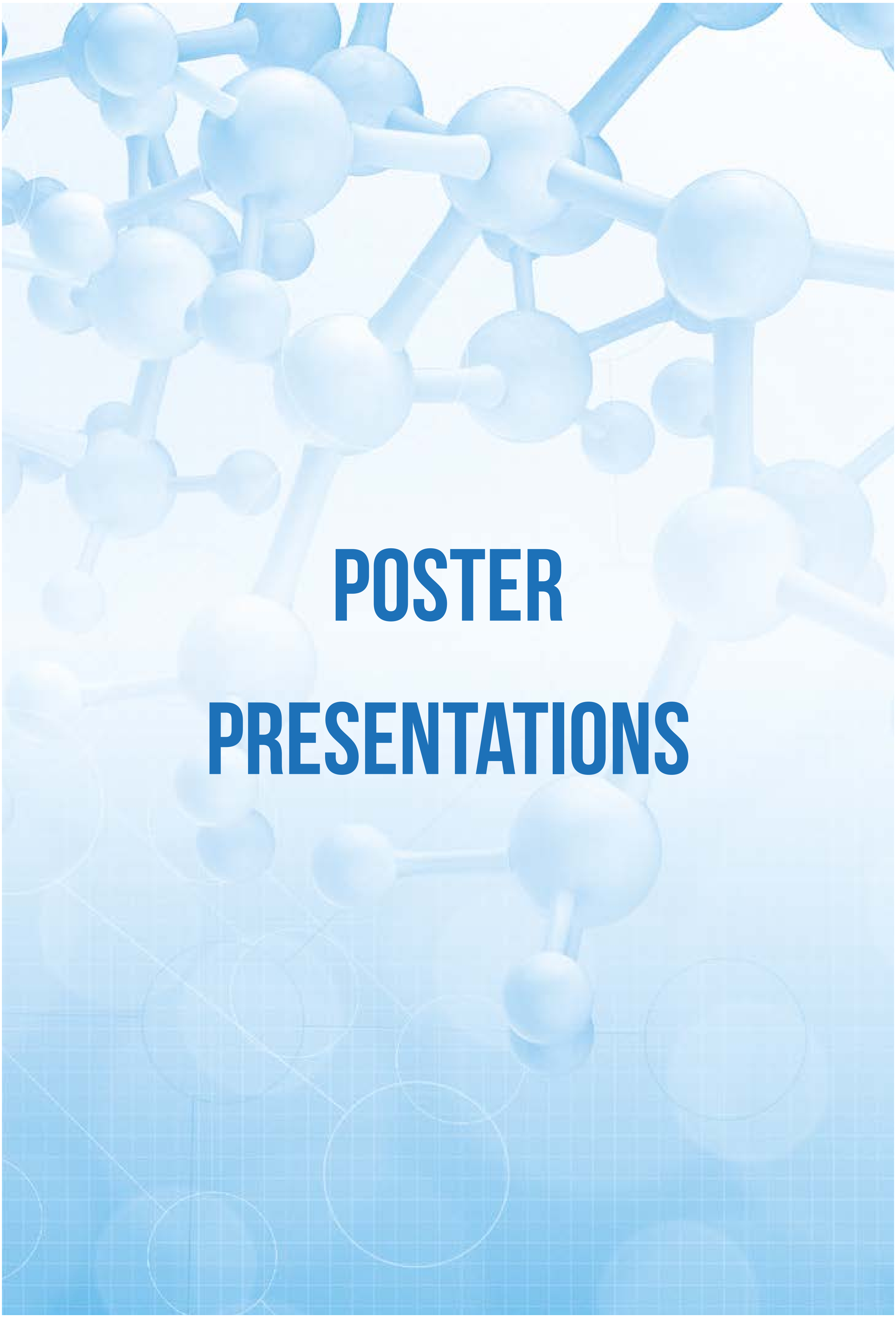
We investigate the biologically active derivatives of berberine, namely its 13-substituted adducts. However, we decided not to stop at 13-mono-substituted berberines and continued to study various 8,13-disubstituted berberines (**c**). In such structures, not only substituent at position C-13 has biological effects, but one at position C-8 can also be considered as an additional pharmacophore group.

Thus, we have developed a new method for modifying alkaloid at the position C-13 without eliminating substituent from C-8 position. We also carried out a series of quantum chemical calculations. So according to calculated logP, compounds (**c**) are amphiphilic, that agree with experimental data. Substances (**c**) were moderately dissolved in water and chloroform.



The developed method of nucleophilic attack at the position C-8 berberines skeleton has a universal character. It allows to consider various C and N nucleophiles as a possible agent for berberine modification. But nucleophiles must meet the main structural requirement. It should have a strong acceptor (EWG) near reaction center (CH_3 or NH_2 group). This method allows the selective use of nucleophiles with multiple reactive sites. To introduce a substituent at the C-13 position of berberine skeleton, we can use activated haloarenes. We can change the biological activity and lipophilicity of berberine derivatives over a wide range by varying the substituents at positions C-8 and C-13.

The reported study was funded by the Russian Foundation for Basic Research (RFBR), project number 20-33-90262.



POSTER
PRESENTATIONS

KEY INTERMEDIATES IN REACTIONS OF NITROALKANES IN PPA

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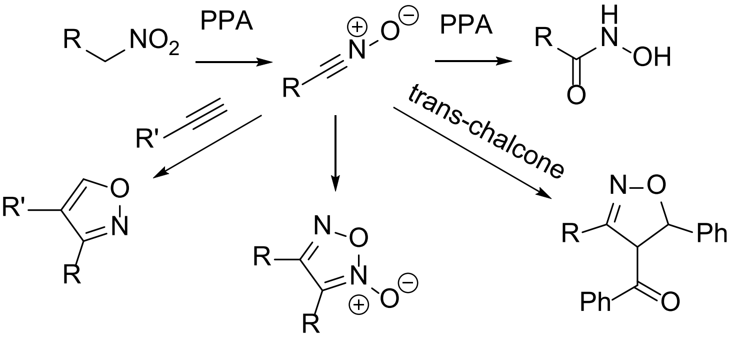
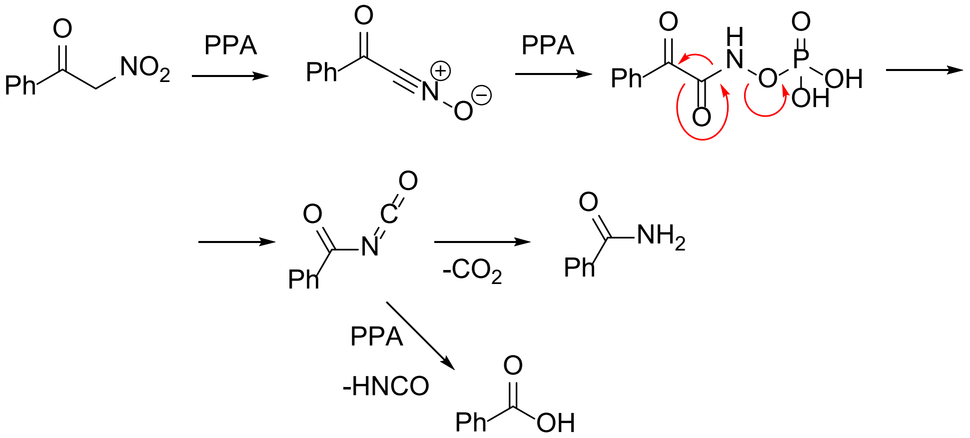
It was previously stated that interaction of nitroalkanes with PPA leads to the formation of electrophilic nitronate species, enabling subsequent reactions with various nucleophiles. Moreover, in the absence of nucleophiles, nitro compounds were converted to the corresponding hydroxamic acids. We set ourselves the task of establishing the intermediate particles formed in the presented transformation. For this, we introduced in PPA medium 2-nitroacetophenones as compounds containing a mobile proton and capable of generating significant concentrations of intermediates. As a result, the reaction led to the formation of the corresponding furoxanes. In the presence of dipolarophiles, the corresponding cycloadducts were formed.



Alternative products have been supplied by the Lossen rearrangement of the resulting hydroxamic acids. Thus, it was possible to fix carboxylic acids and benzamides.



Acknowledgements. This work was supported by a grant from the President of the Russian Federation for state support of young Russian scientists - doctors of science (grant no. MD-3505.2021.1.3), as well as by Ministry of Education and Science of the Russian Federation (grant #0795-2020-0031).

NEW TYPE OF REACTIVITY OF UNSATURATED NITRO COMPOUNDS IN THE SYNTHESIS OF CARBOLINE ALKALOIDS AND ITS DERIVATIVES

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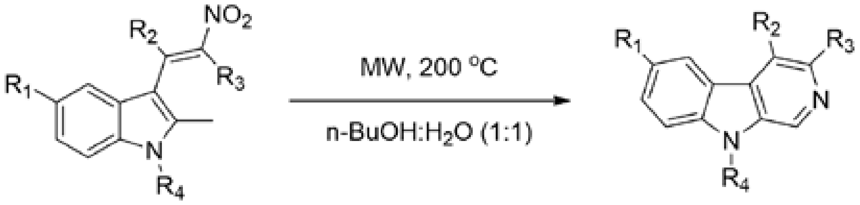
beta-Carboline alkaloids are a large group of natural and synthetic indole alkaloids with different degrees of aromaticity, some of which are widely distributed in nature, including various plants, foodstuffs, marine creatures, insects, mammalians as well as human tissues and body fluids. These compounds are of great interest due to their diverse biological activities. Particularly, these compounds have been shown to intercalate into DNA, to inhibit CDK, Topisomerase, and monoamine oxidase, and to interact with benzodiazepine receptors and 5-hydroxy serotonin receptors.



In a framework of the proposed project, we have developed fundamentally new approaches to the synthesis of carbolines, their derivatives, and precursors, based on readily available starting compounds.

This work was financed by the Russian Science Foundation (grant № 22-23-00159)

SYNTHESIS OF BENZOTHIOPHENE-FUSED ENEDIYNES WITH PROPARGYLAMINE MOIETIES

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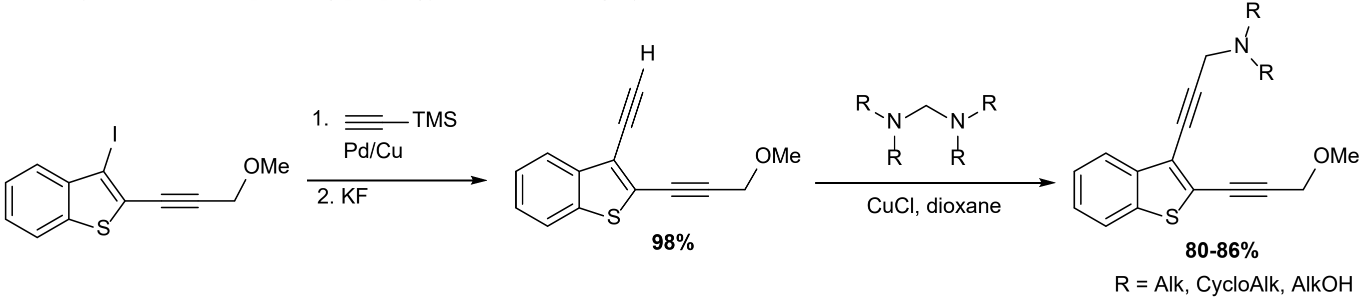
Last years, propargylamines are of increasing interest as one of the most promising class of compounds for different purposes. Propargylamine derivatives are versatile building blocks in the synthesis of different organic substrates and N,O,S-heterocycles, drugs and natural products [1]. One of the traditional synthetic methods toward propargylamines is the copper-catalyzed three components coupling of aldehydes, amines and terminal alkynes [2].

In order to obtain new heterocyclic analogs of natural enediyne antibiotics [3], carrying a propargylamine fragment, the synthesis of 2,3-diethynylbenzothiophene **3** was carried out. The Sonogashira coupling of TMS-acetylene and 3-iodobenzothiophene **1** was performed using diisopropylamine (DIPA) as a base. Subsequent the TMS-group deprotection of 3-ethynyl benzothiophene with potassium fluoride gave the terminal alkyne **2** in high yield. The Mannich reaction of acetylene **2** with bisaminomethanes using CuCl as a catalyst led to corresponding propargylamines **3** in high yields.



In summary, this work provides an efficient and convenient pathway for reaction of bisaminomethanes and terminal alkyne to form acyclic enediynes systems, and the desired products can be obtained up to 90% yield.

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This work was supported by Russian Science Foundation (RSF) (project No. 21-13-00218). The research was carried out using the equipment of the SPbSU Resource Centres: Centre for Magnetic Resonance, Centre for Chemical Analysis and Materials Research.

SYNTHESIS OF 2,5-BIS(THIEN-2-YL)FURAN AND ITS DERIVATIVES

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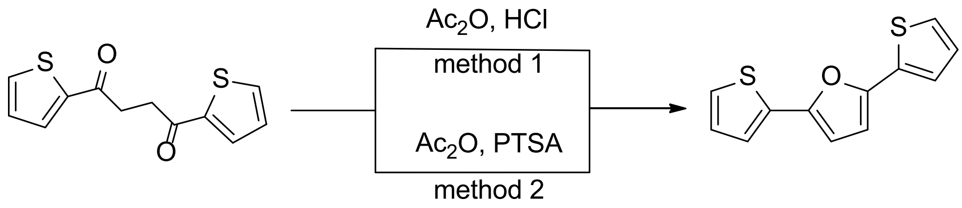
Due to the leading position of oncological desires in the death cases of the population, the searches for new compounds capable of activate the intracellular mechanisms of tumor cell death is an actual direction of medicinal chemistry. One of a promising area for anticancer drug development, is the evaluation of antitumor properties of derivatives of 2,5-bis(thien-2-yl)furan. For example, a 2,5-bis(5-hydroxymethyl-2-thienyl)furan has high affinity to the N-terminal region of the p53 protein, which selectively triggers of apoptosis in the cancer cell, preventing the transfer of damaged DNA to daughter cells. This binding of the inhibitor on 2,5-bis(thien-2-yl)furan scaffold with p53 protein disrupted its interaction with MDM2, a protein involved in regulating the p53-dependent pathway of apoptosis [1].

The key pharmacophoric group of 2,5-bis(5-hydroxymethyl-2-thienyl)furan is 2,5-bis(thien-2-yl)furan moiety. An effective method for preparation of this scaffold based on Paal–Knorr furan synthesis was presented by J. Kagan et al. [2]. In this procedure gaseous hydrochloric acid is passed through a stirred solution of 1,4-di(thiophene-2-il)butane-1,4-dione (**1**) in acetic anhydride at room temperature, that led to 2,5-bis(thien-2-yl)furan (**2**) in good yield (method 1).

We have developed more efficient procedure for cyclization of 2,5- bis(2’-thienyl)furan (**1**). According to this new method butane-1,4-dione **2** was treated with acetic anhydride in the presence of *p*-toluenesulfonic acid (method 2). The yield of 2,5-bis(2’-thienyl)furan is achieved 90%. The solid product was purified by crystallization. The assigned structure and purity of the product **2** were confirmed by TLC-analysis and NMR, ESI-HRMS spectra data.



Further researches will include the development of methods of diversification of 2,5-bis(2’-thienyl)furan (**2**) as well as an evaluation of anticancer activity of the obtained derivatives.

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ACID-CATALYZED DECOMPOSITION OF AZIDES IN THE SERIES OF PYRAZOLECARBOXYLIC ACIDS

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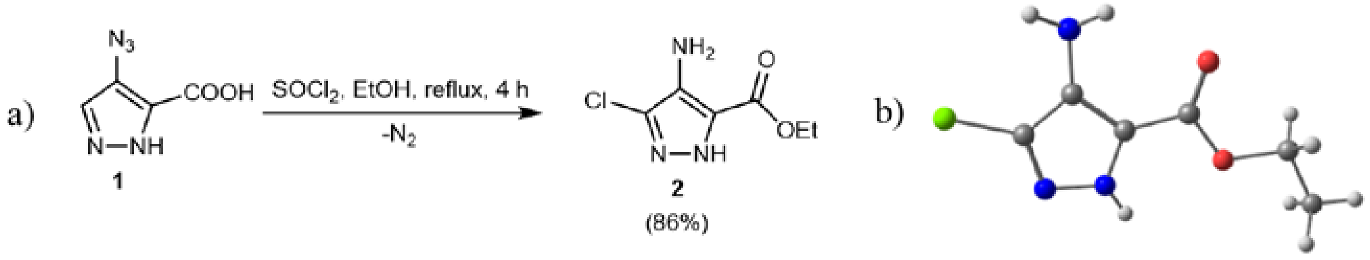
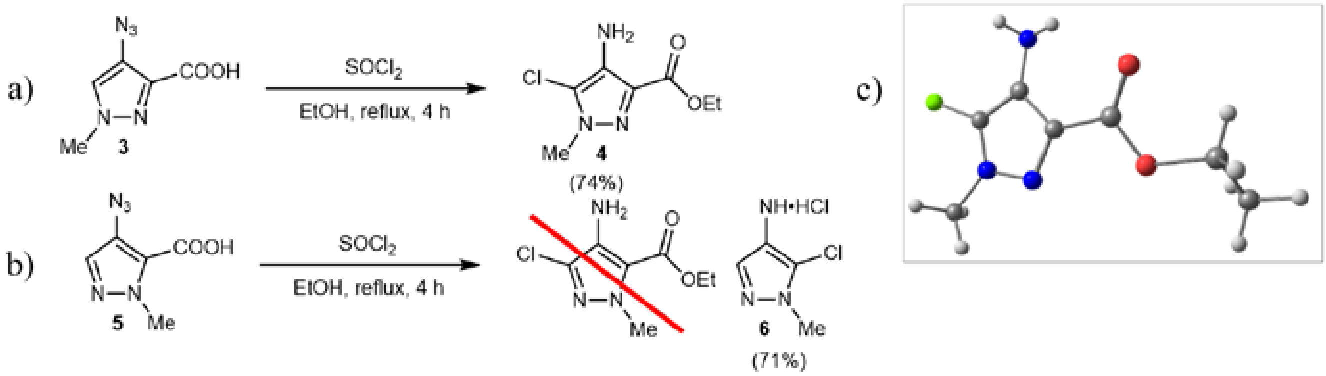
Pyrazoles belong to aromatic heterocyclic compounds widely used in synthetic organic and medicinal chemistry [1]. It is known from the literature about the existence of specific intramolecular noncovalent interactions between the nitrogen atom of the azido-group and the oxygen atom N_β•••O [2]. During the synthesis of isomeric derivatives of azidopyrazole, our group discovered new process (Scheme 1) [3]. The mechanism of the esterification reaction was shown to be affected by the position of azido-group in the pyrazole ring.



Scheme 1. a) Experimental results of the esterification reaction;
b) Molecular structure of 2 according to X-ray study.

Synthetic and quantum-chemical methods have shown that the presence of specific attractive intramolecular interactions between azido- and carboxylic-groups contributes to a decrease of the nitrogen molecule elimination barrier.

Applying the same conditions for the acidic degradation of regioisomeric azides **3** and **5** (Scheme 2), we found, that **3** converts to the expected product **4**, on the contrary its regioisomer **5** undergoes the unexpected decarboxylation reaction resulting in **6**.



Scheme 2. a) and b) Experimental results of the esterification reaction for regioisomers 3 and 5;
c) Molecular structure of 4 according to X-ray study.

Thus, fundamental differences in the reactivity of 4- and 5-azido-1H-pyrazolecarboxylates as well as for the difference in reactivity between **3** and **5** were established and proved by the methods of computational and synthetic chemistry.

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MONITORING OF CATALYTIC TELOMERIZATION BY MALDI MASS SPECTROMETRY

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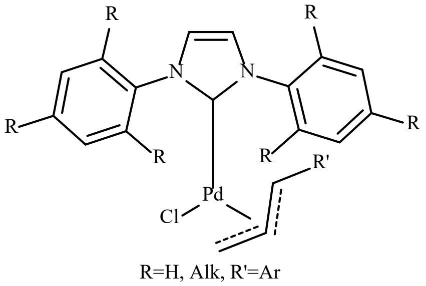
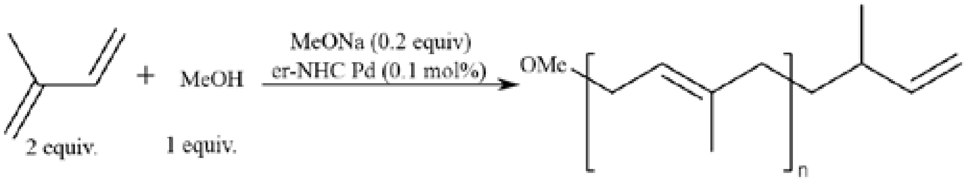
On-line reaction monitoring by mass spectrometry is one of the key instruments allowing establishing kinetics of the formation of intermediates in organic reactions and theirs structures. Such monitoring is usually based on electrospray ionization mass spectrometry and involves direct coupling of reaction vessels with ion source. From the one hand it allows permanent data acquisition, but from the other one it requires a lot of instrument time. An alternative approach can be developed using MALDI mass spectrometry. This soft ionization method also allows detecting intermediates but doesn't require continuous reaction medium flow. In this work we tested this approach to study isoprene telomerization initiated by sodium methylate in the presence of methanol and palladium-based catalysts,.



Rice. 1. Palladium-based catalysts used in the work.

The reaction was carried out in a mixture of isoprene and methanol in a molar ratio of 2:1 at room temperature with constant stirring. A catalyst was added to the reaction mixture, and then the reaction initiator, sodium methoxide:



The samples were spotted on a MALDI target with pre-applied matrix compounds (anthracene, 8,9-diphenylanthracene, picene, rubrene, 1,8,9-anthracentriol, trans-2-[3-(4-tert-butylphenyl) -2-methyl-2-propylidenemalononitrile, 2,5-dihydroxybenzoic acid, 3-indoleacrylic acid were tested). The MALDI mass spectrum was recorded using a Bruker autoflex speed mass spectrometer.

The analysis of the obtained results showed that mass spectra of reaction masses before the introduction of the initiator contain intense peaks of products of elimination of chlorine atom from catalysts' molecules. The intensities of such peaks rapidly decline after addition of the initiator and ion peaks corresponding to the coordination of two isoprene molecules appear. Low-intensity peaks with coordinated telomerization products were also observed. These peaks persists until the complete conversion of isoprene into reaction products.

SYNTHESIS OF POLYTRIAZOLE NANOPARTICLES BASED ON AMPHIPHILIC BIS-NHC DERIVATIVES OF CALIX[4]ARENES WITH OXYETHYLAZIDE/ALKYNYL FRAGMENT

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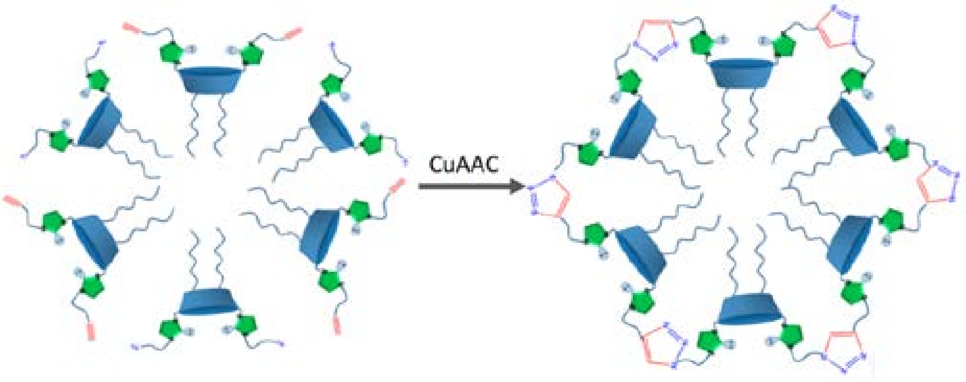
N-heterocyclic carbene ligands (NHC) were isolated in a stable form about 30 years ago. They have caused a rapid revolution in the field of modern organic chemistry. The strong σ-donor and weak π-acceptor properties of these ligands determine the formation of clearly structured thermodynamically stable coordination compounds and, hence, their wide application in metal complex catalysis[1]. Among N-heterocyclic carbenes, polytopic NHC's deserve considerable attention. These ligands provide high stability of the complexes due to the chelate effect and are also a unique framework for the creation of polynuclear homo- and heterometallic coordination compounds[2]. One way to get poly-NHC's are polymeric N-heterocyclic carbenes, obtained by copolymerization of NHC-containing monomers.

Calixarenes are excellent macrocycles for creating such polymer systems. The presence of NHC fragments with azide and alkynyl groups on the amphiphilic macrocyclic platform makes it possible to obtain "click" micellar particles that can act as efficient support for catalytically active palladium nanoclusters.

Herein, we present a polymeric NHC carrier based on successive supramolecular self-assembly and a copper-catalyzed azide-alkyne cycloaddition reaction of amphiphilic imidazolium calix[4]arenes with ethoxylated azide/alkynyl fragments.



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The work was supported by the Russian Science Foundation grant 21-73-10062

SYNTHESIS OF PHOTOACTIVE DIARYLETHENES BY THE TROFIMOV REACTION

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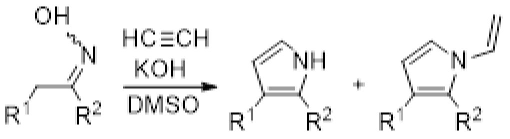
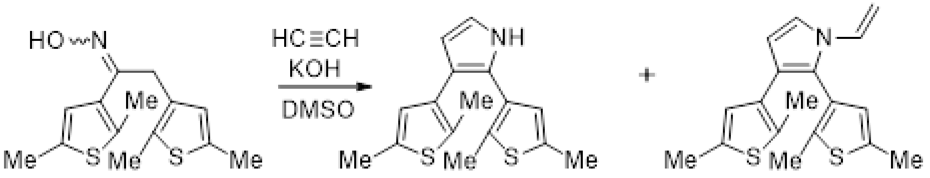
Synthesis of pyrroles from ketoximes 1 and acetylene in the superbase medium KOH-DMSO is known as the Trofimov reaction.1 The reaction provides access to 2,3-disubstituted pyrroles 2 and their N-vinyl-substituted derivatives 3.



1 2 3



4 5 6

In our work, we applied oximes of 1,2-di(hetero)arylethanones in Trofimov reaction for the first time. A number of previously unknown diarylethenes, including compounds 5 and 6, were synthesized. These compounds belong to poorly studied class of diarylethenes with pyrrole ethene “bridge”.2 In our report we will discuss the structure and photochemical properties of a new examples of pyrrole-based diarylethenes.

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The work was carried out with the support of the Russian Science Foundation (grant 21-13-00391).

AMIDATION OF 5-NITROISOQUINOLINE BY DIRECT NUCLEOPHILIC SUBSTITUTION OF HYDROGEN

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Pobedinskaya D.Yu., Borovlev I.V.

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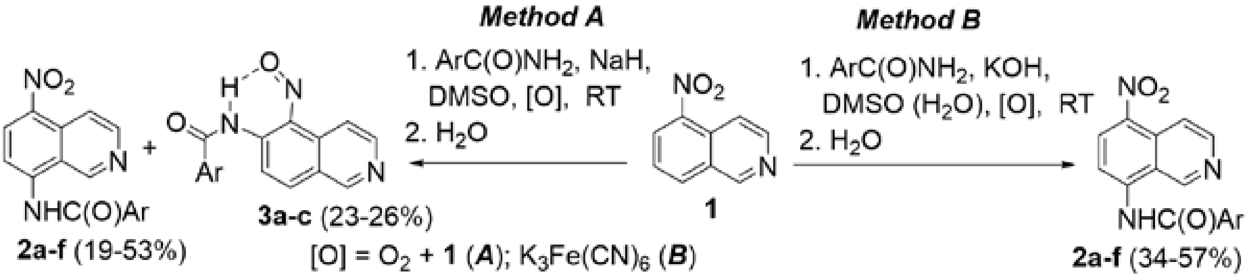
The molecular framework of isoquinoline belongs to a large family of alkaloids with versatile biological and pharmaceutical activity[1]. On research results[2] at least 38 isoquinoline-based therapeutics are in medical use or in clinical trials. Thus, further functionalization of this heterocycle seems to be very promising.

For the S_N^H amidation of 5-nitroisoquinoline, we used two approaches to the reaction conditions, which led to significantly different results.



In the first of them (***method A***), the interaction of 5-nitroisoquinoline (**1**) with amide anions of aromatic acids was carried out in anhydrous DMSO at room temperature, preliminarily generating amide anions by the action of NaH in the same solvent. The process is completed with the formation of a mixture of nitro (**2a-f**) and nitroso products (**3a-c**).

In the second approach (***method B***), we used commercial DMSO containing ~0.5% water, as well as KOH instead of NaH as the base. Under these conditions, the interaction of substrate **1** with amide anions leads to the formation of exclusively nitro compounds (**2a-f**).

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The authors express their gratitude to the North Caucasian Federal University for financial support in the framework of the project to support the projects of scientific groups and individual scientists.

SYNTHESIS OF VINYL ETHERS OF SOME ACETYLENE ALCOHOLS

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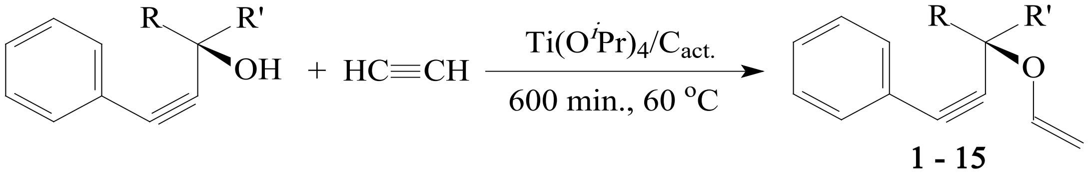
The presence of several active centers in the molecule of acetylene alcohols gives them an important property. It is known that acetylene alcohols undergo an exchange reaction due to hydrogen in the hydroxyl group, so various organic compounds are synthesized on the basis of such alcohols[1-3].

In this study, information was obtained on the synthesis of several vinyl esters (**1-15**) according to the alkylation reaction in the presence of several acetylene using the catalytic system $Ti(O^{i}Pr)_4/C_{act}$.



Here: RR'= −Me (1); R= −Me, R'= −Et (2); R= −Me R'= −Pr (3); RR'= −Et (4); R= −Me R'= –^{i}Pr (5); R= −Me, R'= −^{tr}Bu (6); R= −Me, R'= −Ph (7); RR'= −^{c}Pt (8); RR'= −^{c}Hex (9); RR'= −Me^{c}Hex (10); RR'= −Me^{i}Pr^{c}Hex (11); R= −Me, R'= –H (12); R= −CHCHMe, R'= –H (13); R= −^{c}Hex, R'= –H (14); R= −Ph, R'= –H (15).

The effect of the nature, structure, and spatial location of the substituents on the acetylene alcohol molecule on the formation of vinyl esters was studied, an efficiency series of vinyl reactions were constructed, the reaction mechanisms were proposed, kinetic changes were detected, the structure, composition and purity of the synthesized compounds were proven using modern physico-chemical research methods, alternative conditions of the processes were found.

Based on the results of the study, acetylene alcohols were synthesized with heterogeneous catalytic method using $Ti(O^{i}Pr)_4/C_{act.}$ in the presence of acetylene at temperature of 60 ^{o}C, the amount $Ti(O^{i}Pr)_4$, during 600 minutes, to 8% than mass. of C_{act}, acetylene alcohols vinyl esters with a maximum yield of 1- 92, 2- 88, 3- 86, 4- 85,1, 5- 84, 6- 80, 7- 95, 8- 88, 9- 85, 10- 83, 11- 82, 12- 75, 13- 67, 14- 71 va 15- 84%.

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SYNTHESIS AND REACTIONS OF [1-PERFLUOROALKYL(PHENYL)]-3-HALOGEN ADAMANTANES

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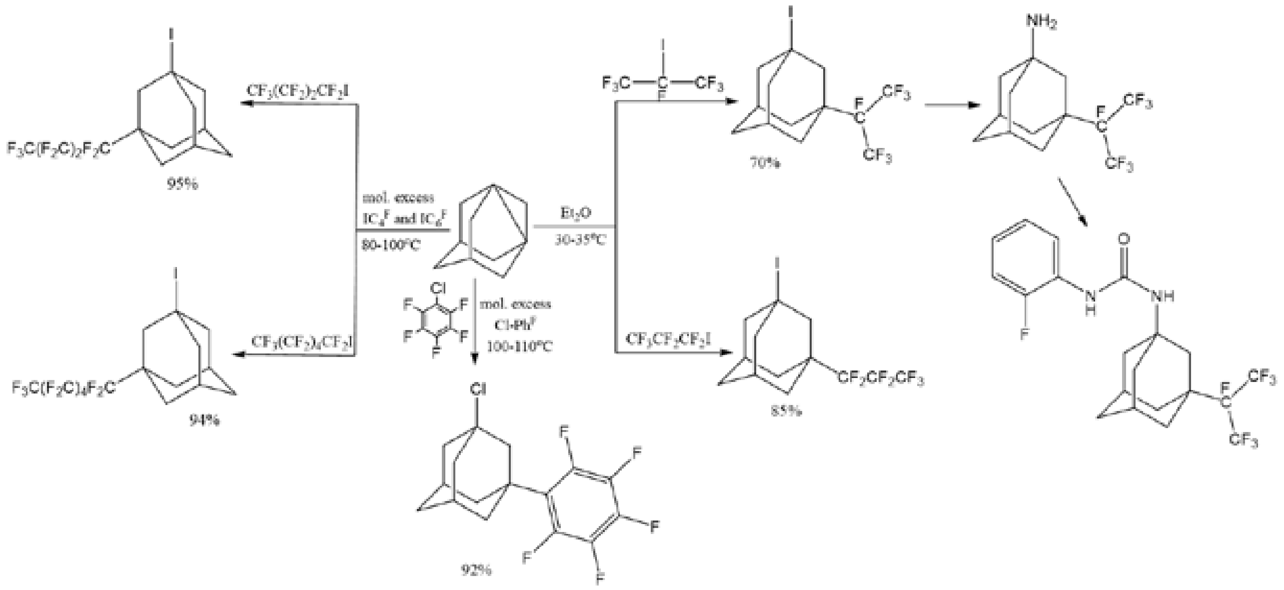
Information on adamantane derivatives containing a perfluoroalkyl group, apart from the trifluoromethyl group, is practically absent. 1-Perfluoroethyladamantane has not been described in the literature, and information on other perfluoroalkyladamantanes and derivatives based on them has not been found.

The main methods for obtaining the perfluoromethyl group is the fluorination of the methyl group or functional groups in adamantane SF_4, CF_3NO, BrF_3, and other fluorinating reagents, which leads to the multistage nature and complexity of the synthesis.

We have developed for the first time a new method for the synthesis of perfluoroalkyl-perfluorophenyladamantanes based on the reaction of 1,3-dehydroadamantane (DHA) with perfluoroalkyl iodides and chloropentafluorobenzene (Scheme 1). The reaction proceeds predominantly with cleavage of the R_F-I, R_{F1}-Cl bond (R_F - perfluoroalkyl, R_{F1} - perfluoroaryl) with the formation of 1-iodo-3-R_F-adamantanes and 1-chloro-3-perfluorophenyladamantane.

Scheme 1



It has been established that the activation of the C–I bond by perfluoroalkyl groups plays a key role in this reaction. Carrying out model reactions of DHA with non-activated haloalkanes: methyl and ethyl iodides, hexyl and octyl bromides under similar conditions showed low DHA conversion and selectivity of the 1,3-DHA insertion reaction at the C-Hal bond. The content of target 3-Hal-1-R-adamantanes did not exceed 10%. In the case of ethyl iodide, along with the target product, 1-ethyl, 1-iodine, and 1,3-diiodine adamantanes were present. This is probably due to the radical mechanism of the reaction, in contrast to the reaction with an activated R_F–I bond.

The reactions of DHA with chlorine and bromobenzene did not lead to its incorporation into the $\mathbf{C}_{Ar}$–Hal bond. Thus, activation of this bond by fluorine atoms facilitates the addition of DHA and leads to the formation of hard-to-reach 3-chloro-1-perfluorophenyladamantane.

The presence of a chlorine and iodine atom in the adamantane molecule makes it easy to carry out further functionalization of perfluorophenyl- and perfluoroalkyladamantanes.

The work was supported by the Russian Science Foundation (grant № 21-73-20123)

SELECTIVE Pd/NHC-CATALYZED BUCHWALD-HARTWIG ARYLATION OF C-AMINO-1,2,4-TRIAZOLES

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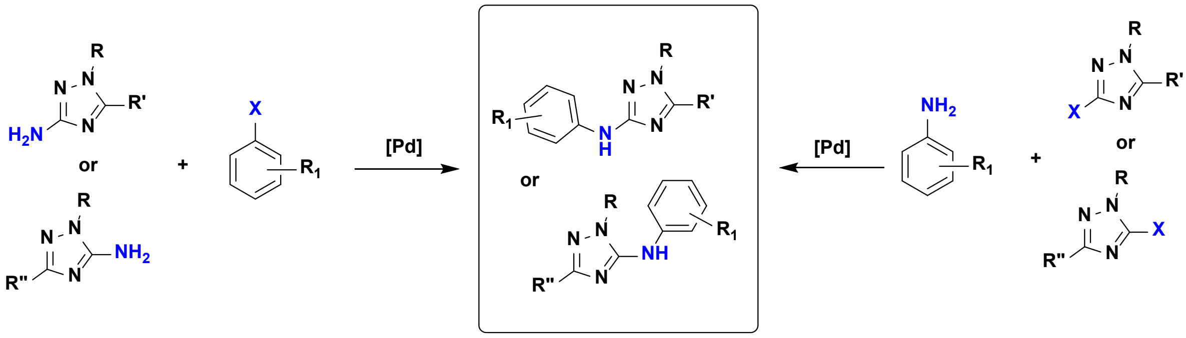
Currently, there are many drugs based on 1,2,4-triazole used in clinical practice for the treatment of various diseases and as biologically active compounds, and they are also a whole group of fungicides with various effects. In addition, 1,2,4-triazole have found wide application as NHC ligands for various Pd/NHC complexes. For example, it was recently shown that palladium complexes with 3-RNH-1,2,4-triazole NHC ligands, capable of ionizing the RNH group in strong basic media can be used as more efficient catalysts [1].

The structure of the heterocycle, in particular, the substituents at N and C atoms of the triazole nucleus, can have a significant effect on the selectivity of reactions of 1,2,4-triazoles, and using of metal complex catalysis can lead to the activation of non-typical reaction centers. It is important to note that the number of stages and wastes of preparation of important nitrogenous heterocycles can be significantly reduce by metal complex catalysis application. However, an important problem in synthesis is the ability of metal complexes to be destroyed during catalytic reactions, which can lead to deactivation of catalytic systems [2, 3].

We have proposed stable catalytic systems using palladium complexes with N-heterocyclic carbenes, allowing the regioselective synthesis of aminotriazole derivatives via the Buchwald-Hartwig reaction, including compounds of great practical importance.



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The study was supported by a grant from the Russian Science Foundation № 22-23-00380, https://rscf.ru/project/22-23-00380/

VINYL DERIVATIVES OF PYRIMIDINES BASED ON PYRAZOLE-4-CARBALDEHYDES

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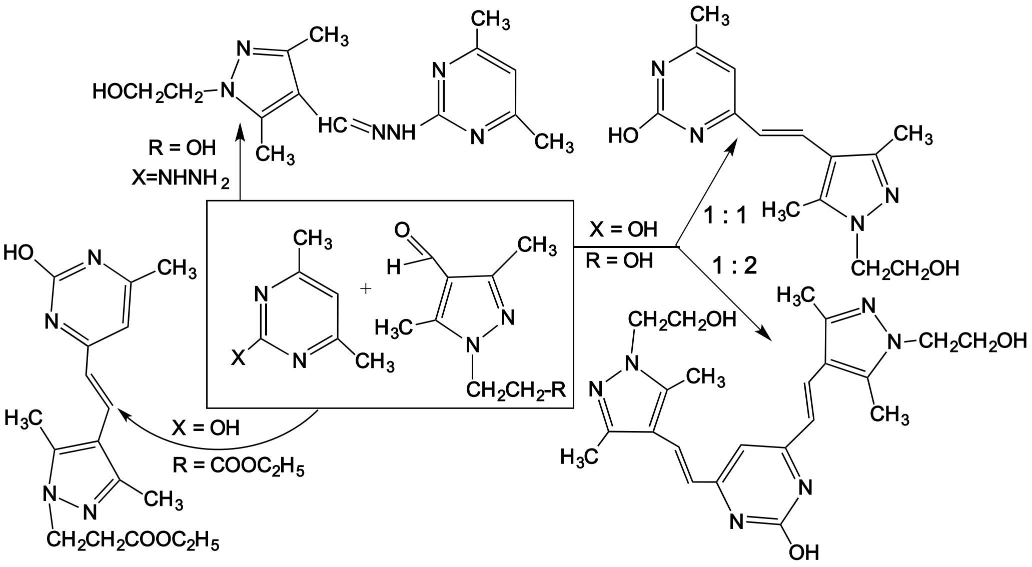
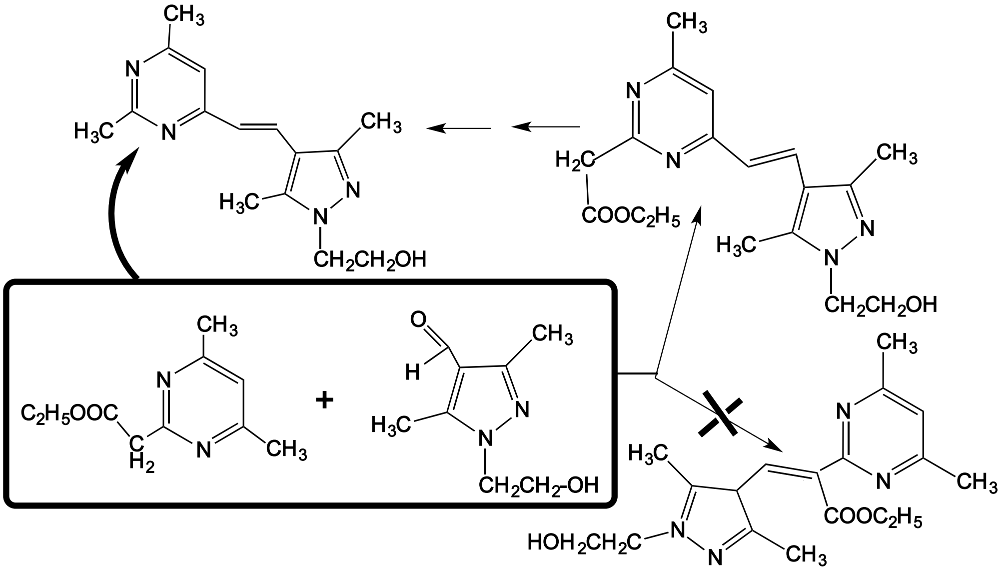
The reactions of pyrimidines with substituted aldehydes of the pyrazole series have been studied. As a result, a series of vinyl pyrimidine derivatives containing conjugated π-bonds were synthesized.



In the reaction of ethyl 2-(4,6-dimethylpyrimidin-2-yl)acetate with substituted 4-formylpyrazole, a condensation product at the 4-methyl group was. isolated.



Support of the State Committee on Science of the Republic of Armenia (project 20RF-138).

SYNTHESIS OF PYRAZOLYLPYRIMIDINES AND THEIR ALKYLATION

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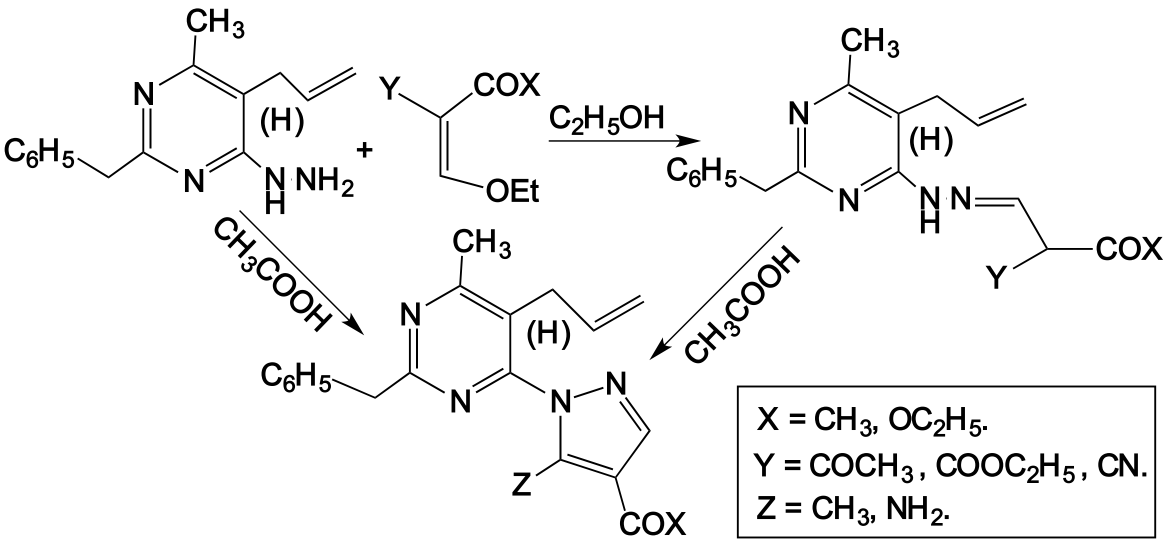
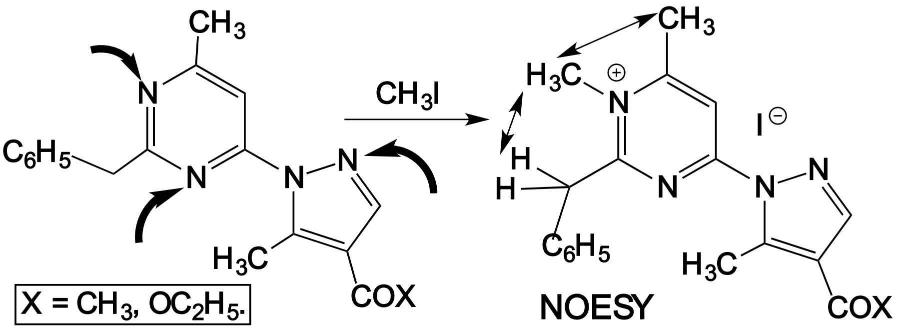
Substituted 4-(pyrazol-1-yl)pyrimidines were synthesized by the interaction of substituted 4-hydrazinopyrimidines with ethoxymethylidenedicarbonyl compounds.



