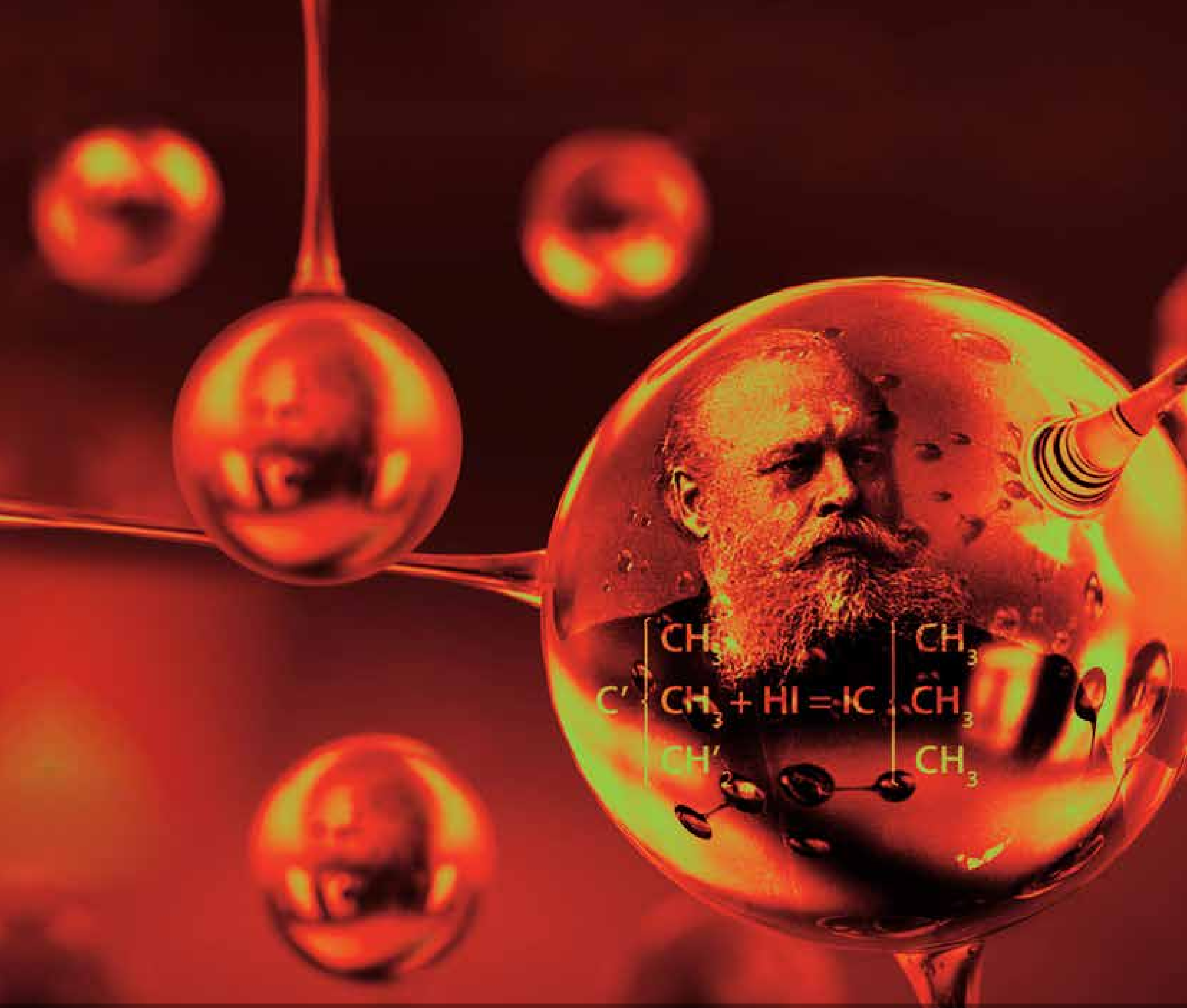

MARKOVNIKOV
CONGRESS
ON ORGANIC
CHEMISTRY

21–28 June 2019
Moscow — Kazan

BOOK OF ABSTRACTS

Markovnikov Congress on Organic Chemistry

21-28 June 2019,
Moscow-Kazan, Russia

Мероприятие проводится при финансовой поддержке
Российского фонда фундаментальных исследований, проект № 19-03-20020.

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ООО «Адмирал Принт», ул. Барклая, 13/2, Москва, 129090

2019 г.

Dear participants, guests and organizers of the Congress!

I am pleased to welcome the participants of the Markovnikov Congress on Organic Chemistry, dedicated to the 150th anniversary of the discovery by the Russian chemist Vladimir Vasilyevich Markovnikov in 1869 of the fundamental rule, which is a classic of the entire world chemical science (Markovnikov's rule). This rule was an important milestone in the development of the structural theory in organic chemistry. For the first time it raised the question of the reactions selectivity.

Vladimir Markovnikov was the founder of the Moscow University School of Chemistry, a graduate of the Kazan Chemical School. V.V. Markovnikov (along with Dmitryi Mendeleev) is one of the most famous Russian chemists abroad. In 1873, Markovnikov headed the chair of chemistry of the natural department of the Physics and Mathematics Faculty of Moscow University, which he headed until 1893 (Academician Nikolai Zelinsky became his successor). V.V. Markovnikov is a person who has entered his name both in the history of our university and in the world of science and culture.

I cordially greet the participants, guests and organizers of the Congress and wish you productive work, opening up new opportunities for developments in the field of chemical science, new scientific contacts, exciting discussions and the implementation of all outlined plans. I am confident that the Markovnikov Congress will be held at a high scientific level and will be an important event in the development of Russian chemical science and international contacts.

I wish success to all participants. Welcome to Congress!

Rector of Lomonosov Moscow State University
Academician Viktor Sadovnichiy

Dear friends!

Kazan Federal University is pleased to announce Markovnikov Congress on Organic Chemistry devoted to the 150th Anniversary of Markovnikov rule during June 24-28, 2019 at Kazan, Russia.

Kazan University is one of the oldest universities in Russia, which will celebrate the 215th anniversary of the foundation in 2019. Outstanding scientists and graduates brought him world fame, and university culture had a beneficial effect on the development of the city of Kazan, Tatarstan and Russia.

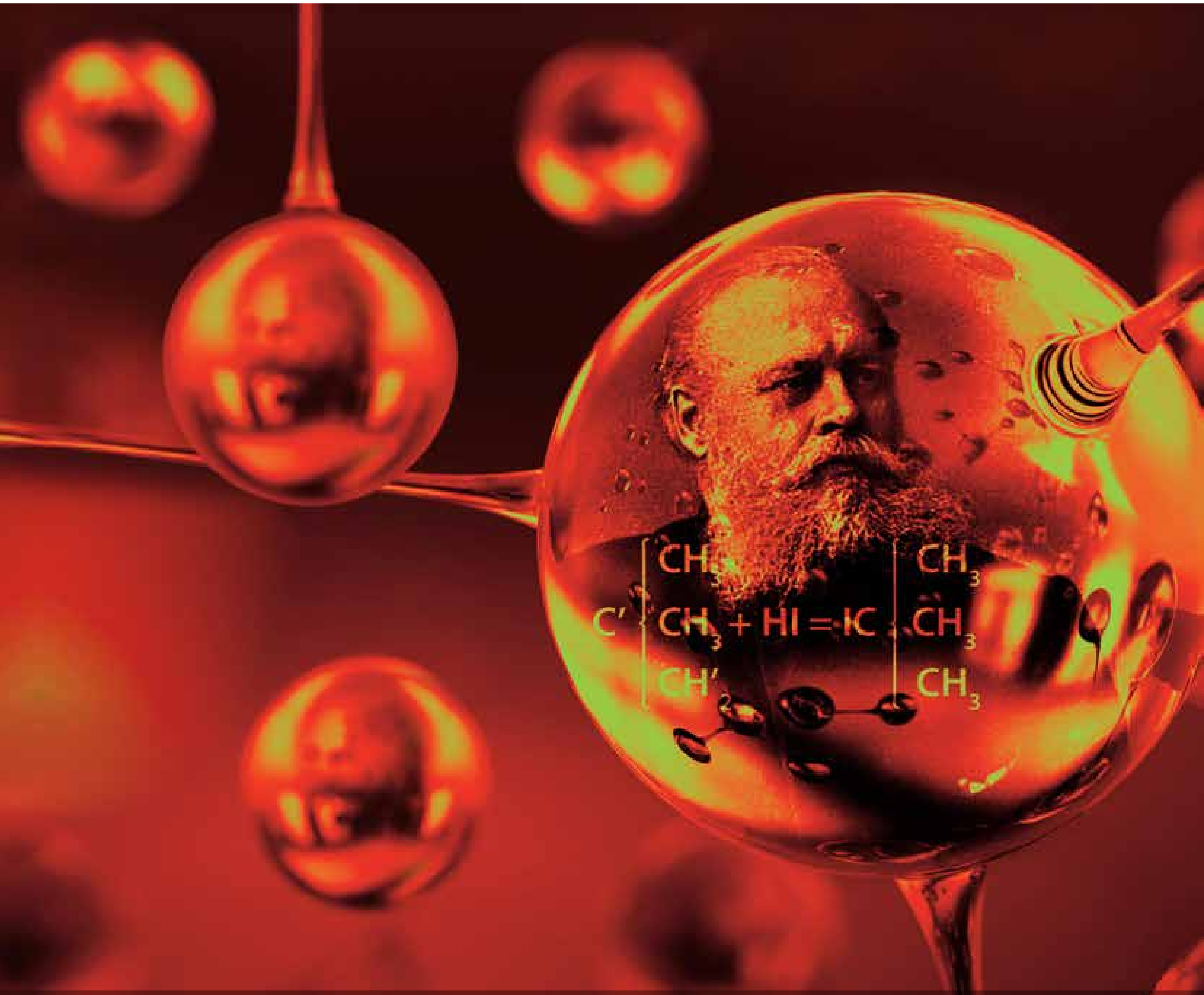
In this context, Kazan Chemical School occupies a special place. Russian tradition in chemistry was born in Kazan University during the 1840's and is associated with the scientific and pedagogical activities of Karl Klaus (1796–1864), Nikolai Zinin (1812–1880), and their disciple Alexander Butlerov (1828–1886). Vladimir Markovnikov was the first and probably the most talented student of Butlerov. He was not only a student of Butlerov but also the main disciple of the Butlerov's theory of chemical structure.

Vladimir Markovnikov is the outstanding representative of the Kazan Chemical School, the one of the founders of the principles of the mutual influence of atoms in organic molecules, who in the walls of Kazan University formulated and proved one of the key rules of modern organic chemistry. In 2019, we will celebrate 150th anniversary of the Markovnikov Rule discovery. It is the famous rule on the regioselectivity of electrophilic addition to unsaturated compounds, which has entered the science to such an extent that it is designated only by the first letter of the author's surname - "M".

Markovnikov left a bright mark not only at Kazan University. In 1873, V. Markovnikov moved to Moscow and started to teach chemistry in the Moscow University. He founded the Moscow Chemical School there.

Markovnikov Congress will be a platform for the presentations and exposures of new trends and advances of the research work to bring together leading academic scientists, researchers and research scholars to exchange and share their experiences and research results on all aspects of Organic Chemistry. Furthermore, it is opportunity to join the international community in your field of interest and experience and explore Kazan, Russia.
I invite you to take this opportunity to join us for academic exchange and visit our city Kazan, Russia.
I am looking forward to seeing you in Kazan, Russia in June, 2019!!!

Rector of Kazan Federal University,
Professor I.R.Gafurov



MARKOVNIKOV CONGRESS ON ORGANIC CHEMISTRY

21–28 June 2019
Moscow — Kazan

POSTER PRESENTATIONS

SYNTHESIS AND BIOLOGICAL ACTIVITY OF 5-ARYLPYRAZOLYL RECEPTORS ON A (THIA)CALIX[4]ARENE SCAFFOLD

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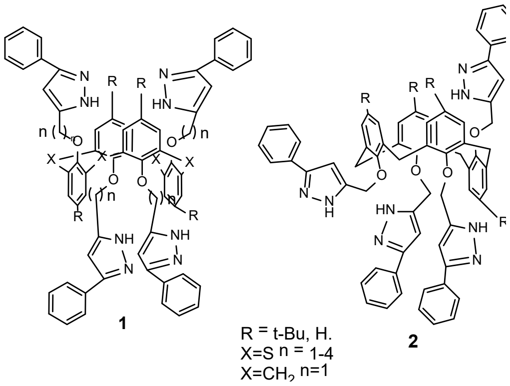
Pyrazole derivatives represent structural units in a number of therapeutical drugs and biologically active compounds, which display anti-inflammatory, antimicrobial, antitumor, and antidiabetic effect. Introduction of heterocyclic groups into the macrocyclic scaffold allows one to combine several pharmacophoric groups in a molecule, as well as to vary conformational mobility of the receptor. Calixarenes macrocycles are relatively accessible and nontoxic; for this reason, the compounds on their basis are attractive for the design of receptors and drug delivery agents.

We previously suggested a facile approach towards heterocycle synthesis from ketoacetylenic precursors of calix[4]arenes, which is new in macrocyclic chemistry [1]. Therefore, the aim of this work is to synthesize arylpyrazole derivatives on a calixarene framework from corresponding ketoacetylenic precursors, where stereoisomeric form, the distance of receptor units from calixarene scaffold, and the size of macrocyclic cavity are varied.



Scheme 1.

As a result of this work, and number of phenylpyrazole derivatives in 1,3-alternate (1) and partial cone (2) has been synthesized in almost quantitative yields from ketoacetylenic precursors (90–96%). These products have been characterized using a number of NMR techniques (COSY, HSQC, HMBC). Toxicological characterization of the pyrazoles 1, 2 has shown their low toxicity towards Gram-positive and Gram-negative bacteria, as well as fungi. In addition, no hemolytic activity of these derivatives towards human erythrocytes has been shown. These results are promising for the development of nontoxic drugs.

This work was supported by the Russian Foundation for Basic Research (project nos. 17-53-10016-KO-A and 17-03-00389-A).

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DESIGN AND BEHAVIOUR IN SOLUTION OF NEW PHOTOSWITCHABLE ORGANIC RECEPTORS BASED ON THIACALIX[4]ARENES AND [1.1.1.1] METACYCLOPHANES BEARING CARBOXYLIC BINDING SITES

Akhmetzyanova Z.V.,[a] Ovsyannikov A.S.,[a,b] Popova E.V.,[b] Solovieva S.E.,[a,b] Antipin I.S.,[a,b]

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Design of supramolecular systems is one of the most developing area in modern chemistry. Light driven photo-switchable systems are very promising for design of new materials with controlled properties (porosity, luminescence etc)[1]. Metacyclophanes, especially calix[4]arenes, composed of four aryl units bridged through methylene groups (for “classical” calix[4]arene) or sulphur atoms (for thiacalix[4]arene) and containing azo-groups present attractive molecular organic receptors for building new photoresponsive assemblies in solution as well as in the solid state. Here we report the synthesis of new low rim tetrasubstituted thiacalix[4]arene and [1.1.1.1]metacyclophane azoderivatives adopting *1,3-alternate* conformation and containing four carboxyl groups as coordinating sites and azo-groups as photoswitchable sites (fig 1). The ability of these compounds to form nanoassociates in solution with d and f metal cations under UV-irradiation have been studied by UV-spectroscopy and Dynamic Light Scattering (DLS).

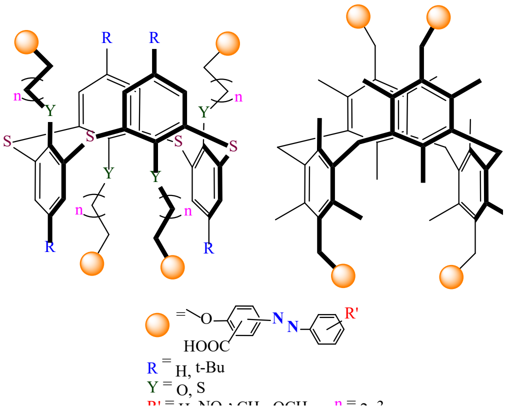

Figure 1

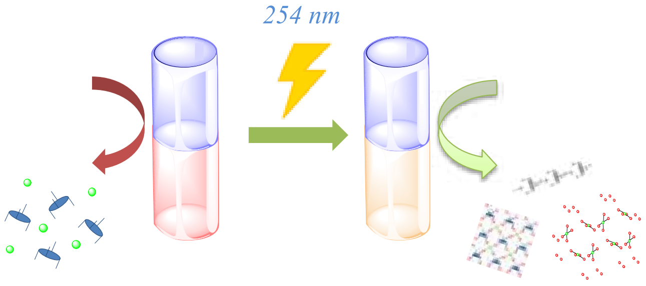

Figure 2

Acknowledgements - This work was supported by the RSF № 17-73-20117.

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2-ARYL-2-FLUORO-2-(3-INDOLYL)ACETOHYDROXAMIC ACIDS DERIVATIVES AS DRUGS AGAINST APOPTOSIS- AND MULTIDRUG-RESISTANT CANCER

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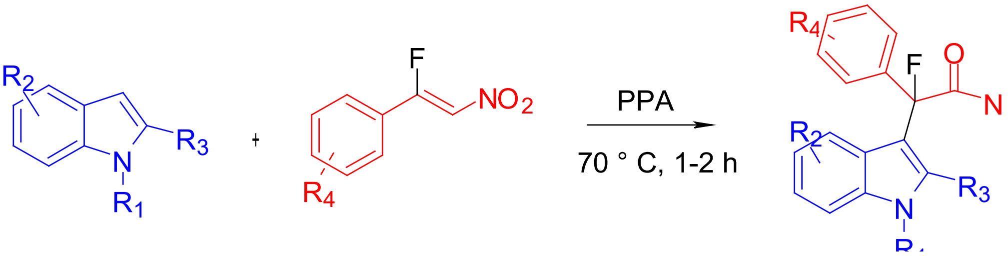
Our recent studies of a reaction of indole derivatives with β-nitrostyrenes in polyphosphoric acid (PPA)20 led to the discovery of an efficient synthesis of 2-aryl-2-(3-indolyl)-acetohydroxamates, that are active against apoptosis- and multidrug-resistant cancer cells as well as glioblastoma neurosphere stemlike cell cultures derived from patients[1].

We suggest that the introduction of the fluorine atom in the α-position of the hydroxamic acid will increase the biological activity (Scheme 1).



Scheme 1.

Financial support from Russian Science Foundation (Grant #18-13-00238) is gratefully acknowledged.

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TRANSITION METAL-CATALYZED CROSS-DEHYDROGENATIVE COUPLING OF CYCLIC NITRONES WITH *NH*-HETEROAROMATICS: A CONVENIENT APPROACH TO CREATING NEW C–C AND C–N BONDS

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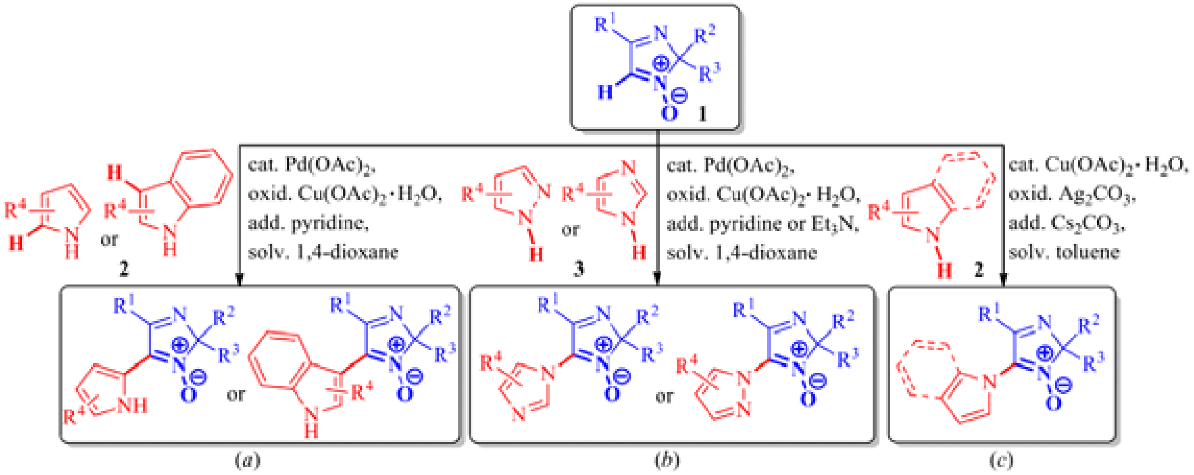
Cyclic nitrones represent a valuable class of non-aromatic unsaturated azaheterocycles, which seems to be of considerable importance nowadays. Due to the presence of an *N*-oxide moiety in their structure, such compounds are known to exhibit versatile properties affording to exploit these substances in various fields of science and technology. In particular, it was shown that spin-trapping features of cyclic nitrone derivatives can be used not only for analytical purposes, but also for therapeutical ones (as potential antioxidant agents). In this connection, the emerging challenge for organic chemists is to develop efficient synthetic strategies allowing one to obtain unexplored functionalized nitrone derivatives.

Our research group has succeeded in elaborating the novel approaches for direct C(sp^2)–H bond functionalization in cyclic aldonitrones, namely, 2*H*-imidazole 1-oxides **1** (Scheme 1). In particular, we have shown that such compounds are able to react diversely with various five-membered *NH*-heteroaromatics under transition metal catalysis, an *N*-oxide function being retained in the products. Thus, for example, aldonitrones **1** can be involved in Pd(II)-catalyzed oxidative C–H/C–H coupling with pyrroles [1] and indoles **2** [2], as shown in Scheme 1a. However, essentially identical catalytic conditions may also promote C–H/N–H coupling in case of interaction of **1** with pyrazoles or imidazoles **3** (see Scheme 1b). Besides, it is interesting to note that in case of interaction with pyrroles/indoles **2**, we have managed to "switch" the course of reaction from the C–H/C–H coupling towards the C–H/N–H one by means of using Cu(II) catalysis, as depicted in Scheme 1c. At the moment, we are continuing to investigate these metal-catalyzed cross-coupling transformations to optimize conditions and to gain higher yields of target products.



Scheme 1. TM-catalyzed C–C and C–N cross-coupling of cyclic aldonitrones with NH-heteroaromatics

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This work was supported by the Russian Science Foundation (Project no. 18-73-00088).

SYNTHESIS OF 1-BUTYL-3,6-DIAZAHOMOADAMANTAN-9-ONE AND ITS DERIVATIVES

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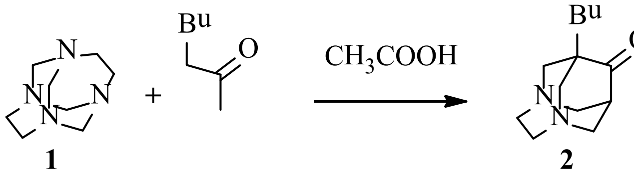
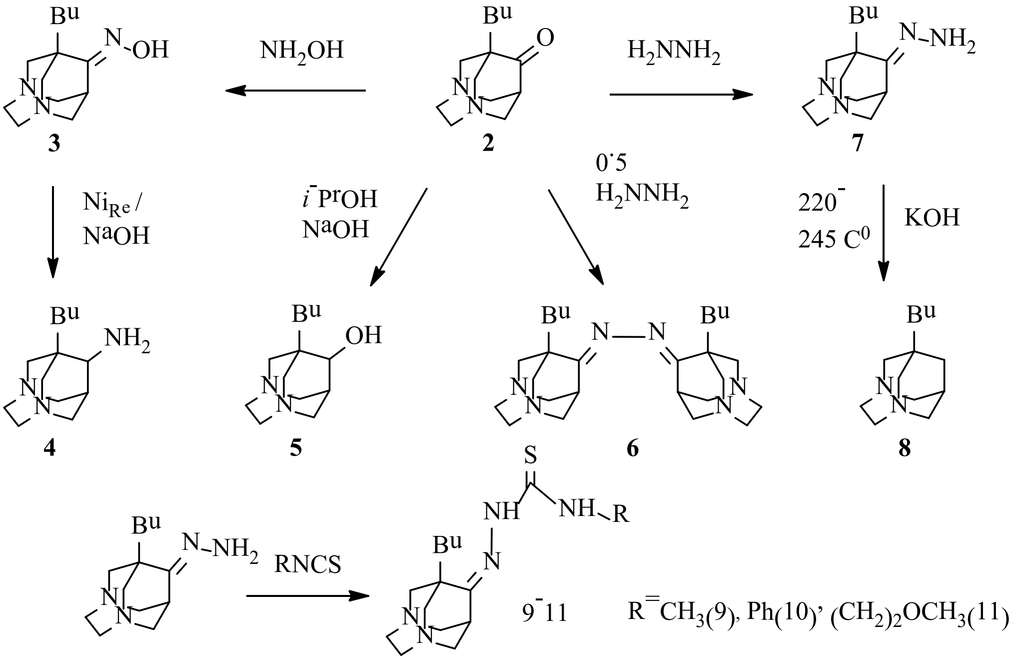
In our work [1], we developed methods of synthesis of different fragrant derivatives of 3,6-diazahomoadamantane. In this work, by condensation of **2-heptanone with** 1,3,6,8- *tetraazatricyclo*[4.4.1.1^{3,8}]dodecane **1, 1-butyl-3,6-diazahomoadamantan-9-one 2 has been synthesized by two methods.**



By reaction of ketone **2** with hydroxylamine, 1-butyl-3,6-diazahomoadamantan-9-one oxime was obtained. Then oxime **3** was reduced with Ni-Al alloy (Raney alloy) in water-alkaline medium into 1-butyl-3,6-diazahomoadamantan-9-amine **4**. By heating of ketone **2** with NaOH in isopropyl alcohol, 1-butyl-3,6-diazahomoadamantan-9-ol **5** was synthesized. Ketone 2 was reduced by the Wolff-Kishner reaction via hydrazone **7** into 1-butyl-3,6-diazahomoadamantane **8**. By heating of ketone **2** with hydrazine, azine **6** has been obtained.

N-substituted thiosemicarbazones **9-11** were synthesized by reaction of different RNCS isothiocyanates with hydrazone **7**. We have obtained previously unknown substances which might be of interest as perspective biological active compounds.



References
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THE STUDY OF ELECTROPHILIC ACTIVATION OF 1-ARYL-3-BROMO-2,2-DIFLUOROPROPAN-1-ONES UNDER THE ACTION OF TRIFLUOROMETHANESULFONIC ACID CF_3SO_3H

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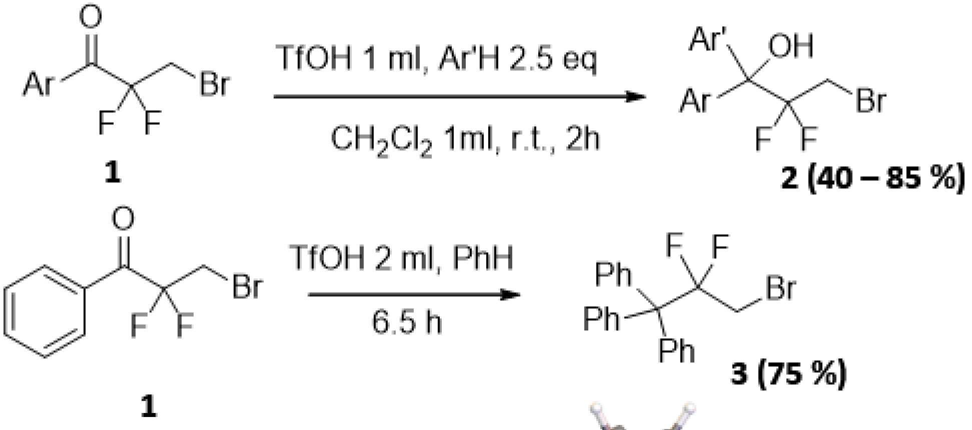
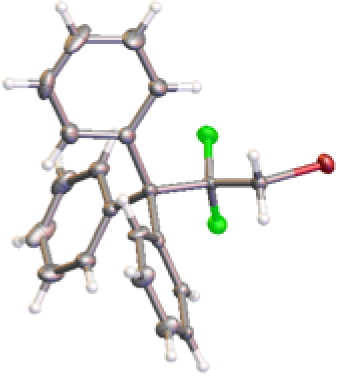
α,α-Difluoroketones **1** represent an important class of organofluorine compounds, which are useful for medicinal chemistry and other fields. In the current work the reactions of 3-bromo-2,2-difluoro-1-arylpropan-1-ones **1** with arenes in trifliuoromethanesulfonic acid (CF_3SO_3H, TfOH) were studied.

Due to significant the electron-withdrawing effect of two fluorine atoms, the carbonyl group can react with various arenes to form 1,1-diaryl-3-bromo-2,2-difluoropropan-1-oles **2** or 1,1,1-triaryl-3-bromo-2,2-difluoropropanones **3** in good yields.





SYNTHESIS OF NEW BIHETEROCYCLIC SYSTEMS BASED ON 3-ETHOXYCARBONYLMETHYLQUINOXALIN-2-ONE

Algaeva N.E., Elena A. Khafizova, Victor V. Syakaev, Olga B. Bazanova,
Ildar Kh. Rizvanov, Shamil K. Latypov, Oleg G. Sinyashin, Vakhid A. Mamedov

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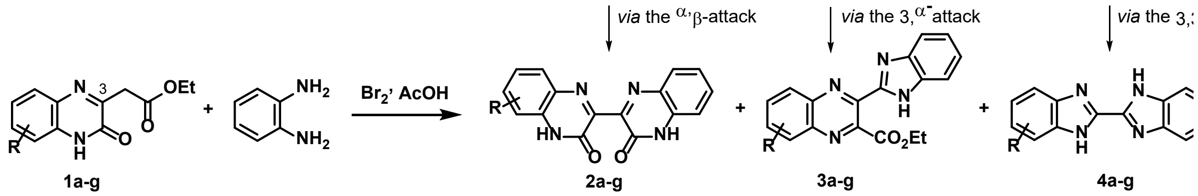
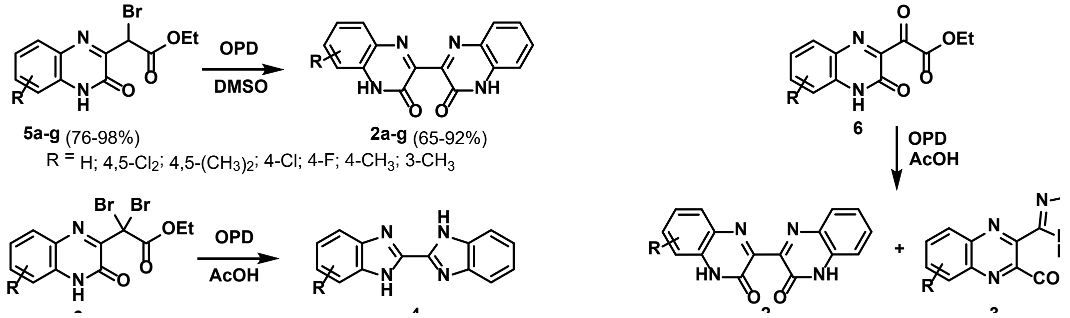
Biheteroaryls which contain two bioactive molecular fragments are an important class of organic compounds. The design and synthesis of new biheteroaryl systems employing carbonecarbon bond-forming reactions through the merging of two heteroaromatic units are highly appreciated in synthetic organic, medicinal and material chemistry. Indeed, biheteroaryl structural motifs containing benzimidazole moieties has attracted considerable attention due to their interesting biological and physical properties and are often found in biologically active molecules and natural products. It is known that the compounds having benzimidazole fused at C2 and C5(6) positions with benzimidazole and quinoxaline heterocycles are an important class of biheterocyclic systems due to their wide applications in the field of medicinal chemistry. In particular, 2,2′-, 5(6′) and 6(5′)-bibenzimidazole, and benzimidazolylquinoxaline derivatives serve as a vital skeleton in the design of drug molecules.

In this report the synthesis of novel 2,2′-bibenzimidazoles, benzimidazol-2-ylquinoxalines and 3,3′-biquinoxaline derivatives through Hisberg-Korner reaction and Mamedov heterocyclic rearrangement using 3-ethoxycarbonylmethylquinoxalin-2-ones and *o*-phenylenediamine (OPD) as precursors is described.



The understanding of the reaction mechanism made it possible for us to develop the regioselective methods for the synthesis of these biheterocyclic systems.



The scope of these reactions and experimental details including spectral peculiarities of the structures will be discussed.

This work was supported by the Russian Science Foundation (RSF) (grant No. 18-13-00315).

ONE-POT SYNTHESIS OF 3-(2-FLUOROALKENYL)INDOLES

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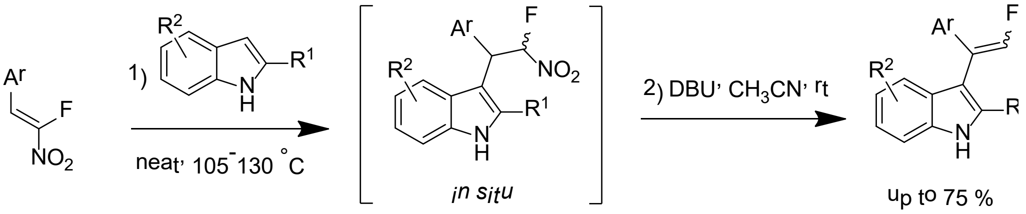
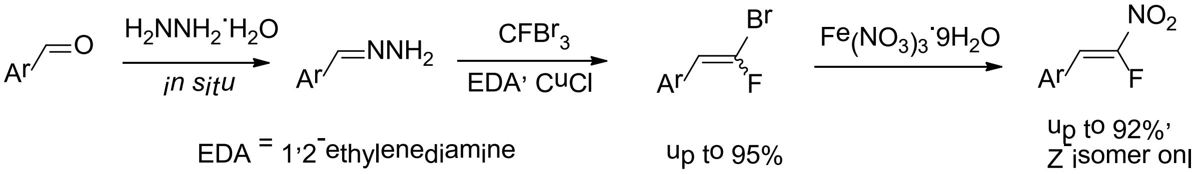
The indole core is one of the most important structural fragments of modern drugs and natural products [1]. In particular, 3-vinylindoles are an important class of functionalized indoles. These molecules have been used as building blocks for the synthesis of a number of significant biologically active compounds [2-5]. Incorporation of fluorine into the molecule is one of the fundamental tools in the development of new drugs and materials. This work is devoted to the synthesis of novel 3-(2-fluoroalkyl) indoles. We developed a one-pot method that involves Michael addition of β-fluoro-β-nitrostyrenes to indoles in neat and catalysts-free conditions and a subsequent elimination of HNO_2 using DBU as a base. (Scheme 1).