The alkylation of the obtained systems was studied. ^{1}H NMR (NOESY) spectroscopy proved the position of attachment of the alkyl group – nitrogen atom N-1 of the pyrimidine ring.



This work was carried out with the financial support of the State Committee on Science of the Republic of Armenia and the Russian Foundation for Basic Research (project 20RF-138 / 20-53-05010 Arm_a /), as well as within the framework of the grant of the Ministry of Education and Science of the Russian Federation for scientific research of the Russian-Armenian University.

SYNTHESIS AND PROPERTIES OF 1,3-DISUBSTITUTED UREAS CONTAINING IBUPROFEN FRAGMENT

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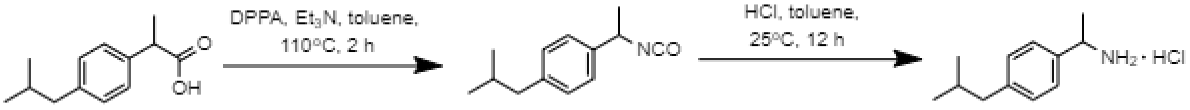
In our work, ibuprofen **1** was used to create 1-isobutyl-4-(1-isocyanatoethyl)benzene **2** by a one-step method, and 1-(4-isobutylphenyl)ethan-1-amine hydrochloride **3** was synthesized on its basis (Scheme 1).

Scheme 1



1 2, 88% 3, 98%

Based on isocyanate **2**, a series of 1,3-disubstituted ureas **5a-e** was synthesized with the participation of celecoxib **4a**, amantadine **4b**, rimantadine **4c**, paracetamol **4e**, trans-4-amino-(cyclohexyloxy)benzoic acid **4d** (Scheme 2).

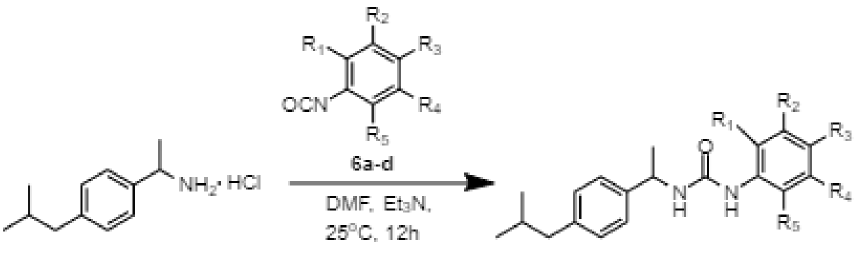
Scheme 2

2 4a-e 5a-e

R = celecoxib (4a, 39%), amantadine (4b, 42%), rimantadine (4c, 83%), paracetamol (4e, 83%), t-AUCB (4d, 69%)

Based on amine **3** and halogen-substituted aromatic isocyanates **6a-d**, ureas **7a-d** were synthesized (Scheme 3).

Scheme 3



3 7a-d

$R_1 = R_3 = R_4 = R_5 = H$, $R_2 = F$ (7a, 53%); $R_1 = R_2 = R_3 = R_5 = H$, $R_4 = F$ (7b, 81%);
$R_1 = R_3 = R_4 = R_5 = H$, $R_2 = Cl$ (7c, 47%);$R_1 = R_2 = R_4 = R_5 = H$, $R_3 = Cl$ (7d, 75%).

The work was financially supported by the Russian Science Foundation (project no. 19-73-10002).

ASYMMETRIC CROTILATION OF ALDEHYDES, CATALYZED BY DERIVATIVES OF AMINO ACIDS

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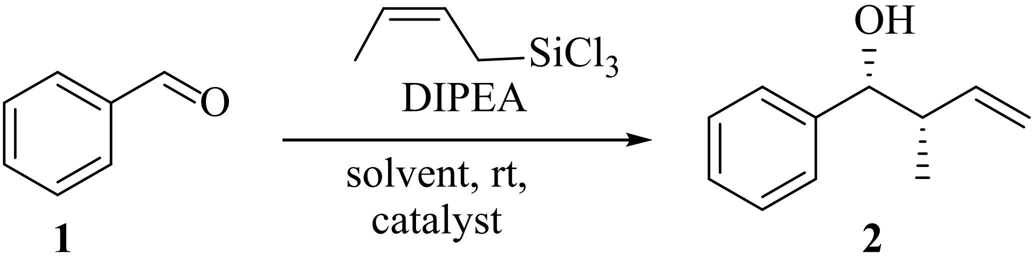
The catalytic synthesis of certain classes of compounds is a complex task. Currently, several methods have been developed, the practicality of which is compensated by the use of expensive and highly toxic reagents, the need for extremely low temperatures, and complex multi-step synthesis of catalysts. These problems have been solved by developing amino acid catalysts [1].

A series of L-valine-based catalysts for the crotylation of aldehydes with Z-crotyltrichlorosilane has been developed. Alcohols with good enantioselectivity were obtained. Practicality is that it is not necessary to resort to extremely low temperatures.



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SULFONYL AND THIYL RADICALS MEDIATED SYNTHESIS OF STABLE ENAMINES

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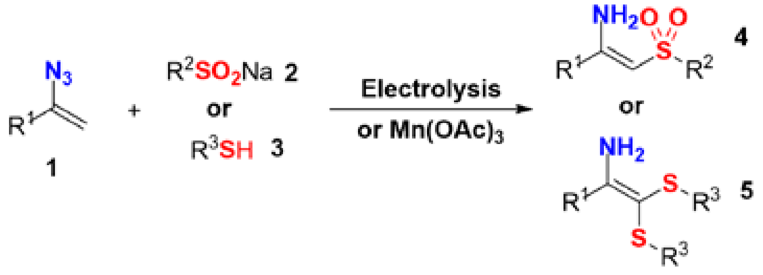
Oxidative coupling techniques are a powerful tool for chemical synthesis, enabling an array of new approaches to the construction and late-stage derivatization of complex molecules. Owing to the plethora of different C−S bonds present in many biologically active molecules, great efforts have been devoted to the site-selective and predictable functionalization with C−S bonds construction in complex targets. Important intermediates in the processes of oxidative sulfonylation and thiolation are sulfonyl[1] and thiyl[2] radicals, the sources of which are often sulfonyl hydrazides, sulfinic acids salts, thiols, and disulfides, respectively.

We carried out an oxidative C-S coupling of sulfinic acids salts and thiols with vinyl azides under the action of both electric current [3,4] and manganese triacetate [5]. Surprisingly, we found that under the action of S-centered radicals vinyl azides formed stable sulfonylated and thiolated *N*-unsubstituted enamines through molecular nitrogen elimination.



Scheme 1

Both electrochemical and manganese triacetate-mediated reactions of sulfinates **2** with vinyl azides **1** give stable enaminosulfones **4**, while simultaneous electrolysis of thiols **3** and vinyl azides **1** results in *gem*-bisthioenamines **5.**

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SYNTHESIS AND PROPERTIES OF 1,3-DISUBSTITUTED DIUREAS BASED ON 1-(ISOCYANATOMETHYL)-3,5-DIMETHYLADAMANTANE

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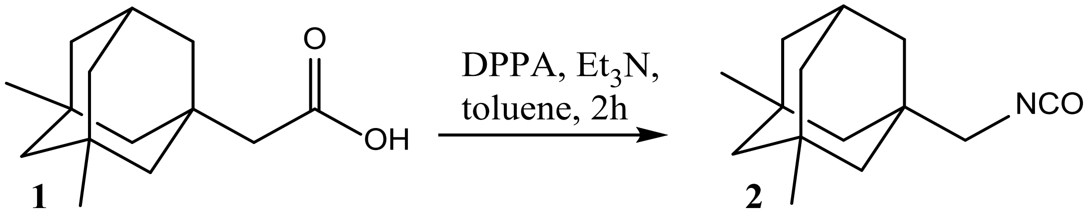
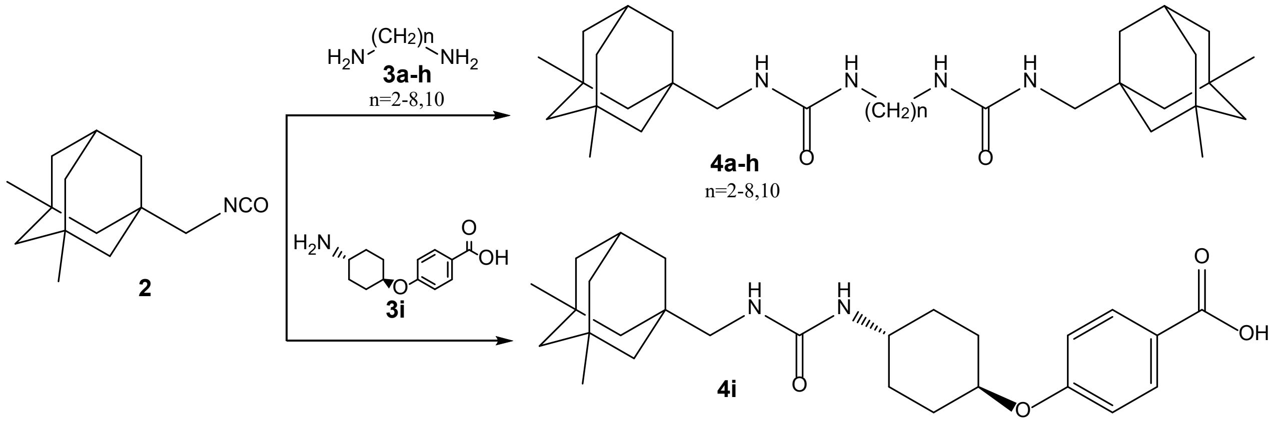
Describes a one-stage method for the preparation of 1-(isocyanatomethyl)-3,5-dimethyladamantane, with a yield of 87% (scheme 1).

Scheme 1



Reaction of 1-(isocyanatomethyl)-3,5-dimethyladamantane with aliphatic diamines synthesized a series of 1,3-disubstituted ureas containing a 3,5-dimethyladamantan-1-yl) methyl radical in their structure, yield of 63-99% (scheme 2).

Scheme 2



Lipophilicity coefficients, melting points and yields of synthesized compounds **4a-i**.

№	n	Mr	LogP*	t *пл*, ºC	***Выход, %***
4a	2	498,74	5.30	212,7	98%
4b	3	512,77	5.58	163,7	99%
4c	4	526,81	5.84	143,5	65%
4d	5	540,82	6.35	127,1	76%
4e	6	554,85	6.86	128,9	98%
4f	7	568,89	7.36	120,4	71%
4g	8	582,92	7.87	109,9	79%
4h	10	610,96	8.63	99,6	94%
4i		454,6	5.32	240,1	63%

The work was financially supported by the Russian Science Foundation (project no. 19-73-10002).

CONTROL OF CHEMOSELECTIVITY BETWEEN CATIONIC 4π AND 6π ELECTROCYCLIZATIONS

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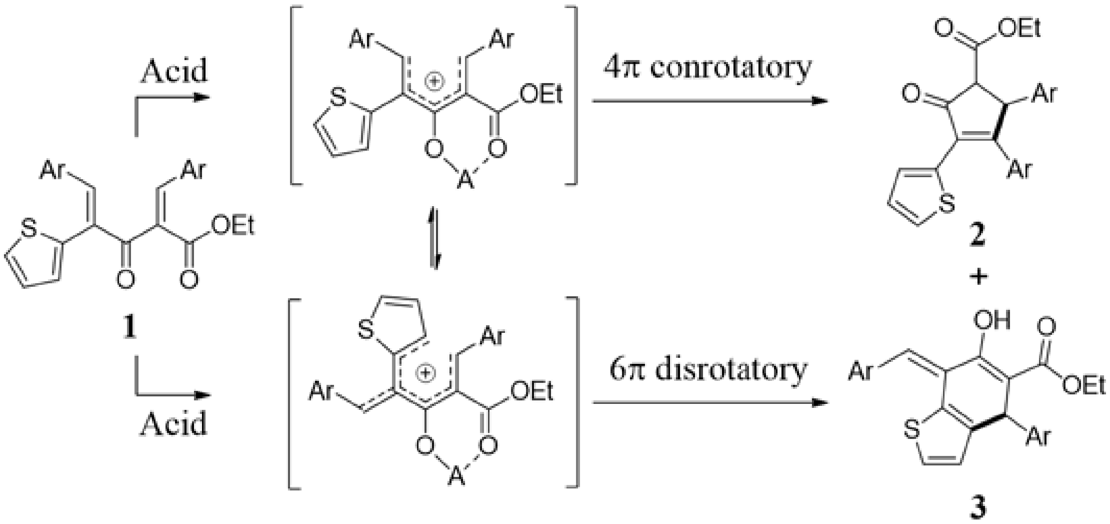
Divinyl ketones (DVK) are important synthons in organic chemistry used in the synthesis of various valuable substances for medicine and material chemistry. Most studies of the Nazarov reaction are based on alkyl-substituted DVKs, although cyclization of aryl-substituted ones may be a promising methodology for the synthesis of natural product derivatives: combretastatins and flavaglins. Recently, in our group, when studying the cyclization of polarized triaryldivinylketones, it was found that, depending on the aromatic substituent at the carbonyl group, the reaction can proceed along two alternative routes: with the formation of cyclopentenone by the Nazarov reaction or with the formation of dihydronaphthalene, probably by intramolecular alkylation. In contrast to benzene derivatives, where the cyclization of divinyl ketones proceeds with high chemoselectivity, the reaction of divinyl ketones **1** containing a thiophene substituent at carbonyl group results in a mixture of products **2** and **3**.



In this work a comprehensive study including the influence of the solvent nature and electronic and steric effects of β-substituents on thienyl substitued DVK **1** cyclization pathway. In addition, we performed DFT-calculations of DVK **1** cyclization, which well-consistent with our experiments and confirm our hypothesis of electrocyclic nature of dihydro benzothiophene **3** formation.

This work was supported by a grant from the Russian Science Foundation (18-13-00308П).

NITROQUINOLINE-*N*-OXIDES IN OXIDATIVE S_N^H-ARYLAMINATION REACTIONS

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Pobedinskaya D.Yu., Borovlev I.V.

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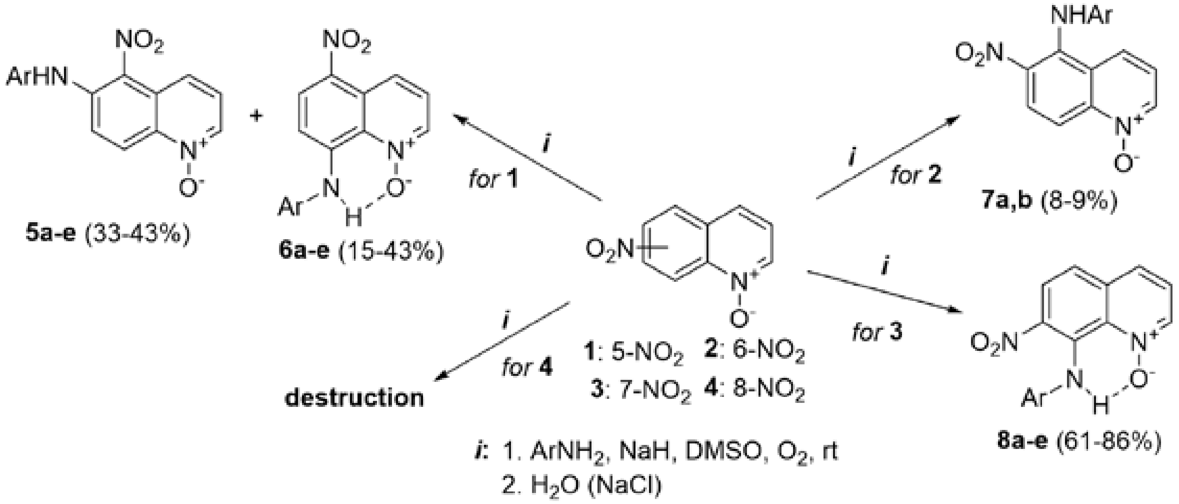
The aim of this work was to study the possibility of oxidative substitution of hydrogen in 5(6,7,8)-nitroquinoline-*N*-oxides for an arylamino group. It is known that heteroaromatic *N*-oxides enter into S_N^H reactions both with the preservation of the *N*-oxide function and with its loss. We carried out the reaction in anhydrous DMSO without isolation from atmospheric oxygen, preliminarily generating the arylamide anion by the action of NaH.



As it turned out, 5- and 7-nitroquinoline-*N*-oxides react most easily, forming substitution products at positions 5 (**5a-e**) and 8 (**6a-e**) in the first case and at the spatially hindered position 8 (**8a-e**) - in the second. 6-Nitroquinoline *N*-oxide reacts with difficulty, giving arylamino derivatives **7a,b** in low yield, while 8-nitroquinoline *N*-oxide undergoes complete degradation under these conditions.

Thus, the *N*-oxides of 5-, 6-, and 7-nitroquinolines react with arylamine anions in anhydrous DMSO, forming only the products of oxidative S_N^H arylamination, while retaining the *N*-oxide function. Note that in the presence of two acceptor groups in the molecule of these substrates, the regioselectivity of the reactions was determined exclusively by the nitro group.

The authors express their gratitude to the North Caucasian Federal University for financial support in the framework of the project to support the projects of scientific groups and individual scientists.

SYNTHESIS, STRUCTURE AND BIOLOGICAL PROPERTIES OF 2-ARYLHYDRAZONES AND 2-ARYLMETHYLIDENE THIAZOLO[3,2-A]PYRIMIDINES

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Litvinov I.A.[a], **Solovieva S.E.**[a,b], **Antipin I.S.** [a,b]

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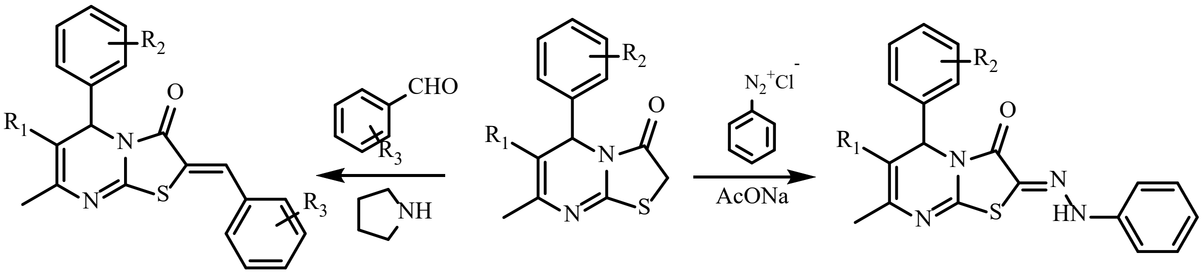
Thiazolo[3,2-a]pyrimidines are promising structural fragments for the development of drugs and anticancer drugs [1].. Hydrazones and arylmethylidene derivatives thiazolo[3,2-a]pyrimidines are known to exhibit bacteriostatic activity, as well as antipyretic, analgesic, antituberculous and antitumor effects. This work is devoted to the synthesis of new 2-phenylhydrazone and 2-arylmethylidene derivatives of thiazolopyrimidines and the identification of the structure – biological activity dependence.



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Acknowledgements. This work was supported by Russian Foundation for Basic Research (project number 20-33-90124).

BENZOFURO[2,3-*b*]QUINOLONES AND NORNEOCRYPTOLEPINES THROUGH EFFECTIVE ONE-POT TRANSFORMATION

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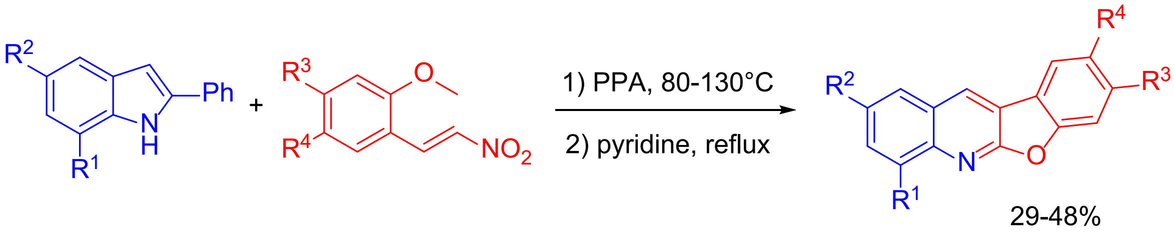
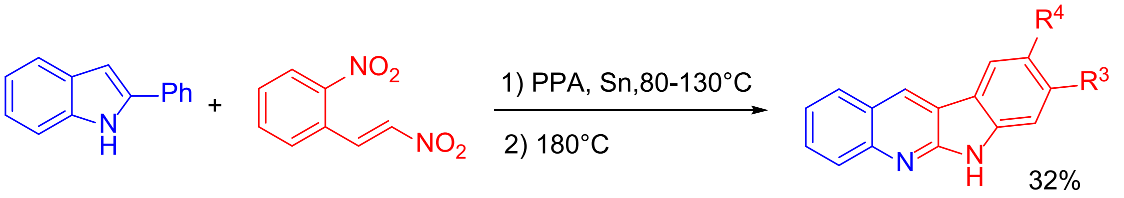
Plants are one of the most important resources for the discovery of new drugs. The potential of natural compounds as new drug leads is clearly illustrated by the discovery and development of many modern medicines. This is an encouraging factor that drives natural products research in the vegetable kingdom. Neocryptolepine is a tetracyclic nitrogen heterocycle isolated from the African climber Cryptolepis sanguinolenta, which is widely used in traditional African medicine in many countries of Central and West Africa. The natural product is one of the representative examples of the small family of indolo[2,3-*b*]quinoline alkaloids, being endowed of multiple biological activities, including DNA-binding and inhibition of the enzyme topoisomerase

Through our latest attempts, we have shown a unique transformation that allows the preparation of 3-substituted-2-quinolones by the reaction of indoles with 2-nitrostyrenes. The significant structural change that this reaction causes can be used to efficient assembly of various quinoline-containing heterocyclic systems. We hypothesized that the reaction of *ortho*-hydroxychalcones should lead to a new heterocyclic system, benzofuro[2,3-*b*]quinolines, also of interest due to their antidiabetic properties. Although hydroxy- derivatives turned out to be inactive in this reaction, we have achieved success using their protected analogues, *ortho*-methoxynitrostyrenes.



The reaction is also excellent for the synthesis of norneocryptolepins. In this case, the amino group was obtained by reduction directly in the PPA medium.



This work was supported by the Russian Foundation for Basic Research (grant #20-33-90049, by the President Grant for State Support of Young Scientists (grant #MK-2035.2021.1.3), and the Ministry of Education and Science of Russian Federation (grant #0795-2020- 0031).

SYNTHESIS OF SUBSTITUTED FURAN-3-CARBOXYLATES BASED ON ETHYL 3-BROMO-3-NITROACRYLATE

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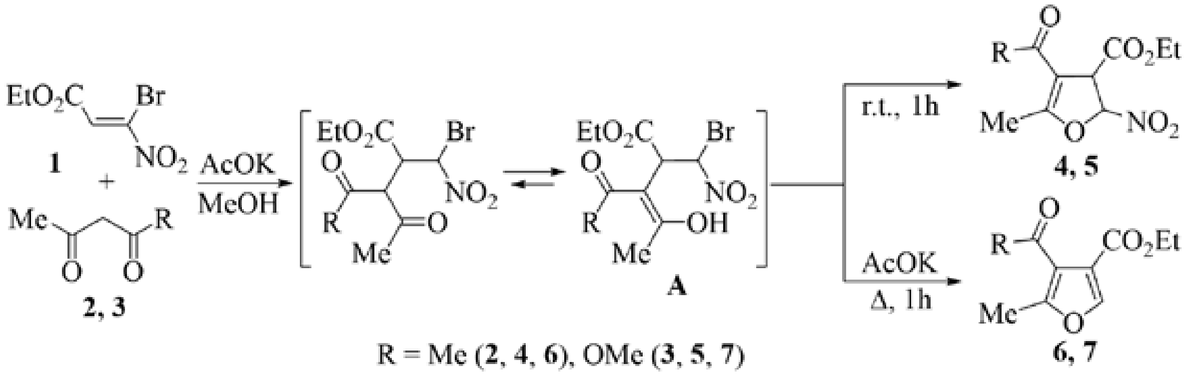
Furancarboxylate derivatives are of undoubted interest due to the presence of important biologically active properties in their representatives. For example, methyl 4,5-diethyl-2-(3-methoxy-3-oxopropyl)furan-3-carboxylate inhibits insulin secretion[1]. At the same time, it is known that alkyl 3-bromo-3-nitroacrylates are convenient starting materials for the synthesis of benzo[*b*]furan-3-carboxylates[2].

We studied the reactions of ethyl 3-bromo-3-nitroac2rylate **1** with pentane-2,4-dione **2** and methyl 3-oxobutanoate **3**, which completed under mild conditions with the formation of 2-nitro-2,3-dihydrofuran-3-carboxylates **4, 5** with a yield of 70-75%.

The interaction proceeds along the path of the initial formation of the Michael adduct **A**, followed by intramolecular *O*-alkylation with the participation of the enol hydroxyl and the bromonitromethyl group.

Therefore, refluxing the reaction mixture with a twofold excess of potassium acetate leads to the formation of substituted furan-3-carboxylates **6, 7** with a yield of 61-68%.



Thus, it has been shown that the reactions of bromonitroacrylate with representatives of acyclic CH-acids, depending on the reaction conditions, lead to the formation of nitrodihydrofuran-3-carboxylates or their denitrated products.

This work was carried out within the framework of a state assignment with financial support from the Ministry of Education of Russia (project No. FSZN-2020-0026).

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ONE-POT SYNTHESIS OF 2-ARYLQUINOLINES AND QUINAZOLINE *N*-OXIDES FROM ARENES AND ELECTROPHILICALLY ACTIVATED NITROALKANES

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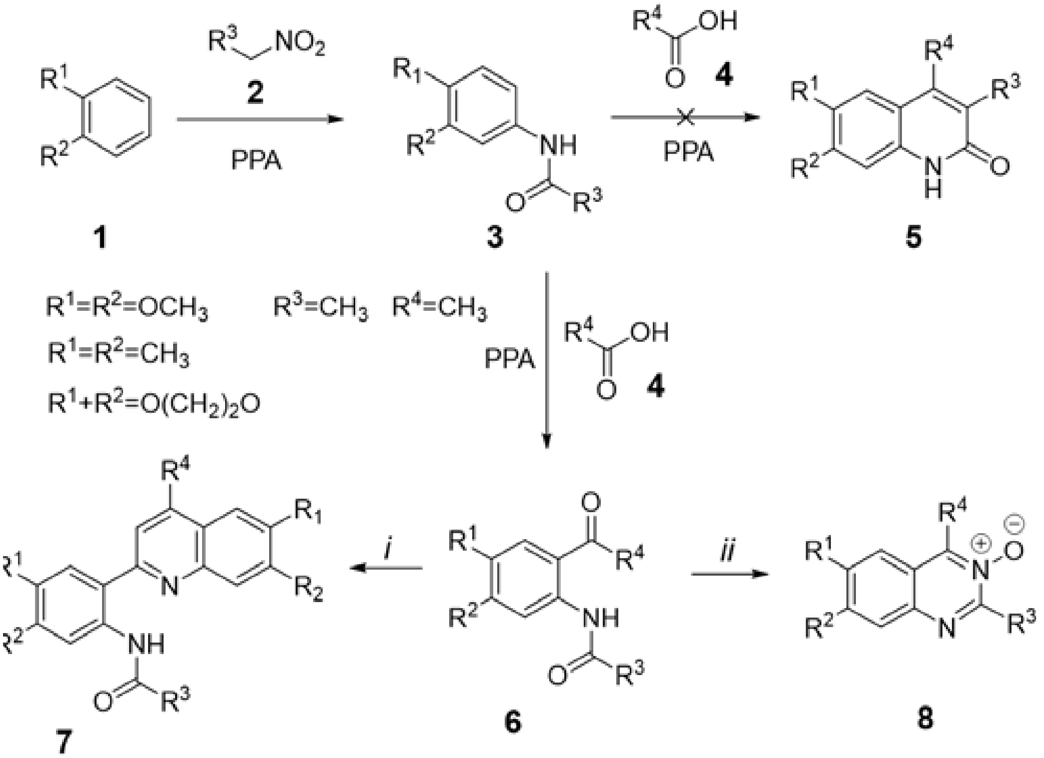
Electrophilically activated nitroalkanes with polyphosphoric acid (PPA) have successfully proven themselves as convenient building blocks in the assembly of frameworks of nitrogen-containing heterocycles. Therefore, in this study it seemed tempting to obtain quinolones **5**, based on arenes **1** and 1-nitroalkanes **2** with the intermediate formation of acetanilides **3**, which, when further treated with carboxylic acids **4**, could lead to quinolones **5**. For the successful implementation of successive acetamination and acylation reactions leading to the formation of compounds **6**, arenes containing two *p*-orientants (EDG) in the *o*-position have been selected.

It has been found that when treated with carboxylic acid **4** (R^4=CH_3) of acetanilides **3** (R^3=CH_3) isolated in pure form, the formation of quinolones **5** is not observed, and with a yield of 95-97% when heated in PPA (86%) for 1-1.5 hours at 105-110 °C, 2-arylquinolines 7 are formed. In the case of one-pot synthesis, which consists in heating a mixture of compounds **1** and **2** in a PPA medium at 105-110 °C for 3-3.5 hours, followed by the addition of carboxylic acid **4** and additional heating for 1-1.5 hours, compounds **7** (yield 15-20%) and **8** (yield 15-20%) are formed.



The structure of the new 2-arylquinolines **7** and substituted quinazoline *N*-oxides **8** is confirmed by ^{1}H, ^{13}C NMR spectroscopy, high-resolution mass spectroscopy and X-ray diffraction data.

Funding: This work was supported by the Russian Foundation for Basic Research (20-33-90027), the Ministry of Education and Science (grant #0795-2020- 0031) and by the President Grant for State Support of Young Scientists (grant # MD-3505.2021.1.3).

THE FIRST REPRESENTATIVE OF A NEW CLASS OF CHARGE TRANSFER COMPLEXES IN *O*-QUINONE SERIES FOR ORGANIC SEMICONDUCTORS

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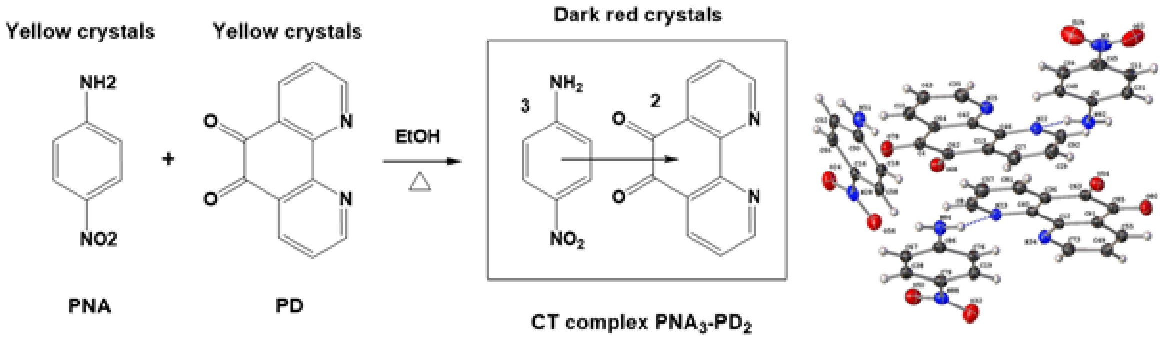
The first stable CT complex in o-quinone series in the crystal state was obtained by the reaction of p-nitroaniline (PNA) with [1,10]-phenanthroline-5,6-dione (PD). The structure of the PNA_3-PD_2 complex was determined by X-ray diffraction studies, which showed that the ratio of donor (PNA) and acceptor (PD) is 3:2. IR spectroscopy and quantum chemical calculations have shown the implementation of several types of donor-acceptor bonds of the PNA amino group with the nitro group of another PNA molecule, PD carbonyl groups and heterocyclic nitrogen atoms.



The diffuse reflectance spectrum of the crystalline powder of the CT complex PNA_3-PD_2 is characterized by a long-wavelength weakly structured absorption band up to 650 nm, which is typical for the CT complex. According to the data of quantum chemical calculations, the resulting complex PNA_3-PD_2 has the properties of direct-gap semiconductors.

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DONOR-ACCEPTOR CYCLOPROPANES IN THE SYNTHESIS OF CARBO- AND HETEROCYCLES: ISOMERIZATIONS, DIMERIZATIONS AND RING EXPANSIONS

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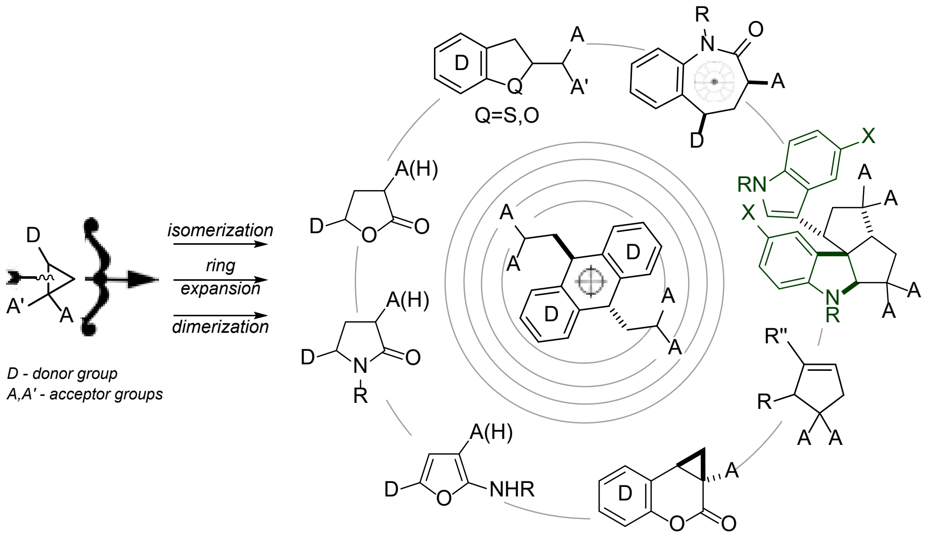
Donor–acceptor (D–A) cyclopropanes are a unique class of substrates which have been proved to be useful building blocks for the synthesis of a broad diversity of cyclic systems. Under the activation with Lewis or Brönsted acid, they undergo three-membered ring opening that can be accompanied by diverse other processes including the participation of multiple reaction centers in D–A cyclopropane molecules. As a result, a broad spectrum of atom-economic processes leading to the significant increase of the molecular complexity has been developed. Herein, we demonstrated several Lewis acid-induced transformations of D–A cyclopropanes *without any reaction partner* [1-5]. These are: a) isomerizations including ring enlargement processes and b) various cyclodimerizations producing a large diversity of carbocycles, from simple ones to complex polycyclic systems. These transformations are promising routes to the synthesis of various bioactive compounds. The process chemo- and stereoselectivity are controlled by the reaction conditions, primarily by the Lewis acid applied, as well as by the nature of donor substituent.



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This work was supported by the Russian Science Foundation (grant № 21-73-20095).

ELECTROCHEMICAL SYNTHESIS OF ORGANONICKEL COMPLEXES OF TYPE [NiBr(R)(bpy)] AND THEIR REACTIVITY TOWARDS ORGANOPHOSPHORUS COMPOUNDS

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The organonickel sigma-bonded complexes are known as key intermediates of various catalytic process of C–P bond formation with participation of chlorophosphines and elemental (white) phosphorus.[1] However, the use of chlorine-containing precursors is unsafe and unenvironmental.[1] Therefore, in this work we describe new approach for the preparation of organophosphorus compounds based on application of organonickel sigma-complexes [NiBr(R)(bpy)], where bpy is 2,2’-bipyridine, with primary phosphines and PH_3.[2,3] Moreover, the use of an environmentally friendly electrochemical methods for the synthesis of this class of organometallics allows to perform *in situ* generation of unstable organonickel sigma-complexes [NiBr(R)(bpy)], where R = Ph, Pr, followed by their interaction with phosphine PH_3, leading to organophosphorus compounds (Figure 1).

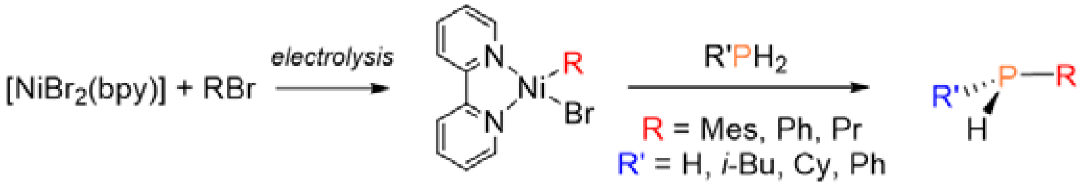

Figure 1. Reaction of an organonickel sigma-complexes with R’$PH_{2.}$

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This work is financially supported by the Russian Science Foundation (project 21-73-00136).

FEATURES OF THE ELECTROCHEMICAL SYNTHESIS OF ORGANONICKEL SIGMA COMPLEXES OF TYPE [NiBr(Aryl)(bpy)]

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The understanding and control of the mechanisms of the catalytic processes is an urgent and important task of modern organic and organoelement chemistry. The reactions of cross- and homo-coupling leading to formation of C–C, P–C and N–C bonds, is an important platform for the synthesis of many organic and organoelement compounds that are widely used in various branches of modern science.[1,2] In this work we describe the peculiar behavior of novel electrochemically synthesized organonickel sigma-complex [NiBr(Tcpp)(bpy)], where Tcpp = 2,4,6-tricyclopentylphenyl, bpy = 2,2'-bipyridine, which, in contrast to its analogues (Figure 1)[3], leads to the formation of new previously not described homo-coupling product, which is difficult to obtain by classical chemical methods.

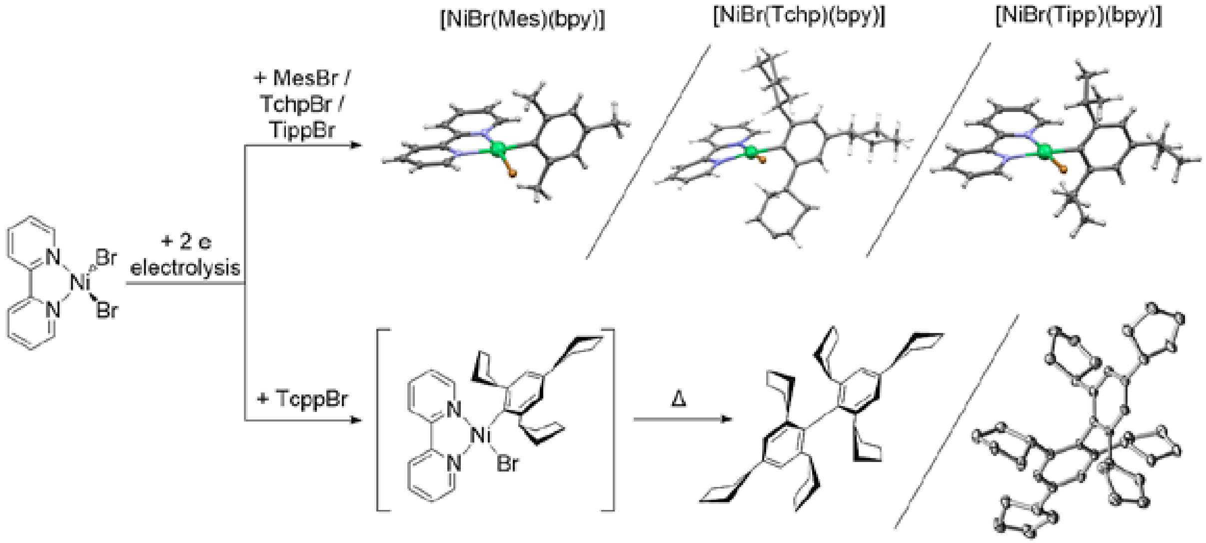

Figure 1. Electrochemical synthesis of organonickel sigma-complexes [NiBr(Mes)(bpy)], [NiBr(Tchp)(bpy)], [NiBr(Tipp)(bpy)] and [NiBr(Tcpp)(bpy)].

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This work is financially supported by the Russian Science Foundation (project 21-73-00136).

UTILIZATION BOUNDARIES OF THE NICHOLAS-TYPE CYCLIZATION IN THE SYNTHESIS OF HETEROENEDIYNE SYSTEMS

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The Nicholas reaction is a general-purpose synthetic tool for the incorporation of a propargylic moiety to different types of nucleophilic organic substrates through stabilized $Co_2(CO)_6$ complexes of propargylic carbocations.[1] Recently the Nicholas-type cyclization was shown to be the key step in the synthesis of 10-membered heteroenediynes.[2]

The aim of the work was to explore the scope and limitations of the intramolecular Nicholas reaction in the synthesis of 10-membered heteroenediynes, including enediynes with additional functional groups.

We tested various nucleophilic groups responsible for the Nicholas reaction (X-LG = OH, S-Ac, NH-SO_2Ar, NH-Bz, NH-Bn) attached to the acyclic enediyne core and additional functional groups, which should stay untouched during the Nicholas-type cyclization(Y = ArNH_2 and COOMe) (Fig. 1). The Nicholas-type cyclization through OH proceeded smoothly giving **2a,b**. It was insensitive towards the additional ester group. S-Cyclization through S-Ac group gave thiaenediyne **2c** in moderate yield. However, the cyclization efficiency through the N-atom was dependent on a substituent (see **2c–g**). The cyclization gave the desired enediyne cycles in good to moderate yield only in the case of sulfonamide derivatives **2d,e**. It is important, that in the case of sulfanilamide function free NH_2-group should be protected by acylation (**2e**).

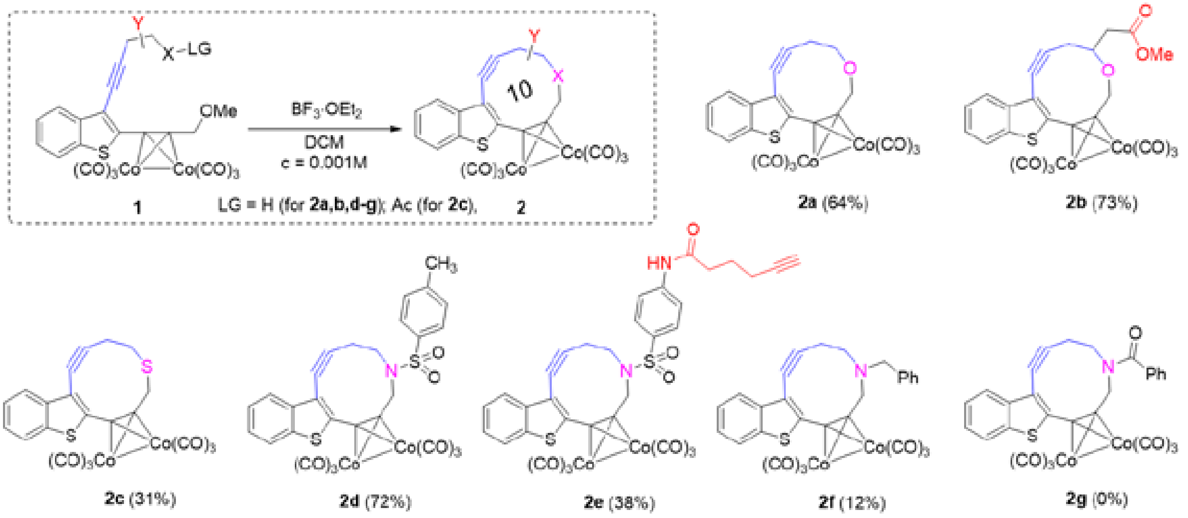

Figure 1. Synthesis of the enediyne Co-complex 3

In summary, both OH and arenesulfonamide groups are good nucleophilic functions for the 10membered ring closure by the Nicholas-type cyclization. The synthesis of active derivatives of enediynes through the additional functional groups (terminal alkyne, ester) is ongoing.