Scheme 1. One-pot synthesis of 3-(2-fluoroalkenyl)indoles

The starting β-fluoro-β-nitrostyrenes were prepared according to the previously developed method (Scheme 2), based on the radical nitration of 2-bromo-2-fluorostyrenes. [5] 2-Bromo-2-fluorostyrenes, in turn, were obtained by the reaction of catalytic olefination from the corresponding aromatic aldehydes. [6]



Scheme 2. Preparation of starting β-fluoro-β-nitrostyrenes

This method opens up a direct way to valuable 3- (2-fluoroalkenyl) indoles, which in turn can be used as precursors for the synthesis of various fluorine-substituted biologically active compounds.

This work was supported by the Russian Science Foundation (RSF) (Grant No. 17-73-10358).
This work was partially supported by the Russian Federation President Grant for leading scientific schools № 4687.2018.3.

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SYNTHESIS OF NEW POLYDIMETHYLSILOXANES WITH DIAMIDE FRAGMENTS BASED ON RENEWABLE RESOURCE

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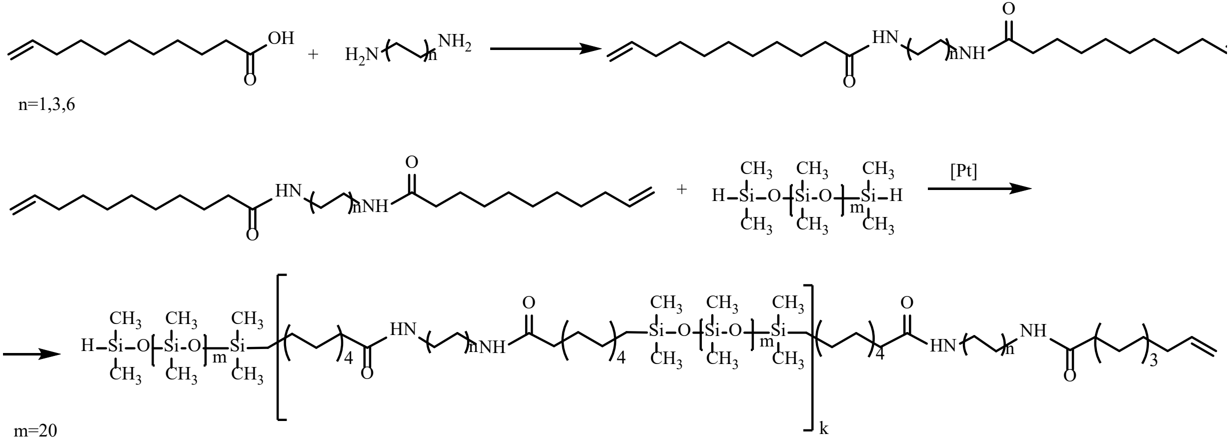
PDMS have high chemical and physical stability, good biocompatibility, optical transparency, hydrophobicity and flexibility. Aliphatic polyamides are important engineering materials with excellent properties, such as a high modulus, good toughness, heat resistance, abrasion resistance. According to the References, the polymers obtained based on amide and siloxane fragments of a linear structure demonstrate interesting morphological, thermal and mechanical properties, which combine the properties of both polysiloxanes and polyamides [1]. In our work, we want to get the complementary data about the possibility of obtaining polymers by hydrosilylation method.



Scheme 1. Synthesis of polydimethylsiloxanes with diamide fragments

We studied effect of the hydrocarbon spacer length in the amide fragment on the properties of obtained polymers. The structures of the products were confirmed by ^{1}H NMR spectroscopy and gel-permeation chromatography. In this work, we explored the properties of these polymers by DSC, TGA and other physical-chemical methods.

This work was supported by Russian Science Foundation (project No 17-73-10327)

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КОНКУРЕНТНЫЕ РЕАКЦИИ ПРИ СИНТЕЗЕ ДИХЛОРДИАЗАБУТАДИЕНОВ

Аскерова У.Ф., Мухтарова С.Х., Шыхалиева И.М., Микаилова Н.Ф., Пирвердиева Н.Р. Ахмедова Н.Э., Шыхалиев Н.Г., Магеррамов А.М

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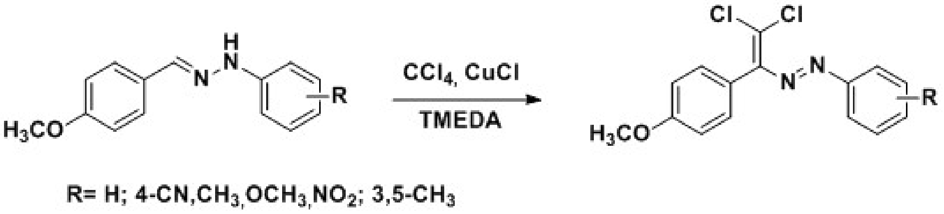
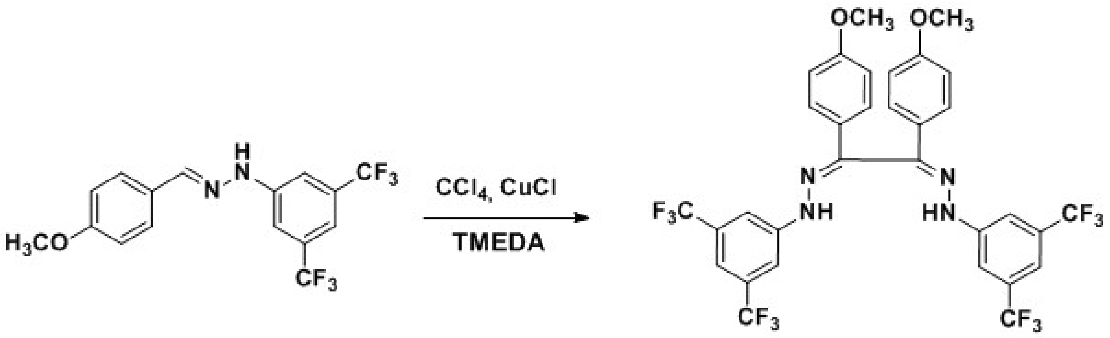
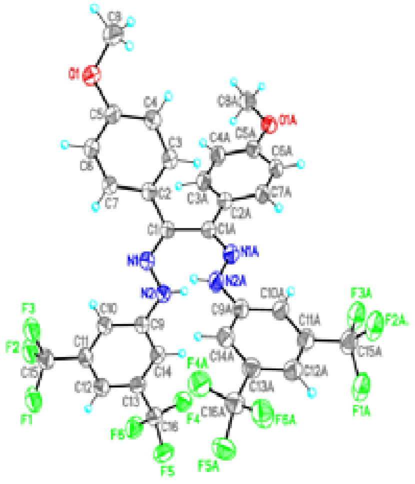
В условиях реакции каталитического олефинирования, на основе фенилгидразонов 4-метоксиальдегида с различными фенилгидразинами, синтезирован ряд дихлодиазабутадиенов. Структура синтезированных соединений подтверждена методами ЯМР и РСА.



R= H; 4-CN,CH_3,OCH_3,NO_2; 3,5-CH_3

Установлено, что при наличии в гидразиновом фрагменте сильной электроотрицательной –CF_3 группы, в отличии от вышеуказанных реакций, диен не является основным продуктом. Образуется новое соединение, продукт конкурентной реакции - сшивки двух молекул соответствующего гидразона. Структура последнего подтверждена методом ЯМР и РСА.





Молекулярная структура (1Z,2Z)-1,2-бис(трифторметил)гидразоно)-1,2-бис(4-метоксифенил)этана

CHEMICAL HYDROLYSIS OF RT-PCR OLIGONUCLEOTIDE PROBES AS QUALITY CONTROL METHOD

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One of the challenges in RT-PCR oligonucleotide probes quality control is to confirm fluorophore and quencher optical properties such as absorbtion (i.e. content) and fluorescence. The results of spectrophotometric and fluorimetric measurements are distorted by intramolecular interactions so fluorophore and quencher have to be separated. We developed two-stage chemical hydrolysis of nucleotide chain method to solve this problem. Fig.1 shows UV-VIS spectra of distortions caused by Cy5 fluorophore and BHQ1 quencher interaction.

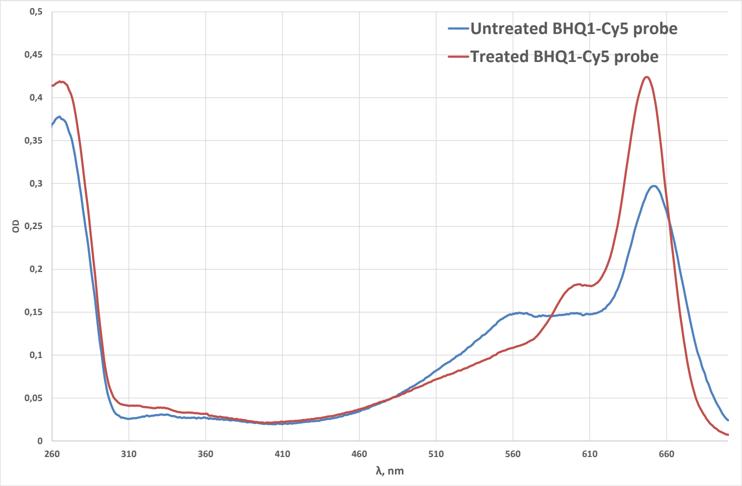

Fig. 1.: BHQ1-Cy5 oligonucleotide probe spectra before (blue line) and after (red line) hydrolysis

Subsequently hydrolysis conditions are optimized to exclude any degradation of dyes commonly used in oligonucleotide probes. Moreover, presented method uses chemicals involved in traditional solid phase oligonucleotide synthesis making it cheap and handy tool for QC on the manufacture. In addition, it shows good reproducibility and faster (2 hours vs overnight) than such alternative as phosphodiesterase digestion of oligonucleotide.

SYNTHESIS AND STRUCTURE OF NOVEL GADOLINIUM COMPLEXES OF CARBOXYLATE PHOSPHONIUM BETAINES

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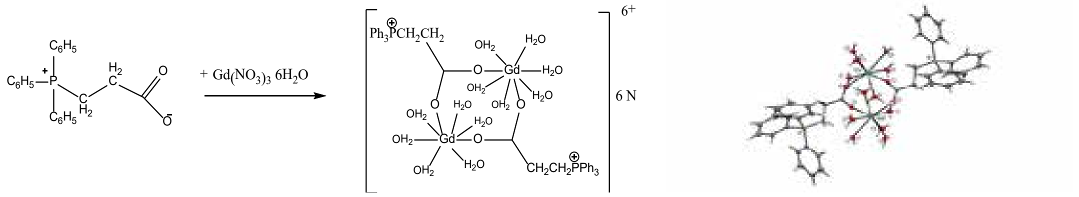
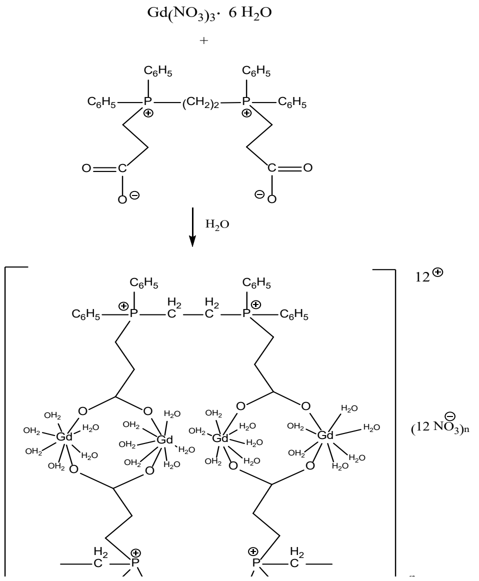
Gadolinium complexes are commonly used to improve the contrast of images obtained by Magnetic Resonance Imaging. Unfortunately, gadolinium ion is highly toxic in its hydrated form $[Gd(H_2O)_8]^{3+}$, its complexation with an organic ligand reduces this toxycity and form thermodynamically very stable compounds [1].

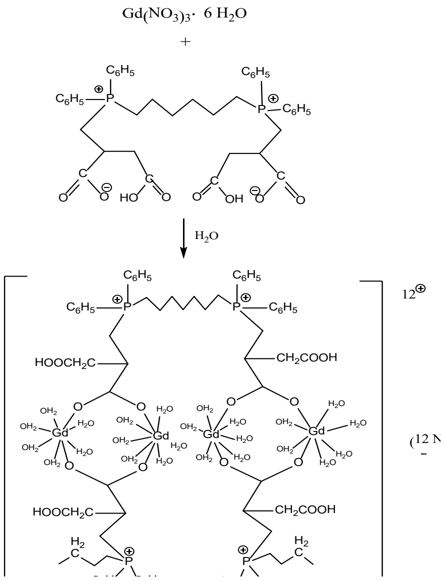
Earler we showed that a series of new mononuclear and heteronuclear complexes of carboxylate phosphonium betaines with biologically important metals (Zn(II), Cd(II), Hg(II) and Cu(II)) were obtained in aqueous media at ambient temperature. X-ray single crystal diffraction showed that carboxylate phosphonium betaines exhibit versatile complexation abilities, producing monomeric, dimeric and tetrameric homonuclear and mixed metal complexes [2].

In this work we have studied the formation of colorless gadolinium complexes with mono- and diphosphonium betaines in aqueous solution.

By reaction of gadolinium nitrate ($Gd(NO_3)_3$ $6H_2O$) with mono- and diphosphabetaines at a ratio 1:1 in water medium we obtained colorless complexes.







The structure of the complexes have been established by comple[of modern chemical, physical, and physicochemical methods. The thermal stability was studied by synchronous thermogravimetry and differential scanning calorimetry (TG-DSC).

This work funded by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (№ 4.5888.2017/8.9).

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OXIDATIVE ACYLOXYLATION OF ETHERS BY CYCLIC DIACYL PEROXIDES

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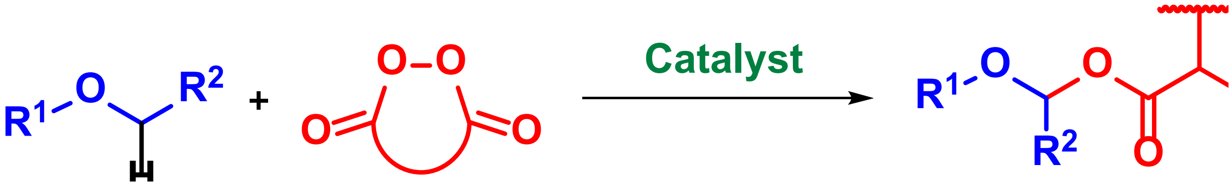
Searching for methods to create a carbon-heteroatom bond in the molecule is one of the relevant problems of modern organic chemistry. Traditionally, ethers are used as solvents and direct functionalization of these inconvenient substrates – a real challenge for organic chemists due to the low reactivity of this class of compounds to many reagents. In particular, the application of classical approaches to the formation of C(sp^3)-heteroatom bonds is complicated by the weak coordination of ethers with transition metals.

Only in recent years, a number of works have been performed on the synthesis of α-acyloxy esters using oxidative C(sp^3)-O coupling, but all methods require the introduction of both a catalyst and an oxidant into the system [1]. As a consequence, the main disadvantage of these methods is the formation of large amounts of waste. As a result, the creation of new selective methods for the C(sp^3)-H functionalization of ethers, corresponding the principles of green chemistry, is a fundamentally important problem.

Here, we presented a new convenient method of oxidative acyloxylation of ethers using cyclic diacyl peroxides both as an oxidant and as a reagent for C–O coupling (Scheme 1).



Scheme 1. A new method of oxidative functionalization of ethers

This work was supported by the Russian Science Foundation (Grant № 18-13-00027).

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USING A NETWORK OF ORGANIC REACTIONS TO PREDICT THE WAYS OF SYNTHESIS OF A COMPOUND

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Development of new high performant synthetic procedures and simplification of structure elucidation procedure lead to great accumulation of data in organic synthesis. In biggest databases amount of reaction data exceeds 100 mln, which rises problem of analysis of big data in chemistry. To simplify searching through existing data, reactions can form an interconnected network. In it, some molecules can exist as reactants in some reactions, and as products in others. An analysis of organic chemistry using the tools of the theory of networks allows us to identify

most of the "central" organic molecules and predict which molecules will be formed in the future [1] Network-based statistical analysis is useful for parallel synthesis optimizaton, assessing chemical reactivity, etc.

In the work we developed an algorythm for creation and analysis of network of organic chemistry. The network was built based on 2.5 million reactions from patents, which contains 1,2 mln unique molecules. A quick search of synthetic pathways for molecules of interest with a step-by-step textual description of the reaction is implemented. Using the CGRdb database, possibility to find similar molecules to a given one was implemented with following extraction of reaction pathways. The algorithm includes possibility to stop the synthesis plan on commercially available compound or return pathway of a given length. Thus, the developed algorythm provide chemist with synthetic routes and description of synthesis leading to compounds of interest or its nearest neighbor.

The work was funded from the Russian Government Program of Competitive Growth of Kazan Federal University, the program of State Assignments for science (Projects No. 4.1493.2017/4.6 and No 4.5151.2017/6.7).

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ACID-CATALYZED TRANSFORMATIONS OF 2-(ADAMANTAN-1-YL)AZIRIDINE

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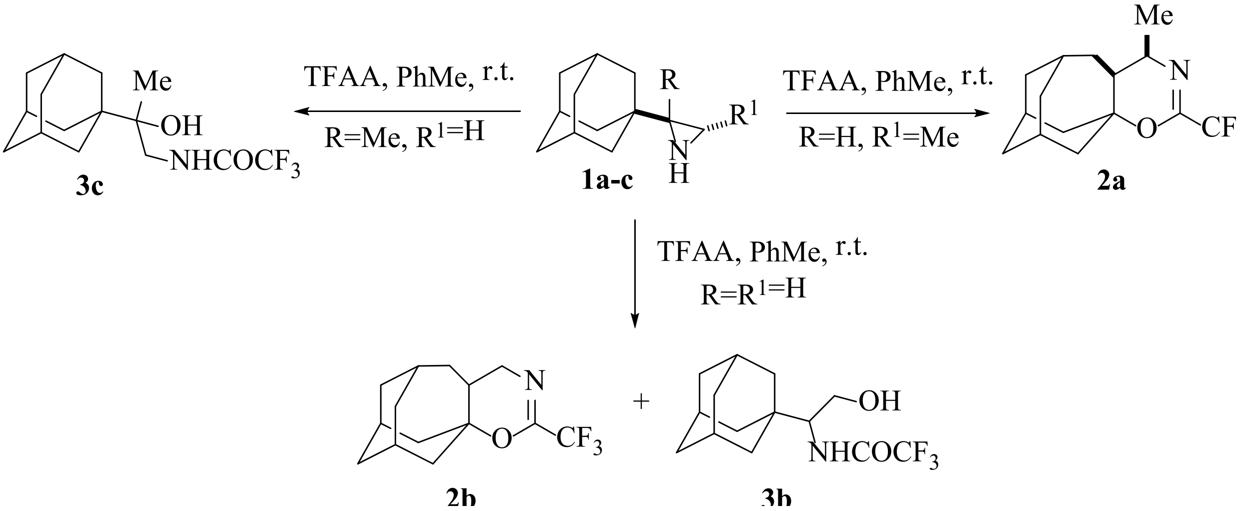
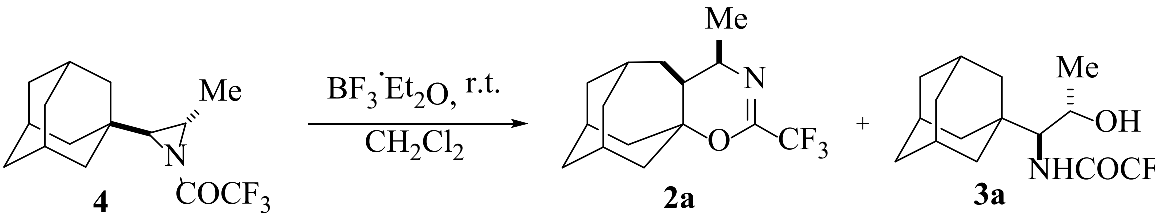
The aziridine fragment is a universal building block for the synthesis of many biologically active compounds. Many natural and synthetic compounds containing the aziridine fragment are applied as anticancer agents. Along with the cytostatic and bacteriostatic activity, aziridine derivatives exhibit an antiviral activity.

We detected an unusual rearrangement of adamantyl-containing aziridines under the action of trifluoroacetic anhydride. In the case of *trans*-2,3-disubstituted aziridine **1a**, 1,3-oxazine **2a** was condensed with a homoadamantane fragment (80% yield). 2-(Adamantan-1-yl)aziridine **1b** leads to a mixture of products **2b, 3b** (1:3). Under the action of TFAA, the aziridine ring is opened to form an adamantylcarbinyl cation and the subsequent skeletal transformation of the adamantane cage into a homoadamantane cage. Further intramolecular cyclization leads to the formation of 1,3-oxazine **2a, b**. 2,2-Disubstituted aziridine **1c** under these conditions gives a single product **3c** (76% yield). The regioselectivity of the opening of the aziridine cycle depends largely on the number and location of substituents in the ring.



Scheme 1. Reaction of 2-(adamantan-1-yl)aziridine with TFAA.

N-Trifluoroacetyl-2-(adamantan-1-yl)-3-methylaziridine **4** under the action of $BF_3 \cdot Et_2O$ results in 1,3-oxazine **2a** and minor product **3a** with 1*S**, 2*R** configuration.



Scheme 2. Reaction of *trans*-aziridine **4** with $BF_3 \cdot Et_2O$.

The structure of the 1,3-oxazine **2a** was proven by NMR and X-ray structural analysis (Lomonosov Moscow State University). A single crystal X-ray diffraction study showed that 1,3-oxazine **2a** has a *cis*-configuration.

This work was supported by the Russian Foundation for Basic Research (project No. 17-03-01292 and 19-03-00929).

STRAIGTHFORWARD SYNTHESIS OF α-TRIFLUOROMETHYLATED VICINAL DIAMINES

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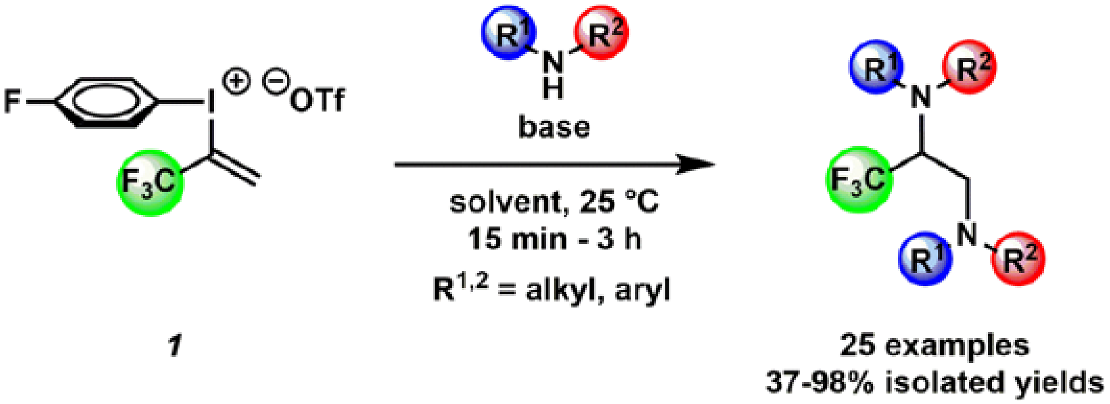
Fluorine containing organic compounds have distinct physico-chemical and biological properties compared to their hydrocarbon analouges. In general, enhanced lipofilicity, metabolic stability and decreased basicity can be attributed to the organofluorine compounds, which features are highly desired in pharmaceutical and agrochemical applications. [1]

Besides these advantages, the synthesis of selectively fluorinated organic compounds suffers from either high electrophilicity of fluorinating agents, low nucleophilicity of floride ion or broad reactivity of organofluorine reagents. Due to these difficulties, development of reagents and synthetic methods for the synthesis of organofluorine compounds are necessary. [2]

Our group has recently published an easily feasible synthesis of 2-trifluoromethyl-aziridines from primary amines and a hypervalent iodine reagent, (4-fluorophenyl)(3,3,3-trifluoroprop-1-en-2-yl)iodonium triflate (**1**) [3]. In continuation of this work, we optimized reaction conditions to achieve simple and mild synthetic procedure for the preparation of 3,3,3-trifluoropropane-1,2-diamines from secondary amines. We have investigated the scope of reaction, regarding the electronic and steric effects of secondary amines, and isolated the corresponding diamines in moderate to excellent yields (37-98%).



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SYNTHESIS AND REACTIVITY OF 2,3-DIHYDRO-1*H*-CHROMENO[3,2-*C*] PYRIDINES

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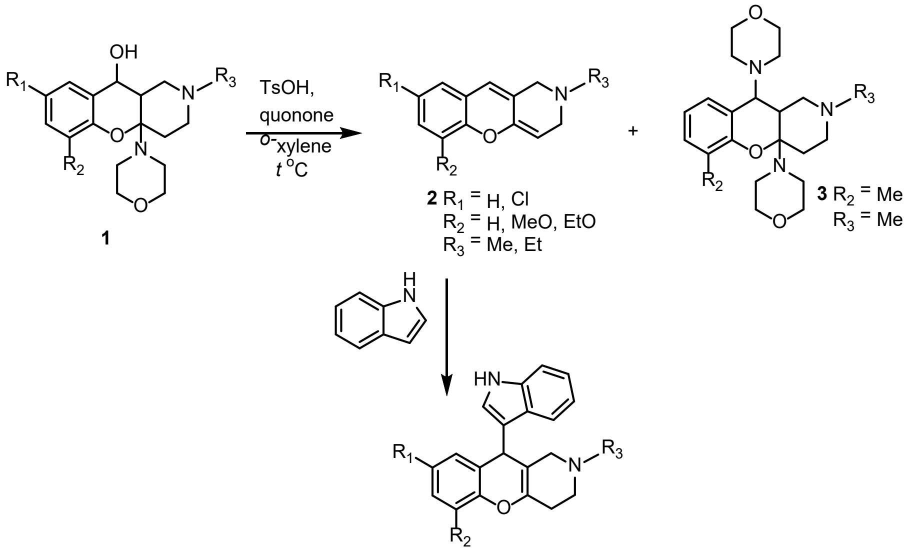
Recently we have studied the reactions of chromeno[3,2-*c*]pyridines with activated alkynes under different conditions [1]. It was shown that chromenopyridines and their derivatives are promising inhibitors of acetylcholinesterase (AChE) and buterylcholinesterase (BuChE)[2]. Continuing this work, we synthesized 2,3-dihydro-1H-chromeno[3,2-c]pyridines **2** and dimorpholyl substituted derivatives **3** from chromenopyridines **1** using acid-catalyzed oxidative dehydration in o-xylene. The structure of an unusual product **3** containing two morpholine fragments was confirmed by X-ray diffraction data (Fig. 1). Assuming that compound **3** is obtained by the nucleophilic addition of morpholine, we used indole as a nucleophile. This allowed us to obtain compound **4**.



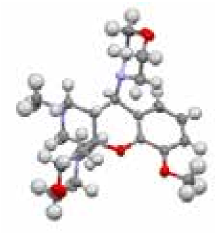


Figure 1. Molecular structure of compound **3**

Mass and IR spectra were registered using instruments of the Shared Research and Educational Center of Physic-Chemical Studies of New Materials, Substances and Catalytic of RUDN. The publication has been prepared with the support of the "RUDN University Program 5-100".

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BASED-ASSISTED FUNCTIONALIZATION OF ISOQUINOLINE BY CYANOPHENYLACETYLENE AND WATER

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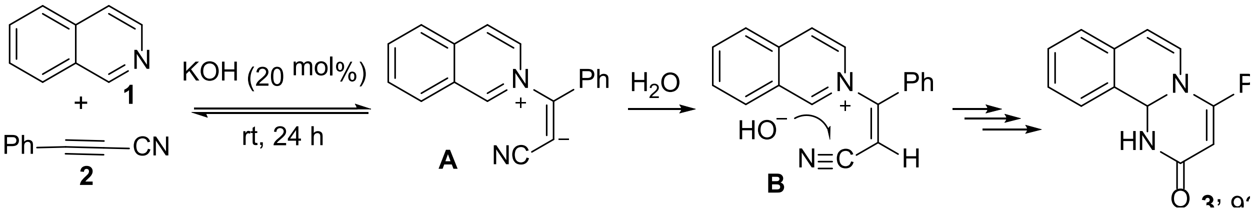
Functionalized isoquinolines are now extensively studied and applied as drugs, their precursors and privileged building blocks in heterocyclic chemistry. Consequently, the search for their expedient and concise syntheses from available starting materials remains a standing challenge in this field.

During our systematic study [1], [2], [3] of the azine functionalization with electron-deficient acetylenes *via* 1,3-dipole (zwitterion) intermediates we have found that isoquinoline, upon treatment with aryltrifluoroacetylacetylenes and water, undergoes an efficient 1,2-annulation to deliver fluorinated oxazinoisoquinolines [4] in a one synthetic operation.

To our surprise, when cyanophenylacetylene **2** is employed as electron-deficient acetylene in the reaction with isoquinoline **1** in an aqueous solution of KOH (**1**:**2**:H_2O = 1:1:5, 20 mol% KOH, 20-25 °C, 24 h), the product of isoquinoline annulation with pyrimidine ring, dihydropyrimido[2,1-*a*]isoquinoline-2-one **3**, have been obtained in almost quantitative yield (Scheme 1).



Scheme 1.

Apparently, the reaction proceeds through the formation of a 1,3-dipole intermediate **A**, the carbanionic center of which is neutralized by a proton from a water to generate *N*-ethenylisoquinolinium hydroxide **B**. Then, the hydroxyl group adds to the cyano function, followed by the domino-sequence to afford product **3**. Noteworthy, hydroxide anions in this reaction act both as catalyst and reactant.

This water-driven, environmentally friendly synthesis, which features the one-pot implementation, atom economy and energy saving, provides for a facile approach to the synthesis of pharmacologically promising compounds.

This work was supported by Russian Foundation of Basic Research (Grant No 18-03-00762)

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$Co(DIPY)_3^{3+}$ IN SILICA CONFINEMENT: DOPING INTO SILICA VERSUS SILICA COATING FOR SIZE MANIPULATION

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Transition metal complexes are on a top of current interest due to their catalytic activity in organic synthesis. However, conversion of molecular complexes into composite nanoparticles is an important prerequisite of their use as nanoheterogeneous catalysts with high recyclability. It is worth noting that both size and content of the composite nanoparticles play significant role in their catalytic activity.

Tris(2,2'-bipyridyl)cobalt(III) doped silica nanoparticles with various sizes from 4.5 to 140 nm were obtained using different methods (Stober's method and a procedure of water in oil reverse microemulsion) and conditions of the synthesis. It is shown that two main processes: silica coating of nanoprecipitates and doping of molecular complexes into silica matrix are of major impact on the size and content of the composite nanoparticles. It is, in particular, highlighted that an order of mixing of components is a powerful tool to tune the size of the composite nanomaterial.

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF NEW ISATIN DERIVATIVES AND HYDRAZONES ON THEIR BASIS

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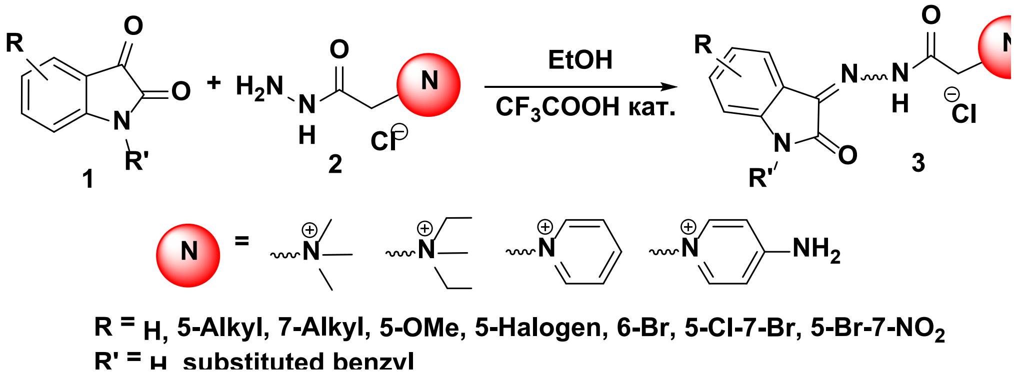
Isatin is a synthetically attractive compound widely used in the synthesis of various heterocyclic systems. The presence of two reactive centers (carbonyl group and lactam fragment) in its molecule makes it possible to consider isatin as a promising platform for the creation of hybrid biologically active substances. Thus, Schiff or isatin-N-Mannich bases exhibit various types of activity (antiviral, antibacterial, fungicidal). However, today the problem of the solubility of isatin acylhydrazones in water remains relevant.