This work was supported by a financial grant from the Russian Science Foundation (211300218)

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DIASTEREOMERIC COBALT(III) COMPLEXES AS HYDROGEN-BOND-DONOR (HBD) CATALYSTS: SYNTHESIS AND EFFECT OF CHIRALITY AT METAL CENTER ON ASYMMETRIC TRANSFORMATIONS

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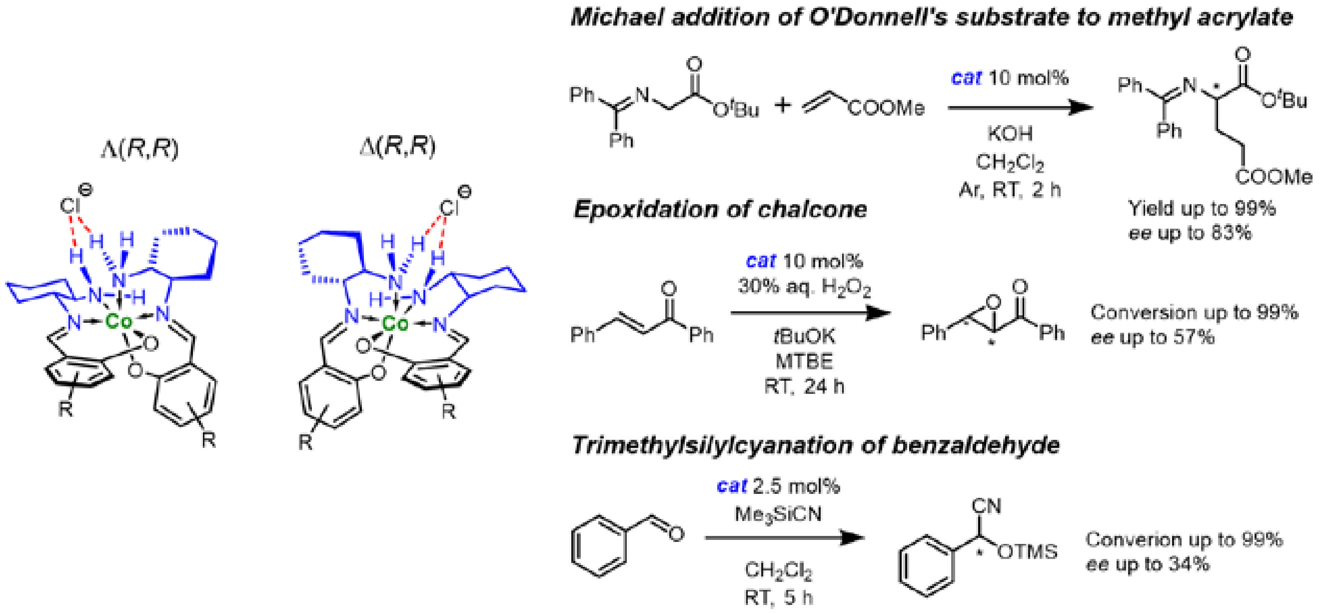
Chiral octahedral cobalt(III) complexes based on coordinated to metal ion chiral ligands are prospective catalysts providing a high stereoselective control in various asymmetric transformations.[1,2] Since Gladysz introduced the concept of “*organocatalysts in disguise*” a new approach in the development of chiral catalytic systems has been intensively highlighted.

Here we introduce a library of the isostructural octahedral chiral-at-cobalt(III) complexes of Λ- and Δ-configurations based on Schiff’s bases of (*R*,*R*)-1,2-diaminocyclohexane and salicylaldehyde derivatives (Figure). The formation of a second Δ-diastereomer for this type of complexes has been observed for the first time. We found that the amount of Co(III) salt and the nature of the salicylaldehyde have a significant influence on the stereoselective assembly. By testing of the diastereomeric Co(III) complexes in three benchmark reactions (Figure), we have demonstrated that the chirality at metal center has a perceptible effect on stereochemical outcome of reaction.[3]



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This work was supported by the Russian Science Foundation, project No. 20-13-00155.

SYNTHESIS OF NOVEL DONOR-ACCEPTOR STAR-SHAPED OLIGOARYLSILANES AND THEIR PROPERTIES IN THE BULK, SOLUTIONS AND NANOPARTICLES IN WATER

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The active development of organic electronics and photonics leads to the search for new materials and new types of devices based on them. A large number of works are devoted to the synthesis and study of both new high-performance polymers and small molecules for use in the field of organic sensors, light-emitting diodes, solar cells, etc. On the way to the final device, the undoubted advantages of small molecules are a certain molecular structure, a known molecular weight, simpler purification methods and good reproducibility [1].

Oligoarylsilanes are one of the well-known and promising classes of molecules for organic electronics and photonics [2]. However, the scope of their application often limits the short-wavelength range of absorption and emission spectra characteristic of this class of compounds [3]. The solution to this issue can be a new molecular design, where the molecules contain fragments of the donor and acceptor types connected to each other by covalent bonds. Such a strategy will make it possible to tune the absorption and luminescence spectra, as well as the energies of the HOMO and LUMO levels and the band gap. As follows from the literature, a few examples of star-shaped D-A arylsilanes have been described. The search for new molecules, the study of their properties is an actual task that will expand our knowledge on this class of compounds.

In this presentation, a multistage synthetic rout, including organometallic synthesis, Suzuki cross-coupling reaction, and the Knoevenagel condensation, with the help of which two star-shaped oligoarylsilane molecules were obtained, differing from each other by the central fragment on each branch, will be described (Fig1). Their optical properties in the film and dilute solutions, thermal and thermoelectric properties were studied. In addition, nanoparticles obtained from these new oligoarylsilanes, their size distribution and stability in water will be presented.

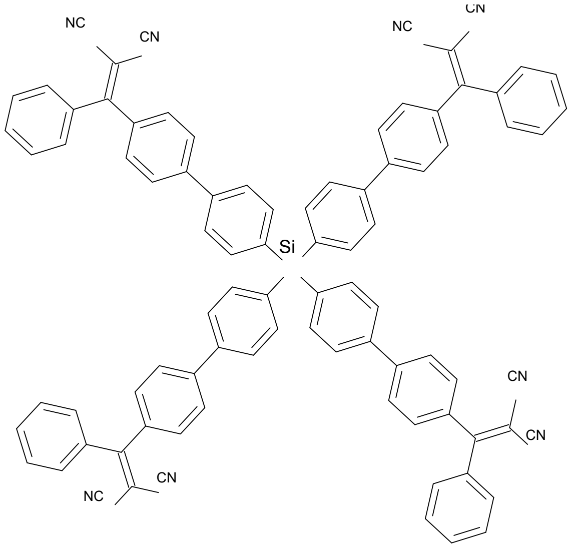

Figure 1. Schematic representation of star-shaped oligoarylsilane molecule.

This work was financially supported by the Russian Science Foundation (grant 19-73-30028).

IN SITU FLUORIDE ACTIVATION OF NEW CHIRAL NICKEL CATALYST FOR SYNTHESIS GABA DERIVATIVES

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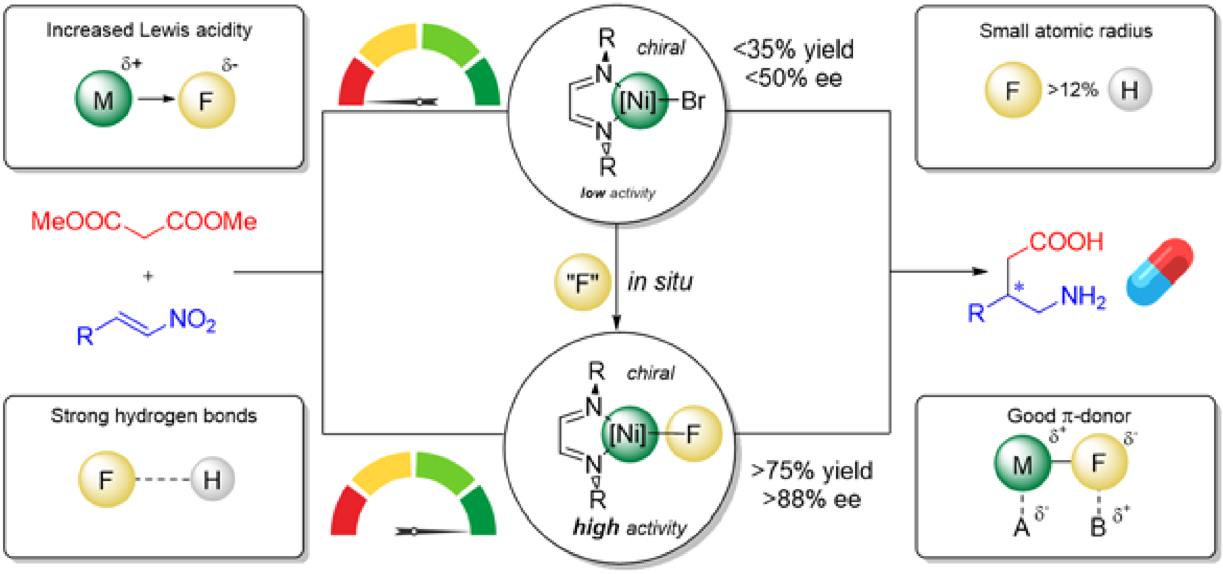
The actual goal of organic chemistry is the development of selective and efficient catalytic systems. It is possible to increase the activity of the catalyst by complicating the structure. Such a strategy has been proven for a long time and works well. However, there is an alternative way: in situ activation of simple catalytic systems. In catalysts containing a metal-halogen bond, it was found that replacing halogen with fluorine can multiply the activity of the catalyst[1].

We have developed and proposed a new nickel diimine catalyst for asymmetric Michael addition. The use of this type of ligand makes it possible to modulate the properties of the complex by a rather simple substitution of an amine, a precursor of the ligand. We have also developed a protocol for the further use of the obtained products of the Michael addition in the synthesis of chiral GABA derivatives with high enantiomeric excess, including drugs.



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STEREOCHEMICAL ASPECTS OF THE SYNTHESIS OF SUBSTITUTED 3,4DIHYDRO2*H*THIOPYRAN AND THEIR TRANSFORMATIONS

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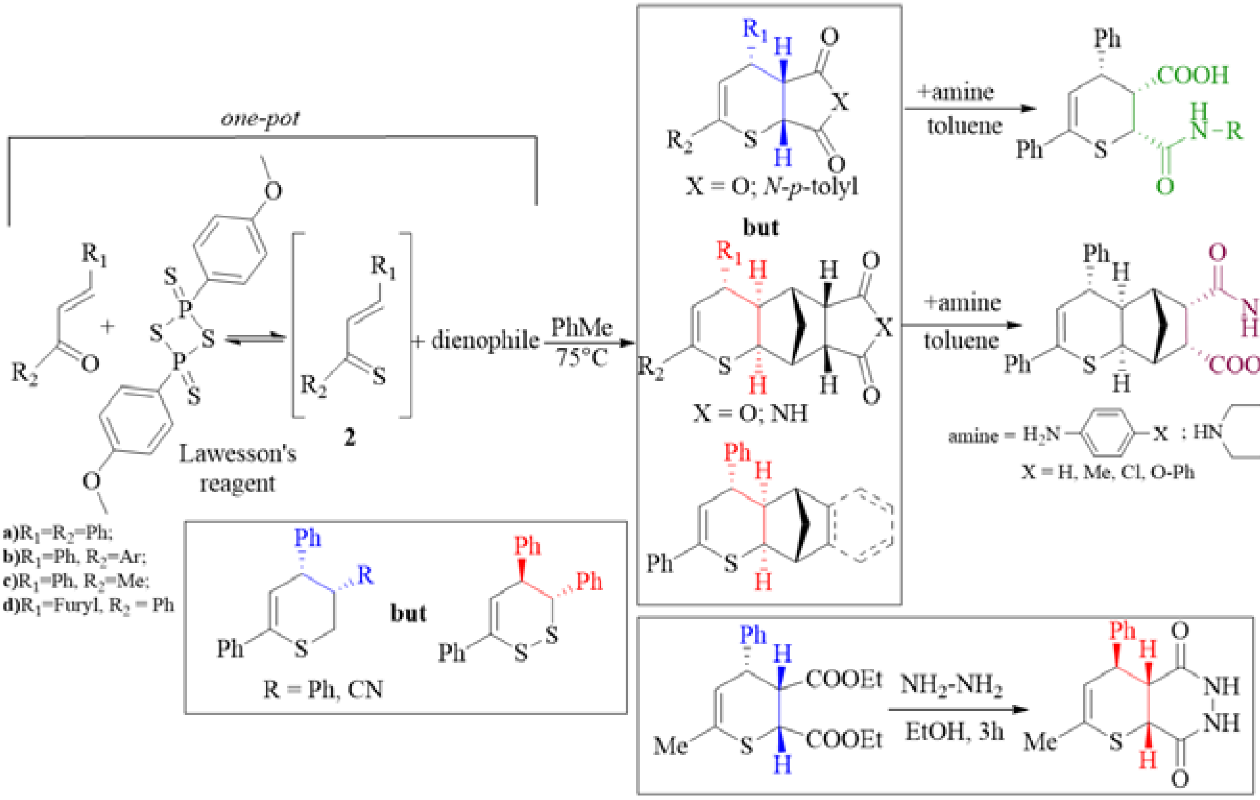
Our research group has developed an original technique for the preparation of hard-to-find functionally substituted compounds of 3,4-dihydro-2*H*-thiopyran series [1], which demonstrate an interesting synthetic potential [2]. The aim of this work is to investigate regio- and stereoselectivity of synthesis 3,4-dihydro-2*H*-thiopyrans via hetero-Diels-Alder reaction and to study subsequent transformation of them. We discovered epimerization of diethyl 6-methyl-4-phenyl-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate in reaction with N_2H_4 and high regioselectivity acylation of amine by anhydrides with 3,4-dihydro-2*H*-thiopyran moiety.



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ARTICLES ON ORGANIC CHEMISTRY IN RUSSIAN CHEMICAL BULLETIN

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Russian Chemical Bulletin is international edition of the prominent Russian journal *Izvestiya Akademii Nauk. Seriya Khimicheskaya* . It was founded in 1936 and has been translated into English since 1952. Currently, *Russian Chemical Bulletin* is published by Springer and Business Media, Inc. The journal is published in paper and electronic forms. The electronic Russian-language version is available on the e-library website (www.elibrary.ru, since 1966), English-language is available on the Springer website (https://link.springer.com/journal/11172, since 1952). At least 350 articles from more than 130 Russian and foreign scientific centers are published annually. The journal is indexed and refereed by leading abstract journals, including Science Citation Index, SciSearch, Journal Citation Reports/Science Edition, SCOPUS, CAS, ChemWeb and other scientific databases. The impact factor of the journal is constantly growing and in February 2022 reaches 1.6 for 2021. The Editorial board of the journal and the Advisory international editorial board include world-renowned scientists. The high quality of the articles is achieved as a result of careful selection of the materials by double reviewing and scientific editing. Well-prepared articles are published in 2–4 months.

Currently, one of the priorities of the journal is to increase the scientometric indicators of authors and Russian scientific organizations. In this regard, the Editorial board of the journal suggests authors to refer actively to their articles, as well as to the articles of their Russian colleagues published in journal during the last two years following the year of publication, since this period has the greatest effect on scientometric indicators.

The journal publishes reviews, analytical and research articles, as well as short reports. The journal covers all areas of chemical science, including organic chemistry. The journal publishes specialized issues, in particular, based on conference materials. The Editorial board of the journal invites the participants of the symposium to participate in the preparation of a specialized issue of the journal, presenting material that has not been published before and reflects fundamental research in organic chemistry and interdisciplinary fields.

Manuscripts could be sent to the editorial office of the journal: incoming@ioc.ac.ru; editorial office phone: +7(499) 137-6997.

SYNTHETIC APPROACHES TO DOXORUBICIN AND *N*-ACETYL-*D*-GALACTOSAMINE CONJUGATES

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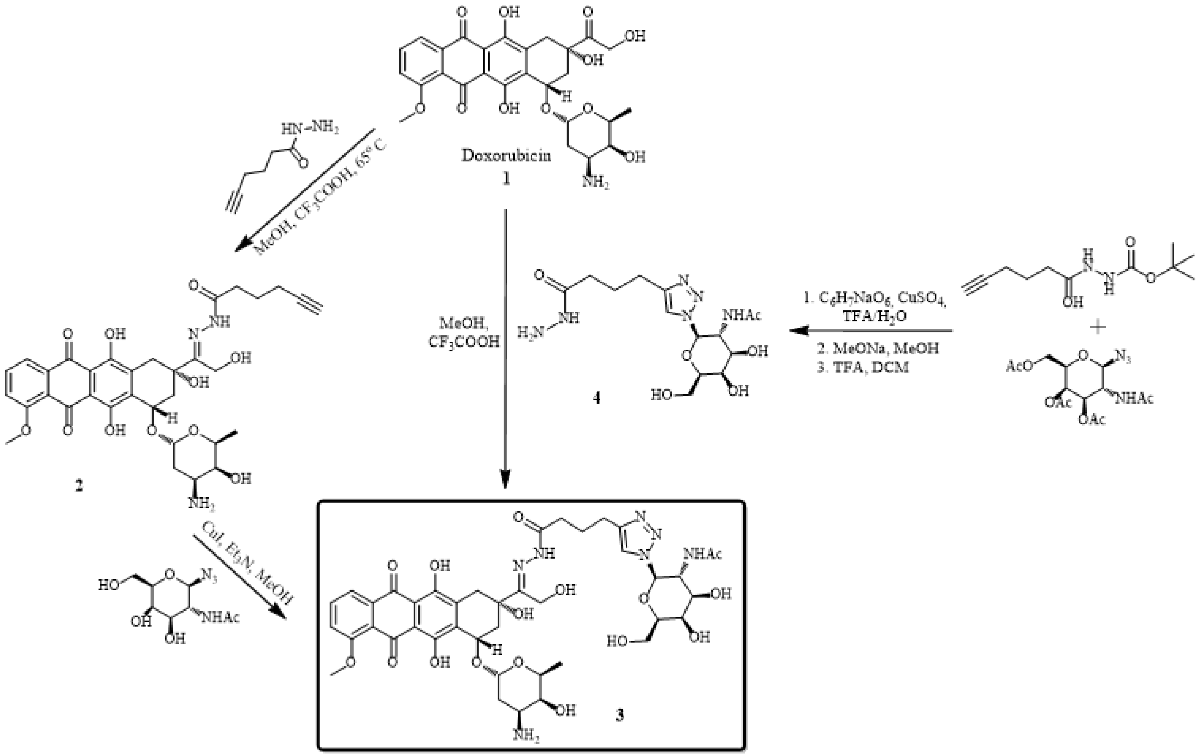
N-Acetyl-*D*-galactosamine derivatives bind to the asialoglycoprotein receptor, a protein expressed on the surface of liver tumor cells. Thereby, the conjugates were designed to deliver doxorubicin directly to hepatocellular carcinoma cells and release the active substance after cleavage. Previously, we synthesized the series of conjugates with amide bond between the active substance and the carbohydrate fragment[1]. However, the compounds didn't show high antitumor activity due to resistance to hydrolysis. The aim of this work was to develop synthetic methodologies for more active compounds, in which doxorubicin is conjugated to *N*-acetyl-*D*-galactosamine derivatives with acid-labile hydrazone bond.



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ONE-POT ELECTROCHEMICAL EXFOLIATION AND METHYLATION OF BLACK PHOSPHORUS

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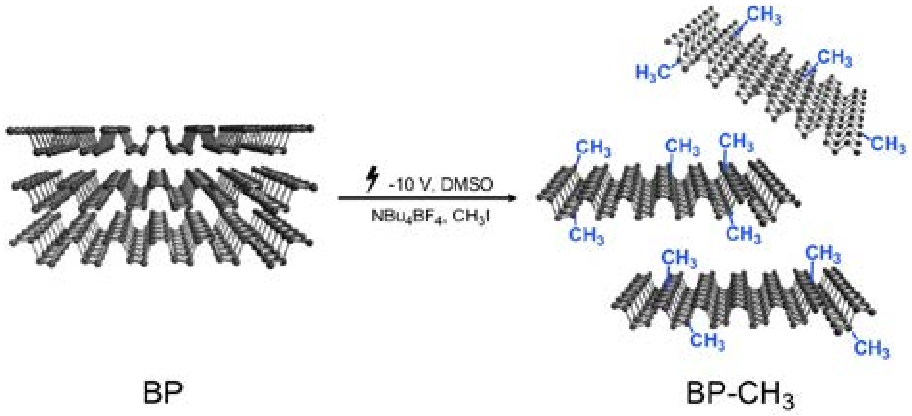
Due to its unique in-plane anisotropic structure, high carrier mobility, and adjustable direct bandgap, 2D black phosphorus (BP) has emerged as an important graphene-like material for various micro- and optoelectronic, energy, catalytic, and biomedical applications [1]. However, low environmental stability severely limits its processing in ambient conditions. Chemical functionalization of BP is an effective tool for increasing the oxidation stability of the material [2].

Herein, we report a *one-pot* approach for electrochemical exfoliation of BP and its functionalization with CH_3-groups. The functionalization proceeds during the electrochemical reduction of CH_3I on the BP electrode at negative potentials in DMSO.



The possibility of the simultaneous exfoliation of BP and CH_3I reduction was confirmed by cyclic voltammetry studies. The dimensional characteristics of the functionalized material (BP-CH_3) were measured by the methods of atomic force microscopy and transmission electron microscopy. The covalent functionalization of BP-CH_3 was confirmed by IR, Raman, and solid-state NMR spectroscopy methods.

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This work is financially supported by the grant of the President of the Russian Federation for supporting of the Leading Scientific Schools (project no. 4078.2022.1.3).

EFFECT OF *N*-SUBSTITUENT IN *PNP* LIGAND ON THE COBALT MEDIATED WHITE PHOSPHORUS ACTIVATION

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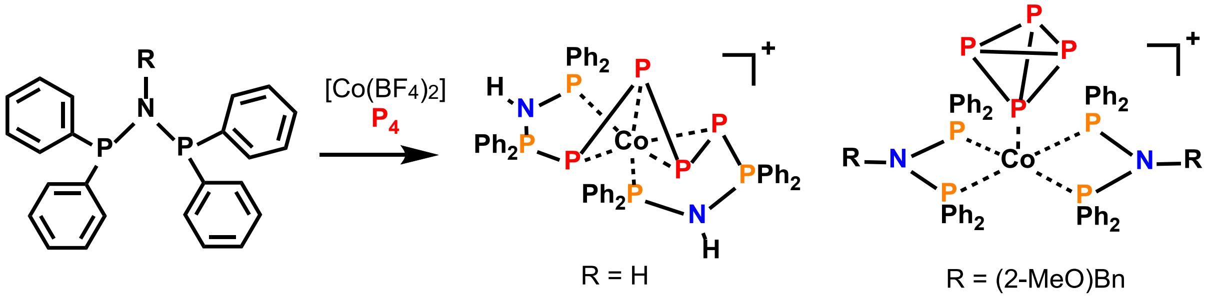
Transition metal-mediated activation and transformation of elemental (white) phosphorus P_4 represents a promising route of ecologically friendly conversion of P_4 into useful organophosphorus products.[1] The complexes of IX group (Co-subgroup) attract particular attention due to their high activity and selectivity in this process.[2-4]

We have found that heating of the mixture containing cobalt complex $[Co(BF_4)_2]$, *N,N*-bis(diphenylphosphino)amine, and P_4 affords the new complex $[Co(Ph_2PNHPPh_2(PPPP)PPh_2NHPPh_2)]BF_4$ in almost quantitative yield. The molecular structure of the obtained complex contains a peculiar *zig-zag* (*PPPP*) moiety. Moreover, the nature of the substituent at *N*-atom of the *PNP*-ligand dramatically impacts on the P_4 activation process. New intermediate of the process – cobalt complex containing intact η^1-coordinated P_4-molecule has been observed in the reaction medium using *N,N*-bis(diphenylphosphino)(2-methoxybenzyl)amine as the ligand.



The obtained results provide new insights on the mechanism of P_4 activation and transformation in the coordination sphere of transition metal complexes bearing organic ligands.

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This work is financially supported by the grant of the President of the Russian Federation for supporting of the Leading Scientific Schools (project no. 4078.2022.1.3).

SOME TRANSFORMATIONS BASED ON THE OXIDATION OF 4-OXOBUTYRONITRILES IN THE PRESENCE OF ALKALI

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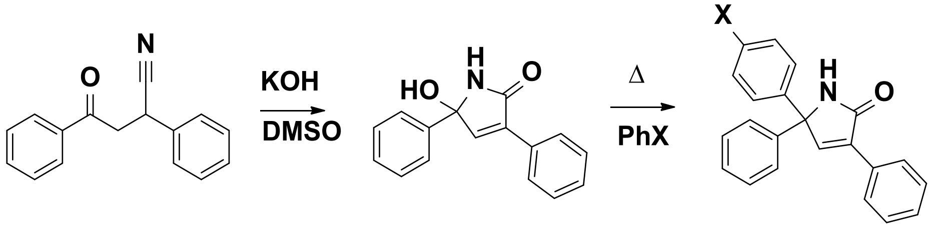
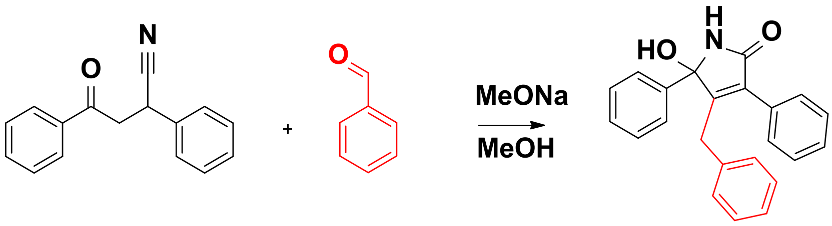
The availability of chalcones with a high diversity of functional groups, combined with a rich and well-studied chemistry, makes them one of the cornerstones of organic synthesis.

Our team also became interested in chalcones.

We found it most interesting to study 4-oxobutyronitriles, which are easily obtained by adding hydrocyanic acid to chalcones. We have previously found that these compounds are unusually easy to be oxidized by the KOH/DMSO system. The hydroxyl group of the resulting 5-hydroxy-3,5-diphenyl-1*H*-pyrrol-2(5*H*)-ones can easily be replaced by various nucleophiles[1].



We have recently found that the introduction of various benzaldehydes and conducting the reaction in the MeONa/MeOH system leads to the formation of various substituted 4-benzyl-5-hydroxy-3,5-diphenyl-1*H*-pyrrol-2(5*H*)-ones. Yields are good to excellent.



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The study was supported by the Russian Science Foundation (grant № 21-73-10029, https://rscf.ru/project/21-73-10029/)

HYDROGEN-BONDED ORGANIC FRAMEWORK AND METAL-ORGANIC FRAMEWORKS BASED ON FUNCTIONALIZED CYCLIC SILOXANES

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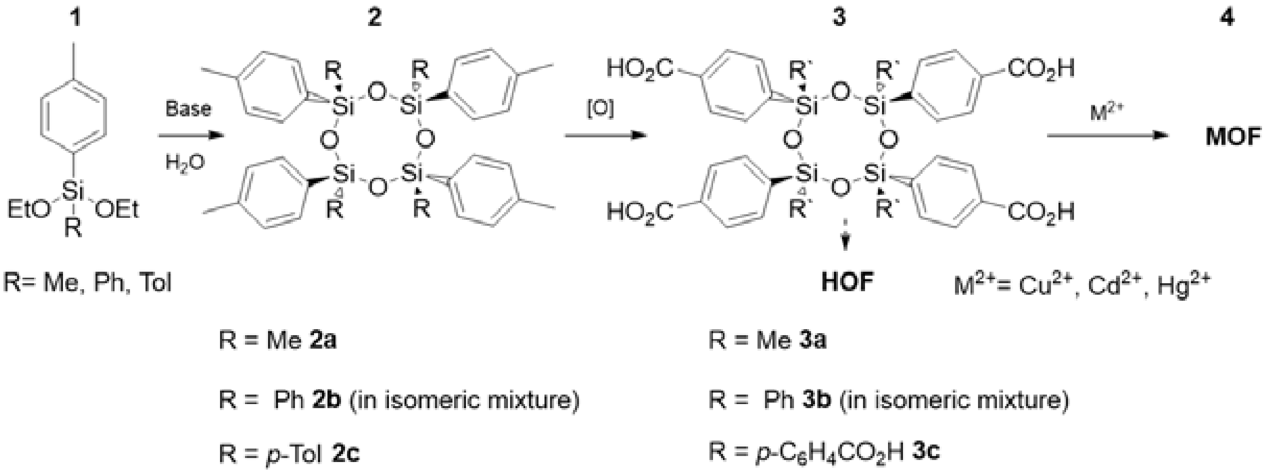
Functionalized organosilicon compounds attracting great interest in context of design of hybrid polymer materials, in particular hydrogen-bonded organic frameworks (HOF's) and metal-organic frameworks (MOF's) which possess complex of unique physical-chemical properties. The last are considered as materials of high porosity, made of metal ions/clusters and organic ligands, oligocarbonic acids in most cases, resulting in wide range of possible applications – gas and liquid separation, catalysts, drug delivery, dye degradation, *etc*. Incorporation of multiple carboxyl-functionalized flexible organosiloxane blocks in structure of ligand can possibly alleviate drawbacks of MOF's, such as low hydrolytic and thermal stability, and greatly increase hydrophobic properties of material.[1] Previously a few organosiloxane-based MOF's have been prepared by this strategy, showing poor porosity.[2][3]

Using catalytic aerobic oxidation of cyclic oligo(*p*-tolyl)siloxanes **2** as a method for functionalization of organosilicon compounds,[4] we synthesized novel cyclic oligo(*p*-carboxyphenyl)siloxane ligands **3** for MOF construction. Cu-, Cd- and Hg-containing MOF's **4** (based on ligand **3a**) was obtained in mild reaction conditions (r.t., 1 atm, *etc.*). Structure of HOF **3a** and MOF's **4** was determined by SCXRD.



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This work was supported by a grant of the Russian Science Foundation (RSF grant 19-73-10172).

UNUSUAL REARRANGEMENT OF 2-(3-OXOINDOLIN-2-YL)ACETONITRILES UPON REDUCTION WITH SODIUM BOROHYDRIDE

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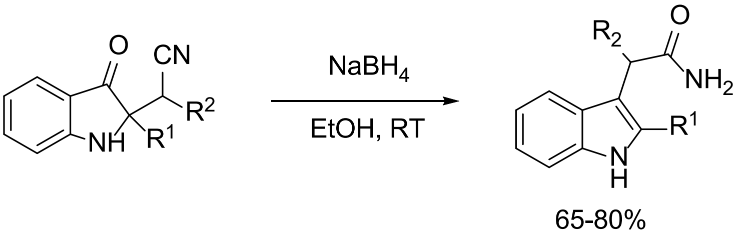
With development of medicinal technologies, cardio-vascular disorders gradually give way to oncological diseases. Indeed, the latter ones are currently causing every sixth death in the World. High lethality of cancer in developing countries is related primarily to the delayed diagnostics and consequently detection of tumor at late stages with active metastasis. Metastatic cells are typically having lower sensitivity to apoptosis inducers, which makes them resistant to a large portion of anti-cancer drugs. In addition, tumor cells are able to mutate quickly adapting to the administered chemical therapy, which becomes a real issue in returning cases. This issue justifies a necessity of continuous search for new anti-cancer drugs, especially those affecting new targets in tumor cells. Most important target molecules would be various indole derivatives, including indolyl acetamides structurally related to previously studied indolyl acetohydroxamic acids, which demonstrated great activity against several lines of drug-resistant cancer cells. We have shown that the reduction of 2-(3-oxoindolin-2-yl)acetonitriles with sodium borohydride in alcohol at room temperature unexpectedly leads to the formation of indolyl acetamides.



New derivatives of indolyl acetamides was synthetized with good yield.

This work was financed by the Russian Science Foundation (grant № 21-73-20051).

SYNTHESIS OF 1,3-DISUBSTITUTED UREAS AND THEIR ISOSTERIC ANALOGUES CONTAINING POLYCYCLIC FRAGMENTS: 1-[(ADAMANTAN-1-YL)METHYL]-3-(FLUORINE, CHLOROPHENYL) UREAS

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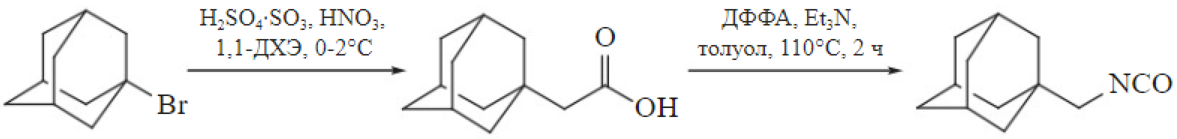
The literature describes a wide range of biological activity of compounds containing urea fragment in their structure. For example, ethyl-2-(4-R-1,4-diazepan-1-carboxamido)benzoates are potential antiviral drugs against RNA viruses such as SARS-CoV, and HIV-1 [1].

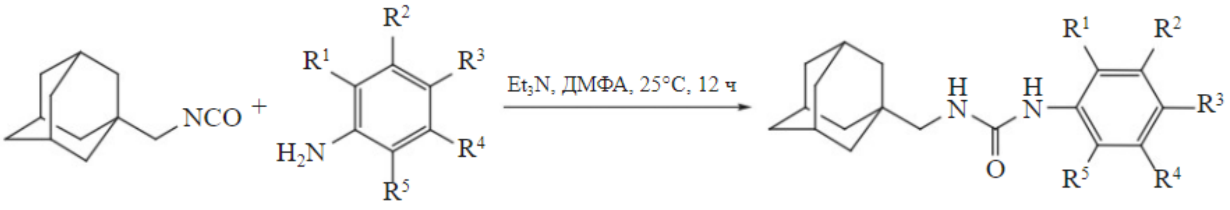
The known synthesis of 1-(isocyanatomethyl)adamantane (**3**) according to the Curtius reaction has a number of drawbacks: the use of toxic thionyl chloride and explosive sodium azide. Therefore, in this work, the synthesis of isocyanate **3** was carried out by a one-step method involving diphenylphosphorylase (DPPA) (scheme 1). Isocyanate **3** was used to synthesize 1,3-substituted ureas **5a-o** in reaction with mono- and dihalogen substituted anilines 4a-o (scheme 2). Yields were 10-92%.

Scheme 1



1 **2** **3**

Scheme 2



3 **4a-o** **5a-o**

$R^1 = R^3 = R^4 = R^5 = H, R^2 = F$ (**5a**); $R^1 = R^2 = R^4 = R^5 = H, R^3 = F$ (**5b**); $R^1 = R^3 = F, R^2 = R^4 = R^5 = H$ (**5c**); $R^1 = R^5 = F, R^2 = R^3 = R^4 = H$ (**5d**); $R^1 = R^4 = R^5 = H, R^2 = R^3 = F$ (**5e**); $R^1 = R^4 = F, R^2 = R^3 = R^5 = H$ (**5f**); $R^1 = R^3 = R^5 = H, R^2 = R^4 = F$ (**5g**); $R^1 = R^3 = R^4 = R^5 = H, R^2 = Cl$ (**5h**); $R^1 = Cl, R^3 = F, R^2 = R^4 = R^5 = H$ (**5i**); $R^1 = R^4 = R^5 = H, R^2 = Cl, R^3 = F$ (**5j**); $R^1 = F, R^2 = Cl, R^3 = R^4 = R^5 = H$ (**5k**); $R^1 = R^4 = R^5 = H, R^2 = F, R^3 = Cl$ (**5l**); $R^1 = F, R^3 = Cl, R^2 = R^4 = R^5 = H$ (**5m**); $R^1 = F, R^5 = Cl, R^2 = R^3 = R^4 = H$ (**5n**); $R^1 = R^3 = R^4 = R^5 = H, R^2 = CF_3$ (**5o**).

All the compounds obtained were confirmed using NMR ^1H, ^{13}C spectroscopy and chromatography-mass spectrometry.

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The work was financially supported by the Russian Science Foundation (project no. 19-73-10002).

DIRECT S_N^H AMINATION AND CARBAMOYLAMINATION OF 5-NITROISOQUINOLINE

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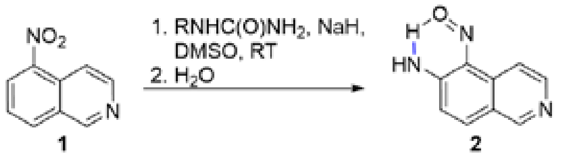
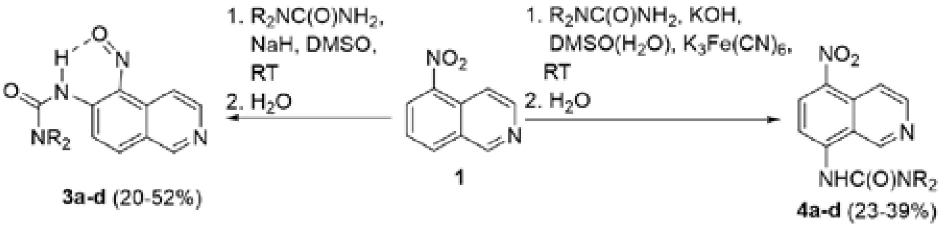
The aim of this work was to study the reaction of 5-nitroisoquinoline with urea N-anions. We found that when 5-nitroisoquinoline (1) is treated with an excess of the anion of unsubstituted urea, tert-butylurea, (1,1-dimethylpentyl)urea and phenylurea in anhydrous DMSO, the reaction proceeds at room temperature and unexpectedly leads to one product - 6-amino-5-nitrosoisoquinoline (2).



R = H (38%), Ph (58%), ^{t}Bu (76%), $-C(CH_3)_2(CH_2)_3CH_3$ (60%)

In the case of 1,1-disubstituted ureas, we implemented two approaches to performing the S_N^H reaction with 5-nitroisoquinoline (1), which differed only in the presence or absence of a small amount of water in the reaction mass and which led to significantly different results. Thus, under anhydrous conditions, anions of 1,1-dimethylurea, as well as amides of pyrrolidine-1-carboxylic, piperidine-1-carboxylic and morpholine-4-carboxylic acids lead to products at position 6, forming ureas based on 5-nitrosoisoquinoline 3a-d .



When using commercial DMSO (water content ~ 0.5%), the reaction of 5-nitroisoquinoline with 1,1-dialkylurea anions proceeds to position 8 with the formation of oxidative S_N^H-dialkylcarbamoylamination products 4a-d.

The authors express their gratitude to the North Caucasian Federal University for financial support in the framework of the project to support projects of scientific groups and individual scientists.

SCANDIUM(III)-CATALYZED C-3 FUNCTIONALIZATION OF IMIDAZO[1,2-A]PYRIDINES

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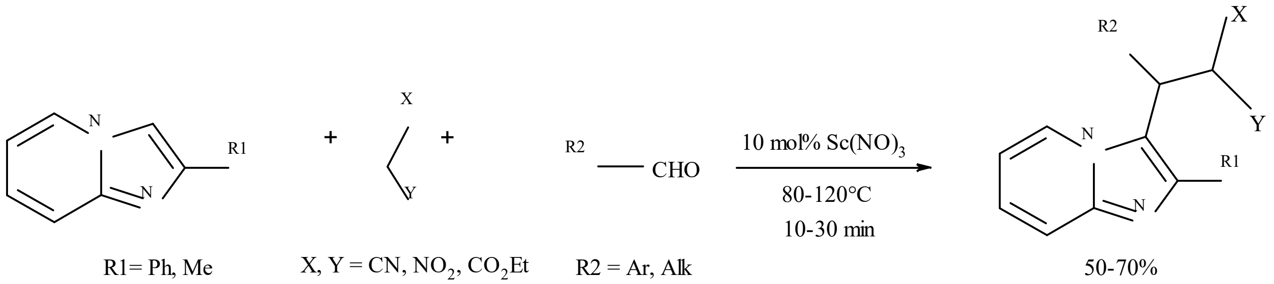
While numerous methods C3-fuctionalization of imidazo[1,2-a]pyridines both metal-catalyzed and catalyst-free are known [1,2], up to date no one-pot, three component Yonemitsu-type condensations [3] were reported regarding this type of substrates. Meanwhile the imidazo[1,2-a]pyridine core is one of the pharmaceutical importance that shows a broad range of biological (anti-cancer, anti-bacterial, antivirus etc.) activities [4] and therefore a tool to facilitate the rapid generation of diverse, chemical libraries of the C-3 functionalized imidazo[1,2-a]pyridine are still needed for use in drug discovery.

Here we would like to report about practical, solvent-free, multicomponent reactions protocol for the construction of aryl/alkyl malonate derivatives of imidazo[1,2-a]pyridine using various aldehydes and active methylene compounds as starting materials in presence of inexpensive $Sc(NO_3)_3$ xH_2O as a catalyst. This procedure is found to be quite rapid and simple providing desirable products with moderate to good yields.



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PHOTOACTIVE HETEROSTYRENES ON FURAN-, BENZOFURAN-, PYRROLE-, AND INDOLE-BASED MATRICES

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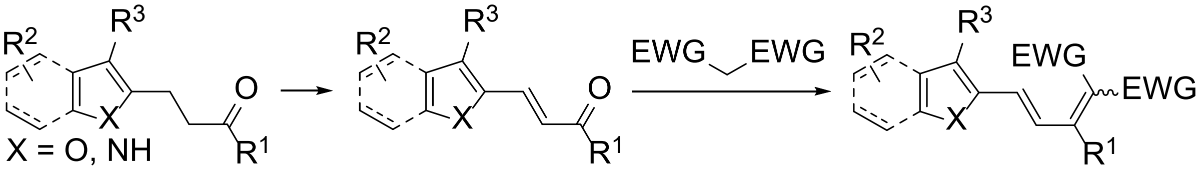
Push-pull chromophores have been extensively utilized as light-absorbing dyes in dye-sensitized solar cells as well as various sensors for detecting trace metals and pH-indicators.

In our ongoing research project aiming at developing straightforward synthetic protocols toward potential push-pull chromophores based on the heterocyclic products obtained via dearomatization of accessible furan platform molecules we engage an alkanone fragment into oxidation/condensation transformation sequence in order to get a set of compounds with high molar extinction coefficients.



Scheme 1. Synthetic strategy toward heterocycle-based push-pull chromophores.

Synthetic details as well as physicochemical, optical, and electrochemical properties of the obtained products will be discussed.

This work was supported by Russian Science Foundation (project 22-23-00505).

SYNTHESIS AND BIOLOGICAL EVALUATION OF THE MERIDIANIN ANALOGS AS POTENTIAL NEW ANTIBACTERIAL AGENTS

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Nowadays, infectious diseases still are the leading problems for science and humanity. Despite the emergence of a variety of antibiotics, which opened the era of effective treatment of bacterial infections, there is still a high morbidity and mortality rates all over the world from infections caused by bacteria, parasites, fungi, and viruses. An urgent task is the development of methods for the synthesis of new highly effective antibacterial agents, preferably with new mechanisms of action. Meridianins, a group of indole alkaloids isolated from the tunicate *Aplidium meridianum*[1], have promising anti-tuberculosis, antimalarial, cytotoxic, and antitumor activities.

In order to search for new antibacterial agents, we synthesized a wide range of meridianin structural analogues under relatively simple reaction conditions, using readily available starting substrates (Figure 1).

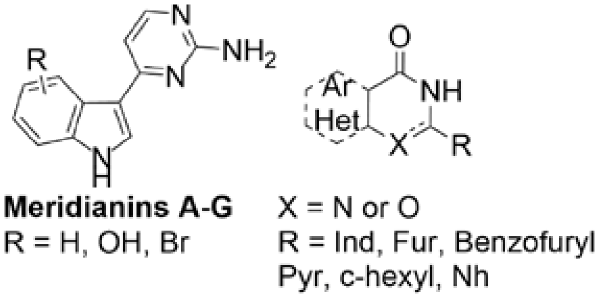

Figure 1.

The optimal reaction conditions were found, the scope and limitations of the developed method were defined. The biological activity of the synthesized compounds was investigated. Research results will be presented in the report.

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This work was supported by Russian Science Foundation, project № 22-23-00503.

SYNTHESIS OF NEW BENZOTHIAZOLE-AND PYRAZOLE-BASED UNSYMMETRICAL PINCER LIGANDS FOR NI-CATALYSED ETHYLENE OLIGOMERIZATION

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Unsymmetrical PCN pincer ligands have unique properties due to the combination of hard (*N*-side) and soft (*P*-side) electron-donors. Such pincer ligands have been successfully used for preparation of various homogeneous catalysts.[1] In this study, we have prepared unsymmetrical benzothiazole- and pyrazole-based PCN pincer ligands and their nickel complexes $[(^{BzTz}PCN)NiX]$ and $[(^{Pyr}PCN)NiX]$ (X = F, Br), which are able to form high active species for ethylene oligomerization into linear α-olefins (TOF up to 200×10^3 h^{-1}) activated by modified methylaluminoxane (MMAO) (Figure 1).[2,3]

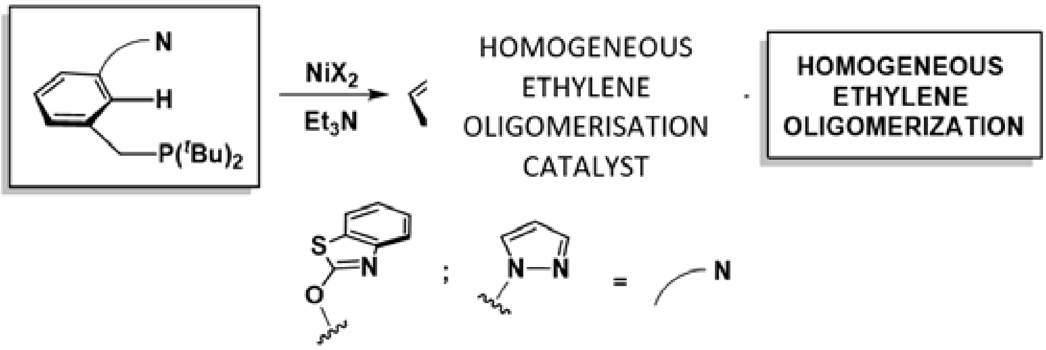

Figure 1. Benzothiazole- and pyrazole-based ligands for nickel-catalyzed ethylene oligomerization.

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This work is financially supported by the grant of the President of the Russian Federation for supporting of the Leading Scientific Schools (project no. 4078.2022.1.3).

SYNTHESIS, STRUCTURE AND PROPERTIES OF NEW AZIDATING REAGENT BASED ON HYPERVALENT IODINE (III) FOR DIRECT AZIDATION OF ORGANIC SUBSTRATES

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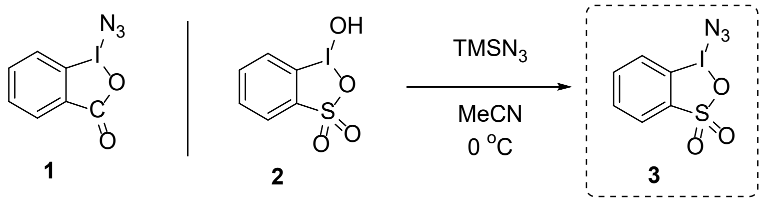
The first organic azide was synthesized and described in 1864 by Peter Griess [1-2], since the time this class of organic compounds was applied in different fields of science and technologies. Azide group is significantly represented in natural and biologically active compounds, its presence and quantity determine the value for high-energy technologies [3-4]. Organic azides are used in synthetic chemistry as precursors to amines and nitrenes, making them key building blocks. Today, many methods are known for the synthesis of azides and their transformations. The existing methods for the synthesis of organic azides have significant drawbacks, such as pre-functionalization and harsh reaction conditions for indirect methods of azide production, and metal catalysis and potential explosiveness for direct methods of azidation.

One of the most promising approaches to the synthesis of aliphatic azides is the use of azidating hypervalent iodine compounds, due to their oxidizing properties and environmentally friendly nature. Only the original azidoiodinane [5-6], which is named as Zhdankin's reagent **1**, has established itself as a highly reactive and convenient "transfer reagent" for the direct azidation of various organic compounds, including natural compounds with a complex structure and labile functional groups. This is evidenced by the number of citations of the first work [6] describing its synthesis and properties: more than 200 citations according to the WoS/Scopus databases. It should be noted that this reagent has a significant drawback (in some works there are cases of explosions during handling), therefore, the development of its analogues and the study of their reactivity attracts considerable attention of world scientists.

We have designed a new azidating reagent – the thia-analogue of well-known Zhdankin's reagent – which possesses high reactivity at mild reaction conditions and is safer for handling. The structure and stability of the reagent **3** were investigated. It was shown the azidoiodinane **3** has cyclic form with quite long, close to ionic, I-O-bond that increases electrophilicity of iodine center.



We have developed a simple and convenient method for the direct synthesis of *α*-azido ketones under metal-free conditions. We also assume that the 2-iodobenzenesulfonic acid resulting from the reaction can be easily recovered from the reaction mixture by simple water extraction, oxidized to 2-iodosylbenzenesulfonic acid **2**, and re-involved in the direct azidation reaction again. Thus, the conditions for carrying out azidofunctionalization using the **2**/$TMSN_3$ system will be as close as possible to "green" chemistry.

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OXIDATIVE RECYCLIZATION OF SUBSTITUTED 2-AMINOPHENYLFURANS

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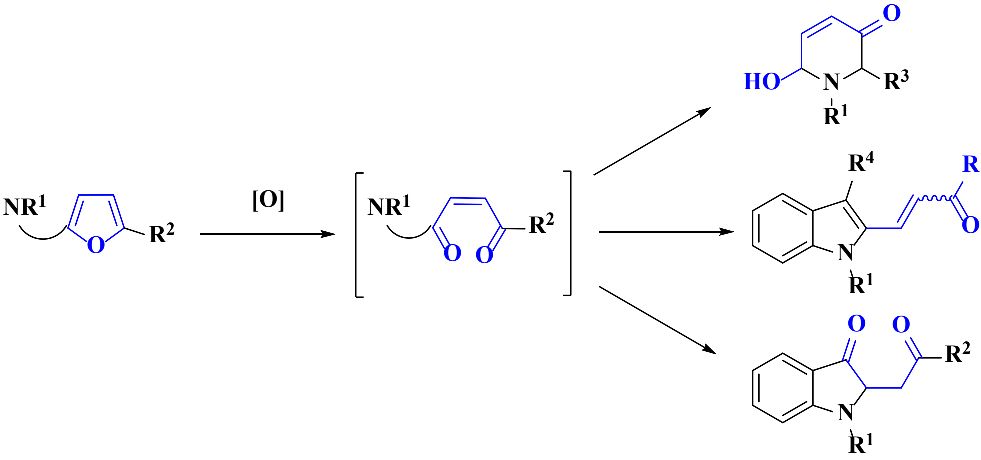
Furans are one of the most important classes of five-membered heterocyclic compounds. The furan core is an integral part of many biologically active and natural compounds, as well as approved drugs. In addition, furans can act as versatile building blocks for the synthesis of various heterocyclic compounds with a set of useful properties.

It is known that the furan core under oxidation is easily dearomatized with the formation of unsaturated 1,4-diketones, and further inter- and intramolecular cyclization leads to the formation of various heterocyclic compounds. Thus, oxidative transformations of furfurylamines give derivatives of pyridinone (aza-Achmatowicz reaction),[1] which is formed as a result of attack by a nitrogen atom of a remote carbonyl group. Oxidation of substituted 2-(2-aminobenzyl)furans, in the structure of which the nitrogen atom and the α-carbon of the furan are bonded by three atoms, the nucleophile can react with the proximal latent carbonyl group, forming five-membered azaheterocycles - derivatives of 2-(2-acylvinyl)indoles.[2] Continuing research in this area, we found that the oxidation of a furan containing an amino group distant from the furan ring by two carbon atoms unexpectedly leads to 2-(2-oxopropyl) indolin-3-ones, resulting from intramolecular Michael addition of the amino function to the formal β -carbon of the furan core.



The report will consider the features of the course of key transformations, the influence of reaction conditions on the efficiency of the recycling reaction and the yields of target products.

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This work was supported by Russian Science Foundation, project № 21-73-10063.

MONOSUBSTITUTED PILLAR[5]ARENE AS CONTAINERS FOR SOME HERBICIDES

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The dispersion of pesticides in the environment as well as their behavior is largely dependent on the mode of distribution and the composition of the applied pesticide. The use of pesticides in the field establishment is usually accompanied by losses due to their volatilization, degradation and photolysis. Thus, most of the applied pesticides and fertilizers do not reach crops. Most of the used agrochemicals end up in surface and groundwater systems that is caused deterioration of water quality, threatening ecosystems and human health. The application of the achievements of supramolecular chemistry and nanotechnology in agriculture is one of the rapidly developing concepts that can solve the problem of food security by reducing the use of pesticides, nutrient losses and increasing yields. One of the existing approaches is the use of macrocyclic compounds for the delivery of plant hormones, pesticides and fertilizers in order to ensure the growth of crops.

The need to design of a new generation of low-toxic supramolecular systems for the effective and safe use of herbicides based on the non-toxic macrocyclic platform pillar[5]arene is primarily due to the possibility of creating "host-guest" systems for the effective and safe use of herbicides. The use of such supramolecular containers will solve the problem of pesticide volatility, reduce their loss during leaching and soil degradation, reduce toxicity and increase safety in their use.

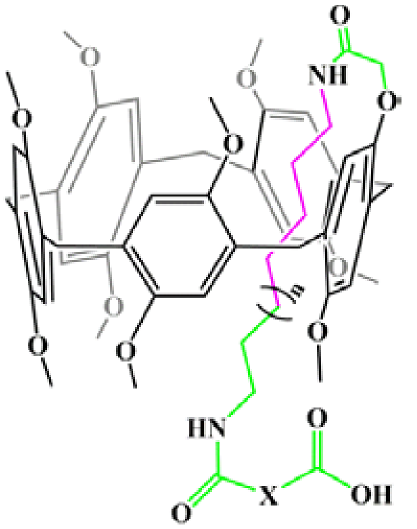

Fig. 1. Monosubstituted pillar[5]arene containing amide and carboxyl functions.

Thus, under this research work methods for the synthesis of monosubstituted pillar[5]arenes containing amide and carboxyl substituents were optimized. The structure of the new synthesized derivatives was fully proved by NMR ^{1}H, ^{13}C, IR spectroscopy and mass spectrometry (MALDI-TOF).

This work was supported by Russian Science Foundation (project no. 21-73-00093, https://rscf.ru/project/21-73-00093/).

A NEW PHOTOCHEMICAL RING EXPANSION REACTION OF PHENOXAPHOSPHONIUM MIXED YLIDES

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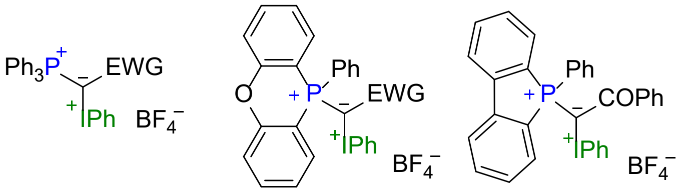
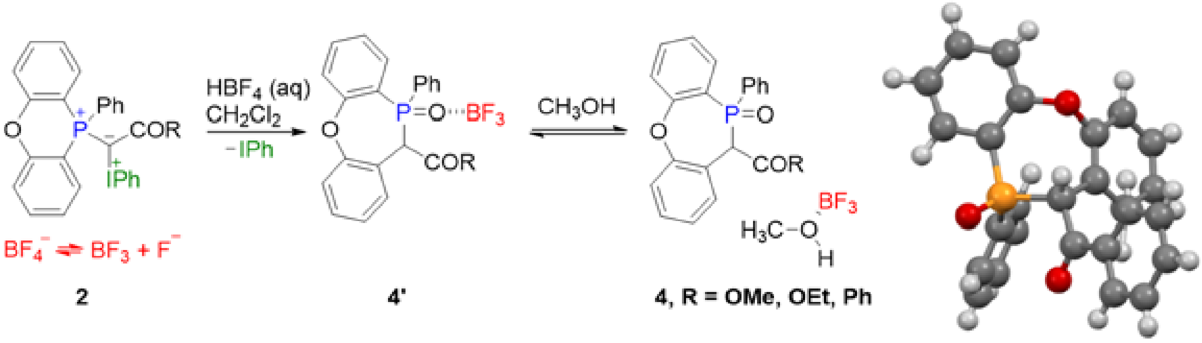
Mixed phosphonium-iodonium ylides **1** have been widely studied since the early 2000s in our research group under the leadership of academician N.S. Zefirov. Recently, we reported a novel type of mixed ylides containing six membered phenoxaphosphonium **2** and five membered dibenzophospholium **3** moieties (**Figure 1**). [1,2]



1 **2** **3**

Figure 1. Various types of mixed ylides.

Within the framework of current research, we report a new process that we observe for P,Oheterocyclic mixed ylides 2. It involves ring expansion and oxidation of the phosphorus atom (Scheme I).



Scheme I. Ring expansion of P,O-heterocyclic mixed ylides 2 under the action of aqueous tetrafluoroboric acid under UV irradiation

As a result of the reaction, seven-membered phenoxaphosphepines **4** are formed. When **R = OMe, OEt** reaction leads to the formation of a mixture of diastereomers, but when R = Ph the process is stereodirected. The major isomer was characterized by RSA analysis.

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The research was supported by the State assignment topic no. 121021000105-7.

RESEARCH ON 4-AMINODIPHENYLAMINE SYNTHESIS

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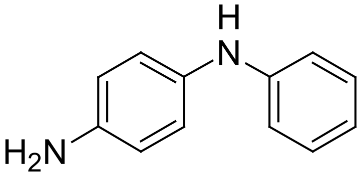
4-Aminodiphenylmethane (4-ADPA) and its 4-N-alkylated derivatives are important products of petrochemical industry, widely used as antioxidants, antiozonants, stabilizers for various polymers etc.[1,2].



Common methods of 4-ADPA synthesis are recently reviewed[3]. Among them are catalytic coupling of aniline or formanilide with *p*nitrochlorobenzene, catalytic reduction of 4-nitrosodiphenylamine (4-NODPA), 4-nitrodiphenylamine (4-NO2DPA) or 4anilinazabenzene, prepared by different synthetic protocols, cleavage of 4-NODPA sulfur derivatives and others. All of them have different drawbacks such as: large amount of wastes with transition metals and/or acids, low yields, multistep process, expensive starting materials and solvents etc.

The most promising synthetic protocol for 4-ADPA synthesis, which is recently under investigation among different research groups both in industry and in academic, is the base catalyzed coupling of aniline with nitrobenzene by nucleophilic aromatic substitution of hydrogen (NASH). The reaction proceeds under mild conditions and leads predominantly to a mixture of 4NODPA and 4NO2DPA together with small amounts of azabenzene in high yields and selectivity. The mixture upon catalytic reduction with hydrogen is converting into 4-ADPA and aniline only.

The major disadvantage of the reaction is the application of quaternary ammonium bases as catalysts. They are expensive, unstable under high concentration and possesses with low stability at temperatures above 60°C.

During our ongoing research we have focused our attention on the new catalysts and catalytic systems for 4-ADPA synthesis by NASH reaction including different synthetic protocols for performing of the process.

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DOMINO-REACTIONS OF CYCLIC NITRONATES UNDER HYDROGEN ATMOSPHERE: APPLICATION FOR SYNTHESIS MERCK'S POTENT HNK$_1$ ANTAGONIST

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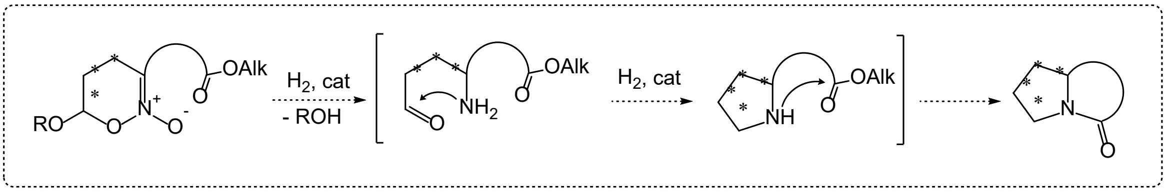
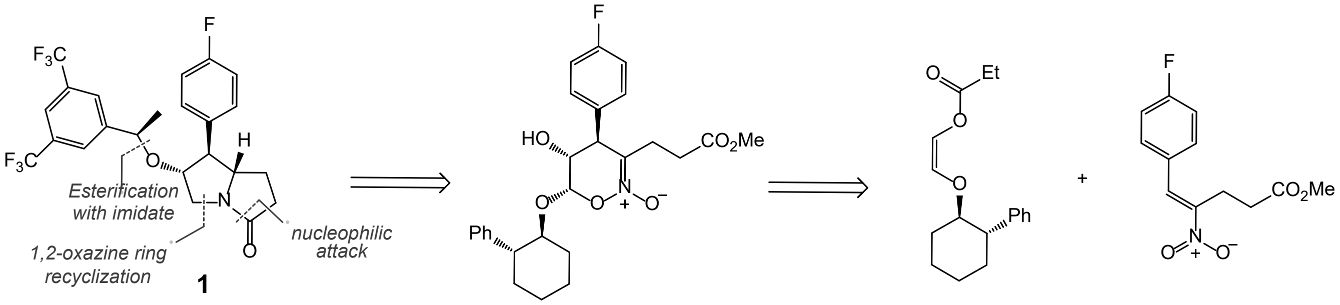
Domino-reactions are one of the major strategies to reduce the number of steps and operations in the synthesis of complex organic molecules. Recently, we proposed a novel approach to construct bicyclic pirrolizidinone system using a stereoselective domino-recyclization of functionalized 1,2-oxazine-*N*-oxides under hydrogen atmosphere.[1] The process involves hydrogenation of the nitronate motif, intramolecular reductive amination and lactamization.

In this work, the proposed domino-strategy was used to accomplish the asymmetric total synthesis of Merck's hNK$_1$ antagonist **1**.[2] The developed synthesis involves a stereoselective assembly of properly substituted 1,2-oxazine-*N*-oxide by the [4 + 2]-cycloaddition and its reductive recyclization as key stages. According to this approach, the target molecule was synthesized in 7 steps with exceptionally high regio- and stereoselectivity.





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This work was supported by the Council on grants of the President of the Russian Federation (grant MD- 3478.2022.1.3).

NEW SERIES OF SEMI-SYNTHETIC WATER-SOLUBLE NATAMYCIN AMIDES AS POTENT ANTIFUNGAL DRUGS

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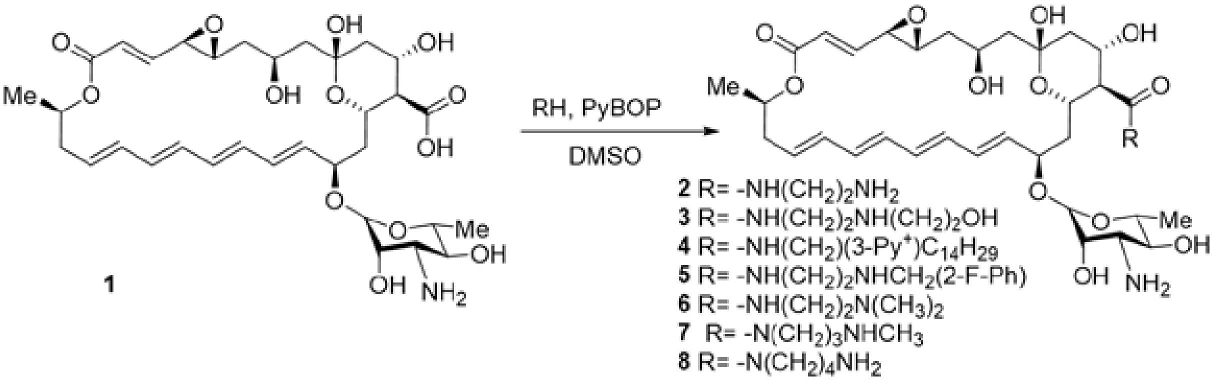
Natamycin (**1**) is a 26-membered polyene antibiotic with potent antifungal activity and is widely used in medicine, agriculture and food industry. The mode of its action is based on specific binding to ergosterol without pore-forming activity.[1] Natamycin as other natural occurring polyenes practically insoluble in water due to its amphiphilic structure and zwitter-ionic character, consequently, has an extremely low bioavailability, so its application is limited to topical administration only. Earlier a series of papers[2,3,4,5] reported that disabling the zwitter-ionic character and introducing an additional basic residue can significantly improve pharmacological profile of polyene antibiotics. So, such modification of natamycin's core is a promising way to obtain new antifungal water-soluble polyenes.

Natamycin (**1**) was condensed with six commercially available diamines with variable chemical nature and with 3-(aminomethyl)-1-tetradecylpyridine hydrochloride. The last one was prepared by quaternization of 3-picolylamine with 1-bromotetradecane by method, described earlier[6]. Reactions were performed in dry DMSO with fivefold excess of amines using benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate (PyBOP) as condensing agent (scheme 1).



Scheme 1. Synthesis of natamycin amides

Natamycin amides in salt forms showed good solubility in water (0.03 – 1 g/ml) as opposed to parent antibiotic **1**. In general, anti-yeast activity against *Candida spp.* of all tested semi-synthetic natamycines **2-8** was comparable to those of parent antibiotic. Among the studied derivatives, amide **8** was chosen for *in vivo* investigations of its efficacy on the model of mice candida sepsis due to the highest *in vitro* activity. It was shown that water-soluble natamycin amide **8** had a systemic therapeutic effect and could protect infected mice from death. The therapeutic index (LD_{50}/ ED_{50}) of **8** is proved to be moderate, but still in 3 times higher than those of amphotericin B.

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This study was funded by RSF, project number 21-74-20102

ONE-POT SYNTHESIS OF 2*H*-THIOPYRANS FROM ENAMIN-3-ONES BY THE DIELS-ALDER REACTION

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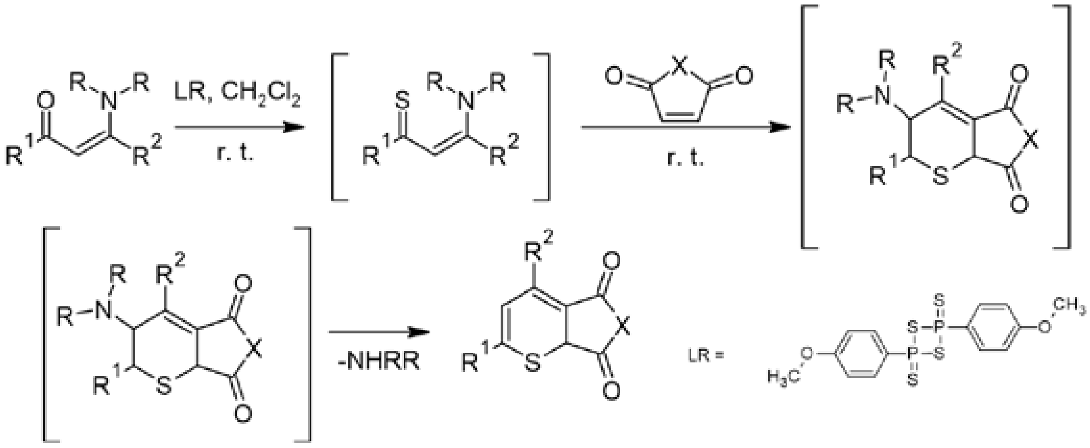
2*H*-Thiopyrans are insufficiently studied organic substances and are of interest for synthetic organic chemistry [1]. One of the effective methods for the synthesis of these compounds is their preparation by the Diels-Alder reaction from enaminothioketones acting as heterodienes [2].

We have developed a *one-pot* method for the preparation of 2*H*-thiopyrans from enaminoketones which involves the thionation of enaminoketones with Lawesson's reagent and the use of the resulting enaminothioketones without isolation in the Diels-Alder reaction with dienophiles.



X = O, N-Ar; R^1 = Me, Ph; R^2 = H, Me; R = $-(CH_2)_4-$

It was shown that the Diels-Alder reaction proceeds only with very active electron-deficient dienophiles at room temperature, while the reaction does not proceed with electron-rich dienophiles even at elevated temperatures. 2-Pyrrolidinyl-2-enones, which were successfully obtained from the corresponding 1,3-dicarbonyl compounds and pyrrolidine, were used as starting enaminoketones [3].

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SYNTHESIS OF 3-SULFANYL-1,2,4-TRIAZOLIUM SALTS AND STUDY AS NHC-PROLIGANDS

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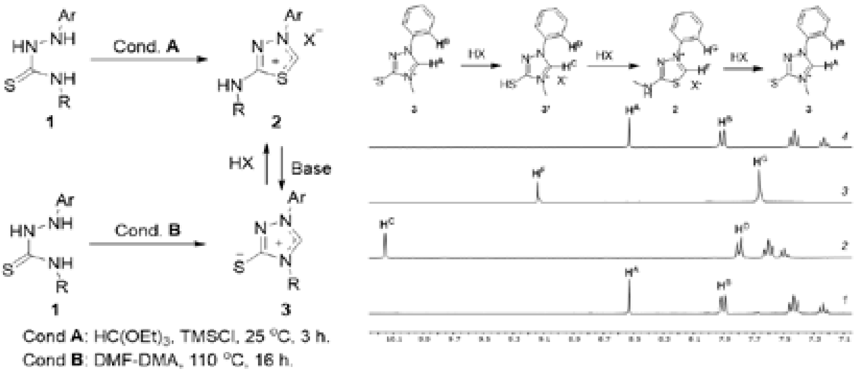
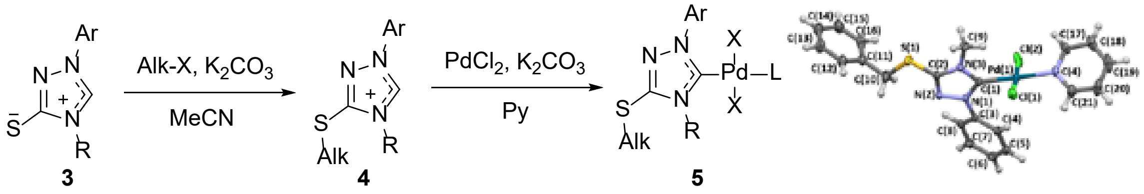
Palladium complexes with NHC ligands based on 1,2,4-triazole are widely used as catalysts.[1] However, methods for obtaining Pd/NHC complexes with 1,2,4-triazole-3-thiols and their S-alkyl derivatives as NHC-proligands are still practically unexplored.

3-Mercapto-1,2,4-triazolium betaines (**3**), products of a cyclization reaction of thiosemicarbazides, were obtained by two ways: reactions with triethylorthoformate, trimethylchlorosilane and treatment with base (**A**) or boiling in DMF-DMA at 110°C (**B**). It is noteworthy that betaines **3** under the action of acid can regroup into thiadiazoles **2**.



a *b*

Thiolates **3** under palladation conditions formed a complex mixture, but their alkylated derivatives can be easily converted to the corresponding Pd/NHC complexes.



Thus, for the first time, the Dimroth rearrangement between 3-aryl-5-(R)amino-1,3,4-thiadiazolium salts (**2**) and 1-aryl-4-R-1,2,4-triazolium-3-thiolates (**3**) was shown and the possibility of using 3-alkylsulfanyl-1-aryl-4-R-1,2,4-triazolium salts (**4**) as new NHC-proligands for the synthesis of Pd/NHC complexes (**5**) was demonstrated.

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The work has been supported by the Ministry of Science and Higher Education of the Russian Federation (project No 075-03-2021-016/4)

SYNTHESIS AND PROPERTIES OF 1,3-DISUBSTITUTED UREAS AND THIOUREAS CONTAINING A NATURAL LIPOPHILIC BICYCLIC FRAGMENT IN THEIR STRUCTURE

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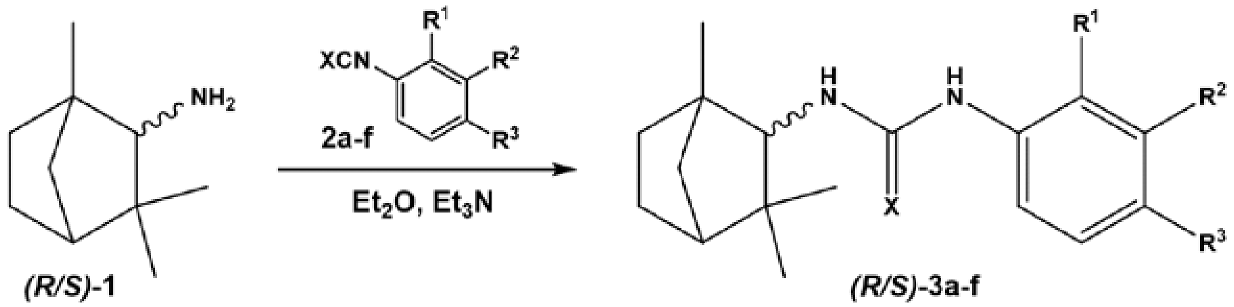
Ureas and thioureas with a highly lipophilic moiety are recognized as effective inhibitors of human soluble epoxide hydrolase (sEH). sHE is an enzyme involved in the metabolism of epoxy fatty acids to the corresponding vicinal diols via catalytic addition of a water molecule. It is a promising target in the treatment of hypertensive, inflammatory, and pain conditions.

However, known ureas and thioureas tested as sEH inhibitors are rapidly metabolized by cytochromes P450 and have poor water solubility due to the presence of a highly lipophilic group in their structure. This limits their use as potential drugs.

As a replacement for the lipophilic adamantane part of the molecule, it is proposed to use a fragment of fenchon. Fenchon is found naturally in plants such as *Foeniculum vulgare Mill.* (fennel), *Pimpinella anisum L.* (anise) and *Anethum graveolens L.* (dill). Such a group of natural origin will increase the water solubility of ureas and can be ignored by cytochromes P450, contributing to an increase in metabolic time.

A directed synthesis of a series of 1,3-disubstituted ureas **3a-d** and thioureas **3e-f** was carried out based on *(S)*- and *(R)*-1,3,3-trimethylbicyclo[2.2.1]heptan-2-amine (**1**) , aromatic isocyanates **2a-d** and isothiocyanates **2e-f** substituted with fluorine and chlorine on the aromatic ring.



R_2=F, R_1=R_3=H, X=O(**3a**); R_3=F, R_1 =R_2=H, X=O(**3b**); R_1=Cl, R_2=R_3=H, X=O(**3c**); R_2=Cl, R_1=R_3=H, X=O(**3d**);
R_2=F, R_1=R_3=H, X=S(**3e**); R_3=F, R_1=R_2=H, X=S(**3f**); R_2=Cl, R_1=R_3=H, X=S(**3g**)

The study of the properties of the synthesized ureas and thioureas showed that the replacement of the adamantane fragment with the natural one positively affects the solubility of the inhibitor in water, increasing it at 1.2-fold, while maintaining a high level of inhibitory activity against sEH. The obtained IC_{50} values are in the range of 0.11-6.4 µM.

The reported study was funded by RFBR (project number 19-33-60024)

S_N^H ARYLAMINATION AS A METHOD FOR THE SYNTHESIS OF NITRO- AND NITROSO-DERIVATIVES OF ARYLAMINOISOQUINOLINES

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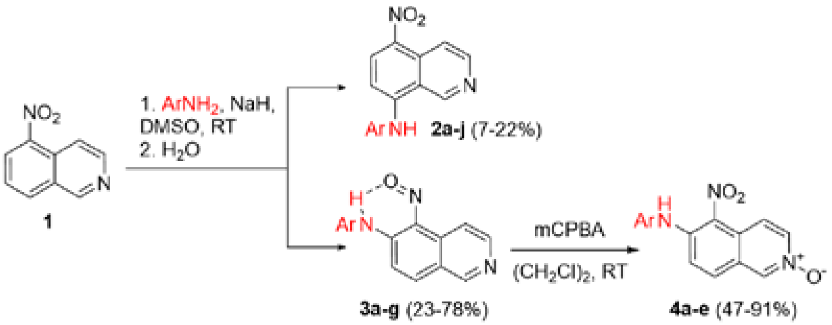
Oxidative S_N^H arylamination reactions are still very rare due to the relatively low nucleophilicity of the arylamide anions commonly used for these processes and, most importantly, their high sensitivity to commonly used oxidizing agents. Previously, direct C–H functionalization with the introduction of an arylamino group was performed using 1,3,7-triazapyrene[1], 3-nitropyridine[2], and nitroquinolines[3] as an example, using anhydrous DMSO and preliminarily generating a nucleophile by the action of NaH on arylamine at room temperature.

We found that the use of N-anions of arylamines as nucleophilic agents in the reaction with 5-nitroisoquinoline (1) in anhydrous DMSO leads to the formation of a mixture of previously unknown 8-arylamino-5-nitroisoquinolines (2a-j) and 6-arylamino-5-nitrosoisoquinolines (3a-g) with a predominance of the latter. Anilines with ortho substituents or relatively bulky meta substituents do not form nitroso compounds.



We further attempted to convert the obtained nitrosamines 3 into the corresponding 6-arylamino-5-nitroisoquinolines using m-chloroperbenzoic acid (mCPBA) as an oxidizing agent. Using an excess of mCPBA (2.2 mol), previously unknown 6-arylamino derivatives of 5-nitroisoquinoline-N-oxide (4a-e) were obtained for the first time; with a smaller amount of oxidant, a complex mixture of products is formed.

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The authors express their gratitude to the North Caucasian Federal University for financial support in the framework of the project to support the projects of scientific groups and individual scientists.

SYNTHESIS AND AGGREGATION BEHAVIOR OF NOVEL LINEAR AND BRANCHED OLIGOTHIOPHENE-CONTAINING ORGANOSILICON MULTIPODS

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The outstanding semiconducting and electro-optical properties exhibited by π-conjugated oligomers and polymers make it possible to utilize such compounds as functional elements for organic electronics and photonics. So far, the most intensive study has been devoted to compounds with p-type conductivity, whose structural geometry varies from linear to hyperbranched macromolecules. Among such materials, oligo- and polythiophenes are of specific interest owing to their high charge carrier mobility, good solubility in organic solvents, and also intensive absorption in the visible spectral range. Thus, the synthesis of different carbosilane-siloxane derivatives of the oligothiophenes with high conjugation lengths followed by the study of the influence of various molecular parameters on their optical and other physical-chemical properties indeed features a critical problem. So, in this work[1] the focus was made on the synthesis of a new family of linear and branched oligothiophene-containing carbosilane-siloxanes with lengths of aliphatic spacers from C3 to C11, various degrees of branching of the end-capping groups (n-hexyl, 2-ethylhexyl or 2-octyldodecyl), and number of conjugated thiophene fragments ranging from quater- (4T) to septithiophene (7T) (Fig. 1).

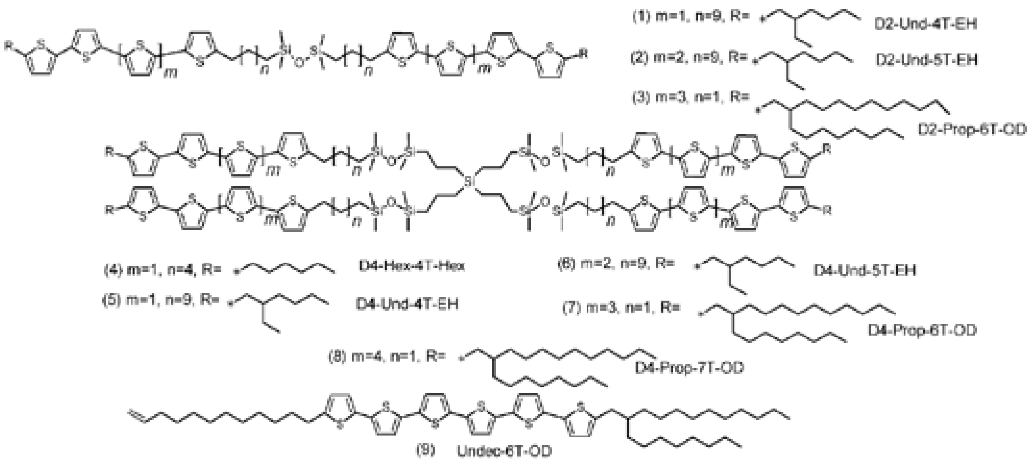

Figure 1. Structural formulas of synthesized oligothiophene-containing carbosilane-siloxanes

The set of compounds with different molecular structures provided a chance to trace the influence of every fragment of the molecule on their phase behavior, aggregation in solution and on the substrate. As a result of the investigation of the optical properties in dilute solutions, it was established that linear and branched end-capping substituents promote different types of aggregates formation. Investigation of these compounds by DSC and POM showed that although some of them can form liquid-crystalline phases, the majority of the linear molecules exhibit a high degree of crystallinity, which decreases with increasing degree of branching. The results of AFM investigations showed that these compounds do have a potential for the application as organic electronics materials.

This work was supported by RSF (project № 19-73-30028).

4-TRIAZINYL DERIVATIVES OF BENZO[*c*]CHROMENE-6-ONES

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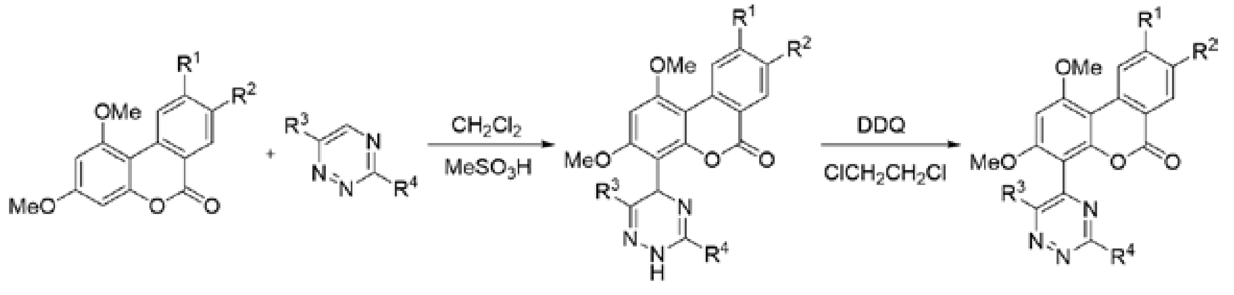
The coumarin scaffold consisting of condensed benzene and α-pyrone rings provides one of the most important photophysically active frameworks. Due to its good photophysical properties, including high quantum yields and excellent photostability, various coumarin derivatives have been studied as reagents in medical photochemistry[3] and organic optoelectric materials, such as laser dyes[1] and dye sensitizers[2]. As a rule, coumarin dyes contain an electron-donating group at C7 and nitrogen-containing heterocyclic moiety, mostly an electron acceptor, at C3 of the coumarin core.

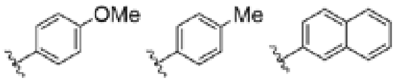
Coumarins containing a pyridyl group are representative examples of pH-sensitive photosensitive drug delivery systems, such as coumarin-benzothiazine-chlorambucil conjugates[3]. The production of pyridines from 1,2,4-triazines under the action of acetylenes, accompanied by nitrogen extrusion (Boger reaction) can be considered as one of the modern approaches to the synthesis of this class of monoazines. Therefore, the aim of the presented work is to obtain 1,2,4-triazinyl derivatives of benzo[*c*]chromen-6-ones for subsequent transformation into pyridines.

We found that the interaction of 1,3-dimethoxybenzo[*c*]coumarins **1** with 3,5-diaryl-1,2,4-triazines **2** in the presence of methanesulfonic acid leads to the interaction products at the 4-position of coumarin with the formation of dihydrotriazines **3**, which can be oxidized into fully aromatic triazines **4** under the action of dichlorodicyanobenzoquinone (DDQ).



1 **2** **3a-n** **4a-n**

a: R^1=H, R^2=H, R^3=Ph, R^4=Ph;
b: R^1=H, R^2=H, R^3=H, R^4=Ph;
c: R^1=H, R^2=H, R^3=Naphth, R^4=Ph;
d:R^1=H, R^2=H, e: R^3=PMP, R^4=Tol;
e: R^1=F, R^2=F, R^3=Ph, R^4=Ph;
f: R^1=F, R^2=F, R^3=H, R^4=Ph;
g: R^1=F, R^2=F, R^3=Naphth, R^4=Ph;
h: R^1=F, R^2=F, R^3=PMP, R^4=Tol;
i: R^1=CH_3, R^2=H, R^3=Ph, R^4=Ph;
j: R^1=CH_3, R^2=H, R^3=H, R^4=Ph;
k: R^1=CH_3, R^2=H, R^3=Naphth, R^4=Ph;
l: R^1=CH_3, R^2=H, R^3=PMP, R^4=Tol;
m: R^1=H, R^2=OMe, R^3=Ph, R^4=Ph;
n: R^1=H, R^2=OMe, R^3=H, R^4=Ph;



PMP Tol Naphth

The obtained triazines **4a-n** can be used as a starting material for the synthesis of 4-pyridinyl derivatives of benzo[*c*]chromen-6-ones by Boger reaction.

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This work was supported by Russian Science Foundation project # 21-73-00214.

SYNTHESIS OF NOVEL TETRAHYDROPYRIMIDINES VIA THE REACTION OF SODIUM 1-(3,3-DIETHOXYPROPYL)UREIDO) METHANSULFONATES WITH *C*-NUCLEOPHILES

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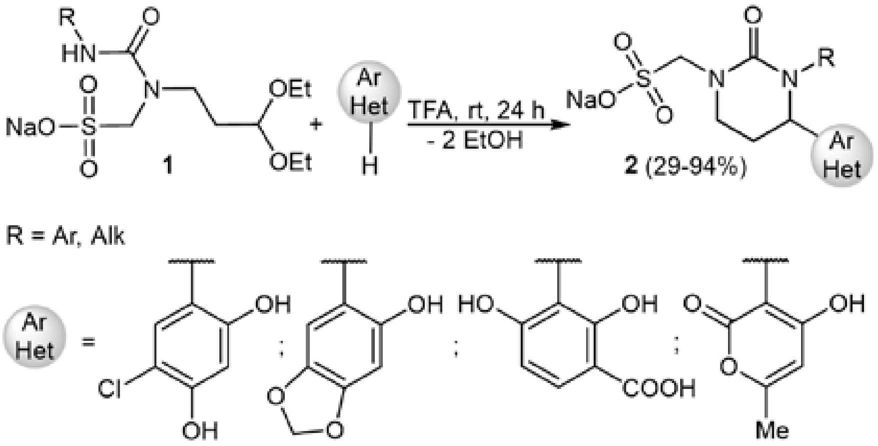
Over the past decades, cyclic ureas continue to be the object of close attention of synthetic chemists and researchers searching for new biologically active substances. Particular attention is paid to substituted tetrahydropyrimidin-2(1*H*)-one derivatives which are predominantly have an inhibitory effect on various enzymes such as HIV protease, dihydroorotase, topoisomerase I, TNF-α-converting enzyme.

In our laboratory we have developed a convenient and simple method of synthesis of tetrahydropyrimidin-2(1*H*)-one derivatives **2** based on acid-catalyzed reaction of sodium (1-(3,3-diethoxypropyl)ureido)methanesulfonates **1** with aromatic and heterocyclic nucleophiles.



The work was supported by a grant from the President of the Russian Federation for support of young Russian scientists (MK-1944.2022.1.3).

NEW AXIALLY CHIRAL BIPYRIDINES AND THEIR APPLICATION IN ASYMMETRIC CATALYSIS

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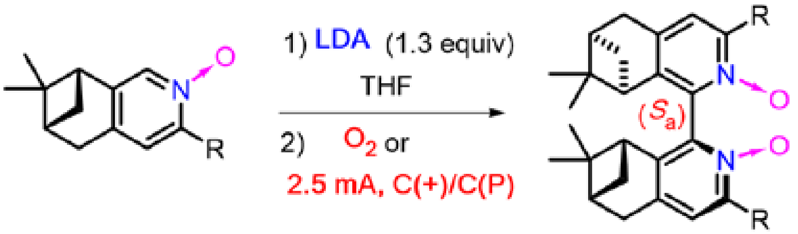
Complexes of chiral bipyridines with transition metals have a very rich chemistry including catalytic asymmetric transformations[1]. Additionally, related bypiridine *N*-oxides have made a considerable impact in enantioselective nucleophilic catalysis[2]. Despite these successes, synthesis and application of axially chiral bipyridine derivatives has not reached the level of maturity, which in part is due to the lack of good coupling methods for joining the pyridine units together in a stereoselective fashion.



Herein, we present an expedient mild procedure for coupling of two chiral pyridine-*N*-oxide units, where the central chirality of the terpene fragment efficiently controls formation of the chiral axis[3]. The synthesised bipyridine-*N*-oxides can be reduced to the respective chiral bipyridines with a complete retention of the axial chirality. Several applications of both bis-*N*-oxides and bipyridines in asymmetric transformations will be presented[5-7]

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This work was supported by the Russian Science Foundation, project # 18-73-10156

MORPHOLOGY AND CONDUCTIVITY OF INDIUM(III) COMPLEXES OF NATURAL PORPHYRIN ANALOGS

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Ethioporphyrins and pheophorbides are heterocyclic compounds of the porphyrin family, the closest analogues of natural chlorophyll. Their interesting photophysical properties are stimulating the research into the application of individual molecules and ordered phases in optoelectronic devices, such as solar cells[1]. The introduction of an indium atom into chelate window causes the macrocycle to deviate from planarity[2] and hence, a change in the ability of the complex to aggregate and form the ordered structures in thin films is expected.

In this work, the films of In(III) complexes of the methyl pyropheophorbide *a*, InCl-MePyroPheo and ethioporphyrin-I, InCl-EtioP-I were synthesized and characterized - Fig. 1. Films of etioporphyrin complex were deposited by vacuum sublimation, while pheophorbide films were deposited by either spin-coating and drop-casting methods[3] due to lower thermal stability.

The spin-coated films of InCl-MePyroPheo showed low photocurrent $I_{light}/I_{dark} = 1,4$ at 10 V DC in contrast to highly photoconductive films of InCl-EtioP-I where the $I_{light}/I_{dark} = 200$. However, the InCl-MePyroPheo films have higher specific conductivity at RT, $\sigma_{300}=1,1\cdot10^{-11}$ Sm/cm compared to InCl-EtioP-I ($\sigma_{300} = 2,7\cdot10^{-12}$ Sm/cm). In sandwich-type cells with the latter compound and Al as the top electrode, a photovoltage of 0.82 V was measured under 1sun illumination.