Scheme 1. General approach to the synthesis of cationized isatin-3-acylhydrazones

In this work, the synthesis of new isatin-3-acylhydrazones containing a positively charged nitrogen atom was first carried out. The approach found makes it possible to obtain, in high yields, isatin-based acylhydrazones soluble in water and organic solvents with high antimicrobial activity and low cytotoxicity. It is established that the presence of a proton or a sterically hindered phenolic substituent at position 1 and halogen atoms (Cl, Br) or alkyl substituents (Me, Et) in the benzo fragment of the heterocycle leads to a significant increase in antimicrobial activity. The data obtained indicate the prospects for further studies of this type of isatin-3-hydrazones as potential antimicrobial agents [1-3].

The authors are grateful to the Assigned Spectral-Analytical Center of FRC Kazan Scientific Center of RAS for technical assistance of research.

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SYNTHESIS AND STUDYING OF ANTIOXIDANT ACTIVITY IN CONDITIONS IN VITRO THE NEW SYNTHESIZED COMPOUNDS.

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Research object: 5 substances were synthesized for the first time at the department organic, bioorganic and medical chemistry of Samara University (Samara, Russia).

Purpose of the study: determination of biological activity for the first time synthesized substances. Objectives of the study: evaluation of antioxidant activity of the first synthesized compounds.

The antioxidant properties of the compounds were evaluated in simple model systems that imitating the most common reactions of free radical oxidation in the humans body and in environments in which was initiated the formation of reactive oxygen forms and the reaction

lipid peroxidation. Registration of of a luminescence was carried out on chemiluminomer «HLM-003» (Russia). Antioxidant activity determined by the degree of inhibition of chemiluminescence and recalculated as a percentage of control. As a comparison drug was selected vitamin C. To identify reactive oxygen forms was used luminol (5-amino-2,3-dehydro-4-phthalazinedione), which oxidizes and forms electronically excited carbonyl chromophores with high quantum yield, resulting in dramatically increased intensity of luminescence associated with the formation of active forms oxygen. Chemiluminescence was recorded for 5 minutes.

The results of the study of compounds on antioxidant activity presented in the table 1:

Table 1.

Comound	Light sum, c.u	Spontaneous luminosity, c.u.	Maximum luminosity, c.u.
Control	29,0 (28,1-29,4)	1,35 (1,31-1,38)	15,6 (15,5-16,3)
Lithium taurate	24,1 (21,4-26,5)*	1,25 (1,24-1,29)*	13,9 (12,7-14,1)*
Magnesium taurate	25,4 (22,4-27,8)*	1,31 (1,27-1,35)	14,3 (13,8-14,9)
Sodium taurate	26,9 (24,3-28,7)*	1,39 (1,37-1,45)	15,2 (14,9-15,6)
Taurine and aminocaproic acid	20,7 (18,3-22,4)*	1,22 (1,21-1,25)*	16,4 (16,1-17,8)
Vitamine C	4,5 (4,3-4,8)**	0,95 (0,92-0,99)**	1,3 (1,29-1,35)**

Note. The median and interquartile range for the results of 10

measurements. The data are reliable in comparison with the control at * $p \leq 0.05$, ** $p \leq 0.001$.

For the initiation of reactive oxygen forms we used 20 ml of phosphate buffer with the addition of citrate and luminol. Buffer composition: 2.72 g. KH_2PO_4, 7.82 g. KCL, 1.5 g. Sodium citrate $C_6H_8O_7Na_3 * 5.5H_2O$ per 1 liter of distilled water. The pH of the resulting solution was adjusted up to 7.45 units by titration with a saturated KOH solution and add 0.2 ml

stock solution of luminol (10-5 M). The formation of ROS initiated the introduction of 1 ml of 50 mm solution of sulphate of iron.

Thus, as a result of experimental work, compounds exhibiting antioxidant properties were found.

The highest level of antioxidant properties was shown for the Sodium taurine and the Magnesium taurate.

SYNTHESIS OF PYRROLO[2,1-*A*]ISOQUINOLINES DERIVATIVES

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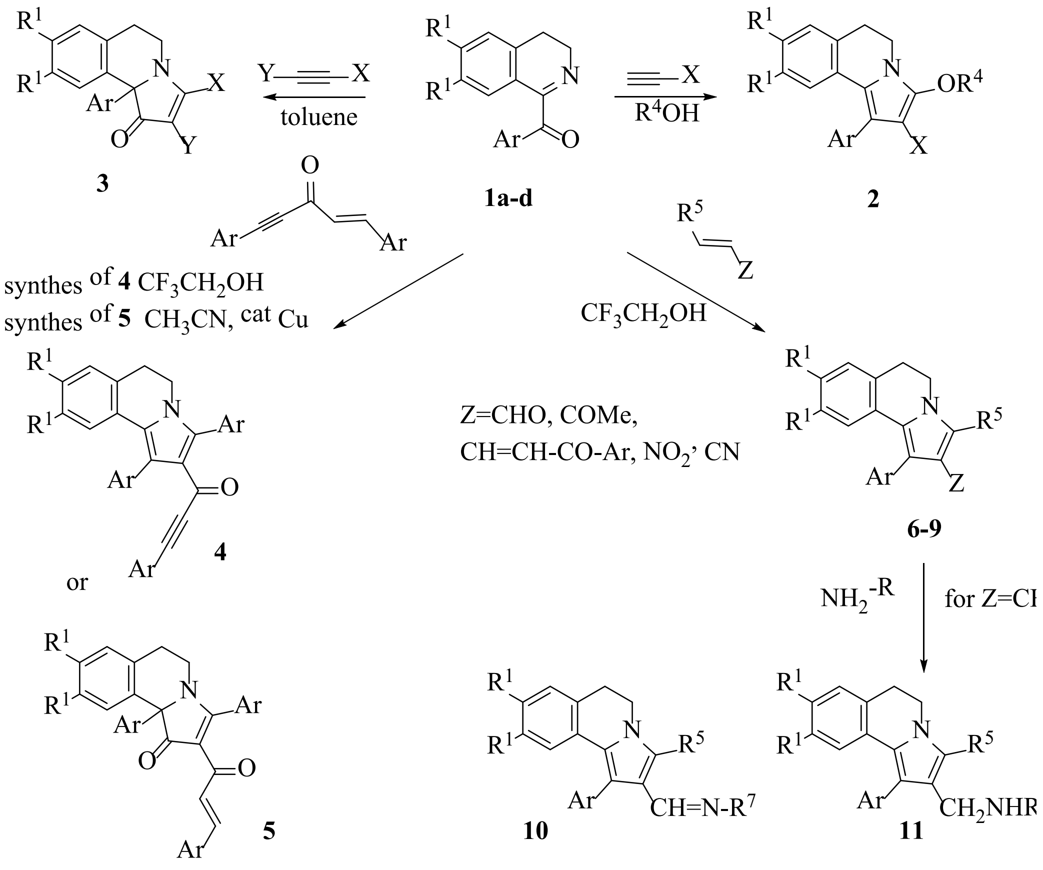
A study of the transformations of 1-aroyl-3,4-dihydroisoquinolines with the participation of electron-deficient alkyls and alkenes has been carried out. It was established that the domino process of the formation of the pyrrolo[2,1-*a*]isoquinoline`s skeleton takes place with the imine-ketone fragment of the starting compound and the double or triple bond of the reagent. As a result, pyrrolo[2,1-*a*]isoquinolines **2–9** with different functional groups in the pyrrole cycle were obtained. The conditions for selectively annulation of the pyrrole ring to 1-aroyl-substituted 3,4-dihydroisoquinolines under the action of vinyl ethynyl ketones were found. Primary bioscreening of a number of the obtained compounds for the presence of cytotoxic activity was carried out. On the basis of pyrroloisoquinolines having a formyl group, azomethines **10** and amines **11** were obtained. Compounds **10** and **11** suppress the action of proteins - “efflux pumps”, which makes it possible to reduce the resistance of cancer cells to a therapeutic drug.



Scheme 1.

This work was supported by the “RUDN University Program 5-100”, RFBR grant № 17-53-560020, RFBR and Moscow city Government according to the research project № 18-31-00001.

POLYFLUOROAROMATIC COMPOUNDS: SYNTHESIS OF SULFANES FROM DISULFANES

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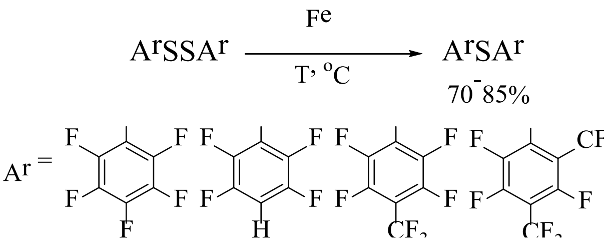
It was reported that diaryl disulfanes suffer desulfurization under the action of Raney nickel with the formation of the corresponding sulfanes [1]. It seemed attractive to extend this approach to polyfluoroaromatic compounds, since fluorinated diaryl sulfanes are of interest for electro-optical applications. Synthesis of unsymmetrical sulfanes from disulfanes and aryl iodides and copper in dry DMF was demonstrated by L.M. Yagupolskiy et al., but direct atom-economy and solvent-free desulfurization procedure has not been studied yet [2].

Our preliminary results demonstrate that direct heating of decafluorodiphenyl disulfane is not effective, obviously, because of the reverse reaction between decafluorodiphenyl sulfane and sulfur and because of the formation of polysulfanes. So, metal powder was added to bind sulfur to metal sulfide and promote the formation of the targeted sulfane. Among the tested metals (Cu, Zn, Fe), iron was the best choice and made it possible to obtain various polyfluoroaromatic sulfanes in good yields (Scheme 1).

We found that the elaborated process is limited to the synthesis of the compounds of symmetrical structure. When unsymmetrical disulfane RSSR´ was involved in reaction, a mixture of sulfanes RSR, RSR´ and R´SR´ in ratio close to 1:2:1 was obtained.

The possible reaction routes are discussed.



Scheme 1

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SYNTHESIS AND IONOCHROMIC PROPERTIES OF *N,N'*-CYCLIC AZOMETHINE IMINES

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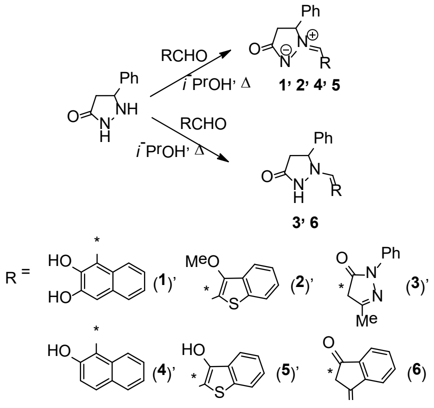
Azomethine imines represent compounds possessing a polar N^--N^+=C fragment, which makes them a valuable precursors in the combinatorial chemistry of heterocycles. *N,N'*-Cyclic azomethine imines are capable of photochromism due to intramolecular photocyclization into diazyridines. We have synthesized *o*-hydroxyaryl(hetaryl)methylidene containing pyrazolidine-3-one-based azomethine imines **1-6** (Scheme 1) and investigated their spectral luminescent and ionochromic properties.



Scheme 1

According to ^{1}H, ^{13}C, ^{15}N NMR spectroscopy and X-ray diffraction data compounds **1**, **2, 4, 5** exist in enol form, and compound **3, 6** – as a keto tautomer. Compounds **1**, **3-6** display fluorescence with a large Stokes shift (ESIPT effect) due to the fast intramolecular O→N (N→O) proton transfer in the excited state. Azomethine imines **1**, **3** are ion-active "naked-eye" switches of spectral properties and can be used for the detection of F^- and $H_2PO_4^-$ anions (Fig. 1).

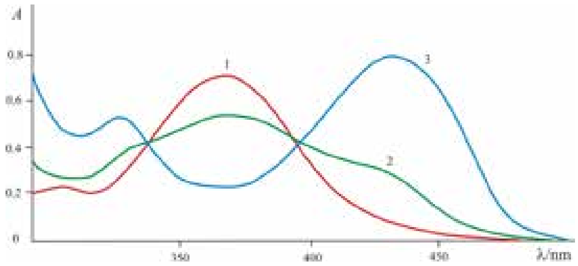


Fig. 1.
Electronic absorption spectra of **1** in CH_3CN ($3.0\bullet10^{-5}$ M) before (*1*) and after addition of Et_3N (*2*) or *n*-Bu4N^+F^- (*3*).

This work was carried out in the framework of the basic part of State task in the sphere of scientific activity (nos. 4.6497.2017/8.9 and 4.5593.2017/6.7) and State task of SSC RAS no. 01201354239.

SYNTHESIS, STRUCTURE AND ELECTRONIC ABSORPTION PROPERTIES OF THE SELECTED QUINOXALINE-BASED COMPOUNDS

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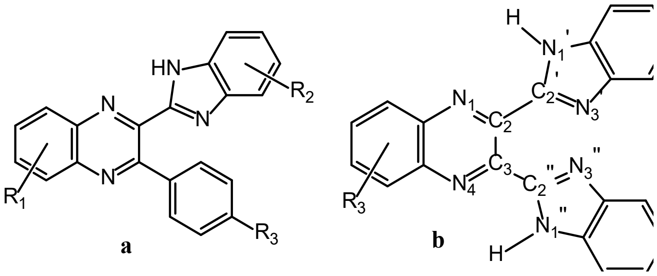
Chemistry of quinoxalines (Q) and benzimidazoles (BI) are recently greatly explored [1-4]. Owing to the remarkable electronic and photophysical properties their various derivatives have been widely employed in the field of light-emitting diodes, organic photovoltaics, dye-sensitized solar cells, organic field-effect transistors, nonlinear optics, and fluorescent optical chemosensors. However, a precise modeling of their excited state properties is still far from being totally achieved representing a challenging subject. Recently, we have proposed[5] a series of novel fluorophores, consisting of a 3-arylquinoxaline moiety and a benzimidazole moiety linked by a single bond (Scheme 1, a). The positions and intensities of the fluorescence maxima in the spectra of these compounds depended rather strongly on environment, while the dependence of the absorption spectra was negligible. All the main spectral features were completely reproduced by time-dependent density functional response theory (TD-DFT) computations[6].



Scheme 1. Chemical structures of considered systems

However, the closely related 2,3-(dibenzimidazol-2-yl)-quinoxalines synthesized in our group and comprising a second BI moiety instead of an aryl group (Scheme 1, b), unexpectedly show a dramatic solvatochromism for the absorption spectra. Conventional TD-DFT based calculations totally failed in reproducing these environmental effects. We showed how the sampling of the ground state potential energy surface based on the analysis of the harmonic vibrational degrees of freedom only, is totally insufficient and a full dynamic exploration using a quantum potential is necessary to correctly describe all the subtle effects.

The reported study was funded by RFBR according to the research project № 18-33-00128 mol_a

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COST-EFFECTIVE COMPUTATIONAL APPROACH FOR EXCITED STATE PROPERTIES IN THE SERIES OF N-CONTAINING HETEROCYCLES

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Organic heterocyclic molecules with extended π-conjugated backbone demonstrate a great potential in a wide range of applications of modern material chemistry. Among them such as non-linear optical (NLO) materials, organic light-emitting diodes (OLEDs), pH/polarity sensors and photovoltaics could be highlighted. Thus an active search for novel candidates with better target properties is a perspective but challenging task. Experimental blind screening among the infinite pool of possible structures is inefficient and wasteful. Computational approach based on quantum chemistry tools and giving reliable predictions of fundamental properties essential for the applications is very convenient and promising way allowing to avoid an extra time and material consumptions. However to recommend computational strategy providing reliable results it should be tested for a wide number of related compounds to determine its the pros and cons, limitations and benefits.

Herein we report on the obtained results on excited state properties of recently synthesized dizine [1-4] and indolizine [5, 6] systems, demonstrating highly stimuli-sensitive emission. Their ground and excited state properties have been treated with density functional theory (DFT), time-dependent density functional theory (TDDFT), MP2 and algebraic digrammatic construction through second-order (ADC2) methods with triple-ζ basis sets. DFT functionals such as local hybrid PBE0, B3LYP as well as long-range corrected cam-B3LYP and ωB97XD functionals have been employed to predict positions of the experimental emission/absorption maxima, electronic absorption band shapes, excited-states natures, conformational and solvatochromic behavior along with intramolecular charge-transfer properties inherent to the push-pull systems[7, 8]. Some intermediate generalization and outcomes are presented

This work was supported RFBR according to the research project № 18-33-00128 mol_a

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TOWARD ACCURATE ELECTRONIC ABSORPTION BAND SHAPES WITH QUANTUM-CHEMISTRY FOR THE SERIES OF PUSH-PULL INDOLIZINE-BASED CHROMOPHORES

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Near-infrared (NIR) absorbing/emitting systems nowadays attract considerable attention of the researchers due to their promising applications in secure displays, night-vision goggles, tissue welding, telecommunications, biological imaging and dye-sensitized solar cells (DSCs). Significant results in solar light to electricity power conversion efficiencies (PCEs) up to >12% for organic molecules have been achieved nowadays. Organic systems possess lower cost, in contrast to the metal-complex analogs, and broad variety for possible chemical functionalization allowing fine-tuning of their photophysical properties. The most perspective systems possess D-π-A architecture and utilize di-/triphenylamine (D/TPA) or indoline fragments as D motifs. However these units have restricted donor strength because of the non-planar twisted structure of the nitrogen lone pair relative to the π-bridges resulting in reduced capability to electron donation into acceptor moiety upon excitation. Recently indolizine-based donors have been found as more efficient donating units [1, 2]. Moreover indolizine-based systems demonstrated intensive electronic absorption/emission up to 700-900 nm revealing themselves as perspective candidates to the role of active layers in DCSs devices or NIR-emitting materials [3, 4].

Herein we report on the study of excited state (ES) properties in series of recently synthesized indolizine-based systems bearing D-π-A architecture. Using the theoretical approaches based on combinations of density functional theory (DFT), time-dependent DFT, Møller-Plesset second-order perturbation theory (MP2) and algebraic diagrammatic construction through second order (ADC2) methods, their ground and excited states features have been effectively rationalized. Employing independent mode displaced harmonic oscillator (IMDHO) approximation the spectral features (band shapes) of experimental electronic absorption/emission spectra have been described and interpreted. It was found that the shape of the lowest-energy electronic absorption bands is strongly influenced by vibronic progressions. In particular, it was shown that the most intensive absorption is located nearby 0-0 adiabatic transition. IMDHO could be utilized for the prediction of electronic absorption properties for a wide range of indolizine derivatives toward light-harvesting applications.

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NMR-PARAMAGNETIC PROBING SYSTEM Mn^{2+} - HEDP- AMC IN ORGANIZED MEDIUM

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Currently, there is lack of information on the complexation of manganese(II) ions with ligands in organized medium. Earlier we found that such ternary systems as manganese(II) - EDTA (DTPA) - polyethylenimine (PEI) [1,2], manganese(II) -hydroxyethylidene diphosphonic acid (HEDP) -PEI, manganese(II) - calixarene - nonionic surfactant revealing high relaxivity, can be considered as models of new positive contrast agents for magnetic resonance imaging (MRI). These complexes are an order of magnitude superior to commercial analogs in the parameter of relaxation efficiency, but are not sufficiently stable. In order to stabilize such systems in physiological media without losing high values of relaxation efficiency, it is necessary to improve the structure of this compositions. In this respect, the compositions of hydroxyethylidene diphosphonic acid (HEDP) and aminomethylated calix[4] resorcinol (AMC) - were used to develop strong manganese(II) complexes with high relaxivity. For this composition there is no information about the influence of the ligand nature, the pH of the medium and the concentration of reagents on the formation of manganese(II) - HEDP - AMC complexes. For this purpose, it is promising to apply the method of NMR-paramagnetic probing. This instrument is especially effective in detecting nanoscale objects formed by manganese(II) ions [3].

In micellar solutions of AMC with pentyl radicals in the Mn(II) -HEDP system, the rise of relaxivity values (up to 2 times) was detected in acidic medium. It was attributed to the stabilization of Mn(II) anionic tris-complex with HEDP by cations of protonated AMC. Using the NMR relaxation method, the degree of substitution of water molecules in the first hydration shell of manganese(II) during the complex formation of Mn (II) with HEDP was quantitatively estimated.

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COMPLEXES WITH CYCLODEXTRINS ENHANCE BIOAVAILABILITY OF SOLUBLE EPOXIDE HYDROLASE INHIBITORS

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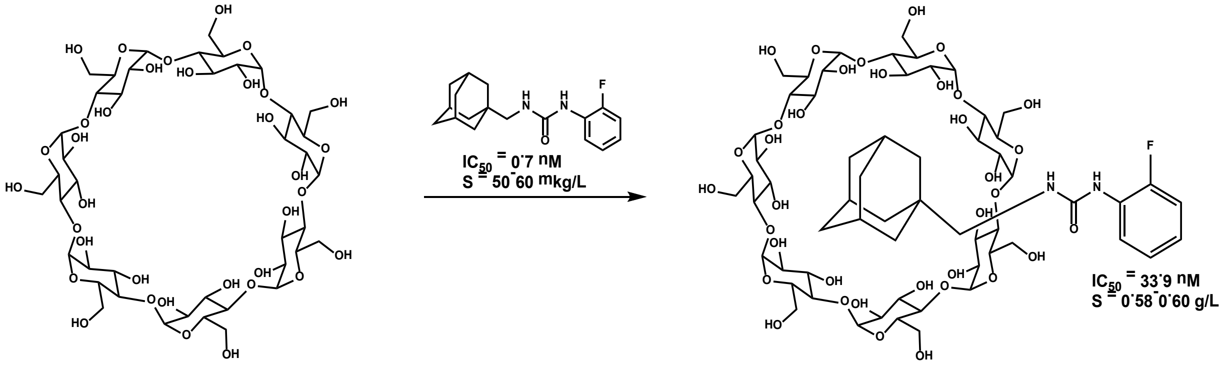
The number of publications devoted to the use of cyclodextrins as encapsulating reagents for drugs has recently increased significantly. The review provides 60 examples of the use of cyclodextrin complexes with drugs [1]. The use of such complexes can improve the hydrolytic stability, photo- and thermal stability, water solubility, as well as reduce toxicity. The creation of a new generation of soluble epoxide hydrolase inhibitors is currently focused on the modification of individual parts of the molecule by isosteric and bioisosteric substitutions in order to improve the activity and physicochemical properties [2]. However, while increasing the lipophilicity of the molecule leads to an increase in inhibitory activity, it also reduces water solubility and metabolic stability.

In this work, it is proposed to encapsulate the lipophilic part of the molecule into the cavity of cyclodextrins. Urea complexes with β-cyclodextrin were obtained by coprecipitation. To the aqueous solution of β-cyclodextrin heated to 70 °C, an adamantyl urea was added with stirring and continued to stir for 10 hours. The turbidity formed at the beginning disappears with time, which indicates the formation of an inclusion complex. The resulting solution was evaporated, and the precipitate was washed with alcohol and dried.



Scheme 1. Synthesis of capsulated inhibitor of soluble epoxide hydrolase.

Our preliminary studies have shown that such encapsulation increases the solubility of inhibitors in water 10,000-fold, while reducing activity 50 times (from 0.7 nM to 33.9 nM). At the same time, the observed decrease in activity is probably associated with a gradual release of the inhibitor from the cyclodextrin cavity, since penetration of the latter into the cavity of the enzyme, apparently, is impossible.

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UNSYMMETRICAL DISULFIDE FORMATION VIA OXIDATIVE S-H/S-H CROSS-COUPLING

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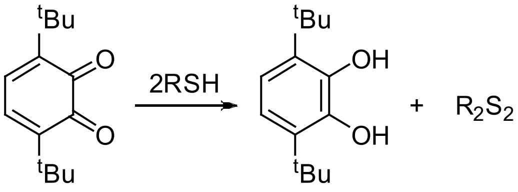
Constructing disulfides remains important in pharmaceutical, agriculture industries and material science. The S-S bond is vital motif found in the structure of various functional molecules. Disulfides can be prepared by using oxidative reagents, for example 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, pyridiniumchlorochromate and etc. [1].

In present work we used 3,6-di-*tert*-butyl-*o*-benzoquinone (**Q**) as one-electron oxidant for disulfide formation via oxidative S-H/S-H cross-coupling.



Q **QH$_2$**

Unsymmetrical disulfides were directly synthesized from the corresponding mixture of thiols R_1SH (1,2 eq.) and R_2SH (0,8 eq.) in the presence of **Q** in N-methyl-2-pyrrolidone (**NMP**) under room temperature (Scheme 1). The choice of solvent is due to its effectiveness in the extraction process of S-contained compounds [2].

$$R_1SH + R_2SH \xrightarrow[QH_2]{\text{r.t., NMP, Q}} R_1SSR_2 + R_1SSR_1 + R_2SSR_2$$

$R_1 = i\text{-}C_3H_7$, $R_2 = C_6H_5$	4.4 %	-	90.6 %
$R_1 = i\text{-}C_3H_7$, $R_2 = C_5H_9$	81.2 %	-	10.6 %
$R_1 = i\text{-}C_3H_7$, $R_2 = C_6H_{11}$	71.5 %	-	21.3 %
$R_1 = i\text{-}C_3H_7$, $R_2 = t\text{-}C_4H_9$	42.8 %	-	49.7 %
$R_1 = i\text{-}C_3H_7$, $R_2 = C_7H_{15}$	59.4 %	-	30.7 %
$R_1 = t\text{-}C_4H_9$, $R_2 = i\text{-}C_3H_7$	80.6 %	9.4 %	-
$R_1 = t\text{-}C_4H_9$, $R_2 = C_6H_5$	5.3 %	-	85.6 %
$R_1 = C_6H_{11}$, $R_2 = C_6H_5$	29.8 %	2.8 %	61.6 %

Scheme 1. The yields of the reaction products.

Unsymmetrical disulfides are principally formed in reactions between different alkyl thiols (42.8 – 81.2%). Reactions with mixture of alkylthiol and thiophenol led to the formation of diphenyldisulfide (61.6 – 90.6%).

This work was supported by Russian Foundation for Basic Research (grant № 18-29-24001)

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THE SYNTHESIS OF 5-ARYL-AZOLO[1,5-A]PYRIMIDINES – PERSPECTIVE ANTI(NEURO)INFLAMMATORY AGENTS

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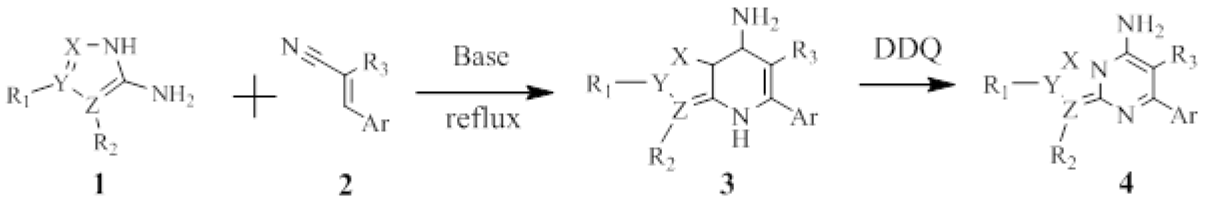
The development of the novel azoloazine-based therapeutic agents is still a relevant area of organic and medicinal chemistry. It has been established that derivatives of azolopyrimidines can be involved in the regulation of a wide range of biochemical processes, among which inflammatory processes take a special position. Thus, one of the most attractive targets for azolo[1,5-a]pyrimidines is the adenosine A2a receptor associated with the development of inflammatory and neuro-inflammatory processes.

The limited range of azolo[1,5-a]pyrimidines 4 was obtained under the reaction conditions of Michael addition from the corresponding aminoazole 1 and benzylidenemalonononitrile previously (2, R2 = -CN) [1].



1 2 3 4

X, Y, Z = N, C
R_1 = -H, -SMe, -CH_3, -furan-2'-yl , -CF_3
R_2 = -H, -COOEt
R_3 = -CN. -NO_2
Ar = -Ph, -Ph(4'-OMe), -Ph(4'-NMe_2), -furan-2'-yl

Scheme 1.

It is proposed to expand the series of azolo[1,5-a]pyrimidines in the present work (Scheme 1). One of the most attractive aspects of this work is the use of arylidene**nitro**acetonitriles(2, R2 = -NO2) [2] as a building block to obtain a previously unknown series of 5-aryl-6-nitro-7-aminoazolo[1,5-a]pyrimidines and corresponding azolo[5,1-b]purines.

High affinity for adenosine A2a receptor in comparison with selective inhibitors was established by docking study for these compounds. One of the lead compounds - 7-amino-6-cyano-3-(2’-furyl)-5-phenyl(4’-methoxy)-[1,2,4]triazolo[1.5-a]pyrimidine has binding free energy -9.71 kcal / mol, which indicates higher affinity towards A2a receptor than affinity of the selective antagonist ZM241385 (ΔG = -9.05 kcal/mol). Thus, compounds of this series can be considered as promising anti-inflammatory agents.

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NEW METHOD FOR THE SYNTHESIS OF (*N*-FUROXANYL)HYDRAZONES

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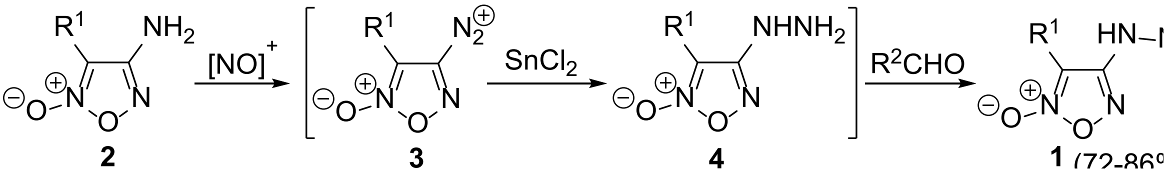
A global trend in modern organic and medicinal chemistry is directed towards the construction of molecular architectures with various degrees of complexity in view of creation of practical technologies and sustainable development [1]. In recent years, enhanced efforts were directed to the synthesis of pharmacologically oriented structures comprising a framework capable of nitric oxide (NO) release, including 1,2,5-oxadiazole 2-oxides (furoxans), which are prone to the exogenous NO release in the presence of thiol cofactors [2]. Furoxan scaffold has attracted considerable attention due to high stability of the furoxan cycle under ambient conditions and absence of nitrate tolerance under continuous therapy [3]. The incorporation of the furoxan motif as potential NO donor into drug candidates with known pharmacological activity became now an efficient tool in the design of novel drug candidates and, as a result, new hybrid structures with various pharmacological activities were revealed [4].

In present work, a novel *one-pot* approach for the construction of previously unknown (*N*-furoxanyl)hydrazones **1** was developed. This method is based on a cascade of one-pot reactions including diazotization of initial aminofuroxans **2**, *in situ* reduction of generated diazonium salts **3** and condensation of formed furoxanylhydrazines **4** with corresponding aldehydes. It is important to note that initial aminofuroxans are readily available compounds which can be easily synthesized on gram-scale according to our recently developed procedure [5].



This work was supported by the Russian Foundation for Basic Research (grant № 19-03-00069).

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PREPARATION OF PECTIN COMPLEXES WITH NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

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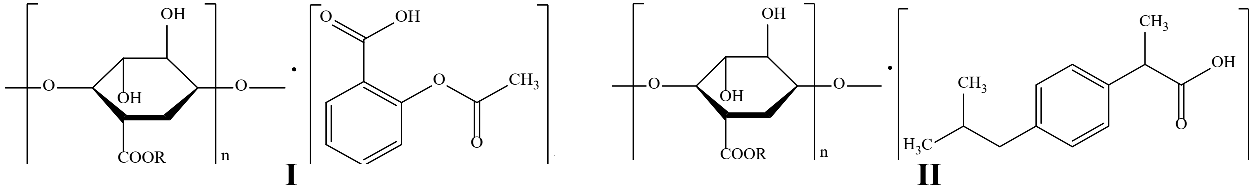
The study of the complexation of pectin with nonsteroidal anti-inflammatory drugs and the physicochemical properties of the obtained complexes is due to the need of creaing new drugs, characterized by high anti-inflammatory activity, prolonged action and reduced ulcerogenic effect [1].

The patterns of pectin complexation with ibuprofen (IBU) and aspirin (acetylsalicylic acid, ASA) were studied. The formulas of the obtained products are shown in scheme 1: pectin complex with ASA **(I),** pectin complex with IBU **(II).**

Scheme 1. Complex of pectin with **ASA** and **IBU**



I **II**

The obtained compounds were investigated using a complex of physicochemical methods (IR and UV spectroscopy, TGA/DSC, dynamic light scattering (DLS)).

The study of the thermal decomposition of the obtained compounds was carried out by the method of synchronous thermal analysis (thermogravimetry/differential scanning calorimetry with FTIR spectroscopy (TGA/DSC-IR-Fourier), which records the change in sample mass depending on temperature with the corresponding thermal effects. Sequential heating of the samples of the complexes and pure pectin is accompanied by two stages of mass loss were shown in table 1. According to the corresponding IR Fourier spectra of the heating of gaseous products in the first stage, evaporation of bound water molecules occurs in the temperature range 86-106 °C with a mass loss of ~5.2-7.9%. The second stage corresponding to decarboxylated polysaccharide is accompanied by mass loss of ~ 40-52% at 242-244 °C.