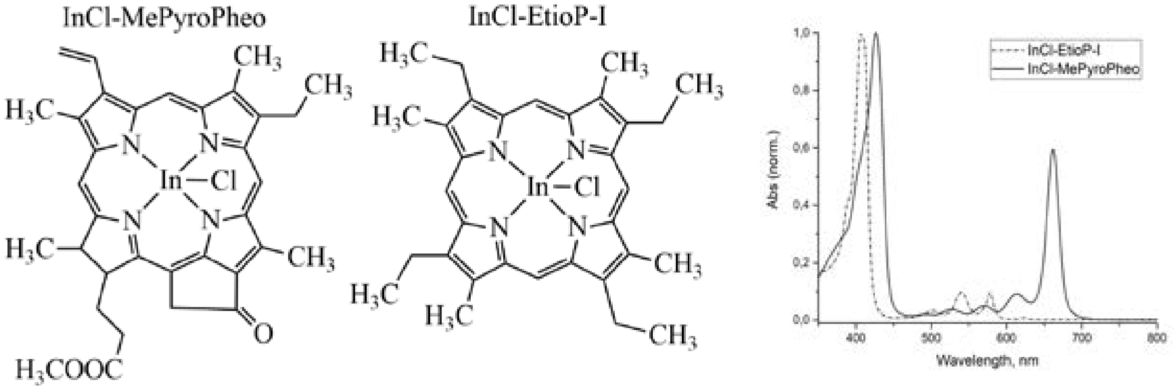

Fig.1. InCl-MePyroPheo and InCl-EtioP-I, and their absorption in toluene.

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This study was supported by the RSF (grant No. 20-13-00285).

SYNTHESIS NOVEL HETEROCYCLIC SYSTEM – PHOSPHININO[3,2-*d*]OXAZOLE

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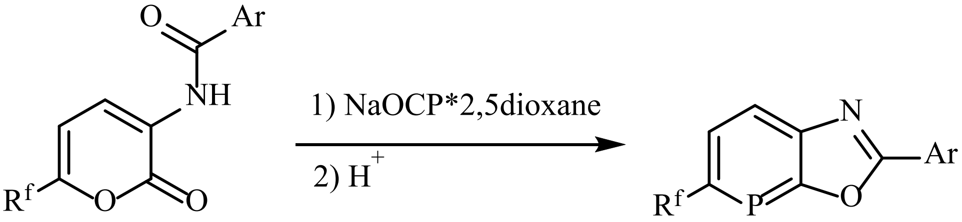
The benzoxazole moiety is widely found in various natural compounds, which are often found to be biologically active. Due to its versatile biological properties, benzoxazole has been incorporated as an essential pharmacophore and substructure in many medicinal compounds. In the past years, numerous benzoxazole derivatives have been synthesized and evaluated for their biological potential. The wide range in therapeutic potential of benzoxazole derivatives is related to the favorable interactions of the benzoxazole moiety with different protein targets[1]. They are also the basic units of an important class of fluorescent organic dyes, particularly attractive due to their high quantum yield, ease of synthesis, and excellent thermal, chemical, and photochemical stability[2].

Herein, we present an expedient mild procedure for one-pot synthesis phosphoric analogues benzoxazoles – phosphinino[3,2-*d*] oxazoles.



The mechanism of reactions and properties of synthesized phosphinino[3,2-*d*]oxazoles is discussed.

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This work was supported by the Russian Science Foundation, project # 18-73-10156

OXIDATION OF 3-CYANOKETONES IN SYNTHESIS OF 2-(3-OXOINDOLINE-2-YLIDENE)ACETONITRILES

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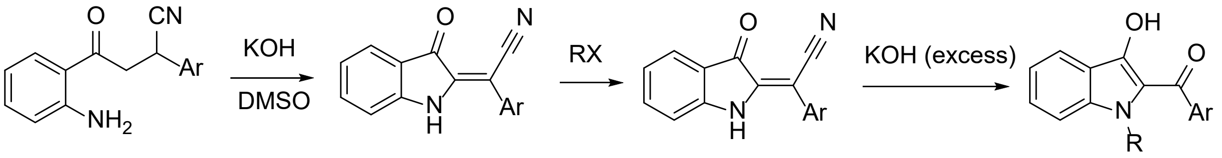
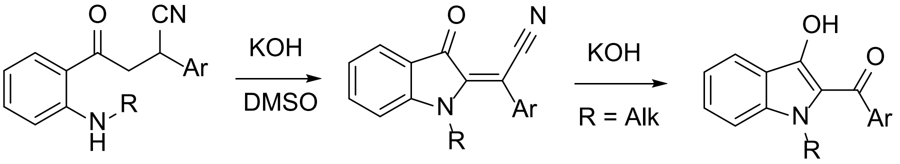
Alkylideneindolin-3-one derivatives bearing a single indoline moiety or two remotely positioned indoline subunits are found in nature and are also endowed with important biological activities. 2-Alkylideneindolin-3-ones bearing a conjugated nitrile function were used as advanced precursors in the synthesis of pyridazino[4,3-b]indoles 2, possessing strong inhibitory activity against Mycobacterium tuberculosis. Recently we have communicated on unexpected formation of 2-alkylideneindolin-3-ones taking place upon treatment of ortho-nitrochalcones with potassium cyanide and acetic acid in methanol.

We were wondering what if ortho-aminochalcones or their derivatives 4-(2-aminophenyl)-4-oxobutyronitriles were used. In this case, instead of reduction, oxidation should proceed with the formation of the desired products. Moreover, the use of an alkaline medium allows the reaction to be combined with *N*-alkylation. The *N*-alkylated product, in turn, converts to 2-benzoyl-3-hydroxyindoles on excess of alkali was used.



A similar result can be obtained using pre-N-alkylated 4-(2-aminophenyl)-4-oxobutyronitrile.



The study was supported by the Russian Science Foundation (grant № 21-73-10029, https://rscf.ru/project/21-73-10029/)

SYNTHESIS AND BIOLOGICAL ACTIVITY OF 2-QUINOLYL-1,3-TROPOLON DERIVATIVES

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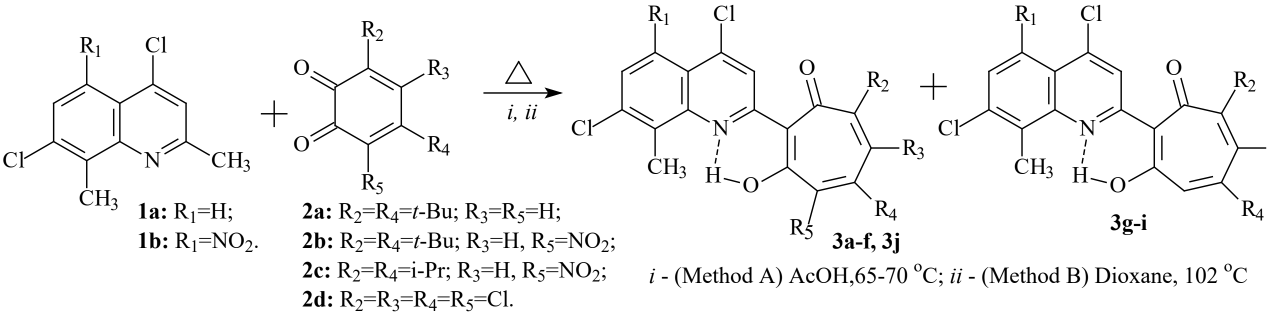
In this study, a series of novel 2-quinolyl-substituted 1,3-tropolones **3** was obtained. The structure of compounds **3** was confirmed by NMR ^{1}H, ^{13}C, IR, mass spectrometry, X-ray analysis.



1a: R_1=H;
1b: R_1=NO_2.

2a: R_2=R_4=*t*-Bu; R_3=R_5=H;
2b: R_2=R_4=*t*-Bu; R_3=H, R_5=NO_2;
2c: R_2=R_4=i-Pr; R_3=H, R_5=NO_2;
2d: R_2=R_3=R_4=R_5=Cl.

3a-f, 3j **3g-i**

i - (Method A) AcOH,65-70 °C; *ii* - (Method B) Dioxane, 102 °C

In subsequent testing for biological activity, compound **3d** and tropolone mixture B of **3i-k** exhibited the broadest and potent activities against six various human cancer cell lines with IC50 values ranging from 0.63 to 3.93 μM. Furthermore, compound **3d** reduced colony formation induced apoptosis in ovarian cancer (OVCAR-3, OVCAR-8) and colon cancer (HCT 116) cell lines. The ERK pathway was broadly induced by **3d** compound, but not by tropolone mixture B of **3i-k** treatment. Taken together, our study suggests that 2-quinolyl-1,3-tropolones are a promising new class of heterocyclic compounds that should be used for the future development of effective anticancer drugs.

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ELECTROCHEMICAL OXIDATIVE COUPLING OF ACTIVATED ALKENES WITH THE USE OF PHTHALIMIDE-N-OXYL RADICAL

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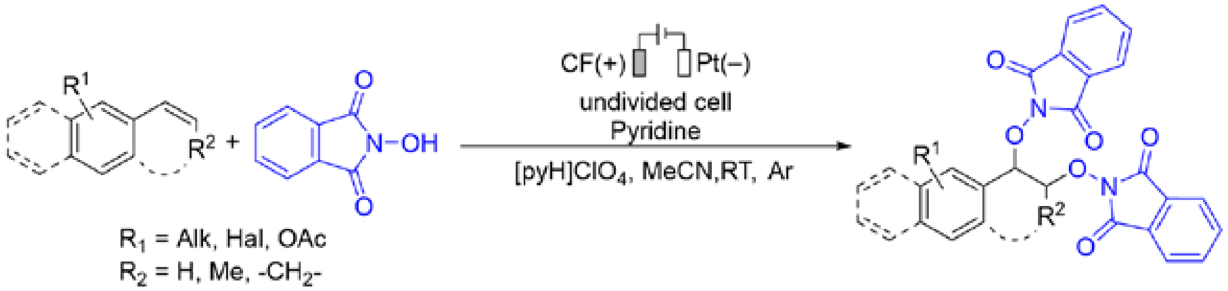
Selective difunctionalization of alkenes is one of the most rapidly developing and studied areas of modern organic synthesis. The methods developed in recent years for the difunctionalization of alkenes with the formation of a C-C or C-Het bond make it possible to obtain valuable intermediates for organic synthesis. [1]

Electroorganic synthesis is a novel approach for the difunctionalization of alkenes that expands the range of suitable substrates, avoids the use of strong oxidizing agents, and minimizes the formation of by-products. Such processes occur during the oxidation or reduction of the initial reagents to radicals. [2]

An increase in the number of reactions of alkenes with imide-N-oxyl radicals is observed, in which the latter are added to the terminal carbon atom of the C=C double bond with the formation of a C-centered radical and its subsequent functionalization. Most of the work in this area is devoted to the radical dioxygenation of vinyl arenes. [3]

In the present work, phthalimide-N-oxyl radicals were used for the radical difunctionalization of vinyl arenes to obtain vicinal dihydroxyphthalimides. [4]



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The work was supported by the Russian Science Foundation grant no. 21-13-00205

SYNTHESIS AND INVESTIGATION OF BISPIDINE-PYRAZOLINE CONJUGATES, POTENTIAL CHIRAL CATALYSTS FOR MICHAEL REACTION

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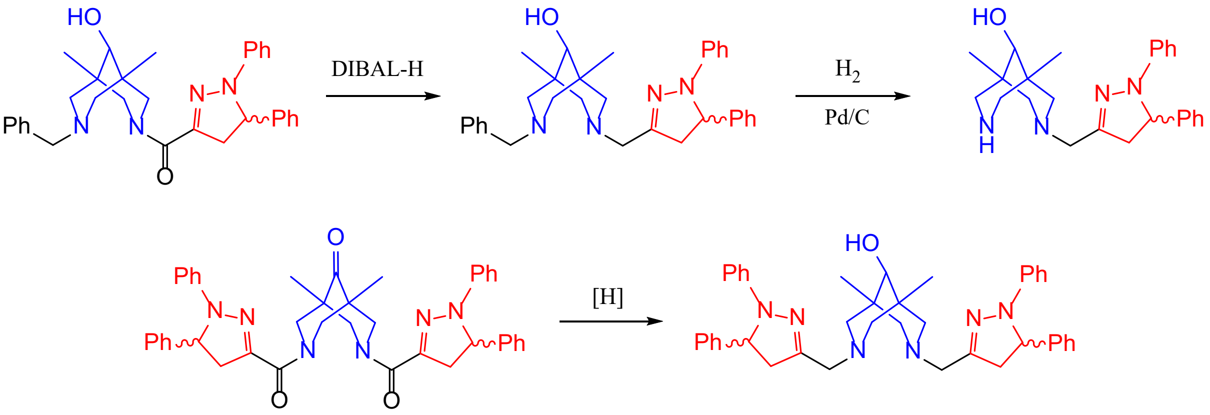
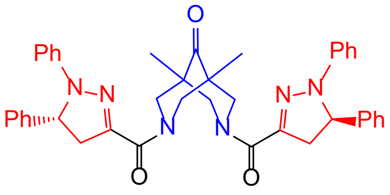
In the present work conjugates of bispidine and chiral pyrazolines were synthesized and characterized. A number of chiral along with non-chiral amides of bispidinone and bispidinol were obtained. The structures of diastereomers of bispidinone bis-amides were predicted by ^{1}H-NMR spectra and then confirmed by means of X-ray studies. Our final aim is to obtain corresponding amines which will be tested for catalytic activity.



Bispidinone bis-amides diastereomers:



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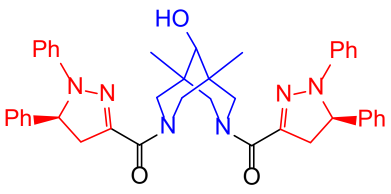

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This work was financially supported by the RSF (grant 19-73-20090).

CHEMICAL MODIFICATION OF AMINOGLYCOSIDE ANTIBIOTIC KANAMYCIN A

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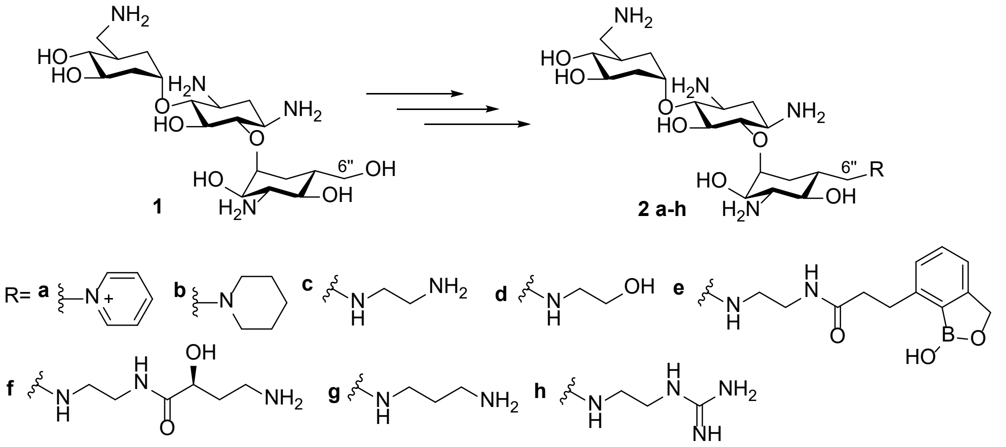
The rapid spread of antibiotic-resistant strains throughout the world determines the relevance of the search for new highly effective antimicrobial agents. Chemical transformation of natural antibiotics is one of the most productive approaches in to a new generation of potent antibacterials.

Though aminoglycosides belong to one of the first class of antibiotics discovered, they still consider as one of the most promising antimicrobial agents due to a wide spectrum of action, i.e., activity against gram-positive and gram-negative bacteria, and mycobacteria.

However, the emergence of pathogen strains with resistance to aminoglycoside antibiotics and their oto- and nephrotoxicity determine the relevance of further development of new generation of this class and antibacterials. The aim of this work was the chemical modification of aminoglycoside antibiotic, kanamycin A, a natural compound produced by Streptomyces kanamyceticus or other related microorganisms.



In this work, new semisynthetic derivatives of kanamycin A containing various substituents in the 6” position were obtained. The synthesis was carried out in several stages, the main of which are: the introduction of protective groups of the urethane type on the amino groups of kanamycin A, the replacement of the 6”-hydroxy group with an easily leaving 2,4,6-triisopropyl benzyl sulfonic acid group, with its subsequent interaction with aromatic and aliphatic amines, and their further modification. Ehe last the step included the removal of the protective groups resulting in the target derivatives of kanamycin A as pentaacetates. The structure of all obtained compounds was confirmed by physicochemical and spectral methods, including ^{1}H and ^{13}C NMR spectroscopy and high-resolution mass spectrometry. The purity of the obtained compounds was confirmed by HPLC.

For all obtained derivatives of kanamycin A, antibacterial activity was studied on various biological models, which made it possible to identify derivatives that are not inferior in activity to the original antibiotic. Further structure optimization of kanamycin A aiming synthesis of new semisynthetic derivatives active against resistant strains is carried out.

The authors are grateful to Ph.D. Grammatikova N.E. (GINA) and Doctor of Chemistry Osterman I.A. (SKOLTECH) for conducting research on the biological activity of the obtained compounds.

INVESTIGATION OF CATIONIC TRANSFORMATIONS INVOLVING 5-ETHYNYL-4-ARYLPYRIMIDINES

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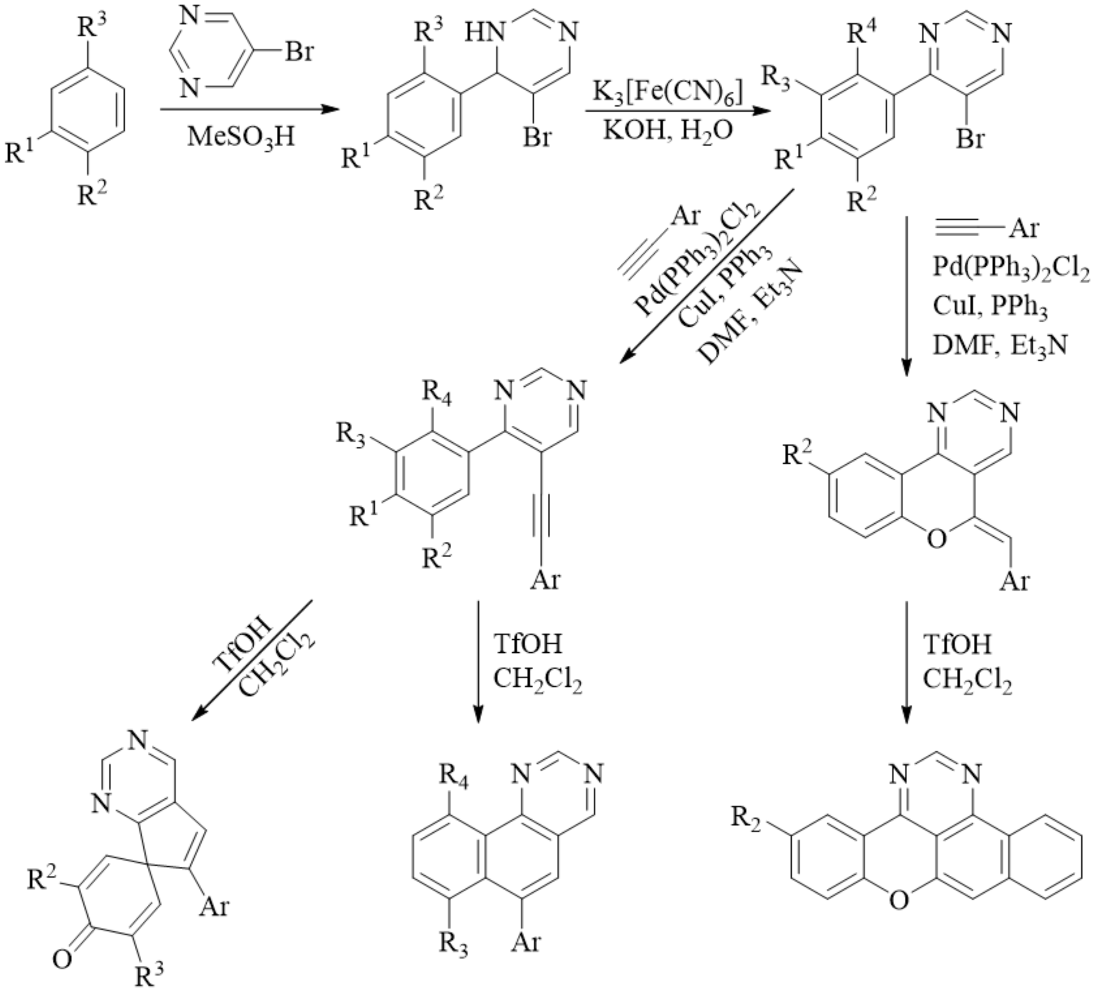
An innovative synthetic approach towards 5-ethynyl-4-arylpyrimidines was developed involving acid-catalyzed electrophilic alkylation of phenols with 5-bromopyrimidine, followed by oxidation and palladium-catalyzed Sonogashira cross-coupling reaction. Reactions of these compounds in the presence of trifluoromethanesulfonic acid were investigated. It was discovered these reactions take a different route for precursors with a different position of phenol group in an arene substituent.



This investigation was supported by Russian Science Foundation (grant #21-73-00057, https://rscf.ru/project/21-73-00057/).

RUTHENIUM(II)-CATALYZED C(3)-H ARYLATION OF FURAN RING IN 2-(FURAN-2-YL)-BENZIMIDAZOLES

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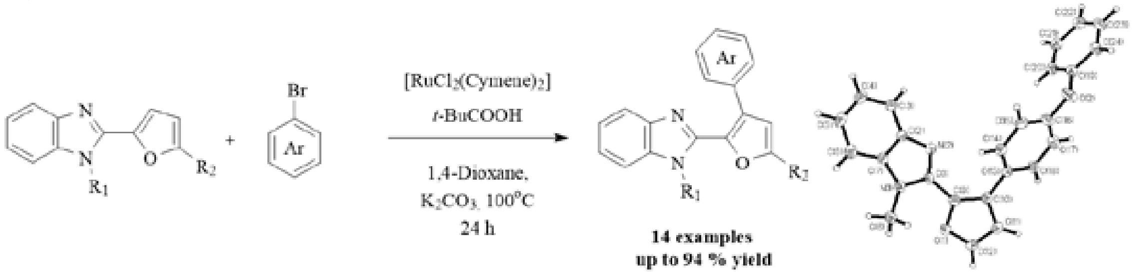
Although the C-H activation of furanes at positions 2 and 5 was extensively studied, the activation of positions and of the furanic core remains a challenging task, usually requiring substituted 2(5) position, sophisticated catalytic systems, special reagents or specific directing groups[1,2]. Therefore, the development of new methods for selective C-H activation of positions 3 and 4 of the furan fragment is an urgent task.

In this work a simple and efficient catalytic system for C(3)-H arylation of 2-(-2-yl)-benzimidazoles with aryl bromides was proposed. A commercially available ruthenium complex [RuCl$_2$Cymene]$_2$ was used as a catalyst and pivalic acid was used as a ligand for the direct arylation of the furan core.



A series of new 2-(3-arylfuran-2-yl)-benzimidazoles have been synthesized with yields up to 94%. The structure of the obtained compounds was confirmed by NMR and ESI-MS spectra, and single crystal X-ray analyses.

1 J. M. J. M. Ravasco, C. M. Monteiro, F. Siopa, A. F. Trindade, J. Oble, G. Poli, S. P. Simeonov, C. A. M. Afonso, *ChemSusChem*, 2019, **12**, 4629.
2 H. H. Al Mamari, U. Grošelj, F. Požgan, H. Brodnik, *J. Org. Chem.*, 2021, **86**, 3138.

This work was supported by the Russian Science Foundation (RSF grant 21-73-0058).

NEW DICATIONIC PROLIGANDS FOR THE SYNTHESIS OF WATER-SOLUBLE M/NHC COMPLEXES

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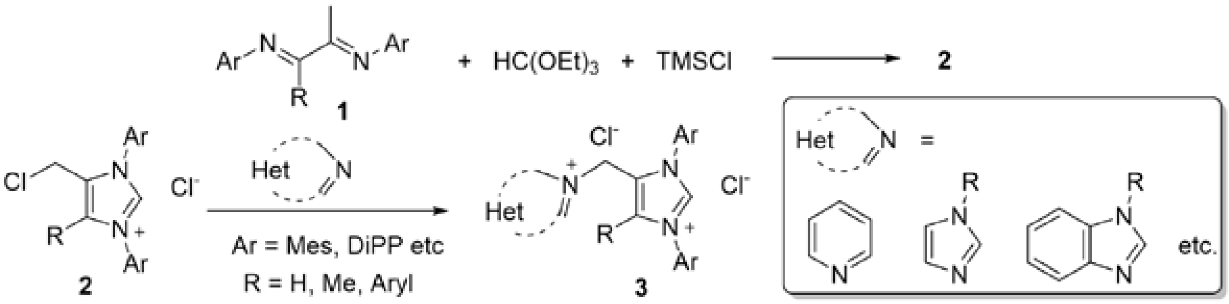
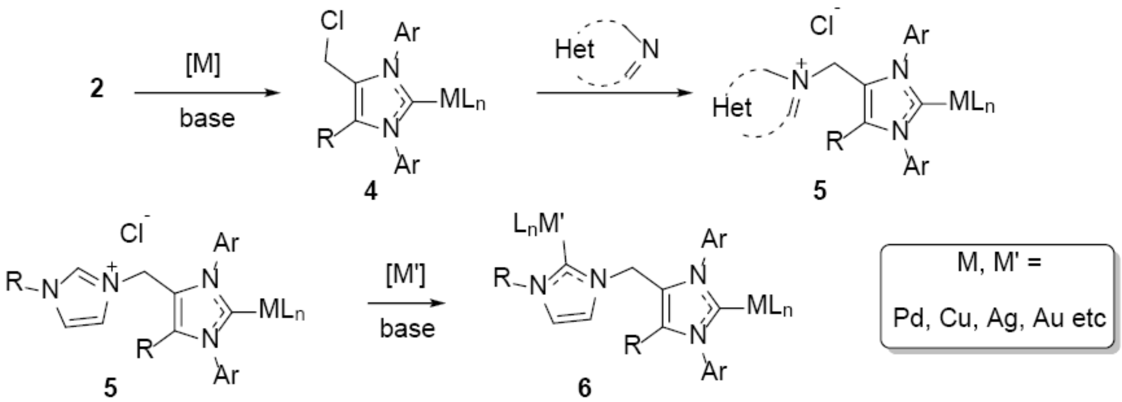
A new cyclocondensation reaction [1] of 1,4-diaryl-2,3-dialkyl-1,4-diazadienes **1** with $HC(OEt)_3$ and TMSCl allowed to obtain numerous 4-chloromethyl-1,3-diarylimidazolium salts **2**. Subsequent nucleophilic substitution of the chlorine atom opens up great opportunities for the synthesis of NHC's containing various functional groups. In particular, by quaternization of N-heterocyclic compounds with salts **2**, dications **3** were obtained, which can be used in the synthesis of practically important M/NHC complexes characterized by high solubility in water despite the presence of bulky substituents on N-atoms.



The properties of the obtained salts **3** and the patterns of their metalation, including the possibility of obtaining bis-metal complexes from azole derivatives, were studied. Chloromethyl-substituted salts **2** itself were metalated to give the corresponding M/NHC **4**, which reaction with azines and azoles lead to the cationic complexes **5**. In the case of azolomethyl substituted **5** their further metalation opens the way to the bis-metallocomplexes **6** with two different metals in molecule.



Compounds **5** were found to be extremely soluble in water and showed good activities in some catalytic reactions in the aqueous media.

References
1) *Angew. Chem. Int. Ed.* **2021**, e202116131

The authors acknowledge Russian Science Foundation grants no 19-73-20085, 22-23-00304.

ADVANCED SYNTHETIC PROTOCOL TO THE H_2O-FREE S,S-DIPHENYLSULFIMINE

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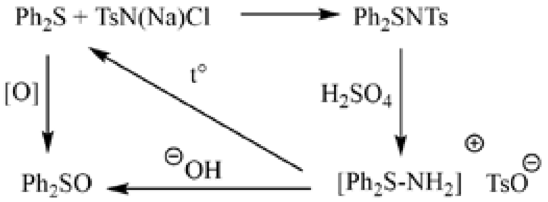
S,S-diphenylsulfimine ($Ph_2S{\rightarrow}NH$) is the key intermediate for coordination chemistry of S^{IV} and S^{VI}. Since the late 1950s, several scientific groups [1-3] have attempted to synthesize $Ph_2S{\rightarrow}NH$. While reproducing these syntheses we have established a number of difficulties that affect the yield of intermediate and target products. S^{IV}-N bond is very labile. Depending on different factors (the intensity of the acid hydrolysis of Ph_2SNTs, exposure to light, heat and oxygen, processing time, base concentration), the presence of by-products, and their yield, varies widely. Total yield of $Ph_2S{\rightarrow}NH$ suffers by formation of by-products on later stages, notwithstanding high yield of TsN group transfer to Ph_2S.



Scheme 1. Synthesis of $[Ph_2S\text{-}NH_2]OTs$ and by-products formation

Commercially available hydrate $Ph_2S{\rightarrow}NH{\bullet}H_2O$ usually has impurities, and in the most cases its additional purification is required. Therefore, the currently known $Ph_2S{\rightarrow}NH$ synthesis protocols are insufficiently developed. The purpose of this work was to understand these difficulties and avoid them. First, we needed to reduce the amount of H_2SO_4 used for hydrolysis of Ph_2SNTs in order to prevent local overheating when quenching it with ice. We have found that the yield of further extraction of the salt $[Ph_2S\text{-}NH_2]OTs$ increases when the potassium tosylate (KOTs) is used to salt it out. Its single crystal was characterized by X-ray diffraction study. It has shown that in the crystal cell $[Ph_2S\text{-}NH_2]OTs$ forms dimer with two of three O-atoms of tosylate and both H-atoms of amino-group are involved in hydrogen bonds formation. Eventually this is the reason why this substance is a stable and non-hygroscopic.

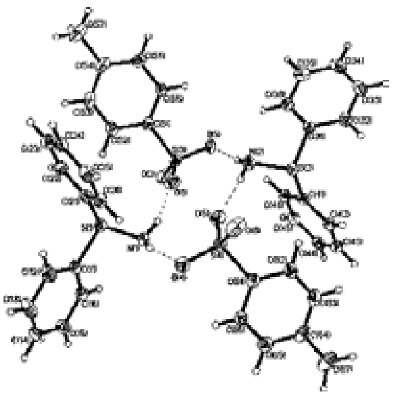


Figure 1. Dimer structure $\{[Ph_2S\text{-}NH_2]^+TsO^-\}_2$

The key stage of obtaining of $Ph_2S{\rightarrow}NH$ from $[Ph_2SNH_2]^+TsO$ is an acid-base reaction. In order to exclude any side-products for which it is optimal to use non-nucleophilic bases, such as ^{t}BuOK, ^{i}PrONa or $(Me_3Si)NNa$. The highest yield of S,S-diphenylsulfimine was achieved by using equimolar amount of ^{t}BuOK in ether at room temperature.

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SYNTHESIS OF BENZOAZINE-BASED CHROMOPHORES AND THE EFFECT OF A HETEROCYCLIC CORE ON OPTICAL PROPERTIES

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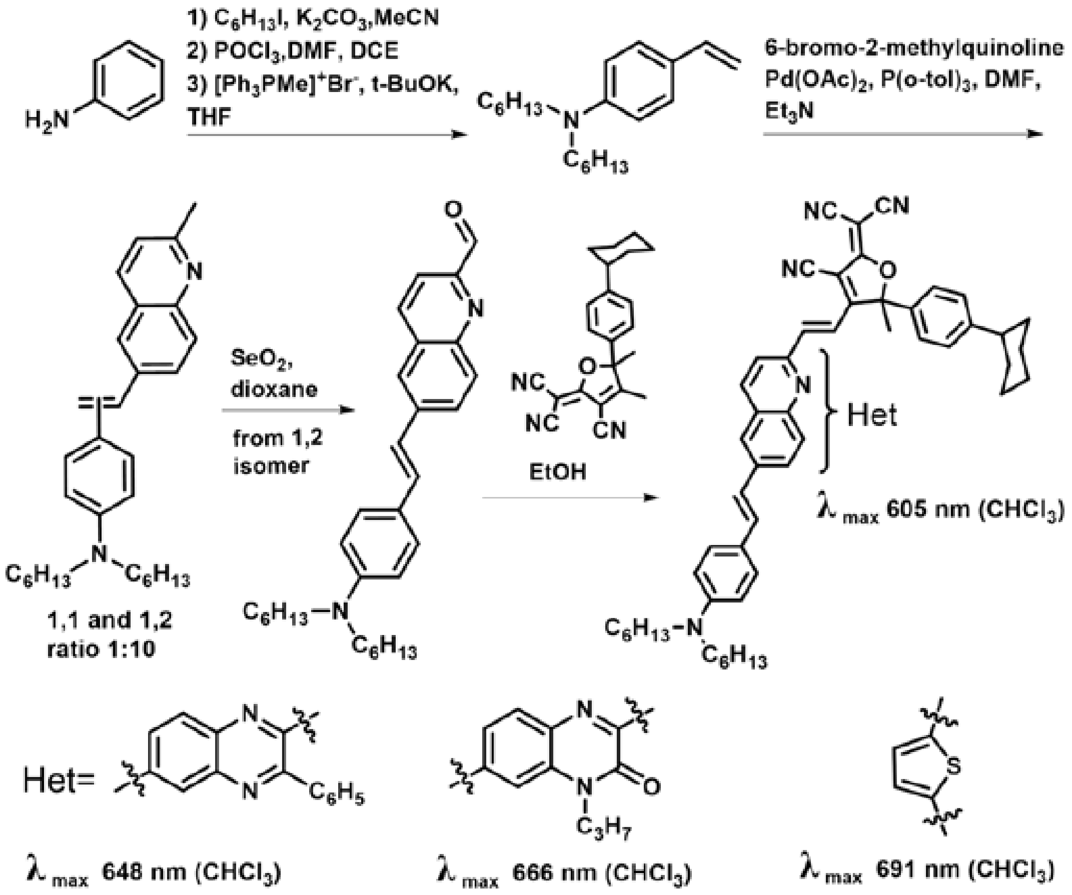
Push-pull chromophores are attracting attention when creating nonlinear-optical (NLO) materials. We have synthesized the first representative of a new class of NLO chromophores with a divinylquinoline conjugated bridge. Photophysical properties of quinoline-based chromophore were investigated both in solution and in polymer composite films. To study the effect of π-bridge heterocyclic moiety new chromophores with other benzoazine cores (quinoxaline / quinoxalin-2-one) and thiophene one were also obtained.



The work was supported by the Russian Science Foundation (grant №21-73-00060).

NANO-SIZED POLYNUCLEAR CAGES: STRUCTURAL DIVERSITY AND INDUCED CHIRALITY

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P.V. Dorovatovskii[c], I.S. Antipin[a, b]

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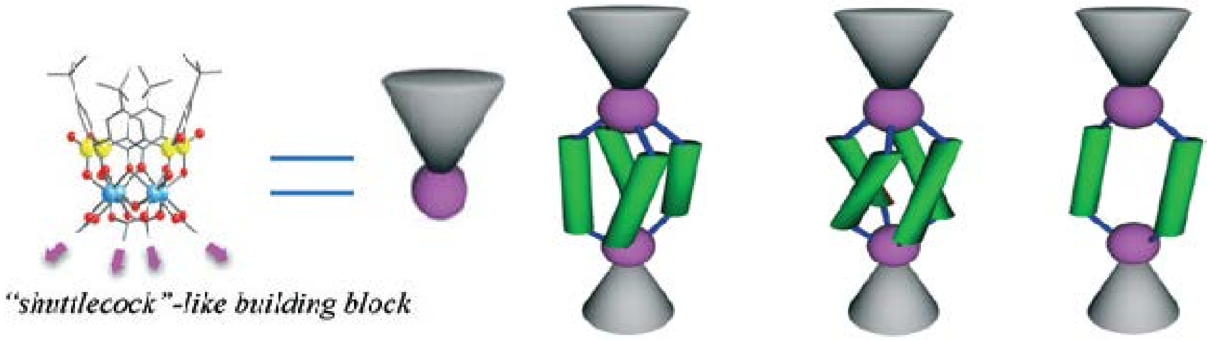
In this work, the formation of adaptative metal–organic nanocontainers or Supramolecular Coordination Cages using the three component approach based on tetrasulfonylcalix[4] arene (TSCA-4H), metallic salts and flexible succinic acid as an organic linker, was achieved. The generation of four new SCCs of three different types, displaying dimeric like structures and differing by the number of involved metallic centers and conformational behavior of succinic acid moieties, has been observed in the crystalline phase. All obtained compounds have been characterized from a structural point of view using single crystal and powder X-ray diffraction. Among them, two complexes $TSCA_2Co_8(suc)_4$ and $TSCA_2Zn_6(suc)_2$ represent the achiral symmetrical species, whereas for the other two isomorphous compounds $TSCA_2M_8(suc)_4$ - M (M = Co or Ni) induced chirality involving the hydrogen bonding between the initially achiral crystal components was observed. It was shown that the crystal structure of the obtained coordination compounds depends on the nature of the used metallic cation, the number of flexible organic linkers and the presence of co-crystallized $M^{II}(DMF)_4(OH)_2$ neutral species within the unit cell. For the obtained chiral nanocontainers, applications in the field of enantiomeric separation, recognition of chiral molecular compounds and asymmetric catalysis are currently under investigation.



The use of tetrasulfonylcalix[4]arene building blocks, when combined with other flexible organic polycarboxylate linkers containing for example longer carbon chains or additional chiral centers anchored within the linker framework, is expected to be a powerful tool to construct new functional adaptative supramolecular nanocontainers.

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This work was supported by the Russian Science Foundation (project no. 19-73-20035).

NOVEL 5,6,7,8-TETRAHYDROPYRAZINO[2,3-*C*] PYRIDAZINE-3-CARBOXAMIDE DERIVATIVES AS DUAL ALK/NUAK1 INHIBITORS

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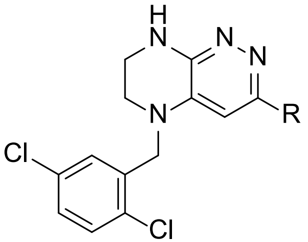
Anaplastic lymphoma kinase (ALK) has been identified in large cell lymphoma cell lines and is now a promising target for therapy of non-small cell lung cancer (NSCLC). Despite the presence of at least 4 approved ALK inhibitors in clinical practice, they are all susceptible to the emergence of resistance and have low kinase selectivity. In this work, we attempted to create a new ALK inhibitor with an improved selectivity profile.

More than 20 new derivatives of 5,6,7,8-tetrahydropyridazino[2,3-c]pyridazine-3-carboxamide of general formula **1** were synthesized, most of which inhibit ALK with an IC50 of about 2-3 nM. The compounds were found to be extremely selective and, except for ALK, inhibited only NUAK1 kinase in the nanomolar range. For the best compounds (e.g. **2**), efficacy on mutant forms of ALK, ADME, PK and *in vivo* efficacy were characterized. Studies of ADME and PK showed no inhibition of hERG at clinically relevant concentrations and low affinity for P-glycoprotein. An *in vitro* efficacy study on ALK+ NSCLC cell lines showed effective growth suppression of cell lines with IC50 in the range of 200-500 nM. In an *in vivo* experiment in murine Ba/F3-EML4-ALK xenografts compound **2** showed effective tumor growth suppression.



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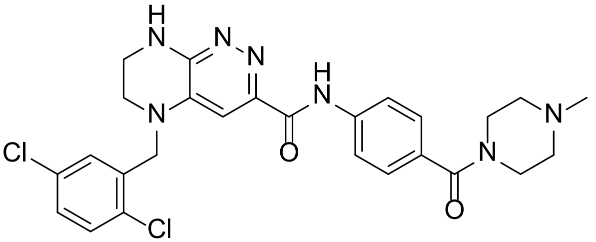

2

NEW CHROMOGENIC SYSTEM BASED ON 2-(HYDROXYPHENYL)BENZOXAZOLES

Tupaeva I.O.,[a] Vetrova E.V,[a] Gusakov E.A.,[a] Sayapin Yu.A.,[b] Krasnikova T.A.,[a]
Demidov O.P.,[c] Minkin V.I.,[a] Metelitsa A.V.[a]

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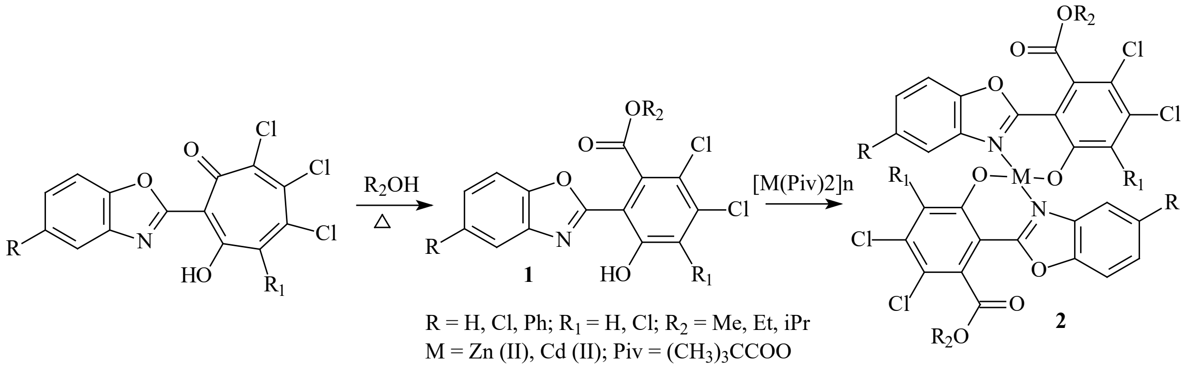
Series of novel polysubstituted 2-(hydroxyphenyl)benzoxazoles **1** was obtained by the original reaction of the contraction of the seven-membered tropone ring (scheme).



R = H, Cl, Ph; R_1 = H, Cl; R_2 = Me, Et, iPr
M = Zn (II), Cd (II); Piv = $(CH_3)_3CCOO$

The chromogenic properties of 2-(2-carbomethoxy-3,4-dichloro-6-hydroxyphenyl)benzoxazole **1** (R = R_1 = H, R_2 = Me), such as fluorescence, solvatochromism, photochromism, and its interaction with metal ions to yield fluorescent complexes have been investigated.

Compound **1** exhibits keto-enol transformations due to intramolecular proton transfer in the ground (GSIPT) states, which is adjusted by the solvent hydrogen-bond basicity. The excited-state intra molecular proton transfer (ESIPT) in molecules of **1** leads to intense fluorescence at 483-494 nm with an anomalous Stokes shift of up to 8493 cm $^{-1}$ and quantum yields of 0.08–0.19.

Ligand **1** interacts with Zn(II) and Cd(II) pivalates to yield bischelate complexes **2** (scheme). The high fluorescence efficiency, “blue” emission, with acceptable levels of resistance to photodegradation allow us to consider complexes **2** as promising luminophores for various applications, in particular, for OLEDs.

References:
1. Vetrova E.V., Tupaeva I.O., Sayapin Yu.A., Gusakov E.A., Nikolaevskii S.A., Demidov O.P., Minkin V.I., Metelitsa A.V. *Dyes and Pigments*, 2020, **180**, 108417.

This research was supported by the Russian Science Foundation № 21-73-00079, https://rscf.ru/en/project/21-73-00079/, at the Southern Federal University.

SYNTHESIS AND REACTIVITY OF SUBSTITUTED 2-(2-NITROBENZYL)FURANS

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The use of compounds of the "*furan platform molecules*" as starting compounds makes it possible to synthesis a wide range of various complex heterocycles. Among the variety of possible derivatives of furan, a special place is occupied by substrates containing in their structure an additional functional group capable of entering into a various cyclization reaction. This type of furans includes substituted 2-(2-nitrobenzyl)furans, which are difficult to access, however have high synthetic potential (Figure 1).

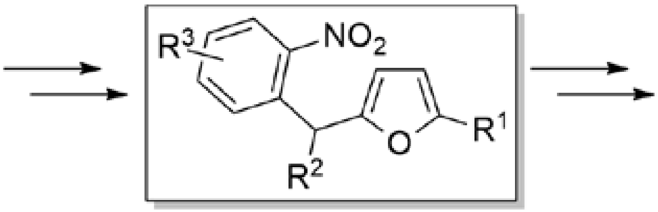

Figure 1.

The report will consider methods for the synthesis of 2-(2-nitrobenzyl)furans containing various substituents; the scope and limitations of the proposed synthetic methods are shown. In addition, the reactivity of 2-(2-nitrobenzyl)furans will be discussed.

This work was supported by Russian Science Foundation, project № 21-73-10063.