Table 1. TGA/DSC data for pectin complexes with ASA and **IBU** and for pure substances

	Stages of mass loss					
	1			2		
	DTG, °C	ΔTG, %	DSC, °C	DTG, °C	ΔTG, %	DSC, °C
Pectin	90.1	7.9	85.8	239.8	51.6	244.4
la (pectin+1.0 ASA)	96.3	5.9	90.1	238.6	46.1	244.1
lb (pectin+0.9 IBU)	79.3	5.2	106.2	236.7	40.4	241.8
IBU	-	-	-	289.3	99.7	291.1
ASA	-	-	-	231.5	38.8	234.6

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BIS-1,3,2-DIAZAPHOSPHOLIDINE BASED ON 9,10-DIHYDROANTHRACENE

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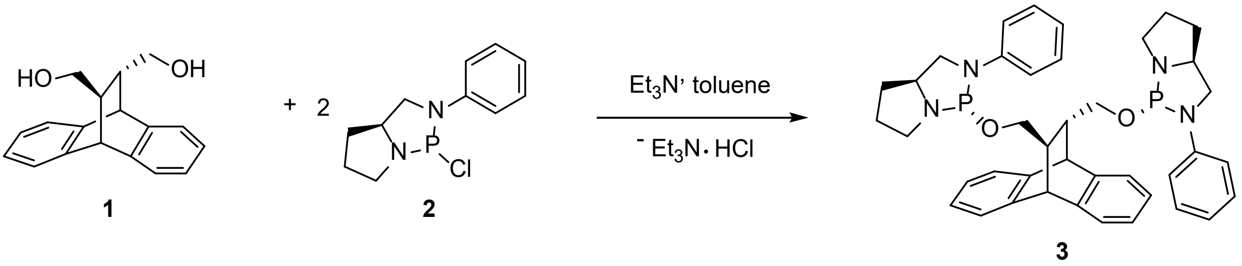
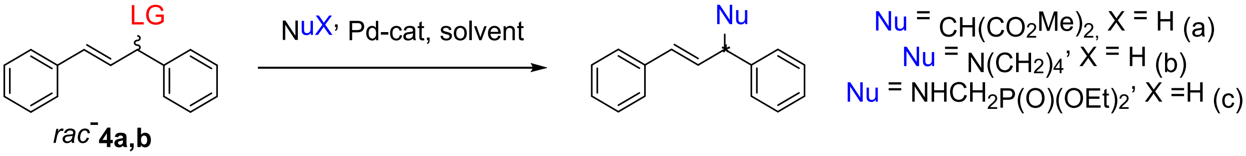
Bis-1,3,2-diazaphospholidine **3** was synthesized by the reaction of ((9*R*,10*R*,11*S*,12*S*)-9,10-dihydro-9,10-ethanoanthracene-11,12-diyl)dimethanol **1** [1] with (5*S*)-2-chloro-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane **2** [2] in toluene in the excess of Et$_3$N as an acceptor of HCl (Scheme 1).



Scheme 1. Synthesis of 1,3,2-diazaphospholidine **3**

Determination of the chemical and enantiomeric purities, composition, structure, and stereochemical features of **3** was implemented by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy (including homo- and heteronuclear correlation techniques APT, DEPT, ^{1}H,^{1}H - COSY, ^{1}H,^{1}H - NOESY, ^{13}C,^{1}H - HSQC, ^{13}C,^{1}H - HMBC, and ^{31}P,^{1}H - HSQC), mild mass spectrometry (MALDI TOF/TOF), IR spectroscopy, polarimetry, HPLC on enantioselective stationary phases and elemental analysis.

In the near future, ligand **1** will be tested as an asymmetric inducer in the Pd-catalyzed allylic substitution of substrates *rac*-**4a,b** using dimethyl malonate, pyrrolidine and diethyl aminomethylphosphonate as nucleophiles.



Scheme 1. Pd-catalyzed asymmetric reactions.

This work was supported by the Ministry of Education and Science of the Russian Federation (State Task № 4.12776.2018/12.2).

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NOVEL *N*-HETEROCYCLES OF 1,5-DIAZACYCLOOCTANE SERIES ON THE BASIS OF ACROLEIN AND OPTICALLY ACTIVE AMINO ALCOHOLS

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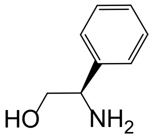
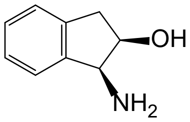
Heterocyclic compounds constitute the largest and most varied family of organic compounds significant to almost all aspects of modern organic chemistry, medicinal chemistry, and biochemistry. The present work is devoted to structure, synthesis and properties of nitrogen heterocycles of 1,5-diazacyclooctane series. Due to the presence of two nitrogen donor atoms and unique conformational features of the eight-membered ring, 1,5-diazacyclooctanes attract great interest as ligands in transition metal complexes, starting and intermediate compounds in organic synthesis, as well as biologically active substances.

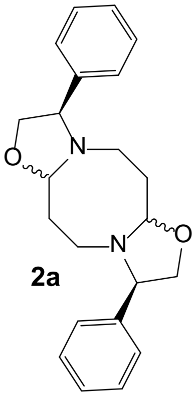
It was previously shown that α,β-unsaturated imines derived from 1,2-ethanolamine derivatives and acrolein participate in «head-to-tail» [4+4] dimerization and give eight-membered heterocyclic products [1, 2]. Derivatives of dioxazolidin-[1,5]-diazacyclooctane **2a** and **2b** obtained from the reaction of acrolein with optically active amino alcohols ((*R*)-2-phenylglycinol (**1a**) and (1*S*,2*R*)-1-amino-2-indanol (**1b**)) were further subjected to alkylation by various Grignard reagents.



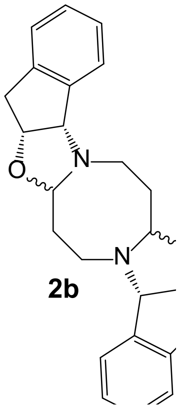
1a



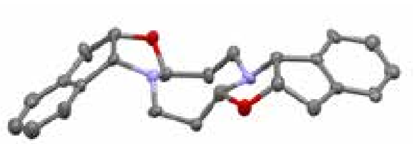
1b



2a



2b



Thus, series of novel derivatives of 1,5-diazacyclooctane with alkyl, alkenyl or aryl substituents at positions 2 and 6 of the eight-membered ring was synthesized in stereochemically pure form. Subsequent catalytic hydrogenolysis led to the formation of optically active *N*-unsubstituted 2,6-dialkyl-1,5-diazacyclooctanes which are hardly available by other methods. Structure of pure stereoisomers of novel diazacyclooctane derivatives have been characterized in detail by NMR spectroscopy and single crystal X-ray diffraction.

This work was supported by the Russian Government Program of Competitive Growth of Kazan Federal University.

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SYNTHESIS OF NEW DERIVATIVES OF PYRIDO[2,3-B]THIENO[3,2-D] PYRIMIDINES, CONDENSED WITH SATURATED HETEROCYCLES

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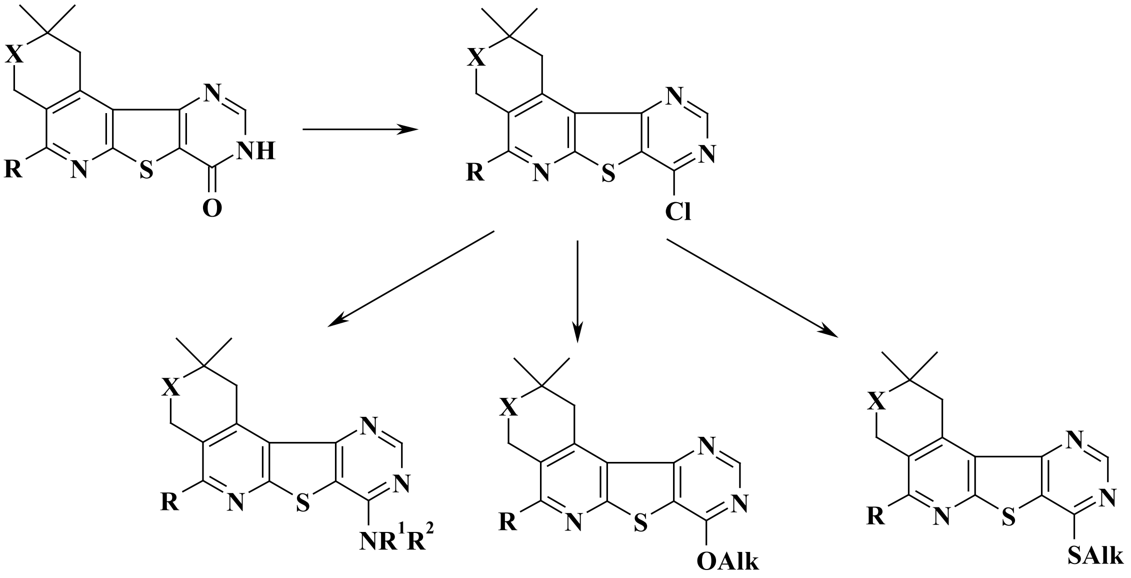
The derivatives of thieno[3,2-d]pyrimidines are the biologically active substances [1,2]. Tetracyclic condensed systems conteining pyrido[2,3-b]thieno[3,2-d]pyrimidines and saturated heterocycles such as pyran or thiopyran ring are potential biological active new heterocyclic systems.

In this report we have developed new methods for obtaining of functionalized pyrano(thiopyrano)[4',3' :4,5]pyrido[2,3-b]thieno[3,2-d]pyrimidines. This compounds were synthesized starting of corresponding condensed thieno[3,2-d]pyrimidin-ones. By reacting the latters with $POCl_3$ were synthesized chloro derivatives, which under the action of various of amines conversion into the amino derivatives. As well as synthesized the oxyalkyl and thioalkyl derivatives on thes based chloro derivatives in the follow scheme.

The new compounds were found to have neurotropic properties. The investigations was showed that some of the synthesized compound cause anxiolytic or activating effects.



X = O, S; R = morpholino, pyrrolidino, piperidino; R^1R^2 = H, Alkyl, cycloalkyl, Aryl.

This work was supported by the RA MES State Committee of Science, in the frames of the research project № 18T-1D066

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SYNTHESIS OF α-AMINOPHOSPHINEOXIDES WITH LONG ALKYL CHAINS BY THE PUDOVIK REACTION

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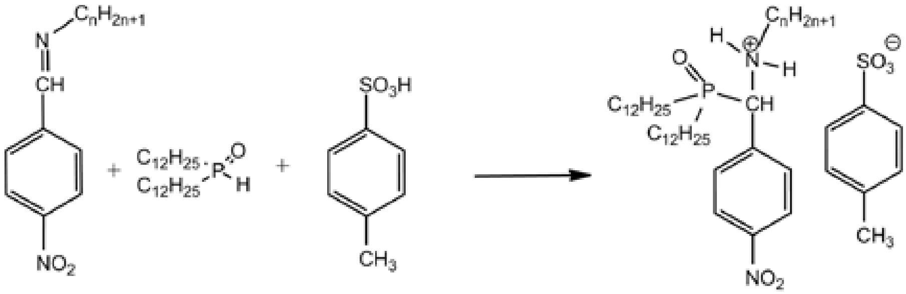
The Pudovik reaction is a method for preparing of the various aminophosphinoxides in organophosphorus chemistry. Various aromatic imines were mixed with didodecylphosphinic acid an equimolar amount of *p*-toluenesulfonic acid in benzene. The reaction mixture was heated for several hours at the boiling point of the solvent (Scheme 1). According to the ^{31}P NMR spectra, α-aminophosphineoxide and a small amount of by-product were obtained.



Scheme 1. Synthesis of α-aminophosphineoxides

The solvent was removed on a rotary evaporator and dry residue obtained. To remove impurities the mix of diethyl ether/ethanol in ratio 3:1 was added, because the by-product did not dissolve in this mixture. The compounds, containing as substituents at the nitrogen atom dodecyl, hexadecyl, octadecyl fragments at the nitrogen atom were obtained and they were amorphous powders.

Product has a tetradecyl substituent at the nitrogen atom formed needle-like crystals suitable for X-ray analysis (Fig. 1).

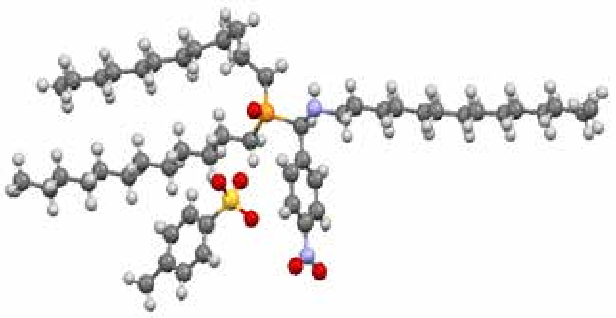


Fig. 1. General view of a molecule of *p*-nitrophenyltetradecylaminodidodecylphosphorylmethane salt with *p*-toluenesulfonic acid in the crystal

According to X-ray diffraction analysis, the molecule of *p*-toluenesulfonic acid was present in the crystal structure of the compound. In the crystal packing, alternation observed the lipophilic tetradecyl fragments at the nitrogen atom and two dodecyl fragments at the phosphorus atom.

This work funded by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (№ 4.5888.2017/8.9).

SYNTHESIS OF NEW LIPOPHILIC AMINOPHOSPHABETAINES

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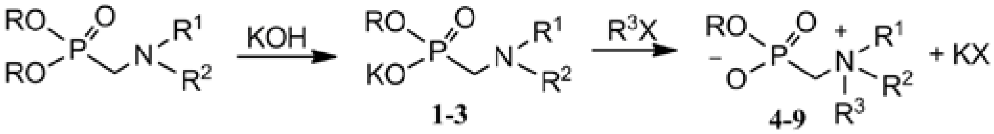
Over the past decades, the importance of chemistry of organophosphorus compounds has been continuously increasing in the pharmaceutical and chemical industries, which is associated with the creation of effective substances having complexing, antibacterial and antiviral properties. Organophosphorus betaines are no exception: they are analogs of organic amino acids and they have a wide range of potential chemical and biological properties.

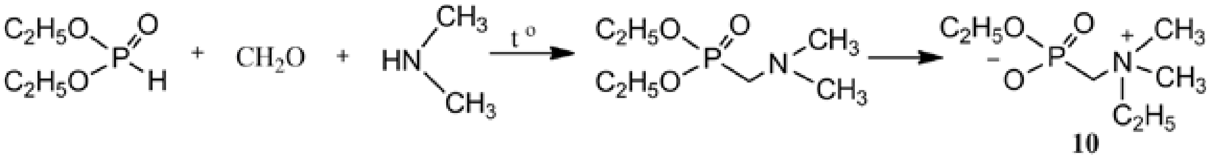
We have obtained a new series of lipophilic phosphorylated betaines, including containing long-chain alkyl fragments at the nitrogen atom. To obtain the desired products, we used a one-put synthesis method. In the first stage by the reaction of Kabachik-Fields in acetonitrile O,O'-dialkyl-α-aminophosphonates (**1-3**) were prepared. Isolated compounds used in alkaline hydrolysis in boiling hydrous 1,4-dioxane. Targeted aminophosphabetains (**4-9**) synthesized quaternization reaction with corresponding organohalides (Scheme 1) [1]



R = C_2H_5, $R^1 = CH_3$, $R^2 = C_8H_{17}$, $R^3 = CH_2C_6H_5$, X= Cl (**1, 4**); R = *i*-C_3H_7, $R^1 = R^2 = CH_3$, $R^3 = CH_2C_6H_5$, X= Cl (**2, 5**), $R^3 = C_8H_{17}$, X= Br (**6**), $R^3 = C_{10}H_{21}$, X= Br (**7**), $R^3 = C_{12}H_{25}$, X= Br (**8**); R = *i*-C_3H_7, $R^1 = CH_3$, $R^2 = C_8H_{17}$, $R^3 = CH_2C_6H_5$, X= Cl (**3, 9**);

Scheme 1. Synthesis of aminophosphabetaines

We first obtained aminophosphabetaine (**10**) using a one-pot synthesis method in system diethylphosphite/paraform/dimethylamine in azeotropic mixture water-benzene (Scheme 2).



Scheme 2. Synthesis of aminophosphabetaines

The O,O'-diethylaminophosphonate formed by the reaction of Kabachnik-Fields, is converted to the betaine form in consequence of intramolecular ethylation at the nitrogen atom.

This work funded by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (№ 4.5888.2017/8.9).

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Cu(II) CATALYZED N-VINYLATION OF NITROAZOLES AND 5-SUBSTITUTED TETRAZOLES BY E-STYRYLBORONIC ACID.