THE SYNTHESIS AND PROPERTIES OF SILOXANE-CONTAINING ESTERS AND AMIDES

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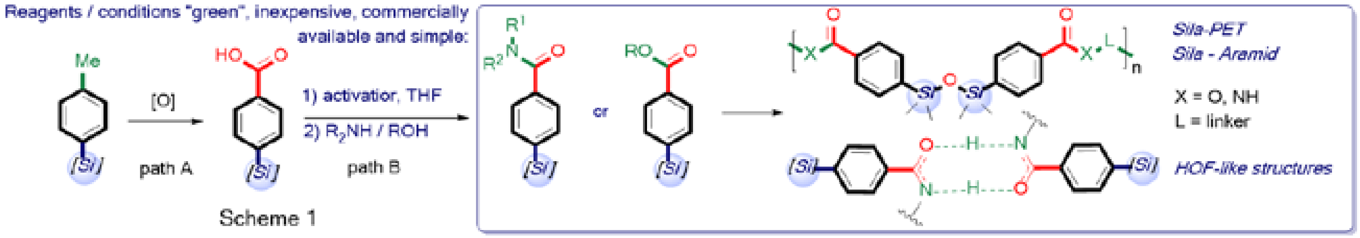
The preparation of organosilicon compounds with a "polar" functional group is one of the fundamental problems in modern organoelement chemistry that requires mild conditions and high selectivity. Previously, we proposed a highly efficient method for the preparation of *p*-carboxy-phenyl-siloxanes (*Scheme 1, path A*).[1]

This research presents a method for the synthesis of siloxane-containing amides and esters via the mild activation of carboxylic group in *p*-carboxy-phenyl-siloxanes (*Scheme 1, path B*).



Scheme 1

Amides bearing N–H-units with different chemical structures were discovered to form HOFs in crystalline state. Propargyl derivatives are perspective for "click chemistry".

Furthermore, bifunctional amines and alcohols served as precursors for the production of "*Sila*-PET" and "*Sila*-Aramid", analogs of industrially important polymers, bearing useful properties of organosilicon compounds.

References

1. Goncharova, I. K., Silaeva, K.P., Arzumanyan, A.V. et. al. *J. Am. Chem. Soc.* **2019**, *141*(5), 2143-2151.

The research was supported by a grant of the Russian Science Foundation (19-73-10172)

A NEW VERSATILE CLASS OF WATER-SOLUBLE DIARYLETHENES

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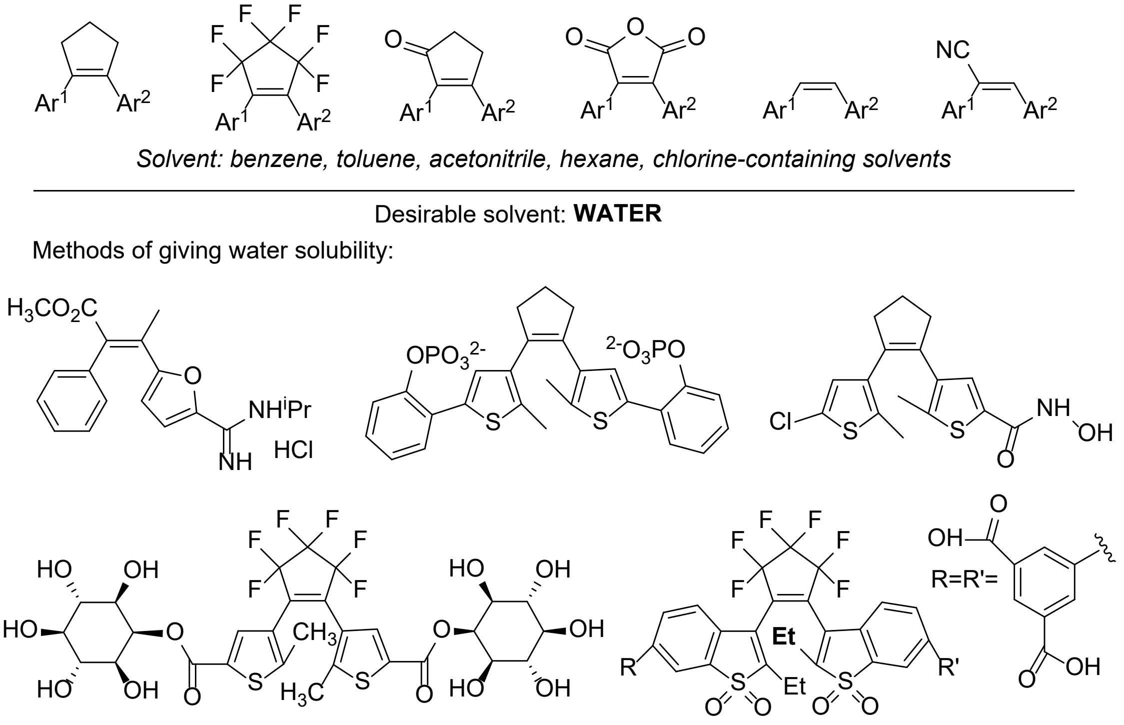
Photochemical reactions of diarylethenes (DAE) are actively used in the chemistry of materials and in organic synthesis. The vast majority of DAE are highly soluble in organic solvents, but poorly soluble in water. To increase solubility, various approaches are used, in particular, associated with the introduction of solubilizing groups (charged ions, non-ionic groups, fragments of hydrocarbons, etc.)[1]. Obviously, these methods are not universal.



Solvent: benzene, toluene, acetonitrile, hexane, chlorine-containing solvents

Desirable solvent: **WATER**

Methods of giving water solubility:

In our work, we propose the first universal class of diarylethenes, whose representatives are distinguished by excellent solubility in water. These compounds obtained from available precursors retain the full spectrum of photoactivity in water (without the addition of organic co-solvents) and undergo into irreversible reactions of oxidative cyclization and photorearrangement, as well as reversible photocyclization and *E*-/*Z*-isomerization (photochromism) depending on the structure.

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The work was supported by the Russian Science Foundation (grant 21-13-00391).

INTERRUPTED TRANSITION METAL-CATALYZED FURAN-YNE CYCLIZATION: OPTIMIZATION OF REACTION CONDITIONS

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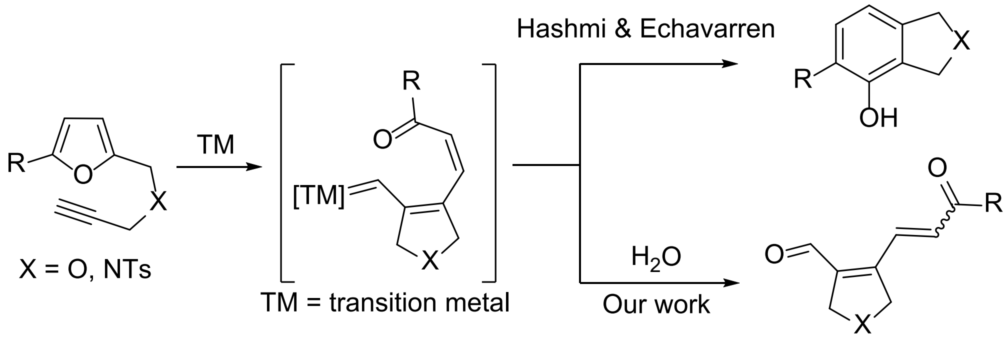
Synthesis of heterocyclic compounds via intramolecular dearomatization of the furan ring with transition metal acetylene complexes as electrophiles was proposed to be an effective synthetic strategy toward complex organic molecules.[1,2] The research groups of Hashmi and Echavarren independently reported a cascade transition metal-catalyzed transformation of furyl-tethered acetylenes into substituted phenols.[3,4] The reaction was proposed to proceed through the intermediate formation of metallocarbene species, which was experimentally supported by isolation of the dicarbonyl by-product formed via water addition to the carbine center in trace amounts.

Driven by high potential synthetic utility of such dicarbonyl compounds we started a research project aiming at finding optimal reaction conditions toward their selective formation.



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Scheme 1. Synthesis of dicarbonyl compounds

Details of the optimization studies as well as some further synthetic prospects of the obtained products will be discussed.

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This work was supported by Russian Science Foundation (project 21-73-10063).

SYNTHESIS OF NOVEL EFFECTIVE (p)ppGpp PRODUCERS' INHIBITORS

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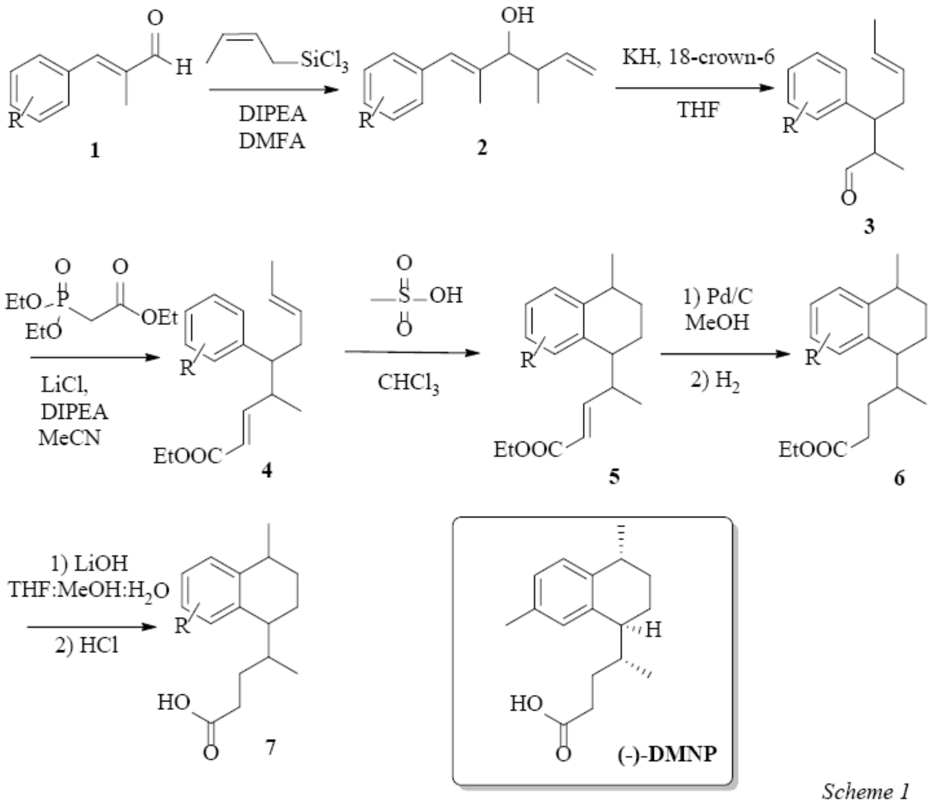
Tuberculosis (TB) is a communicable disease that is a major cause of ill health and one of the leading causes of death worldwide. Until the coronavirus (COVID-19) pandemic, TB was the leading cause of death from a single infectious agent, ranking above HIV/AIDS[1]. Bacterial persistence coupled with biofilm formation is directly associated with failure of antibiotic treatment of TB. Previously, we identified 4-(4,7-dimethyl-1,2,3,4-tetrahydronaphthalene-1-yl)pentanoic acid (DMNP), a synthetic analog of diterpene, as a lead compound that was able to suppress persistence and destroy biofilms in Mycobacterium smegmatis. DMNP targets structural sites common to RelMsm, RelZ, and presumably several other as yet unidentified (p)ppGpp producers[2]. In our search for effective (p)ppGpp producers' inhibitors, we synthesized novel derivatives DMNP (Scheme 1).



Scheme 1

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The work was supported by Russian Science Foundation (project № 18-73-10156).

CUTTING-EDGE POLYMER MATERIALS FUNCTIONALIZED WITH [1]BENZOTHIENO[3,2-b][1] BENZOTHIOPHENE (BTBT) DERIVATIVES

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[1]Benzothieno[3,2-b][1]benzothiophene (BTBT) is a promising molecule that attracts interest of researchers due to its excellent electrical performance [1-3]. Consecutive fused aromatic rings and sulfur atoms give BTBT an extensive conjugated system. Such a specific structure gives adequate spatial distribution of highest occupied molecular orbital (HOMO) for effective π-orbital overlap, leading to highly efficient charge carrier transport. In addition, large band gap (> 3 eV) of BTBT compounds has been known to afford high air-stability [4]. BTBT shows high electrical properties both in the composition of low molecular weight semiconductors and in the composition of polymer semiconductors. Recently, we developed various BTBT-based devices that show good charge mobility in different applications [5-7]. We assume that special individual mechanical and morphological characteristics of polymers functionalized with BTBT are important for producing various flexible electronic devices with high electric properties. Apart from it, such frameworks are manufacturable and low cost meaning they are essential in producing a large area electronics.

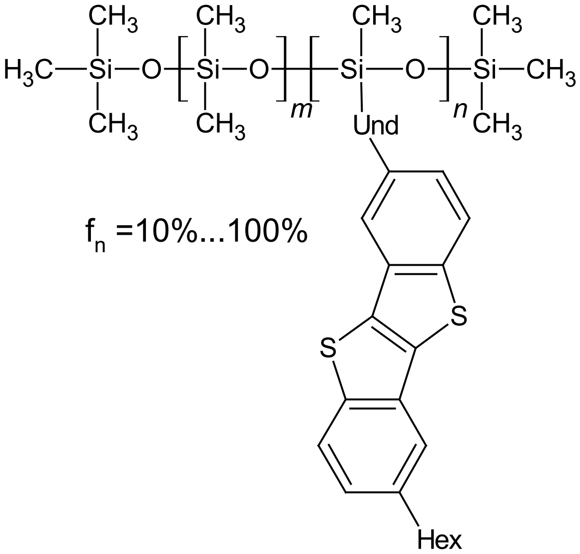

Fig.1 Scheme of polymers functionalized with BTBT-derivatives

In this work, we report on a synthesis of a range of polymers functionalized with BTBT-derivatives (Fig.1) and compare their properties. The amount of functionalized group ranges from 10% to 100%.

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This work was supported by the Russian Science Foundation (project no. 19-73-30028).

DISTANT PARTICIPATION

A NEW THREE-COMPONENT DOMINO REACTION FOR THE SYNTHESIS OF PYRROLES

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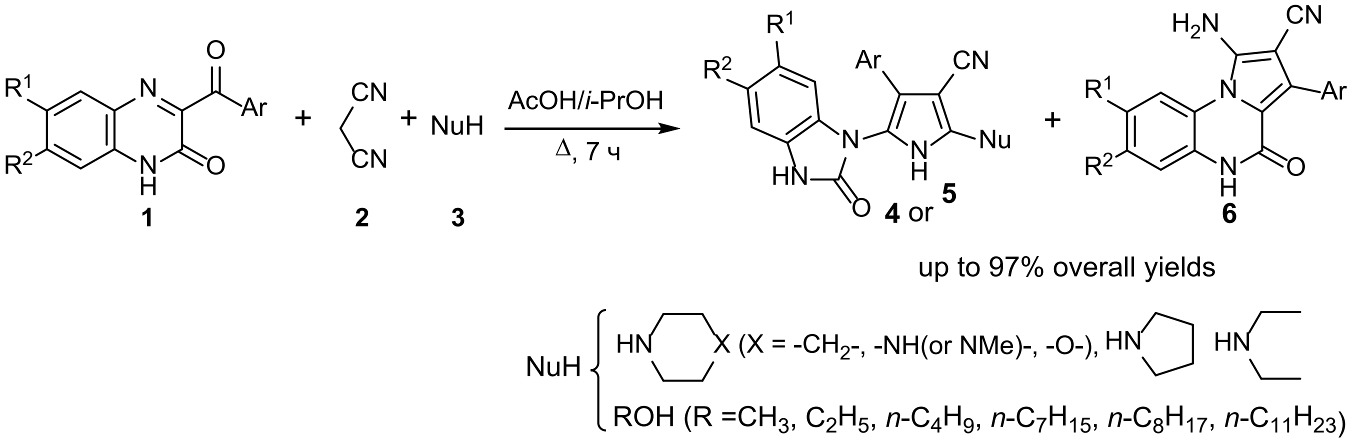
A three-component domino reaction (3-aroylquinoxalin-2-ones **1**, malononitrile **2**, and a secondary cyclic amine (or primary alcohols) **3**) as an alternative method for divergent synthesis of bi- and tri-heterocyclic fused pyrroles with different substitution patterns by varying 3-aroylquinoxalin-2-one, a secondary cyclic amine (including piperidine, morpholine, piperazine, pyrrolidine), and primary alcohol substrates has been developed. One of the competing reactions pathways proceeds by quinoxalinone–benzimidazolone rearrangement (type II Mamedov rearrangement) leading to 5-(benzimidazol-2(3*H*)-on-1-yl)pyrrolecarbonitriles **4** and **5** in good yields through amination or alkoxylation, showing that the synthetic route allows us to build libraries of pyrrole derivatives with a wide diversity of substituents. Another direction of the competing pathways gave the differently substituted patterns on the fused pyrrole frameworks **6** through intramolecular pyrrolo[*a*] annulation. Features of this strategy include the mild condition(s), convenient one-pot operation, ready availability of a variety of 3-aroylquinoxalin-2-ones, secondary cyclic amines, and primary alcohols, and excellent regio- and chemoselectivities. We hope that this new approach to the construction of functionalized pyrroles will add significantly to the modern arsenal of methods to assemble such types of rings.



This work was financially supported in part by the Russian Science Foundation (18-13-00315-п).

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DEVELOPMENT OF A TECHNIQUE FOR OBTAINING A HYDROGEL COMPOSITION BASED ON GELLAN GUM AND ALGINATE

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Researchers have defined hydrogels in different ways over the years. The most common of them is that a hydrogel is a polymer mesh swollen in water and cross-linked, obtained as a result of a simple reaction of one or more monomers. Hydrogels have received considerable attention in the last 50 years due to their exceptional prospects in a wide range of applications [1]. Thus, in this paper, several hydrogels based on harmless natural polymer compounds are considered.

Hydrogels are polymeric substances whose structure is represented by interconnected lines. Hydrogels can be used as the main candidate for the supply of medicines [2]. The concepts of regulated release, as well as drug delivery, have a tremendous impact on medical technological processes, and improve numerous available medicinal substances. Providing an opportunity to apply new methods of treatment. However, there is currently a scientific and technical obstacle in the use of hydrogels. To do this, it is necessary to create a new approach in order to eliminate the barrier, and also show the advantages in therapeutic treatment. When reacting to external stimuli, hydrogels, due to their own sensitivity, emit a medicinal substance. This role provides an opportunity to form a controlled system for the delivery of pharmaceutical substances.

This work involves the use of cyclodextrin as one of the polysaccharides for the synthesis of supramolecular hydrogel, which will have the function of transporting the drug compound and removing liquid from the environment. Cyclodextrins belong to the class of carbohydrates, namely oligosaccharides derived from starch. The main and distinguishing feature of them is the creation of host-guest complexes. For example, the creation of films based on hydrogels with embedded cyclodextrin molecules will give a more favorable interaction effect. Firstly, cyclodextrins increase the solubility of the drug, due to the formation of an inclusion complex. Secondly, polysaccharides - natural compounds that belong to renewable sources, are easily available. Due to their connection, the medicinal substance will be effective in the treatment of knee, hip joints and open wounds.

The objective of this work was to create a scientific and technical scheme for the extraction of hydrogels based on gellan gum and alginate. Cyclodextrin and sulfadimesine were considered as the released active substance. Cyclodextrins belong to the class of carbohydrates, namely oligosaccharides derived from starch. Cyclodextrins increase the solubility of the drug, due to the formation of an inclusion complex. In nature, cyclodextrins are formed with the help of soil bacteria and the enzyme cyclodextringlucotransferase.

The physicochemical, mechanical, adhesive and antibacterial properties of polymer materials based on gellan gum, alginate, cyclodextrin and sulfomedisine were investigated in the course of the work. The dependences and regularities of the composition of each component are determined by various physico-chemical methods, in particular IR spectroscopy, differential calorimetry, etc. This study confirms a relatively inexpensive, environmentally friendly, non-toxic and effective method of modifying hydrogels to deliver pH-controlled molecules. New hydrogels have also been synthesized, which are suitable as a carrier for the controlled release of therapeutic substrates.

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COMPLEX FORMATION IN THE SERIES OF PYRAZOLYL DERIVATIVES

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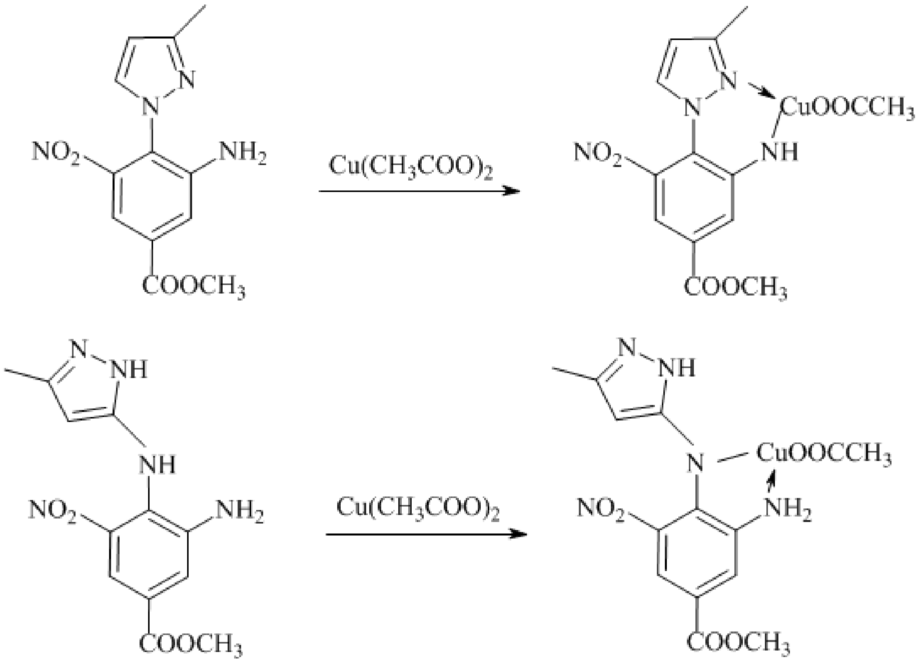
Pyrazolyl and aminopyrazolyl derivatives were obtained by the reaction of nucleophilic substitution of a chlorine atom in 3,5-dinitro-4-chlorobenzoic acid methyl ester with 3(5)-methylpyrazole and 5(3)-amino-3(5)-methylpyrazole. After selective reduction of pyrazolyl and aminopyrazolyl derivatives and subsequent reaction thereof with soluble copper salts, complexes of composition 1:1 were obtained and studied[1-3].



All reaction products were isolated, purified and characterized by spectral methods (IR-spectroscopy, ECS and mass spectrometry). The complex of the amino pyrazole derivative is more stable.

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RENEWABLE FURANS IN CYCLOADDITION REACTIONS

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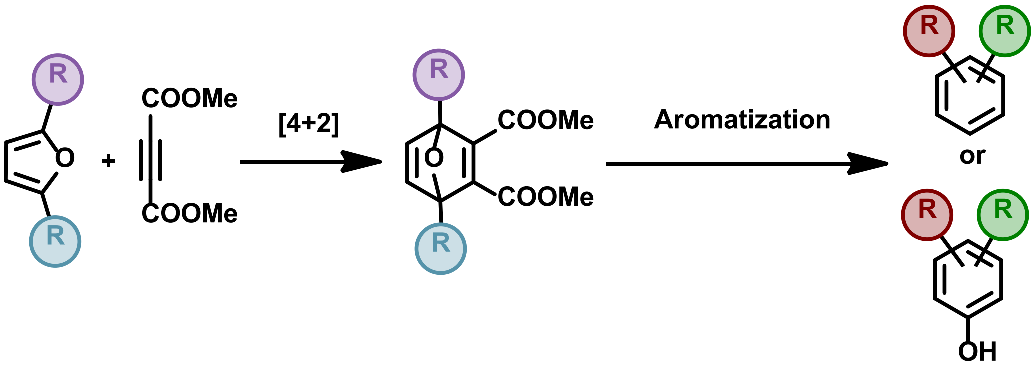
The biomass processing methodology developed in recent years opens up access to furan “platform compounds” [1], their derivatives are perceived as key elements of the transition to a renewable economy. Despite advances in the production of furans from biomass, access to aromatics is a key issue to fully address the challenge of developing a renewable chemical industry and building a sustainable carbon-neutral cycle. The transformation of furan compounds into benzene derivatives can be achieved using Diels-Alder reactions of furans with dienophiles and subsequent aromatization of the obtained adducts [2].



Scheme 1. Cycloaddition reactions of renewable furans and subsequent aromatization of adducts into benzene and phenol derivatives [3].

A systematic study of the activity of various renewable furans in the cycloaddition reaction with dimethyl acetylenedicarboxylate was made (Scheme 1). The relationship between the structure and activity of furans was analyzed experimentally and using quantum chemical calculations. A number of new 7-oxanorbornadienes have been obtained. Two catalytic systems have been developed for the aromatization of adducts into benzene and phenol derivatives.

Acknowledgment. The authors are grateful to the Scientific School program (grant NSh-5199.2022.1.3) for the support.

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TAUTOMERIC FORMS OF PYRAZOLES OF THE COUMARIN SERIES

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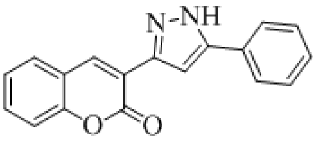
In order to study the photochemical transformations of 3-(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)coumarins and their derivatives, two pyrazoles were synthesized[1] – 3-(5-phenyl-1*H*-pyrazol-3-yl)coumarins **1** and **2**:



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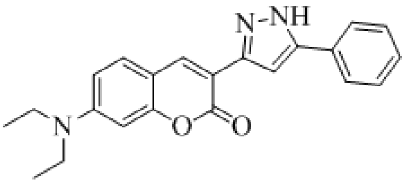
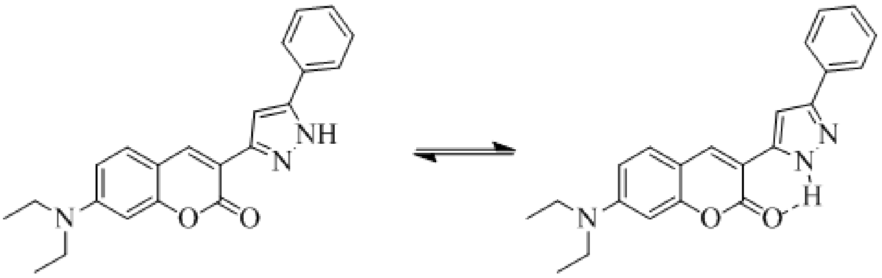


2

According to NMR data, these compounds were found to exist in DMSO-d_6 as an equilibrium mixture of tautomeric enamine forms. To identify structural isomers, their two-dimensional HH spectra were recorded in the ROESY mode. The structure of the most stable tautomer was determined by DFT calculation and X-ray powder diffraction. According to the results of the studies, it was shown that in the preferred enamine form, the NH-hydrogen of the pyrazole ring participates in hydrogen bonds with the neighboring carbonyl group of the coumarin fragment. Moreover, this connection seems to be more effective when the 7-diethylamino group is present in the coumarin residue:



2, enamine form **I** **2**, enamine form **II**

The found structural features of the 3-(5-phenyl-1*H*-pyrazol-3-yl)coumarins can be of interest for an objective assessment of the mechanisms of the biological activity of 3,5-diaryl-1*H*-pyrazoles.

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N-CYANOACETYLATION OF HETEROCYCLIC AMINES AS THE ROUTE TO N,S-POLYHETEROCYCLIC COMPOUNDS

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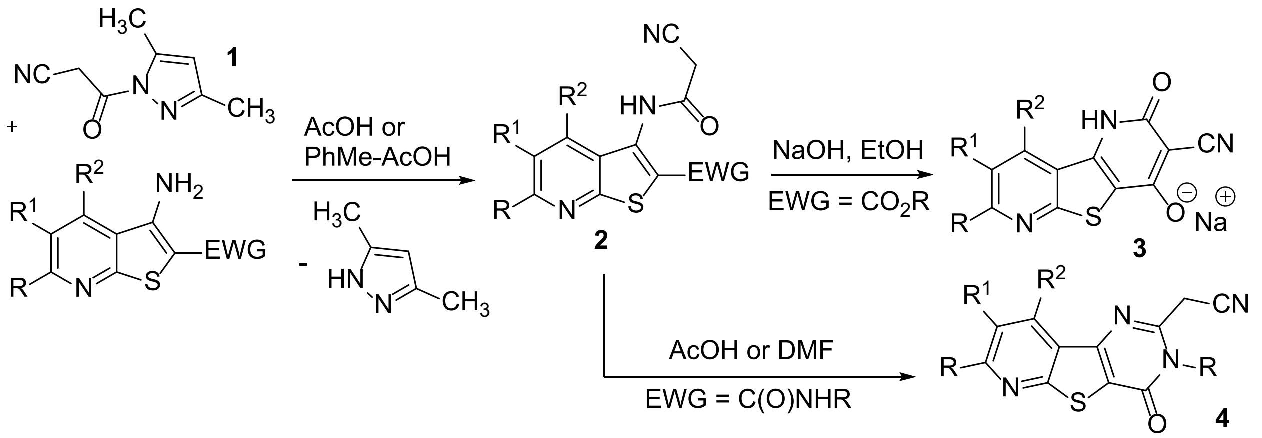
Cyanoacetamides are important reagents for the preparation of a variety of heterocyclic systems and biologically active compounds. N-(Cyanoacetyl)-3,5-dimethylpyrazole **1** has been recognized as the one of the most convenient reagents for cyanoacetylation [1-3]. We obtained a series of new N-(hetaryl)cyanoacetamides by reaction of azolide **1** with heterocyclic amines. Further cyclization of cyanoacetamides **2** afforded thieno[2,3-b]pyridines **3**,**4** of the expected biological activity.



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This work was financially supported by the Administration of the Krasnodar Region and the Russian Foundation for Basic Research (project no. 19-43-230007 p_a_) and the Ministry of Education and Science of the Russian Federation (topic 0795-2020-0031).

DOMINO REACTIONS OF *N*-(PROPARGYL)INDOLE-2-CARBONITRILES

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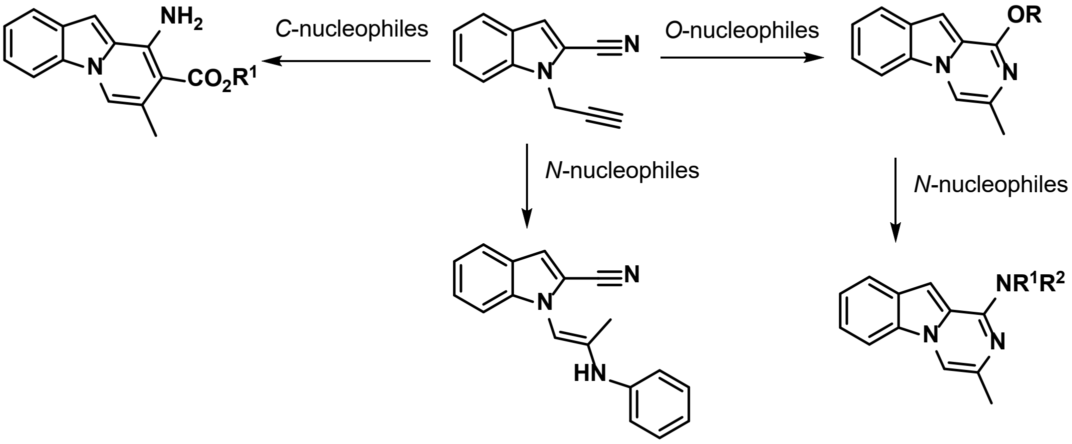
N-(Propargyl)indole-2-carbonitriles can act as valuable precursors for obtaining annulated indoles. In this work, we studied their reactions with various *O*-, *C*-, and *N*-nucleophiles. It turned out that valuable heterocyclic products, pyrazino[1,2-*a*]indoles, can be obtained in reactions with alcohols [1]. Control experiments show that the reaction starts with an alkyne-allene rearrangement followed by the formation of imidate. Nucleophilic cyclization of the imidate at the allene moiety completes the sequence. Interaction with such C-nucleophiles as nitromethane or diethylmalonate results in the formation of another heterocyclic system, pyrido[1,2-*a*] indoles [2]. The use of *N*-nucleophiles makes it possible to effectively isolate the products of allene hydroamination, and one-pot conversion of *N*-(propargyl)indole-2-carbonitriles to 1-aminopyrazino[1,2-*a*]indoles.



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The work was prepared with the support of the RUDN Program of Strategic Academic Leadership, RFBR and Moscow Government grant № 21-33-70007.

β-CARBOLINES: A GENERAL METHOD FOR THE SYNTHESIS OF ALKALOIDS NORHARMANE, EUDISTOMINE O, AND BAUERINES A-C

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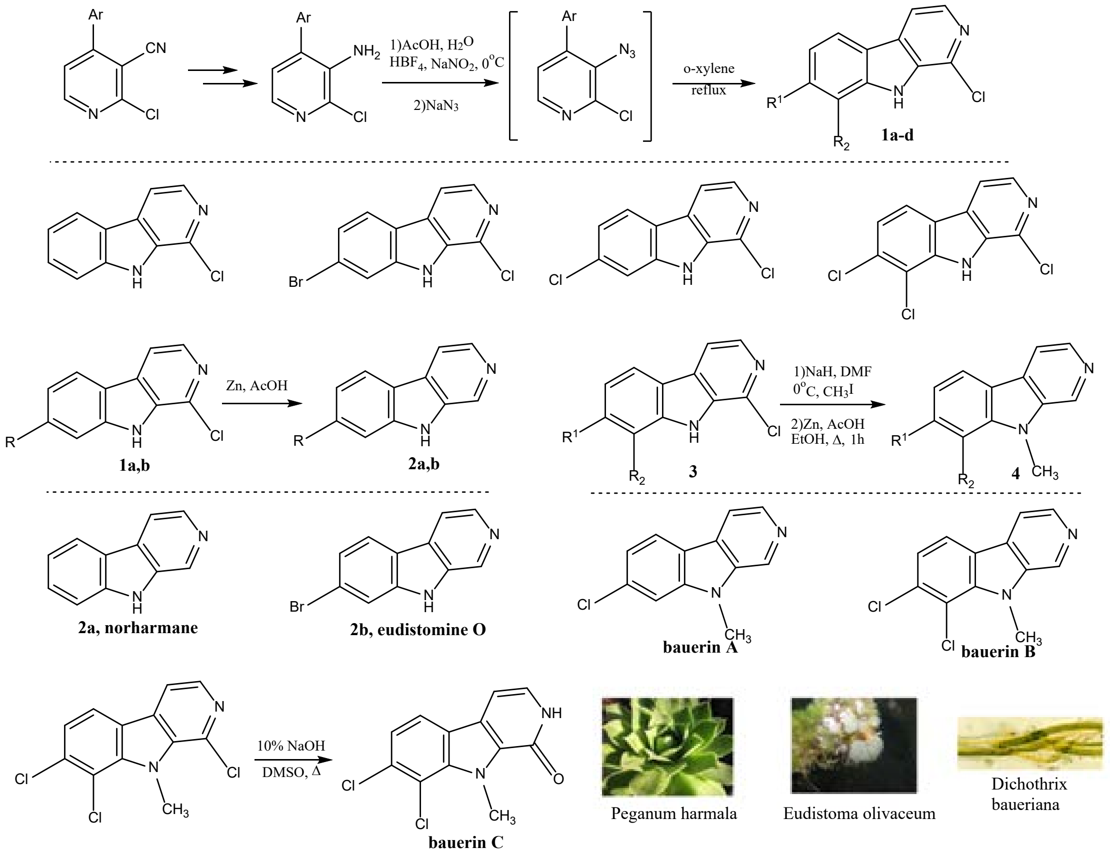
A new scheme for the synthesis of β-carboline alkaloids has been developed, which makes it possible to introduce halogen atoms into specified positions of the benzene ring. This made it possible to create a general method for the synthesis of four β-carboline alkaloids. Thermolysis of 3-azido-4-arylpyridines was used to obtain 1-chloro-β-carbolines **1a–1d** substituted in the benzene ring. Reductive dechlorination of 1-chloro-β-carboline **1a** and 1-chloro-7-bromo-β-carboline **1b** Zn in AcOH/EtOH gave norharman **2a** and eudistomin O **2b**.



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SYNTHESIS OF RHODAMINE-4(5)-ISOTHIOCYANATE

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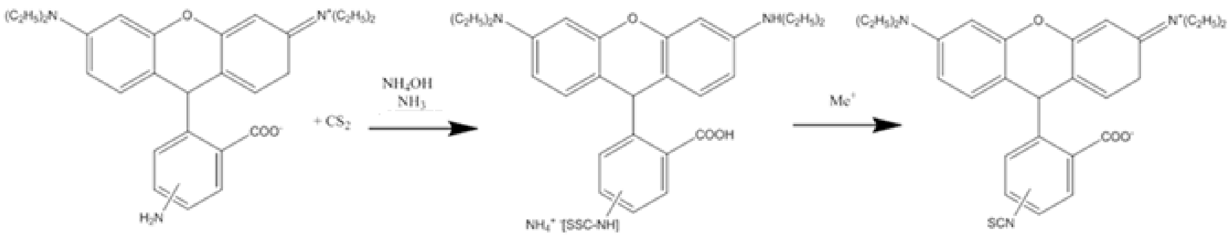
For the rapid diagnosis of viral infections, immunofluorescence staining is used in medicine, which is based on the interaction of an antigen with antibodies labeled with fluorochrome found in cells and tissues.

Xanthene dyes from the alkylrodamine class, namely rhodamine isothiocyanate (RITZ), are used in analytical chemistry, fluorescence microscopy biotechnology for the preparation of luminescent serums and in medicine as fluorescent protein taps for the rapid diagnosis of viral infections.

The preparation of this compound by the treatment of tetraethylaminorodamine with thiophosgene in an acetone medium was described earlier [1,2]. We have developed a method for obtaining rhodamine isothiocyanate by thermal decomposition of heavy metal salt rhodamine-4(5)-dithiocarbomate, in a technological way that provides a high yield and the necessary purity of the final product -4(or5)-isothiocyanates according to the above scheme, by the reaction of tetraethylaminorodamine with carbon disulfide in the presence of ammonia with the formation of ammonium salt rhodamine-dithiocarbamic acid, obtaining heavy metal salt from it and its thermal decomposition of salt.



Spectral characteristics of the obtained dyes:

	Wavelength, λ, nm	Intensity in dimethylformamide, E_1	Intensity in ethyl alcohol, E_2
RITZ-4	558	7700	6800
RITZ-5	560	9100	8750

The substances showed a high intensity of luminescence. Binding to proteins 90%.

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СИНТЕЗ ФЛУОРЕСЦЕНТНЫХ 1-АРИЛ-3-АРИЛЭТЕНИЛ-1*H*-ПИРАЗОЛОВ

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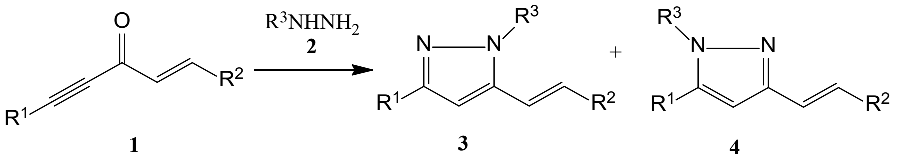
Полизамещенные производные пиразола представляют интерес в качестве фотоактивных материалов, флуоресцентных материалов, материалов для нелинейной оптики, компонентов жидких кристаллов, органических фотопереключателей. Поэтому разработка новых подходов к синтезу таких соединений является актуальной задачей [1].

Особый интерес представляют производные пиразолов, содержащие в качестве заместителей ненасыщенные фрагменты (–C=C–, –C≡C–)[2, 3]. Одним из возможных путей к синтезу подобных соединений является циклоконденсация сопряженных енинонов с замещенными гидразинами. Однако известно, что взаимодействие винилацетиленовых кетонов с арилгидразинами может протекать с образованием двух изомерных пиразолов (схема 1) [2].

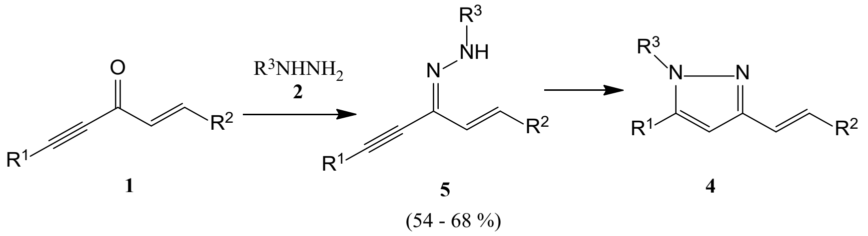
Схема 1.



В работе [4] было показано, что в реакциях арил- и гетарилзамещенных кросс-сопряженных енинонов с арилгидразинами, проводимых в нейтральной среде (этанол), происходит образование 5-арилэтенил-1H-пиразолов **3** (атака β-атомом азота гидразина по β-атому углерода тройной связи). В продолжение этой работы, для тех же исходных веществ **1**, **2**, были подобраны условия селективного синтеза изомеров этих соединений – 3-арилэтенил-1H-пиразолов **4**.

Для этого синтез проводился в 2 этапа. На первом этапе создавались условия селективного образования арилгидразинов енинонов (схема 2). Для этого реакцию проводили в кислой среде, что способствовало протонированию карбонильной группы и способствовало увеличению электрофильности соответствующего 3-го атома углерода сопряженной пентады енинона.

Схема 2.



a: $R^1 = R^2 = R^3 = Ph$; b: $R^1 = p$-Tolyl, $R^2 = R^3 = Ph$; c: $R^1 = R^3 = Ph$, $R^2 = $ 2-Furyl; d: $R^1 = R^3 = Ph$, $R^2 = p\text{-}O_2NC_6H_4$;
e: $R^1 = p\text{-}MeOC_6H_4$, $R^2 = R^3 = Ph$; f: $R^1 = R^3 = Ph$, $R^2 = o$-Tolyl;
g: $R^1 = R^2 = $ 5-Bromo-2-furyl, $R^3 = Ph$; h: $R^1 = R^3 = Ph$, $R^2 = p\text{-}ClC_6H_4$;
i: $R^1 = R^3 = Ph$, $R^2 = $ p-Tolyl; j: $R^1 = R^2 = Ph$, $R^3 = p\text{-}FC_6H_4$; k: $R^1 = H$; $R^2 = R^3 = Ph$.

Ранее [4] не удалось подобрать условия циклизации этих соединений в производные пиразола или пиразолина. Мы же показали, что при кипячении гидразонов **5** в ДМФА в течение 1 ч происходит образование продуктов циклизации гидразонов - пиразолов **4**. Пиразолы представляют собой бесцветные или светло-желтые, устойчивые при хранении кристаллические соединения.

Их строение и состав подтверждается данными спектроскопии ЯМР ^{1}H и ^{13}C и данными элементного анализа.

Исследованы спектрально люминесцентные характеристики полученных соединений: измерены спектры поглощения и люминесценции, определены коэффициенты экстинции, стоксовы сдвиги, оценены относительные квантовые выходы.

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SYNTHESIS OF A TARGETED DELIVERY SYSTEM OF A CHLORIN-e_6 PHOTOSENSITIZER TO TUMOR CELLS BY USING A BIOORTHOGONAL REVERSED ELECTRON DEMAND DIELS-ALDER REACTION

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Photodynamic therapy is currently an effective method of treating and diagnosing cancer, and chlorin-based photosensitizers are widely used in clinical practice. Their main disadvantage is the low selectivity of accumulation in tumor cells, which can lead to damage to healthy tissues.

Synthetic scheme for hybrid biological vector consisting of a targeted fragment (biotin), a linker and a tetrazine has been developed. A photoactive (therapeutic) agent based on chlorin-e_6 [1] selectively binds to the tetrazine fragment *in vivo* using the Diels-Alder reaction and forms a photoactive system that generates singlet oxygen when irradiated, thereby causing the death of a tumor cell (Fig. 1.).

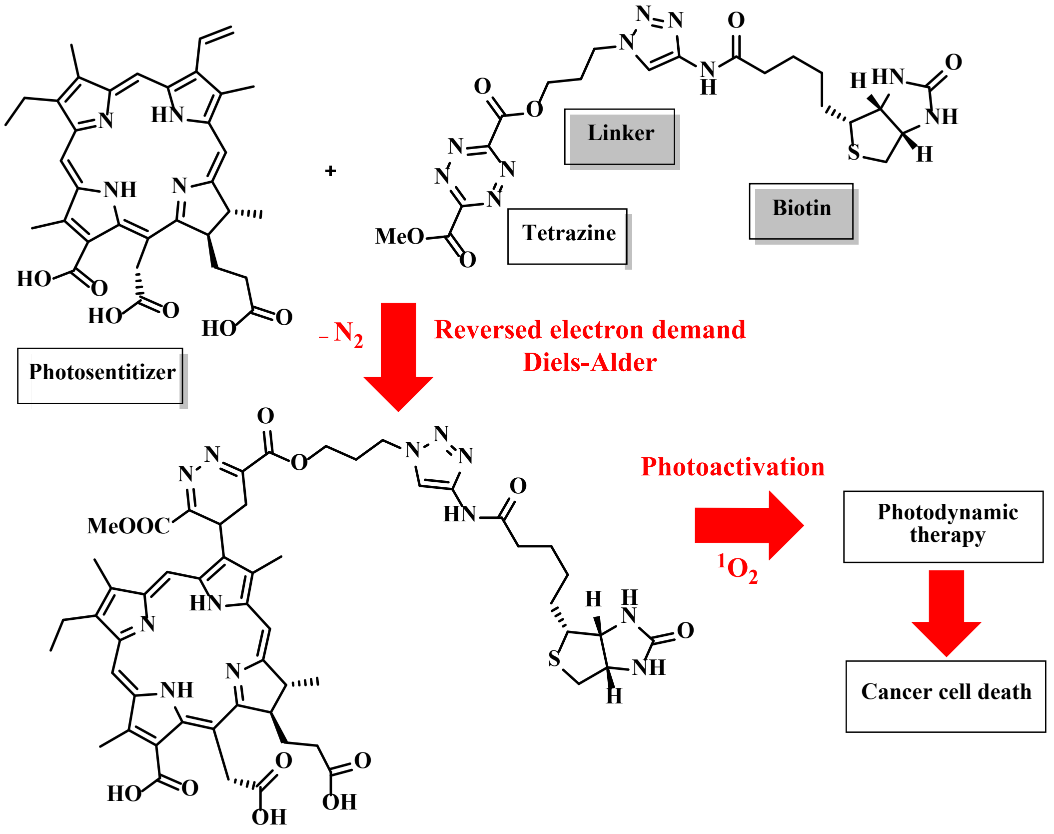

Fig. 1. Strategic molecules for targeted photosensitizer delivery and subsequent formation of a photoactive system

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[1] Otvagin V. F., Nyuchev A.V., Kuzmina N.S., Grishin I. D., Gavryushin A. E., Romanenko Yu. V., Koifman O. I., Belykh D. V., Peskova N. N., Shilyagina N.Yu., Balalaeva I. V., Fedorov A. Yu. // European Journal of Medical Chemistry. 2018. vol. 144. pp. 740-750.

The proposed synthesis technique and the resulting conjugate can become the basis for the creation of new targeted diagnostic and/or therapeutic drugs. *This work was supported by the Russian Science Foundation under Grant No. 21-73-10230.*

SYNTHESIS OF ANALOGUES OF FURAN CHALCONES AND THEIR REACTIONS WITH BENZENE IN BRØNSTED AND LEWIS SUPERACIDS

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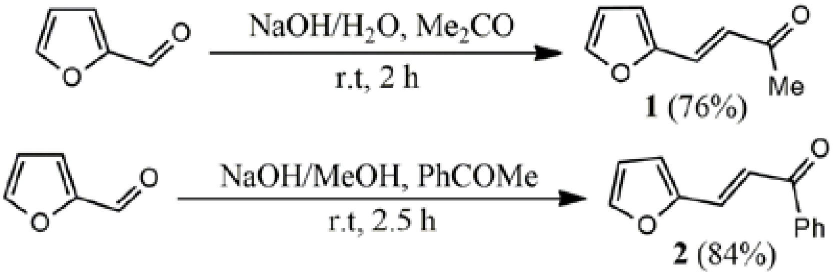
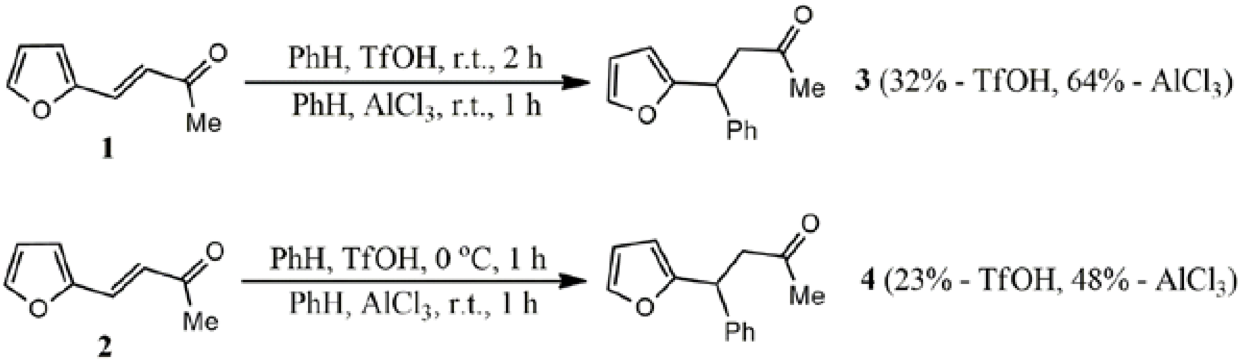
Currently, much attention is paid to the processing of renewable wood and plant raw materials. Various ways of replacing of non-renewable raw materials, oil, and natural gas, by renewable ones, wood, plants, and agricultural waste, are being actively developed. Furfural, 5-hydroxymethylfurfural (5-HMF) and other furan derivatives obtained by chemical processing of renewable plant resources are actively used as secondary energy resources, in the production of synthetic resins, lacquers, polymers, as well as for the synthesis of medicines.

In this work, furan analogues of chalcones **1** and **2** have been synthesized from furfural by condensation with acetone and acetophenone, respectively.



We have found, that under superelectrophilic activation conditions with Brønsted superacid CF_3SO_3H (triflic acid, TfOH) or strong Lewis acid ($AlCl_3$), compounds **1** and **2** in reaction with benzene give rise to products of hydrophenylation of the side chain carbon-carbon double bond, compounds **3** and **4**, respectively. The yields of target products are higher in $AlCl_3$-promoted reactions.



The obtained compounds open up new possibilities for synthesis of furan derivatives based on products of processing of plant raw materials.

SYNTHESIS AND STUDY OF WATER-SOLUBLE UNSYMMETRICAL CATIONIC PORPHYRINS AS POTENTIAL PHOTOINACTIVATORS OF PATHOGENS

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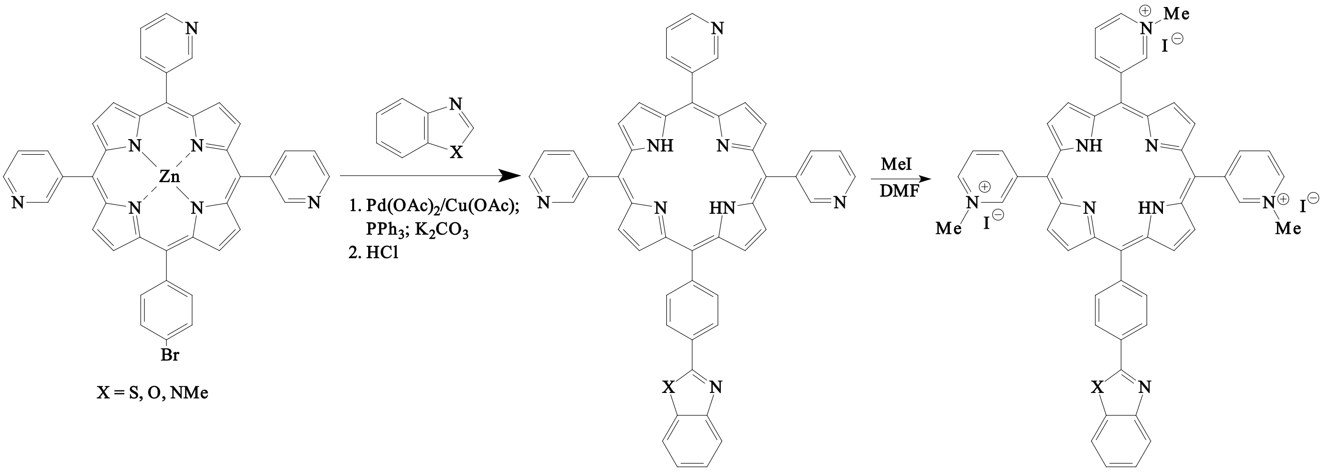
Photodynamic inactivation is the most promising method for combating drug-resistant pathogens. Its undeniable advantage is its indirect effect on the pathogen and, for this reason, the absence of addiction to the drug. A promising target for pathogens is genetic material. For intercalation targeting of a photosensitizer to DNA, the photosensitizer must be in its cationic form. In this case, the "tuning" of the photochemical and complexing properties of the photosensitizer can be carried out by introducing heterocyclic fragments of molecules into the composition of peripheral substituents. The purpose of this work was to introduce benzoxazole, N-methylbenzimidazole, and benzothiazol residues into the porphyrin molecule using the CH-activation method [1, 2] and study the effect of the heterocyclic porphyrin substituent on binding to DNA.

A targeted synthesis of water-soluble triiodides of 5-[4'-(1,3-heterocycl-2-yl)]phenyl]-10,15,20-tris(3'-N-methyl-pyridyl)porphins was carried out. To "introduce" a heterocyclic fragment into the porphyrin molecule, the strategy of palladium-catalyzed coupling of bromoporphyrin and heterocycle was chosen. The starting 5-(4'-bromophenyl)-10,15,20-tris(3'-pyridyl)porphine was obtained by the condensation of pyrrole and a mixture of 3-pyridaldehyde and 4-bromobenzaldehyde, which was further converted into a Zn complex for the subsequent stage of hetarylation. The hetarylation reaction takes an average of 48 hours to form hetarylporphyrins. The reaction products were separated using column chromatography. The quartenization reaction took place in DMF at boiling for an hour.



Scheme 1. Synthesis of asymmetric cationic porphyrins

It has been established that the synthesized porphyrins with DNA form semi-intercalation complexes with abnormally high affinity, which makes it possible to count on the inhibitory ability of genome replication.

The work was conducted with financial support of RSF No. 21-73-20140.

PROMISING MATERIALS FOR THE PRODUCTION OF LABORATORY CHEMICAL FDM MICROREACTORS

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The production of individual laboratory chemical equipment using additive technologies (3D printing) is a complex but relevant task. Recently, the demand for such products in fine organic synthesis and other various fields has increased significantly [1–3], since 3D printing allows organizing compact production directly in a scientific laboratory and allows optimizing the design of products in a short time.

The purpose of this study is to search for modern thermoplastic materials that can be used for the production of laboratory chemical reactors. The range of materials studied included polylactide (PLA+), thermoplastic polyurethane (TPU), polycarbonate (PC), polyamide (PA), carbon fiber filled polyamide-6 (PA6-CF), polypropylene (PP), and glass fiber filled polypropylene (PP- GF). Determination of the mechanical strength of FDM products in the form of standard samples was carried out using a universal testing machine. It is shown that the strength of materials decreases in the series: PA6-CF > PC > PLA+ > PP-GF > PA > TPU > PP. The chemical stability of materials was studied in an experiment specially designed by the authors for a number of the most common organic solvents. It has been shown that PA6-CF, PA, PP-GF, PP are stable in these solvents for 24 hours. PLA+, TPU and PC are stable for 24 hours only in ethanol, in the environment of other solvents they have different degrees of stability.

Within the framework of this work, it is planned to carry out transfer hydrogenation reactions on Pd-NHC catalysts in FDM-printed tubes and compare the results obtained with the data established during reactions in standard glass tubes, in addition, it is planned to develop a methodology for the production of structured catalytic cartridges by extrusion fusing using thermoplastic materials filled or coated with catalytically active particles. Study of the efficiency of the obtained catalytic systems in fine organic synthesis reactions is anticipated.

Acknowledgment. The authors are grateful to the Scientific School program (grant NSh-5199.2022.1.3) for the support.

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СИНТЕЗ НОВЫХ ФУНКЦИОНАЛЬНО ЗАМЕЩЕННЫХ ИЗОИНДОЛОВ, ПИРИДО[3′,2′:4,5]ПИРРОЛО[2,1-*a*]ИЗОИНДОЛОВ И СПИРОБЕНЗОФУРАН-2,1′-ИЗОИНДОЛИНОВ

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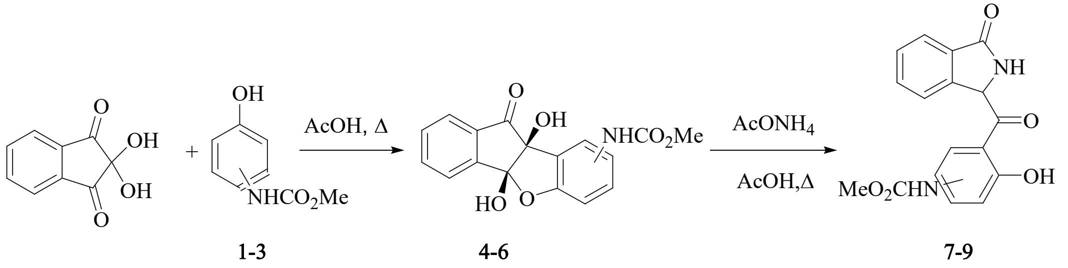
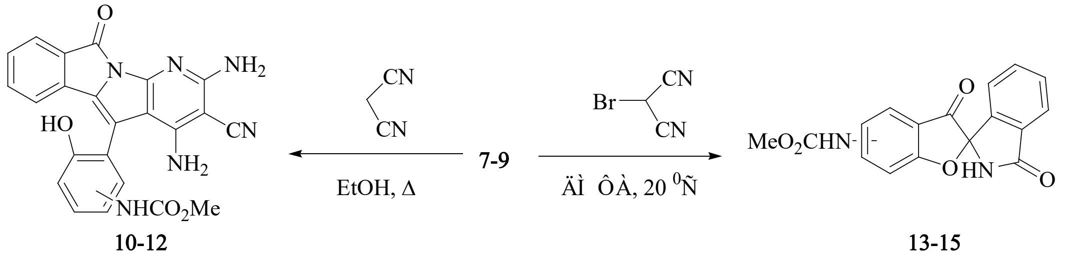
Аддукты фенолов с нингидрином представляют собой ценные соединения в синтезе новых конденсированных и спирогетероциклических соединений.

Ранее нами сообщалось о получении аддуктов (**4**-**6**) взаимодействием изомерных гидроксизамещенных метил-N-фенилкарбаматов (**1**-**3**) с нингидрином в уксусной кислоте [1]. В данной работе нами изучена *one-pot* реакция нингидрина с фенолами (**1**-**3**) в ледяной AcOH, при последующем добавлении к реакционной массе ацетата аммония. Установлено, что реакция приводит к получению производных изоиндола (**7**-**9**) с выходом (65-67%).



Изоиндолы **7-9** далее введены в реакцию с малононитрилом в присутствии Et_3N и моноброммалононитрилом в ДМФА в присутствии K_2CO_3. Установлено, что реакции приводят к получению соответственно конденсированных систем **10-12** (выход 70-74%) и спиросоединений **13-15** (выход 65-72%**).**



2-$NHCO_2Me$ (1,4,7,10,13); 3-$NHCO_2Me$ (2,5,8,11,14); 4-$NHCO_2Me$ (3,6,9, 12,15).

Строение новых соединений доказано методами ИК, ЯМР^{1}H, ^{13}C спектроскопии.

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DARZENS CONDENSATION IN THE SYNTHESIS OF (-)-MENTHYL-3-ARYLGLYCIDATES

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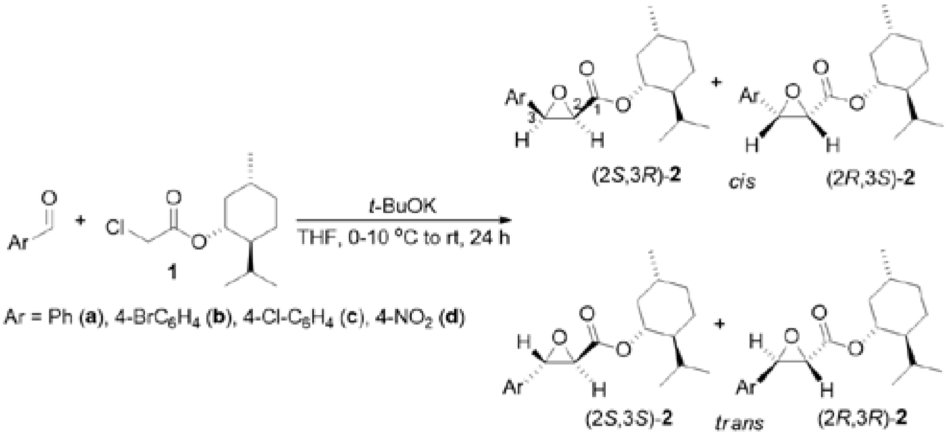
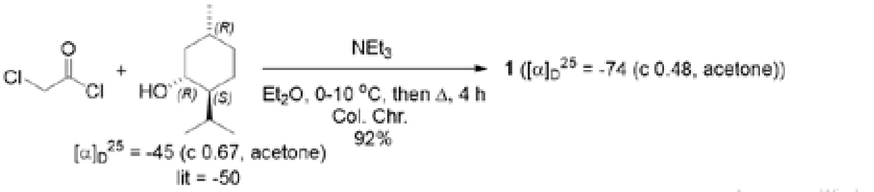
Menthyl-3-arylglycidates are obtained by the reaction of aromatic aldehydes with (-)-mentylchloroacetate under the Darzens condensation condition.1 The introduction of a chiral fragment into the molecule made it possible to observe the formation of four enantiomers in the 1H NMR spectra of the crude products. During prolonged standing (48 h) of the Darzens condensation products, one of the *cis* enantiomers in each case crystallized in an oily mixture and was easily separated from the oil. One of the trans enantiomers was isolated by column chromatography in each case. The configuration of all chiral carbon atoms in crystalline samples *cis* and *trans* **2a-d** was determined by X-ray single crystal analysis.

(-)-Mentylchloroacetate **1** was synthesized from (-)-menthol and chloroacetyl chloride.





This work was financially supported in part by the Russian Science Foundation (18-13-00315-n).

Reference

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SYNTHESIS AND REARRANGEMENT OF 3-HYDROXY-4-ARYL-3,4,5-TRIHYDRO-2*H*-BENZ[*B*][1,4] DIAZEPIN-2(1*H*)-ONES

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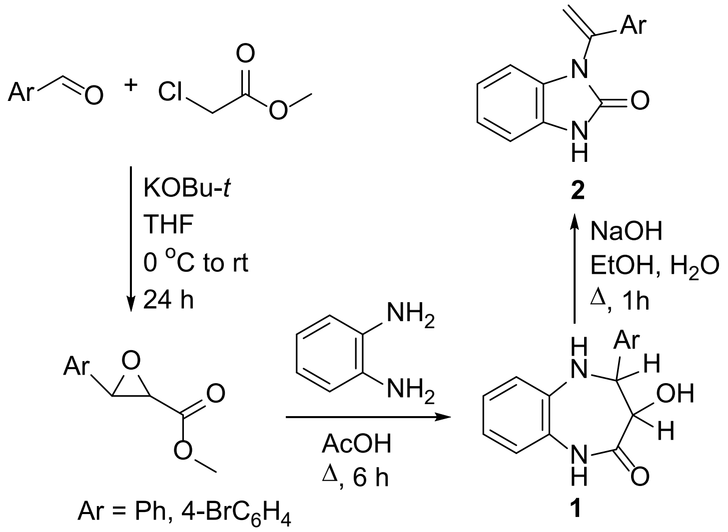
3-Hydroxy-4-aryl-3,4,5-trihydro-2*H*-benz[*b*][1,4]diazepine-2(1*H*)-ones (**1**) were obtained by heating at reflux in AcOH the mixtures of *o*-phenylenediamine and corresponding 3-aryl glycidates synthesized, in turn, under Darzens condensation condition from aromatic aldehydes and methyl chloroacetate.1 Diazepine-2-ones **1** were subjected to the rearrangement with the formation of 1-(1-arylvinyl)-1*H*-benzo[d]imidazolo-2(3*H*)-ones (**2**) under refluxing in an aqueous alcoholic alkaline solution.



This work was financially supported in part by the Russian Science Foundation (18-13-00315-n).

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NOVEL CLICK PRECURSORS ON THE BASE OF THIA- AND CALIX[4]ARENE DERIVATIVES WITH FREE LOWER RIM

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Calix[4]arenes are cyclic macromolecules consisting of four phenolic fragments linked together by methylene groups (or thiol groups in the case of thiacalix[4]arenes). The presence of several reaction centers (upper and lower (-OH groups) rim) in their structure makes it possible to obtain compounds containing various functional groups, as well as exhibiting certain specified properties. The introduction of azide fragments into the structure of calix[4]arenes makes it possible to use these macrocycles as reagents in "click reactions" to obtain a wide range of water-soluble compounds under mild conditions.

As a result of this work, a procedure for obtaining a universal synthetic platform based on thia- and calix[4]arene derivatives was developed. This strategy consists in consecutive azo coupling (or nitration for thiacalixarene derivatives), reduction and diazotization reactions (Fig. 1). The obtained tetraazide derivatives can be used to obtain various triazoles with free hydroxyl groups, which can be modified with the necessary functional fragments.

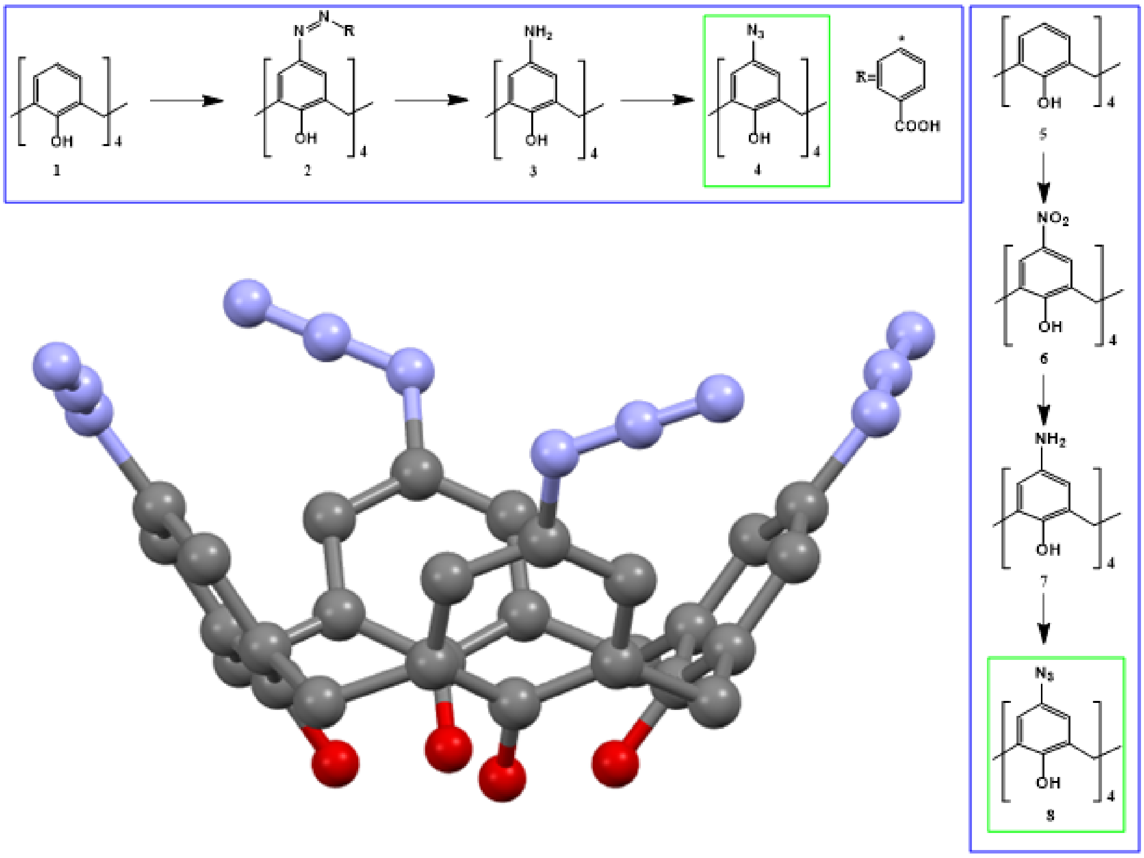

Fig.1. Synthetic strategy for obtaining target compounds and X-ray diffraction of calixarene 4

This work was supported by Russian Scientific Foundation № 21-73-10062.

DIVERSITY-ORIENTED SYNTHESIS OF PHOSPHACOUMARINES AND BENZOXAPHOSPHOLENES FROM 2-ALKENYLPHENOLS

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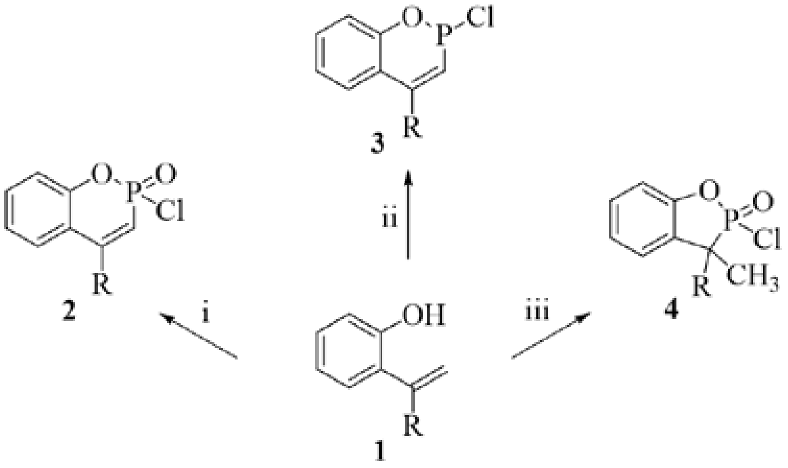
An increasing interest in the development of the synthesis methods of phosphorus-containing heterocycles in recent decades is due to wide spectrum of their biological activity[1-3].

Herein, we report a facile diversity-oriented synthesis of phosphacoumarines and benzoxaphospholenes from 2-alkenylphenols. We have found that the reaction of 2-alkenylphenols (**1**) with phosphorus pentachloride leads to the formation of phosphacoumarins (**2**). The interaction of 2-alkenylphenols (**1**) with phosphorus trichloride leads to the cyclization and formation of chlorophosphorines (**3**). When catalyzed by Lewis acid, the main reaction pathway became the formation of benzoxaphospholenes (**4**).



i.1.PCl_5,2.SO_2; ii. PCl_3; iii.PCl_3, $ZnCl_2$

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This study was funded by Russian Science Foundation grant № 22-23-01134, https://rscf.ru/project/22-23-01134/

SYNTHESIS OF THE PRINCIPAL BUILDING BLOCKS OF AMPHIDINOLIDE FAMILIES B, D, G, H, L

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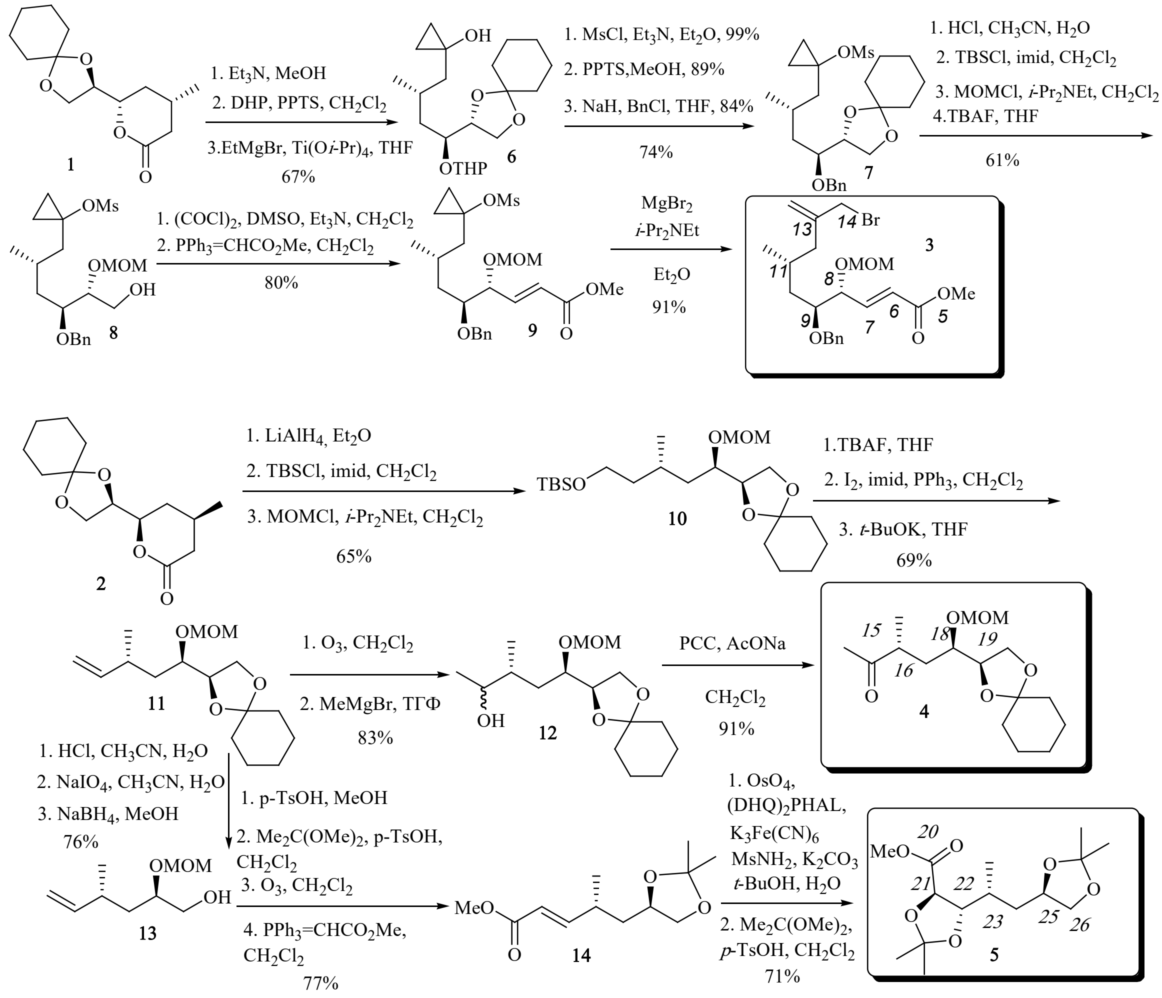
Lactones **1** and **2** obtained by diastereoselective allylation reactions followed by reduction were used in a divergent scheme for the synthesis of the main building blocks of amphidinolide families B, D, G, H, L **3**, **4**, **5**.



A QUANTUM-CHEMICAL STUDY OF N-METHYL-N'-METHOXYDIAZEN-N-OXIDE THERMAL DECOMPOSITION MECHANISM

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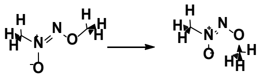
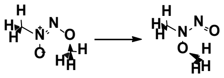
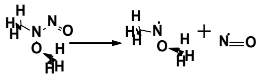
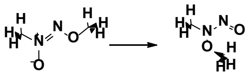
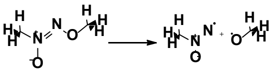
Alkoxy-NNO-azoxy compounds (AZC) [1] are actively studied due to their similarity in elemental composition with secondary nitramines used as explosives and components of solid rocket fuels. In addition, substituted AZC are widely used in pharmaceutics due to their ability to release NO under physiological conditions. Our work is devoted to quantum-chemical calculation (Table 1) of the mechanism of N-methyl-N'-methoxydiazen-N-oxide (1) thermo destruction [2,3]. The experimental enthalpy value of the thermal decay activation of compound **1** (at the average experiment temperature T_{av} = 573 K) is 199.2 kJ/mol [1].

Table 1. The activation enthalpies (kJ/mol) of the most likely alternative mechanisms of the primary act and secondary reactions of N-methyl-N'-methoxydiazen-N-oxide the gas-phase monomolecular thermo destruction at various temperatures (K).

Process	Method	PBE	B3LYP		wB97XD				wB97X		G4
	Basis	L11	6-31G(2df,p)		6-31G(2df,p)		Def2TZVP		Def2TZVP		
	Temp.	298	298	573	298	573	298	573	298	573	298
	1→2	17.7	15.8	13.6	14.0	11.8	17.0	14.8	17.1	14.9	15.9
	2→3	156.6	183.9	183.6	198.1	197.7	201.1	200.7	206.6	206.1	195.1
	3→4	143.1	111.4	111.4	119.4	119.6	112.8	113.1	108.1	108.3	121.5
	1→3	203.4	224.7	225.1	237.0	237.1	238.3	238.5	245.2	245.2	233.9
	1→5	236.8	221.4	220.9	238.2	237.8	225.3	225.0	227.6	227.3	255.3

The isomerization of **1→2** has a low enthalpy of activation, so secondary reactions will be limiting. The most energetically advantageous development of the process is associated with the transfer of the CH_3 group between O atoms (**2→3**), followed by the formation of experimentally observed decomposition products of compound **1** [1]: N_2O, CO, CO_2, H_2, H_2O, etc. For the NO breakaway channel (**3→4**), an energetically acceptable subsequent decomposition path has not yet been found, i.e. it is probably a dead end [2, 3].

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TRANSFORMATIONS OF AZACYCLIC ALLENES UNDER MICROWAVE IRRADIATION

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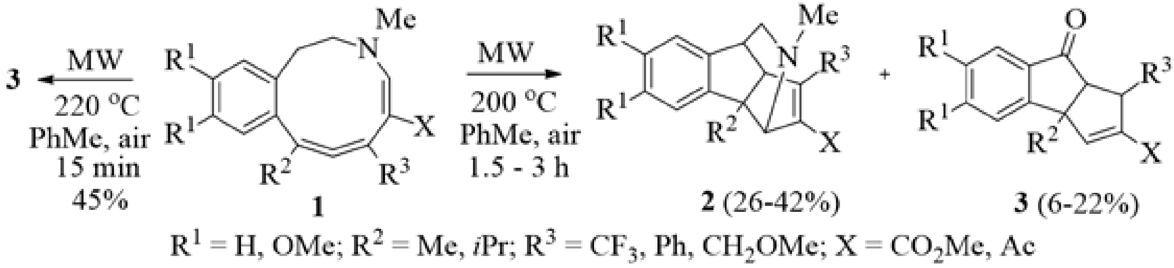
Recently, there has been a growing interest in the chemistry of allenes, as evidenced by a large number of publications on this topic. Cyclic compounds with a heteroatom, in particular with a nitrogen or sulfur atom, can be attributed to hard-to-reach and, as a result, poorly studied allenes. We have previously shown that such systems can have high physiological activity[1], and also be the starting point for the construction of various complex framework compounds[2-4].

While studying the transformation of a number azacyclic allenes under microwave irradiation at 150°C, we synthesized cyclopropa[*cd*]azulenes and N-bridged cyclopenta[*a*]indenes[3]. However, in some cases, depending on the substituents, the reactions were not started at 150°C, and at 180°C they proceeded for a long time (more than 7 hours) with significant tarring. Raising the temperature to 200°C promoted the formation of cyclopentaindenes **2** and **3**, while the reaction time did not exceed 3 hours, but thermolysis at 220°C led to the formation of only one product **3** and a reduction in reaction time to 15 minutes. Comparing the reactivity of 6-trifluoromethyl allenes **1** with 6-phenyl substituted analogues, it is possible to observe a lower activity of fluorinated derivatives in thermal transformation reactions.



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The reported study was funded by RFBR and VAST, project numbers 21-53-54002 and QTRU 01.05/21-22.

THE INVESTIGATION OF CATALYSIS NATURE IN Pt_2dba_3-CATALYZED HYDROSILYLATION REACTION

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The “cocktail” or dynamic type of catalytic system is a new mechanistic concept in transition metal catalysis [1]. It involves the equilibration between species of metal complexes and metal nanoparticles and clusters formed during the reaction. The investigation of dynamic catalytic systems involves the usage of a combination of different analytic methods enabling the characterization and identification of the species involved [2].

The hydrosilylation reaction is widely used in laboratory practice and industry. The dynamic nature of alkene and alkyne hydrosilylation reaction catalyzed by Pt/MWCNT (multi-walled carbon nanotubes) was found earlier (Fig.1) [3].

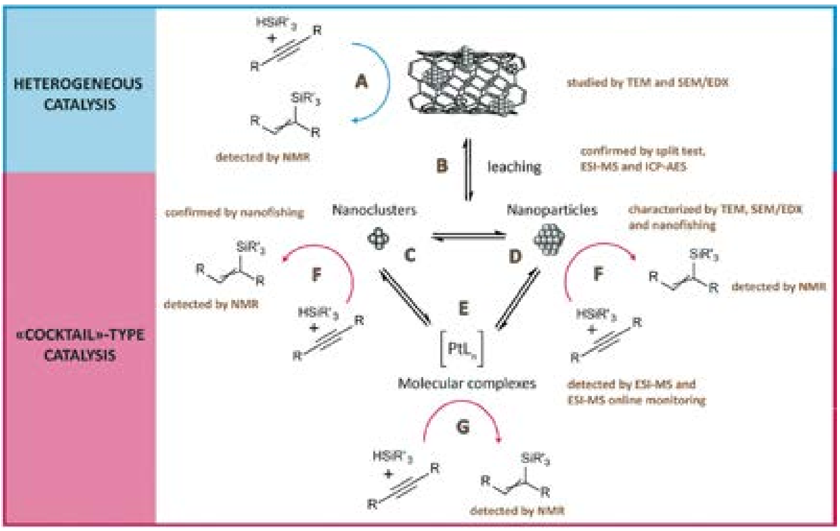

Fig.1. The mechanistic investigation of Pt/MWCNT catalyzed hydrosilylation reaction [3].

In this work, we are going to investigate the nature of the catalysis in Pt_2dba_3-catalyzed hydrosilylation reaction of alkenes and alkynes. The catalytic activity evaluation and mechanism investigation are planned as well.

Acknowledgment. The authors are grateful to the Scientific School program (grant NSh-5199.2022.1.3) for the support.

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CATIONIC DOMINO REACTION IN THE SYNTHESIS OF 3-HYDROXYINDOLINES

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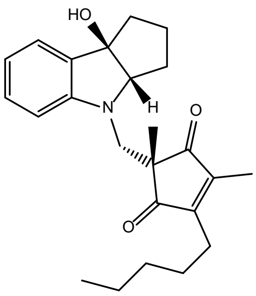
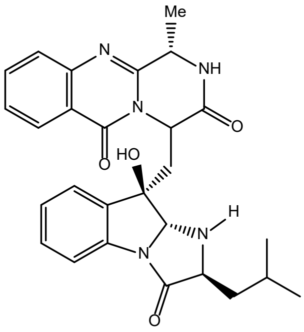
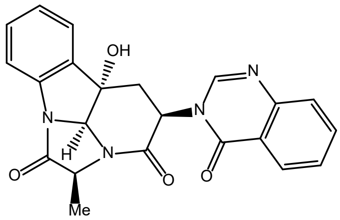
The indoline nucleus is the basis of the structure of some alkaloids, as well as the precursor of indoles. The presence of an acetyl and a secondary amino group in the structure of **1** inspired us to a new method for the synthesis of 3-hydroxyindolines. A complete surprise was the appearance of a domino reaction during the acylation of the secondary amino group, which ended with the synthesis of 3-hydroxyindoline **2**.



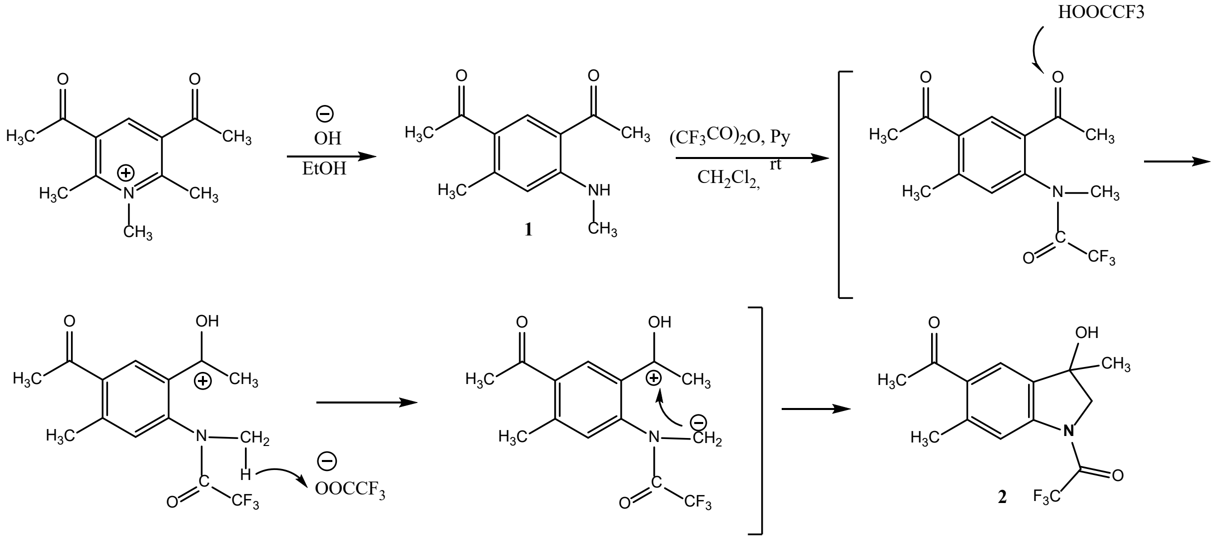
(+)-Madindoline A

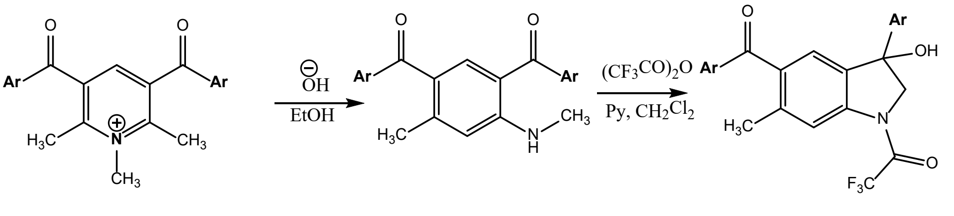


fumiquinazoline I



(-)-chaetominine





Ar = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 3-$MeOC_6H_4$, 4-ClC_6H_4.

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THE SYSTEM APPROACH IN CHEMISTRY AND CHEMISTRY EDUCATION

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Modern chemistry face the greatest conceptual and positional crisis since Justus von Liebig created the existing system of chemical education. Chemistry of our days has no understandable objectives for people, no breaking discoveries and no persons who could speak to society. Moreover, such a phenomenon as chemophobia is quite common - hostility and fear of everything «chemical». The popularity of classical chemistry education is declining from year to year. Obviously, chemistry as a science must be reinvented.

In many ways, the current situation is due to the dominance of the reductionist, analytical approach in chemistry. While chemists are considering isolated phenomena and processes, they cannot be included in the integral problematic field of the modern world [1]. The same can be said about chemistry education: it is impossible to educate a modern scientist by transmitting knowledge that is divorced from a practical context.

The «new chemistry» should be based on a system approach, which, in contrast to the reductionist one, is addressed not to the elements of the system separately, but to the whole, the interconnections and dynamics of the system. Systems thinking, on the one hand, allows seeing the place of chemistry in a new way in the general scientific and social context, and on the other hand, it has a huge educational potential [2]. Learning based on the principles of systems thinking, new chemists will be able to solve complex problems, effectively participate in cross-disciplinary interaction, learn not just to do their job, but to act in the interests of society and see long-term consequences.

The report will consider the prospects for the practical implementation of the principles and methodology of systems thinking in chemistry and chemical education.

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ACYLATION OF ARENES BY MUCONIC ACID. SYNTHESIS OF CONJUGATED DIENE-1,6-DIKETONES

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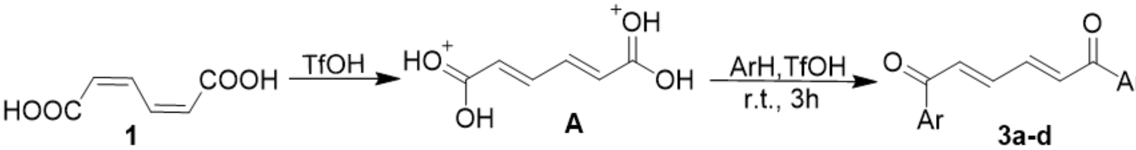
Muconic acid, as a compound obtained from lignocellulosics, is a perspective molecule for the development of the synthesis of new organic compounds.

The aim of this work is the acetylation of arenes by muconic acid under the action of Bronsted and Lewis superacids.

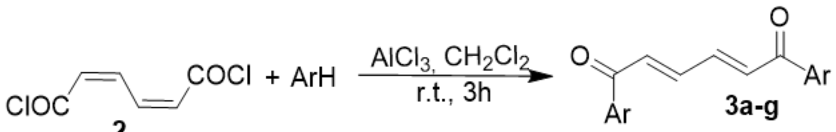
Protonation of *cis*-*cis*-muconic acid **1** in Bronsted superacid CF_3SO_3H (TfOH) forms dication **A**. This species reacts with arenes leading to acylation products *trans*-*trans*-**3a-d**. This reaction does not take place at C=C bonds of dication **A**.



3a (100%), **b** (96%), **c** (89%), **d** (91%)

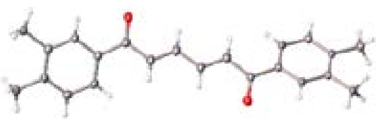
3: Ar=C_6H_nR: **R**=3,4-Me_2(**a**), 2,4-Me_2(**b**), 2,5-Me_2(**c**), 2,4,6-Me_3(**d**)

Compounds **3a-g** may be also obtained by reaction of chloroanhydride **2** with arenes under the action of $AlCl_3$.



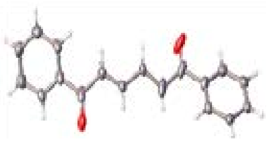
3a (100%), **b** (96%), **c** (89%), **d** (91%), **e** (100%), **f** (92%), **g** (90%)

3: Ar=C_6H_nR: **R**=H(**e**), 4-OMe(**f**), 2,3,5,6-Me_4(**g**)



X-ray of 3a

X-ray of 3d



X-ray of 3e

This work was supported by Grant of the President of the Russian Federation № MK-1014.2021.1.3

P-AMINO-CYCLOPENTADIENYLIDENE-PHOSPHORANES

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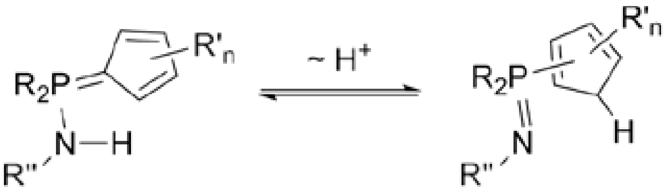
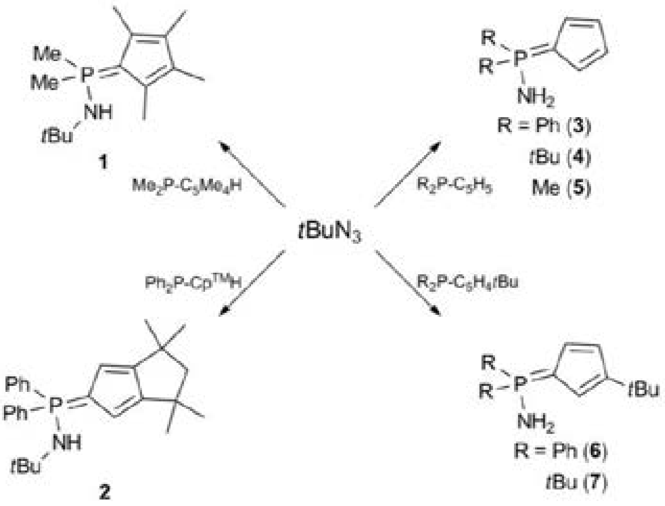
In the course of systematic investigations of ambident organophosphorus(V) donor ligands of the general type [R2P(X)Z]$^-$ (X, Z = S, NR', CHR', {Cp}) synthesis of a new compound class *P*-amino-cyclopentadienylidene-phosphoranes (*CpPN*) was developed.

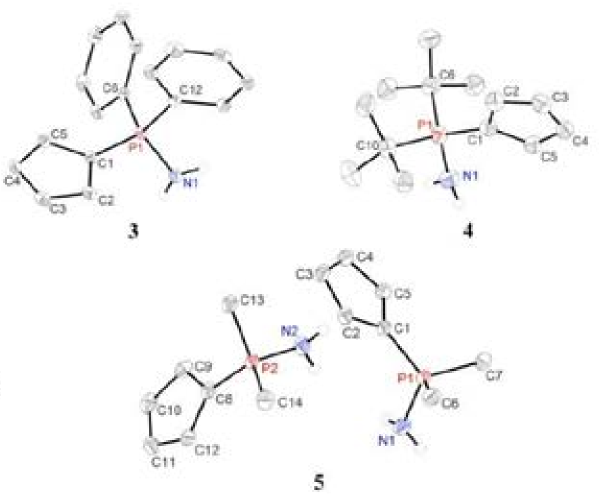
The synthesis was carried out by the Staudinger reaction of an appropriate Cp-phosphane and an organic azide. Relative Brønstead acidity of the (R)*n*Cp–*H* and RN–*H* protons is re- sponsible for occurrence of *CpPN* in one of their two possible tautomeric forms: *P*-amino- cyclopentadienylidene-phosphorane or *P*-cyclopentadienyl-iminophosphorane (Scheme 1).



Scheme 1. Tautomerizationof *P*-amino-cyclopentadienylidene-phosphorane (left) and *P*-cyclopentadienyl-iminophosphorane (right).

Formerly we reported on the reactivity of 3,4-disubstituted and *tetra*-methyl-substituted Cp-phosphanes with *t*BuN3, that led to the regular products exclusively as *P*-amino- phosphorane tautomers Me2P(=C5Me4)NH*t*Bu (**1**) and Ph2P(=Cp^{TM})NH*t*Bu (**2**).





Scheme 2. Syntheses of P-amino-Cp-phosphoranes 1–7. Fig. 1 Molecular structures of 3–5.

Absolutely unexpectedly, we found that the reaction product of *t*BuN3 with ring- unsubstituted Ph2P-C5H5 reveal no resonances of *t*Bu-group. Instead, ^{1}H NMR showed signif- icantly broadened resonance at 2.84 ppm close to the range of the NH-protons of **1** and **2**, but with 2*H* overall integral intensity. Further ^{13}C-NMR, HRMS and elemental analyses revealed that this product refers to *P*-NH2-cyclopentadienylidene-phosphorane **3** (Scheme 2).

Similarly, ring-unsubstituted *t*Bu2P–C5H5 and Me2P–C5H5 give *P*-amino-phosphoranes **4** and **5** also characterized by an X-ray structure analysis (Fig.1).

Next, mechanistic studies to ascertain the role of substituents in the Cp-moiety in for- mation of unexpected *P*–amino-cyclopentadienylidene-phosphoranes **3**–**7** will be discussed.

TWO TYPES OF VICINAL SUBSTITUENTS IN REACTIONS OF BIMOLECULAR NUCLEOPHILIC SUBSTITUTION AT A SATURATED ATOM

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The kinetics of the reaction of vicinal bromoethane derivatives with a number of sulfur-containing nucleophilic reagents (thiourea, sodium thiosulfate, sodium thiophetolate) was studied by radiochromatography. The non-observance of the isokinetic dependence and the Taft equations for all substituents was shown, and the fulfillment for two separate reaction series, one of which is satisfactorily described by the Taft equation, which takes into account the inductive and steric effects of substituents. Based on the data obtained, the existence of two types of vicinal substituents with different mechanisms of influence on the reactivity of bromine at a saturated carbon atom is assumed [1]. For the first type of substituents (H, OH, Br, Cl, F, CH_3, C_6H_5, SO_3Na), the main factors determining the reactivity are the inductive and steric effects of the substituents. For these substituents, the Taft equations are satisfied. The second type (COOH, $COOC_2H_5$, CN, NH_3Br, $N(CH_3)_3Br$, $SC(NH_2)_2Br$, $N(CO)_2C_6H_4$), which do not obey the Taft equations, includes charged or highly polar groups with the corresponding orientation, which allows us to expect manifestation of the field effect, which leads to additional stabilization of the transition state [2]. Other possible mechanisms of the effect of vicinal substituents on reactivity are discussed. The reaction kinetics was studied in various solvents (dimethylformamide, methanol, ethanol, acetonitrile, ethyl acetate, acetic acid). The splitting into two types of substituents is also observed when considering the dependence of reactivity (lgk x) and chemical shifts in the C13 NMR spectra on the carbon atom of the reaction center. Apparently, the general regularity of bimolecular reactions of nucleophilic substitution at a saturated carbon atom is manifested here. In the light of these ideas, the difficulties in interpreting the effect of neighboring electron acceptor substituents in the reactions of bimolecular nucleophilic substitution at a saturated carbon atom and unsuccessful attempts to search for simple quantitative patterns using empirical constants of the Hammett-Taft type become understandable.

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SYNTHESIS AND STRUCTURE OF NEW TYPES OF SULFOLANOCROMENONES

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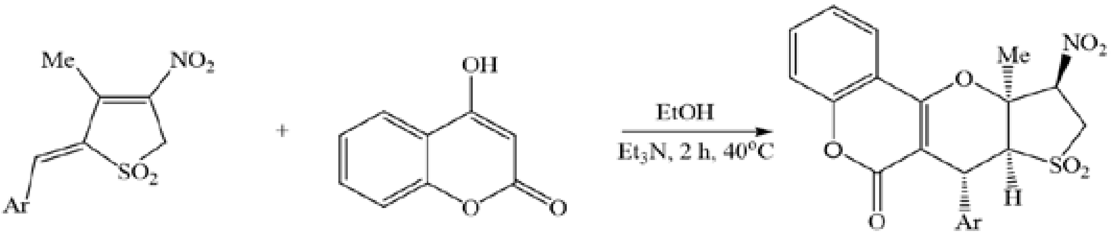
s-trans-Fixed nitrosulfodienes **1a-h** are convenient substrates for constructing fused sulfolane-containing polycycles with pyrazolidine, isoxazolidine, and hydrochromenone rings[1]. The research of the reaction of dienes **1a-h** with 4-hydroxycoumarin, carried out under mild conditions (ethanol, 40°C, cat. TEA, 2 h), led to the synthesis of a new derivatives type of the sulfolanopyranochromenones **2a-h** series with yields up to 90%.



1a-h Ar: Ph **1a**,**2a**; 2-MeC$_6$H$_4$ **1b**,**2b**; 4-MeC$_6$H$_4$ **1c**,**2c**; 2-ClC$_6$H$_4$ **1d**,**2d**; 4-ClC$_6$H$_4$ **1e**,**2e**; 2,4-Cl$_2$C$_6$H$_3$ **1f**,**2f**; 2-BrC$_6$H$_4$ **1g**,**2g**; 4-BrC$_6$H$_4$ **1h**,**2h**.

2a-h (67-90%)

Compounds **2a-h** are crystalline substances, their structure was established on the basis of IR, ^{1}H, and ^{13}C NMR spectroscopy data using homo- (^{1}H–^{1}H COSY, ^{1}H–^{1}H NOESY) and heteronuclear (^{1}H–^{13}C HMQC, ^{1}H–^{13}C HMBC) two-dimensional experiments, as well as X-ray diffraction analysis.

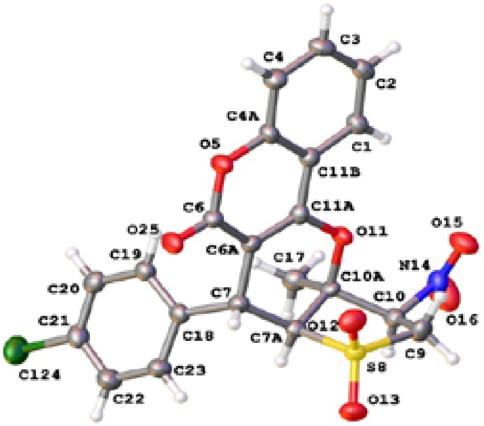


Fig 1. Molecular structure of polycycle 2e in crystalline boundedness

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This study was carried out with the financial support from the Russian Foundation for Basic Research within the framework of scientific project No. 20-33-90071.

PREPARATION OF AROMATIC DINITRILES WITH HETEROCYCLIC SUBSTITUENTS

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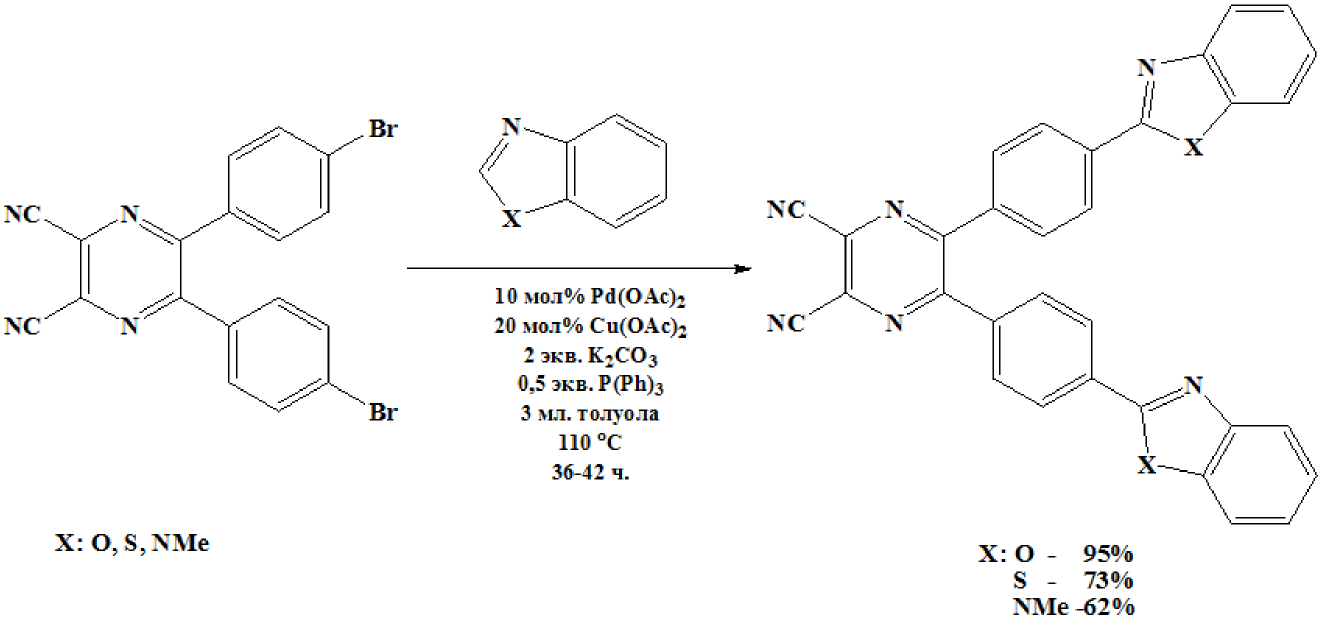
Aromatic nitriles are important building blocks in the synthesis of porphyrazines and phthalocyanines. Traditional methods for the synthesis of nitriles include Sandmeyer, Rosenmund-von Braun reactions, dehydration of aldoximes and amides. A success in modern nitriles chemistry has been the metal-catalyzed cyanation of aryl halides with transition metal complexes. The development of new methods for the synthesis and modification of dinitriles is of considerable interest and makes it possible to expand the range of symmetrical and asymmetric porphyrazines synthesized from them in order to obtain new functional materials.

In our work, we propose the synthesis of new dinitriles using palladium-catalyzed CH-functionalization. Initially synthesized 5,6-bis(4-bromophenyl)pyrazine-2,3-dicarbonitrile was introduced into a heteroarylation reaction with a number of heterocycles having an “acid C-H bond”. The reaction products were obtained in good yields. This technique opens up prospects for the introduction of benzothiazol, benzoxazole, and N-methylbenzimidazole subunits into dinitrile molecules.



Syntheses were conducted with financial support of the Council for Grants of the President of the Russian Federation, project MK-3863.2021.1.3.

The identification was carried out using the resources of the Center for Shared Use of Scientific Equipment of the ISUCT (with the support of the Ministry of Science and Higher Education of Russia, grant No. 075-15-2021- 671).

SYNTHESIS AND SELF-ASSEMBLY OF ANTIMICROBIAL AMPHIPHILIC ISATIN DERIVATIVES BASED ON 1,4-DIAZABICYCLO[2.2.2]OCTANE

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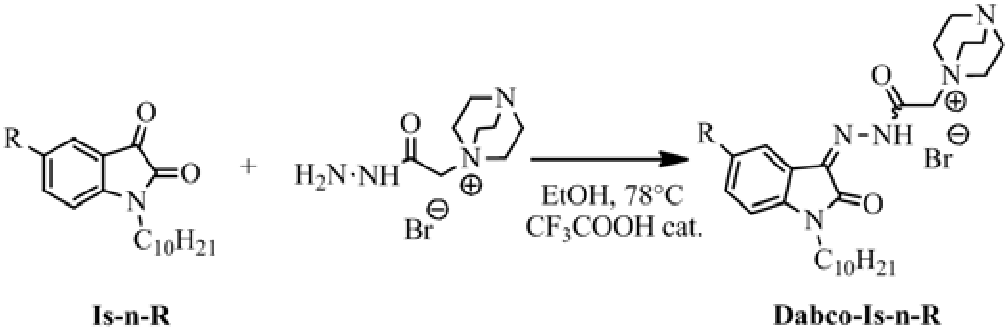
The creation of supramolecular assemblies based on amphiphilic quaternary ammonium salts is one of innovative strategy for improving their antimicrobial activity. Quaternized derivatives of 1,4-diazabicyclo[2.2.2]octane (Dabco) have low toxicity and distinctive features in aggregation behavior from classical ammonium derivatives. Isatin provides a rich platform for the synthesis of compounds exhibiting biological activity due to the presence of two reaction centers - a carbonyl group in position 3 and an endocyclic nitrogen atom.

In this work, we synthesized a new cationic isatin derivatives (Dabco-Is-n-R) containing in their structure the Dabco fragment, different alkyl substituents in position 1 (C_nH_{2n+1}, where n = 10, 12, 14, 16, 18) and substituent of various natures (R = H, CH_3, Cl) in position 5.



R = H, CH_3, Cl
n = 10, 12, 14, 16, 18

The self-assembly of Dabco-Is-n-R was studied by tensiometry, conductometry, dynamic light scattering and spectrophotometry. The critical association concentration of Dabco-Is-n-R is an order of magnitude lower than for classical quaternary ammonium surfactants. The solubilization capacity of Dabco-Is-n-R toward hydrophobic dye (Sudan I) increases with the increase of alkyl chain length from the decyl to its octadecyl analogue by 2.5 times.

The most effective antimicrobial compound against *S. aureus* and *C. albicans* is Dabco-Is-12-H. MIC values of Dabco-Is-12-H are lower than for a topical antiseptic Miramistin, Is-12 and Dabco-12 trimethylammonium derivatives.

The authors gratefully acknowledge the CSF-SAC FRC KSC RAS for providing necessary facilities to carry out this work.

SYNTHESIS AND ANTIVIRAL ACTIVITY OF CONDENSED TRIAZOLOPYRIDAZINE DERIVATIVES

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The development of antiviral drugs has become especially relevant in recent years, which is primarily due to the widespread prevalence of coronavirus infection SARS-CoV-2.

Of particular importance are the development of broad-spectrum antiviral drugs (ADs) and/or specifically targeting SARS-CoV-2. Among modern antiviral agents, the most effective drugs belong to the group of nucleoside analogues (NAs) or abnormal nucleosides - antimetabolites of natural DNA and RNA monomers. Depending on the structure and position of the hydrophobic substituent, such nucleosides can either block the penetration of viruses into cells or inhibit the stage of replication of their genomes. In connection with the above, the purpose of our work was to study the possible AV activities of original drugs related to bicyclic heterosystems with different conjunction of pyridazine cycle with 1,2,4-triazole ring, which has a wide range of physiological activity [1-4]. In this regard, a number of 3-(pyrazole-1-yl)-1,2,4-triazolopyridazine derivatives with various substituents in the triazole ring have been synthesized on the basis of the starting 3-(pyrazole-1-yl)-6-hydrazinyl-pyridazine.

SARS-CoV-2 isolates were propagated in Vero and VeroE6 cells in medium with Eagle-MEM (Sigma) containing 10% fetal bovine serum at 37 °C. All experiments with SARS-CoV-2 were performed in enhanced biosafety level 3 (BSL3). SARS-CoV-2 from the nasal and oral mucosa was determined by means of biological titration in Vero E6 cells. These data were duplicated using qRT-PCR. The study revealed an effective prophylactic effect of the two studied drugs (SR-321 и GT-2007), when the drug inhibited viral activity for 72-2224 hours. The iral activity was almost completely suppressed up to dilutions of 100 TCD50/ml inclusive.

Given the promising antiviral activity of SR-321 and GT-2007 in vitro, we next evaluate their in vivo efficacy by infecting Syrian hamsters with SARS CoV-2 using a combination of intranasal and ocular infection patterns. All investigated in in vivo conditions preparations SR-321 and GT-2007 in the form of an injection led to the complete disappearance of the virus from the mucous membranes of the nose and mouth by 5 dpi. Micro-CT analysis revealed serious lung abnormalities in all infected animals, which were absent in the control animals (treated with saline). Syrian hamsters are characterized by lung damage starting from 32-48 hours after inoculation of the virus. This lesion is described as typical lung pathology. Total viral loads as measured via qRT-PCR in oronasal swabs were 1–2 log10 lower in treated animals. Also, positive probes for SARS Cov-2 in treated hamsters significantly decreased compared to the oronasal swabs obtained from animals from the virus control group and disappear on 7 dpi while in hamsters from the virus control group positive probes disappears only after 7-9 dpi.

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REDOX BEHAVIOR OF 1H-XANTHEN-1-ONE DERIVATIVES IN ORGANIC SOLVENTS

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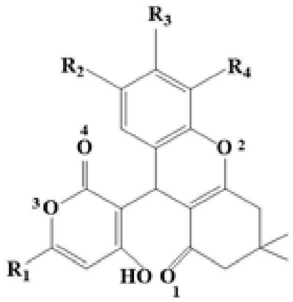
Compounds containing a xanthene fragment belong to an important group of oxygen-containing heterocyclic compounds due to their specific properties, high biological activity, and the possibility of their use in the synthesis of drugs [1, 2]. Depending on the type of substituent and its localization in the structure, polyfunctional xanthenes exhibit various biological activities. Synthetic and natural derivatives of 1H-xanthene attract much attention due to a wide range of pharmacological actions: anticoagulant, antispasmodic, anti-inflammatory, antianaphylactic, antiviral, antifungal, anti-HIV and antibacterial. Recently, special interest has been drawn to this class of compounds in view of the determination of their antitumor activity [3].



I: R_1=Me; R_2=R_3=R_4=H;
II: R_1=Ph; R_2=R_3=R_4=H;
III: R_1=Ph; R_2=R_3=H; R_4=OH;
IV: R_1=Ph; R_2=R_4=H; R_3=OH;
V: R_1=Ph; R_2=Br; R_3=R_4=H

The electrochemical behavior of 1H-xanthen-1-one derivatives **I**–**V** obtained on the basis of the procedure described in [4] was studied by the CV method. The electrochemical properties of derivatives of 1H-xanthen-1-ones on platinum in organic solvents (CH_3CN, CH_2Cl_2) have been studied. It was found that the oxidation of derivatives of 1H-xanthen-1-ones proceeds stepwise by the ECE mechanism. At the first stage of transformations, unstable radical cations are generated, the fragmentation of which proceeds with the elimination of a proton. The presence of carbonyl groups in the compounds under study enhances the protonation tendency in an acidic medium.As a result of electrochemical oxidation of derivatives of 1H-xanthen-1-ones, the products of their O-heteroaromatization are formed. Analysis of the CV curves of the oxidation of compounds **I-V** made it possible to determine the values of anodic potentials, which correlate with the value of their ionization potential (Table).

Compound	CH_3CN		CH_2Cl_2		CH_2Cl_2
	E_{pa1}, V	E_{pa2}, V	E_{pa1}, V	E_{pa2}, V	PI, eV
I	1,60	1,82	1,64	1,88	5,89
II	1,68	1,90	1,72	1,96	6,05
III	1,48	1,72	1,58	1,80	5,77
IV	1,42	1,68	1,54	1,76	5,72
V	1,64	1,88	1,70	1,94	6,01

The oxidation (E) and ionization (PI) potentials of 1H-xanthen-1-ones depend on the structure of the compounds. The direction of secondary transformations of polyfunctional derivatives of 1H-xanthen-1-ones under the conditions of an electrochemical experiment was determined by the method of quantum chemistry. From the point of view of thermodynamic evaluation, the stage of protonation of substituted 1H-xanthen-1-ones is energetically favorable (-970÷(-1150) kJ/mol. The propensity of oxygen atoms of heterocyclic compounds to protonation is described by the following sequence: 2<3<4<1. Using the PASS program, computer prediction of the potential biological activity (anaphylactic, antihypoxic and antitumor) of the studied compounds was carried out.

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The work was supported by the Russian Foundation for Basic Research (grant no. 20-03-00446a)

THERMAL REARRANGEMENT AND HYDRAZINOLYSIS OF *N*PHTHALIMIDOAZIRIDINES, CONTAINING 1,2,4-OXADIAZOLE MOIETY

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1,2,4-Oxadiazole and aziridine derivatives are widely used in medicinal chemistry and pharmaceutical production as active pharmaceutical ingredients, therefore their synthesis and study of their properties is important. Herein we repot synthesis of *N*-phthalimidoaziridines, containing 1,2,4-oxadiazole moiety, and subsequent thermal rearrangement and hydrazinolysis of aziridines.

N-Phthalimidoaziridines were obtained by oxidation of *N*-aminophthalimide with lead tetraacetate in presence of 5-alkenyl-1,2,4-oxadiazoles. The reaction was performed at -10 °C in CH_2Cl_2 [1]. Starting 5-alkenyl-1,2,4-oxadiazoles were prepared through one-pot procedure from aromatic amidoximes and carboxylic acids in presence of KOH in *N*,*N*-dimethylacetamide [2].

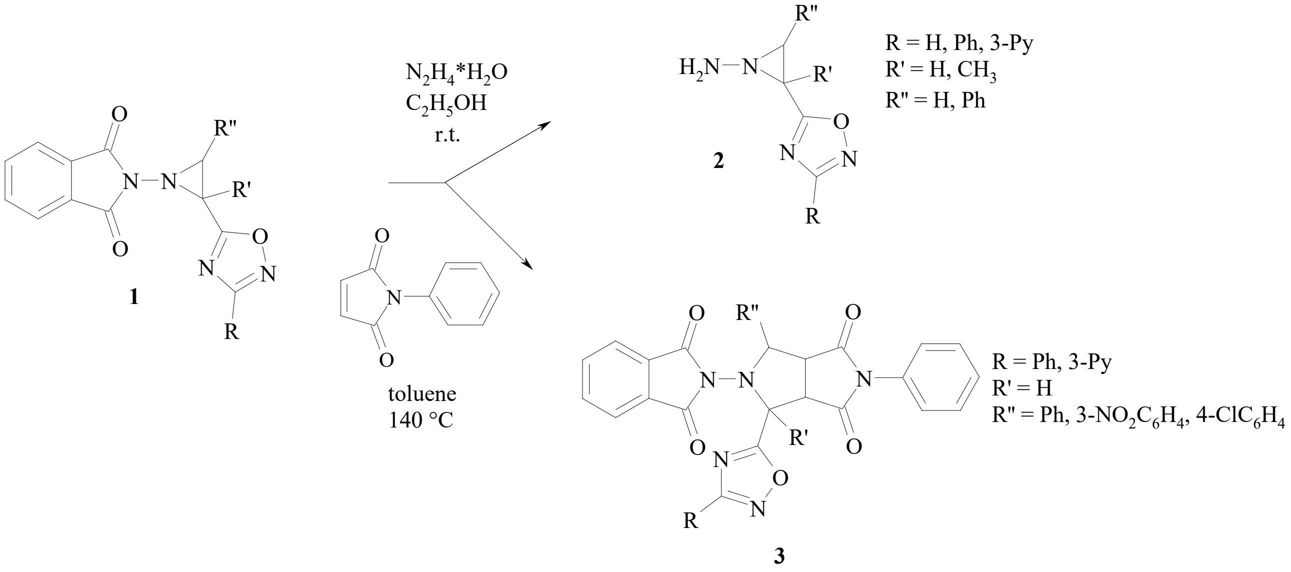

Figure 1

N-phthalimidoaziridines (1) underwent hydrazinolisis at room temperature in EtOH. As a result corresponding N-aminophthalimides (2) were obtained.

N-phthalimidoaziridines (1) were heated in toluene in presence of dipolarophile (*N*phenylmaleimide). As a result of C-C bond breaking 1,3-dipoles were formed and reacted with *N*phenylmaleimide to give corresponding products (3). However, mono-substituted aziridines resisted thermal rearrangement.

Structures of synthesized compounds were confirmed by their IR and ^{1}H and ^{13}C NMR spectra.

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VISIBLE LIGHT-INDUCED CATALYSIS OF N-HETEROCYCLIC CARBENES IS A USEFUL TOOL IN SYNTHETIC GREEN CHEMISTRY

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To meet the requirements of modern chemistry, the use of photocatalytic reactions is attractive, since they allow the generation of reactive radicals under mild conditions. Visible light sensitization initiates organic reactions and reduces the proportion of side reactions that often occur when using high-energy UV radiation [1].

In addition to photocatalysis, organocatalysis has an important potential for initiating organic transformations [2]. N-heterocyclic carbenes (NHCs) have recently become an exciting chapter of organocatalysis, however, NHC catalysis through single electron transfer processes, despite the possibility of achieving chemical transformations of inert chemical bonds and the use of green reagents, is a difficult task in organic synthesis [3].

Recent advances in this field have shown that the combined use of NHC and a photocatalyst can significantly increase the efficiency and selectivity of the reaction, which are unattainable when using systems with a single catalyst [4, 5].

In this work, it is planned to study the catalytic activity of systems containing NHC directly bound to an organic photoactive molecule. The design of such a structure will significantly increase the environmental friendliness of the reaction by eliminating the additional introduction of metal-containing photocatalysts without loss of efficiency, as well as solubility in water, which is important for the functionalization of valuable water-soluble natural compounds. As a result, photoredox-active NHC systems will be synthesized and their activity in the reactions of C-C bond formation will be studied.

Acknowledgment. The authors are grateful to the Scientific School program (grant NSh-5199.2022.1.3) for the support.

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TARGETED SYNTHESIS AND STUDY OF A WATER-SOLUBLE PORPHYRIN WITH A TYRAZILINE FRAGMENT TO INHIBIT SARS-CoV-2

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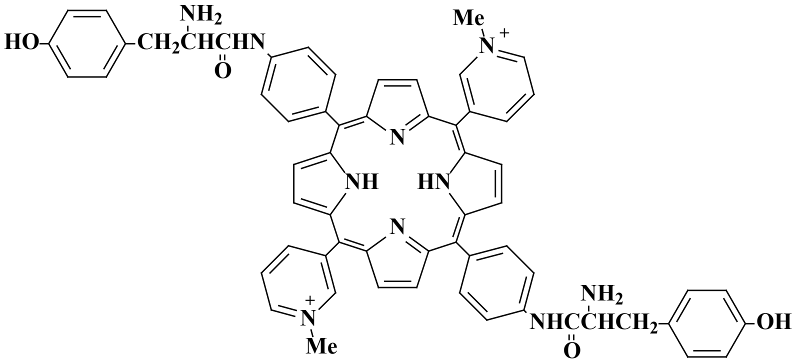
The COVID-19 epidemic began in the Chinese city of Wuhan in 2019 and has spread to all countries of the world. To date, the total world statistics of infection is more than 474 million people, with a fatal outcome in more than 6 million cases. The causative agent of the disease is the zoonotic virus SARS-CoV-2. On the surface of the virion is the Spike protein, which consists of three chains. Each chain includes two subunits: S1 and S2. The S1 subunit binds to the host cell receptor, and the S2 subunit is responsible for the fusion of the virus and host cell membranes. The S1 subunit contains a receptor-binding domain (RBD) that binds to the host cell's ACE2 receptor. It should be noted that RBD is the most common target for the inhibition of protein functions; however, it is RBD that is subject to the most frequent mutations. Therefore, the aim of this work was the targeted synthesis of a porphyrin capable of binding to the conserved part of the S protein (with S2 subunits). The nature of the interaction of the porphyrin with 2 or 3 S2 subunits should prevent the change in protein conformation required for membrane fusion. To achieve this aim, at the first stage of the work, molecular docking of a wide range of porphyrins with the Spike protein was carried out, and the dependences of the effect of the porphyrin molecular structure on its localization were established. This made it possible to design the porphyrin 5,15-bis(4'-L-N-tyrosinylamidophenyl)-10,20-(pyridin-3'-yl)porphine diiodide), the nature of its interaction with the S-protein corresponds to the aim of the work. At the second stage of the work, a method for its synthesis was developed. 5,15-bis(4′-nitrophenyl)-10,20-bis(pyridin-3′-yl)porphin was used as the initial porphyrin, which was obtained by condensation of meso-(pyrid-3′-yl)dipyrrolylmethane and 4-nitrobenzaldehyde in propionic acid and then was reduced with tin dichloride to 5,15-bis(4′-aminophenyl)-10,20-bis(pyridin-3′-yl)porphine. Acylation of the amino derivative was carried out with L-di-BOC-tyrosine using dicyclohexylcarbodiimide as an activating agent. Further, the resulting 5,15-bis(4'-*LN,O*-di-tert-butyloxy-carbonyltyrosinylamidophenyl)-10,20-bis(pyridin-3'-yl) porphin was methylated at the pyridyl moiety, after which the BOC protection was removed by trifluoroacetic to-you. The structure and purity of all obtained compounds were proved by the methods of electronic, ^{1}H NMR spectroscopy and mass spectrometry (MALDI TOF).



The work was funded by the RFBR (research project No. 20-04-60067).

SYNTHESIS OF TERMINAL ACETYLENE ALCOHOLS BASED ON CALSIUM CARBIDE AND SOME KETONES

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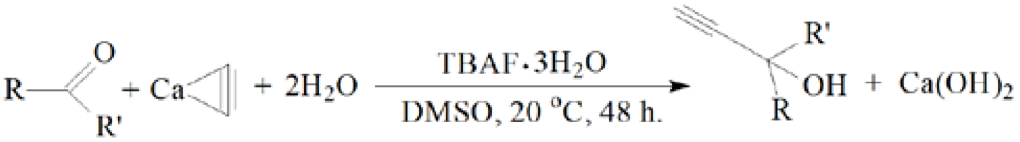
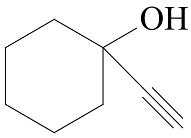
The presence in the molecule of acetylene alcohols and dioles of a triple bond, a hydroxyl group (s) and mobile hydrogen in it, functional groups retained a heteroatom and substituents with different structures that based on such a series of compounds increases the ability to synthesize and produce valuable, chemically stable and biologically active compounds[1,2]. Recently, a new generation of vitamins, antibiotics, biocides, polymers, rubber and electronic materials, based on acetylene alcohols are being produced[3].

In this study, the synthesis of the corresponding terminal acetylene alcohols (**1-4**) based on the reactions of cyclohexanone, acetophenone, para-chloroacetophenone and adamantanone with calcium carbide was studied. The alkylation reaction of selected ketones was carried out in DMSO, THF and methanol solution in the presence of TBAF·3H_2O, the reaction duration, temperature, catalyst, reagent and substrate quantities were studied. The reaction scheme was proposed as follows[4].



Here: RR′= -$_c$Hex (1); R= -Me, R′= Ph (2); R= -Me, R′= Ph$_p$Cl (3); RR′= -Ad (4)



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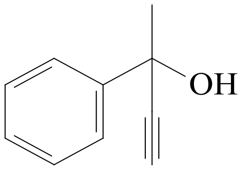

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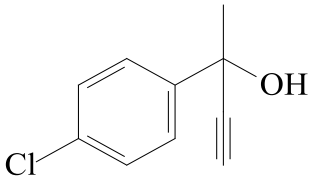

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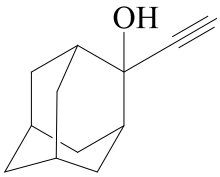

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REACTION OF 2-ETHOXYPYRROLIDINES WITH CARBONYL COMPOUNDS – AN EFFICIENT METHOD OF SYNTHESIS OF NOVEL NORHYGRIN DERIVATIVES

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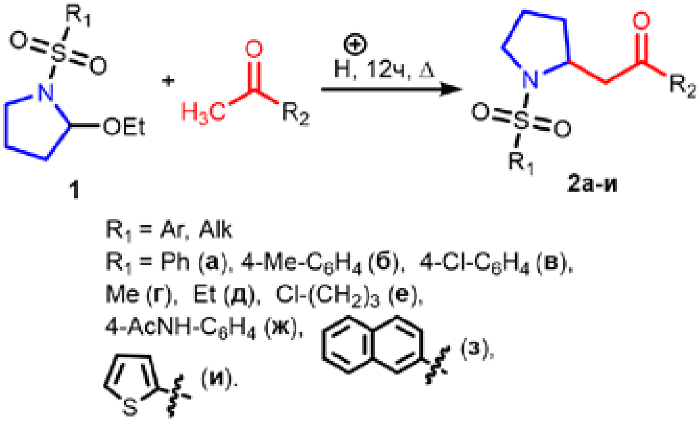
Pyrrolidines are one of the most important and widespread classes of heterocyclic compounds. Of particular interest are norhygrin and its derivatives, since they have different physiological activities. Among them, the alkaloids hygrin, cuscohygrin, ruspolinon, norruspolinon, etc. can be noted. Therefore, the development of new methods for the synthesis of compounds of this class is an urgent task.

We have developed a method for the synthesis of pyrrolidines containing a terminal carbonyl group based on the reaction of 2-ethoxypyrrolidines with carbonyl compounds. The proposed method is distinguished by operational simplicity and the availability of reagents and catalysts.



The study was supported by the Russian Science Foundation grant № 21-13-00022, https://rscf.ru/project/21-13-00022/

SYNTHESIS AND BIOLOGICAL ACTIVITY OF PROTIC AND APROTIC IONIC LIQUIDS BASED ON 5-HMF

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Ionic liquids (ILs), which are low-melting salts with bulky organic cations, have found wide applications in various fields of science and industry. They are used as unique reaction media for chemical reactions, conductive media for electrochemical processes, biocompatible media for biological objects, and solvents for cellulose. However, the high cost of the initial reagents for their synthesis, as well as the difficulties associated with the purification and regeneration of ILs, are a serious constraint on their wide industrial application. The use of initial reagents obtained from renewable raw materials will significantly reduce the cost of ILs and their environmental burden. A good alternative to non-renewable aromatic sources is 5-hydroxymethylfurfural (5-HMF) (platform compound) derived directly from cellulose [1].

We have developed flexible methods for the synthesis of protic and aprotic ammonium ILs based on 5-HMF [2]. The synthesis of protic ILs includes two stages: reductive amination of 5-HMF and subsequent protonation with strong inorganic acids. To obtain quaternary ammonium salts after reductive amination, quaternization of the nitrogen atom is necessary, followed by replacement of the anion. Thus, the use of a quaternary ammonium cationic center makes it possible to obtain ILs with anions of weak acids. Additional functionalization of the IL cation is also possible, which can be included in the protonation/quaternization step or carried out later. The ability to change the cations and anions of IL opens up prospects for tuning their physicochemical properties, biological and antimicrobial activity.

Acknowledgment. The authors are grateful to the Scientific School program (grant NSh-5199.2022.1.3) for the support.

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SYNTHESIS OF AMIDES AND PEPTIDES OF 4-AMINO-*N*-ARYLPYROGLUTAMIC ACIDS

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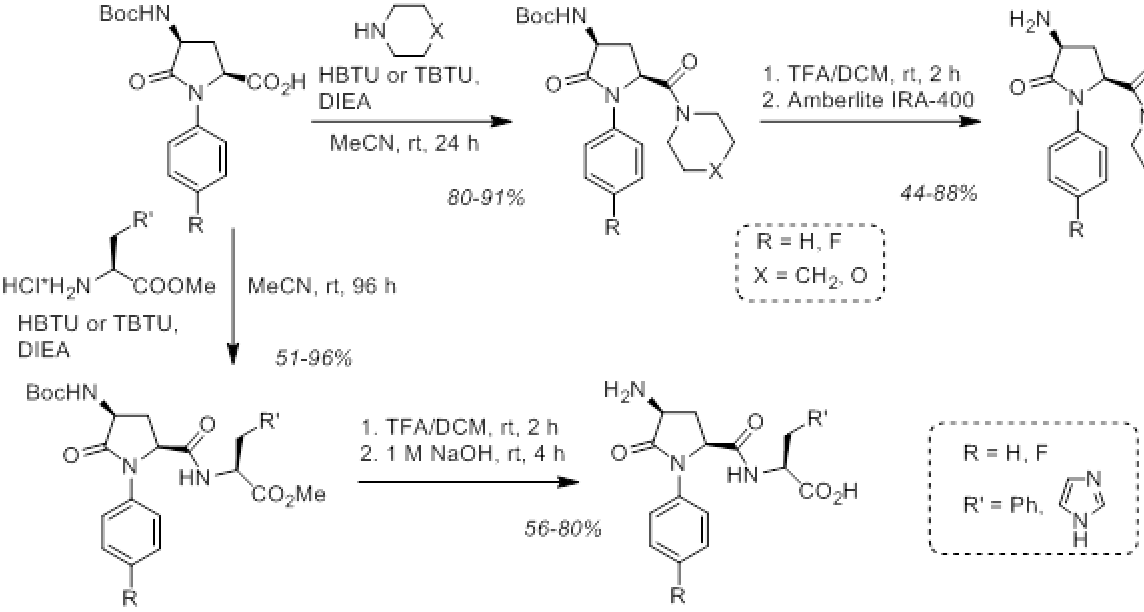
The derivatives of pyroglutamic acid exhibit diverse biological activities and are used as chiral building blocks in organic synthesis. In continuation of the work on the synthesis and study of derivatives of 4-amino-*N*-arylpyroglutamic acids, among which compounds with psychotropic[1,2] and antithrombotic activity were identified, we synthesized amides of (2*S*,4*S*)-4-amino-*N*-phenyl- and (2*S*,4*S*)-4-amino-*N*-(4-fluorophenyl)-pyroglutamic acids with piperidine and morpholine, as well as peptides with (*S*)-phenylalanine and (*S*)-histidine.



4-*N*-Boc-Protected pyroglutamic acids were used as the starting compounds; the coupling reaction was carried using HBTU or TBTU as the coupling agents, Boc protection was removed by the action of trifluoroacetic acid, the methyl ester was removed as a result of alkaline hydrolysis. Structures of the synthesized compounds were confirmed by NMR spectral and elemental analysis data.

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The work was financially supported by the Russian Foundation for Basic Research (project no. 20-43-660045).

SYNTHESIS, STRUCTURE OF *N*-(2,3-dimethyl-1*H*-indol-7-yl)-2,2,2-TRICHLOROACETAMIDE WITH ANTIMICROBIAL ACTIVITY

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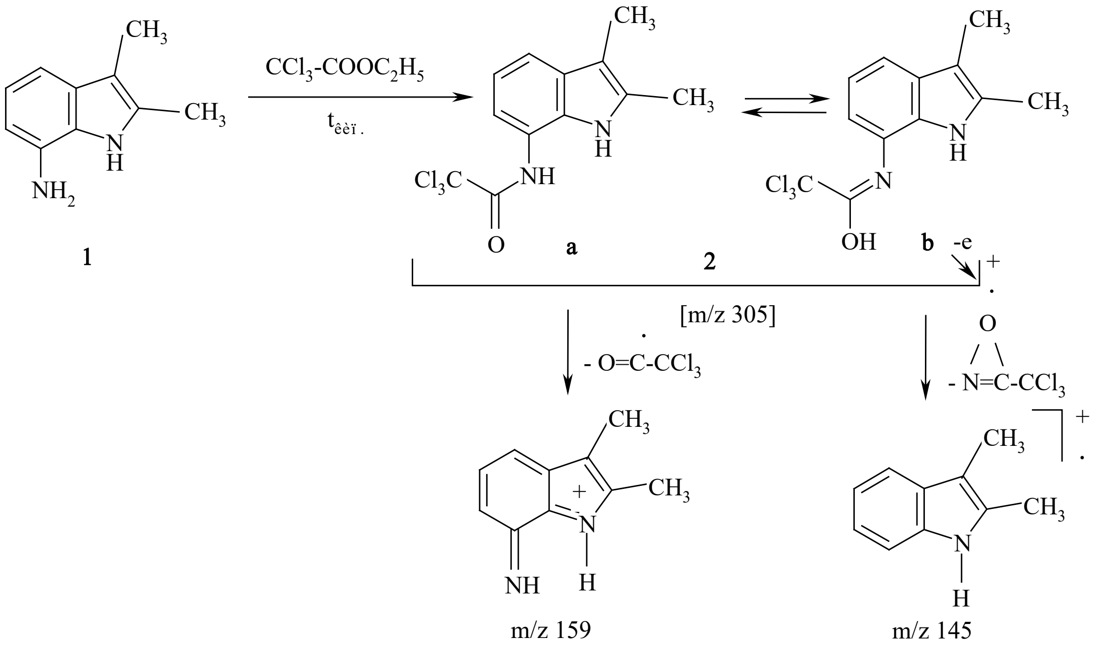
We are searching for new compounds with antimicrobial activity based on substituted 1H-indolylamines [1]. It has been established that *N*-(2,3-dimethyl-1*H*-indol-7-yl)-2,2,2-trichloroacetamide is formed upon prolonged boiling of aminoindole 1 in toluene with ethyltrichloroacetate (**2**). If this reaction is carried out in excess of boiling trichloroacetic acid ethyl ester (169 °C), then it ends within 1 h. Spectral data (NMR, mass spectra) indicate two possible **a**- and **b**-tautomeric forms of compound 2.



For example, this is evidenced by fragment ions with m/z 145 and m/z 159 in the mass spectrum, which are formed, respectively, by the elimination of the 3-(trichloromethyl)-1,2-oxazirin molecule and the trichloroacetyl radical (O=C*-CCl_3). Bioscreening of amide **2** with respect to test strains of microorganisms *(Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Streptococcus pyogenes)* indicates its antimicrobial activity comparable to or exceeding the activity of the reference drug dioxidine.

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НАСТОЛЬНЫЙ ЯМР-СПЕКТРОМЕТР
100PRO

- Рабочая частота 100 МГц
- Чувствительность более 220:1
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- Стабилизация ^{2}H / без дейтерия
- Стандартные ампулы диаметром 5мм для ЯМР
- Цветной сенсорный экран с возможностью работы в перчатках
- Открытый API для внешних программ
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- Постоянный магнит 2,35 Тл, не требующий криожидкостей

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- одномерные эксперименты
- T1 (спин-решёточная релаксация)
- T2 (спин-спиновая релаксация)
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