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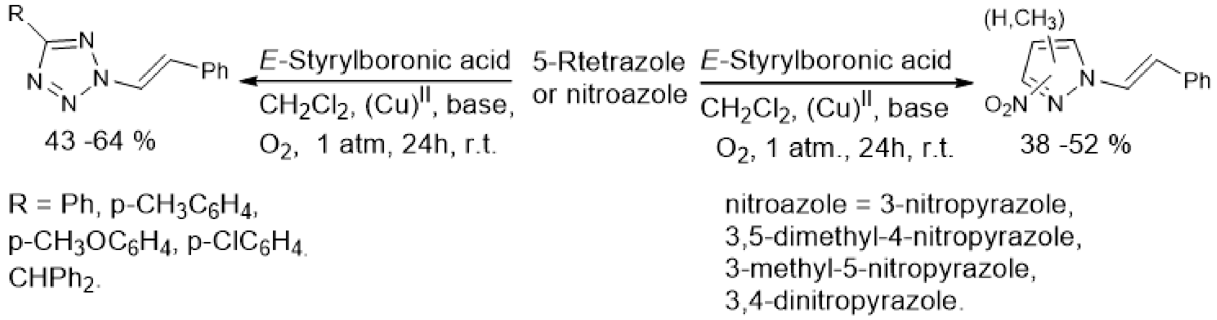
N-Modified nitroazoles **[1]** and tetrazoles **[2]** are famous classes of pharmacologically active molecules broadly used in medicine. So for example N-vinylnitroazoles possess antiparasitic activity and are precursors for the synthesis of nucleoside analogue, while N-vinyltetrazoles are used as monomers for preparation of polimers with various medical and indastrial properties. According to chemical References interesting N-styrylnitroazoles were synthesized only by multistep classical processes. In our opinion, the optimal method of N-styrylazoles synthesis is direct selective styrylation of these azoles by appropriative reagents.

Earlier, we have proposed methods for the selective N-arylation of some tetrazoles **[3]** and nitroazoles **[4]**. by diaryliodonium salts in the presence of copper salts. However we were failed to synthesize target N-styryltetrazoles and N-styrylnitroazoles by this method. We could not obtain desirable products using Pd-catalyst also **[5]**. The synthetic success was reached only with *E*-styrylboronic acid as reagent in the presence of Cu(II) salts according to Chen-Evans-Lam coupling reaction **[6]**. For all substrates the main product was N-styryl-isomer with the participation of the less sterically hindered nitrogen atom eliminating 3-methyl-5-nitropyrazole, where the ratio of isomers was near 2:1 in favor of 1-*E*-styryl-3-methyl-5-nitro-pyrazole:



The structures of products obtained were correctly established by spectroscopic methods (NMR ^{1}H, NMR ^{13}C, NOE-experiments and HRMS).

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BENZO[*B*]THIENO[2,3-*D*]THIOPHENE-BASED HETEROACENES AS PROMISING P-TYPE ORGANIC SEMICONDUCTORS: SYNTHESIS AND PHYSICAL PROPERTIES

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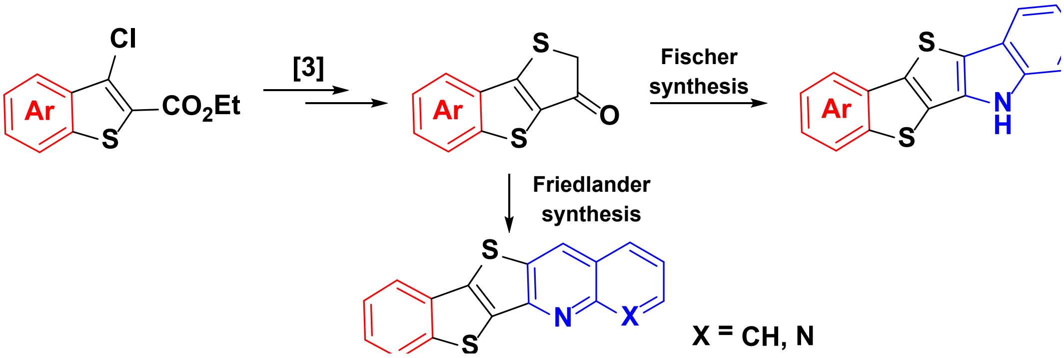
Heteroacenes, having π-excessive system, are attractive as p-type semiconductors due to the better environmental stability, coursed by low-lying HOMO energy levels, as compared with fully carbon-cored acenes. [1] Among them, benzo[*b*]thieno[2,3-*d*]thiophene-based (BTT) compounds are of the most promising organic semiconductors to their excellent stability and high charge-carrier mobility. [2] So we would like to present effective synthetic protocol to obtain different BTT-based hereacenes via a sequence of transition-metal-free reactions, including the Fiesselmann thiophene, the Fischer indole or Friedländer quinoline synthesis condensations (Scheme 1). Semiconductor properties of some obtained were studied by preparing thin solid films and measuring the charge carrier mobility.



Scheme 1. Consecutive synthesis of BTT-based heteroacenes

This work was supported by the Russian Foundation for Basic Research, project 18-33-20083, and by the Council on grants of the President of the Russian Federation (grant MK-1460.2018.3).

LIPOTRIPEPTIDES AS COMPONENTS OF THE COMPLEX SIRNA TRANSPORT PLATFORM

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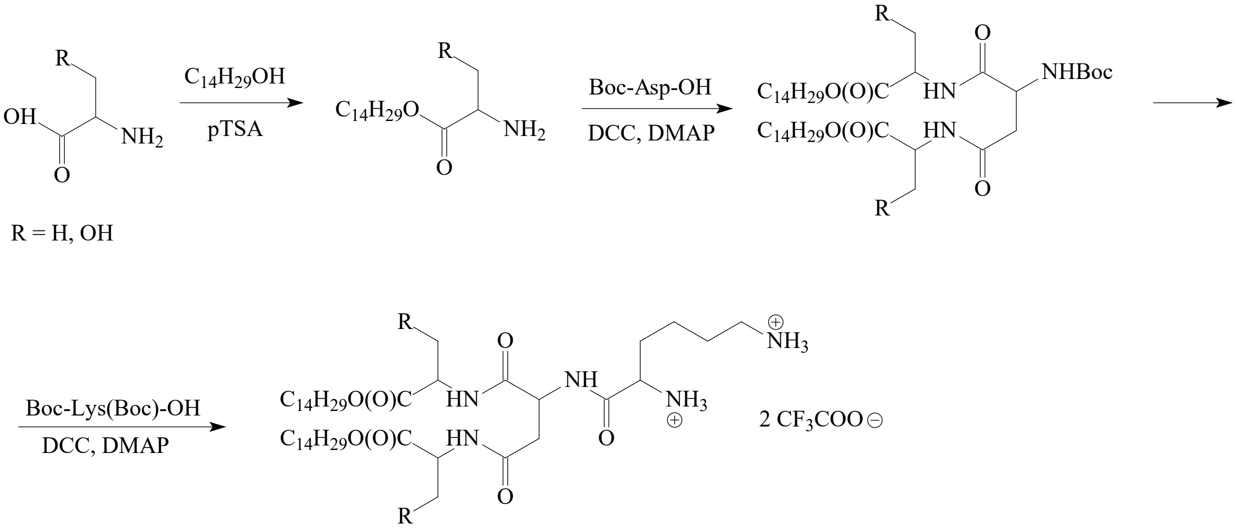
Small interfering RNA (siRNA) is attracts a lot of attention from specialists all over the world as a promising method of gene therapy due to the molecular mechanism of negative regulation of gene expression [1]. The main advantages of using siRNA are high specificity in suppressing the activity of any target gene with a known nucleotide sequence. Successful application of such drugs is determined by the efficiency of the nucleic acids delivery system to the cells. Among these systems, cationic liposomes have become widely spread [2]. We have developed a scheme for obtaining cationic amphiphiles based on natural L-amino acids (Scheme 1) as components of a complex platform to transport biologically active substances. The synthesized substances are designed to study the dependence of structure - functional properties, in particular, the effect of the side functional group in the linker on various aspects of the intracellular promotion of lipoplexes, including the efficiency of escape from endosomes. The polar block of amphiphiles is represented by the L-Lysine residue [3]. The hydrophobic domain is formed by derivatives of tetradecyl alcohol.



Scheme 1. The synthesis of cationic amphiphile.

This work was supported by the Russian Foundation for Basic Research (grant no. 19-04-00775).

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SYNTHESIS OF 2-FURANONES FROM ACETYLENE DERIVATIVES UNDER THE ACTION OF WITH VARIOUS ACIDIC REAGENTS

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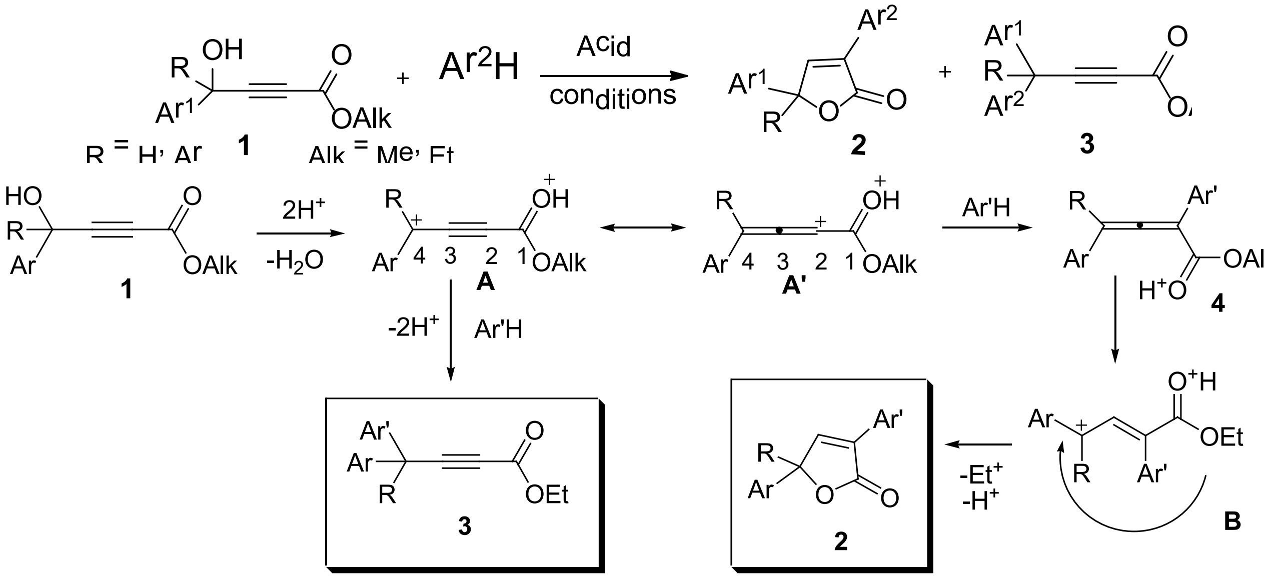
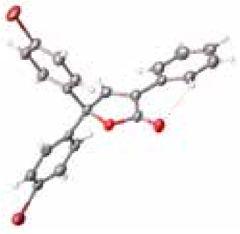
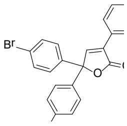
Furanones are of interest from the point of view of their biological activity. These compounds possess anti-malarial, anti-microbial, antituberculor and anticancer properties, and many other activities [1]. Furanones inhibit the expression of bacterial exo-enzymes, that actively degrade components of the immune system thereby enhancing the immune response [2].

In this study, 2-furanones **2** were obtained by the reaction of acetylene compounds 1 **1** with various arenes under acidic conditions. Alkynes **1** (R = H, Alk = Me) in TfOH at room temperature give rise to compounds **2** and **3** in moderate yields (20 – 40%). Compounds **1** (R = H, Alk = Et) can react with arenes in the presence of acidic zeolites CBV-720 at 120ºC (glass autoclave), affording the target compounds **2** and **3**. Diarylated substances **1** (R = Ar, Alk = Et) give selectively only furanones **2** in higher yields (up to 80%) in TfOH at room temperature. Intermediate cationic species **A** and **B** of this reaction were studied by means of DFT calculations to elucidate their reactivity and the reaction mechanism.







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REACTION OF 2-CHLORO-1-PHENYLBENZO[E]-1,3,2-AZAOXAPHOSPHORIN-4-ONE with 2-benzylideneaminoalcohols and 2-benzylideneaminophenol: formation of stereoisomeric cage 1-aminophosphonates

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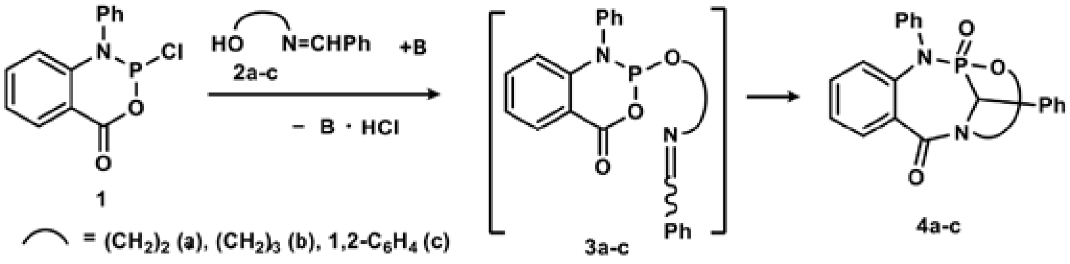
1-Aminophosphonates possess important practically useful properties, such as high biological activity [**1**] and capability to form complexes with many metals [**2**]. In this study, we successfully implemented a new modification of our intramolecular approach [**3**] to the synthesis of cage 1-aminophosphonates using the reaction of 2-chloro-1-phenylbenzo[*e*]-1,3,2-azaoxaphosphorin-4-one **1** with 2-benzylideneaminoalcohols **2a,b** and 2-benzylidene aminophenol **2c** in the presence of a base to avoid the opening of the anhydride moiety (Scheme 1). The formation of P(III) derivatives **3a-c** was detected by ^{31}P NMR (□p□ 120 ppm). Compounds **3a-c** gradually turned into cage 1-aminophosphonates **4a-c** upon standing at room temperature.



Scheme 1.

Aminophosphonates **4a-c** were isolated by column chromatography on SiO$_2$ as a mixture of two diastereoisomers in good yields. The structures of the diastereoisomers were determined by ^{1}H, ^{13}C, ^{31}P NMR, XRD and mass spectra.

This approach can be extended to related cyclic systems where a phosphorus atom is bound to an exocyclic C=N bond through different possible spacers.

The work was financially supported by the Russian Foundation for Basic Research (Project No. 19-03-00730).

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SYNTHESIS, STRUCTURE, AND COMPLEXATION OF NITROBENZOAZACROWN ETHERS

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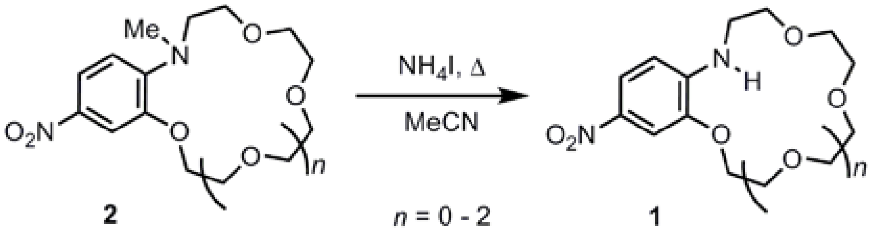
Previously, we developed a new strategy for the synthesis of formyl and nitro *N*-alkylbenzoazacrown ether derivatives with different macrocycle size and macrocycle nitrogen atom being linked to the benzene ring. It is based on the stepwise transformation of the macrocycle of accessible benzocrown ethers used as synthons [1, 2]. We also synthesized dinitrodibenzodiazacrown ethers by one-step transformation of the *cis*-dinitrodibenzo-18-crown-6 ether macrocycle on treatment with aliphatic diamines [2]. And we prepared formyl derivatives of benzoazacrown ethers with N–H group in the macrocycle using two methods [3]. Nitrobenzoazacrown ethers **1** containing NH group in the macrocycle have been unknown until now.

We elaborated a method for the synthesis of nitrobenzoazacrown ethers **1** by *N*-demethylation of *N*-methyl-nitrobenzoazacrown ethers **2** on treatment with ammonium iodide, resulting in the formation of benzoazacrown ethers in 95–100% yields [4].



Scheme 1. Synthesis of benzoazacrown ethers **1** by demethylation of *N*-methylbenzoazacrown ethers **2**

The spatial structure of nitrobenzoazacrown ethers and their complexation behaviour towards alkali and alkaline-earth metal cations, ammonium ions, and fluoride anions were investigated using X-ray diffraction and ^{1}H NMR spectroscopy. It was shown that the stability of host–guest type complexes of nitrobenzoazacrown ethers with metal and ammonium cations in MeCN-d_3 is lower than the stability of complexes formed by *N*-alkyl-substituted analogues with the same macrocycle size. It was shown that fluoride anions in DMSO-d_6 or MeCN-d_3 can bind to nitrobenzoazacrown ethers via hydrogen bonding with the NH group of the macrocycle [4].

The resulting nitro benzoazacrown ethers are of interest as synthons for the synthesis of functional derivatives at the macrocycle nitrogen atom.

This work was supported by the RFBR (grant No. 16-03-00267), the Ministry of Science and Higher Education within the State assignment FSRC «Crystallography and Photonics» RAS.

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METAL ORGANIC FRAMEWORKS BASED ON FC-LINKERS FOR ENERGY STORAGE IN BATTERIES AND SUPERCAPACITORS

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The energy crisis has gradually become a critical problem that hinders the social development and ultimately threatens human survival. Electrochemical energy storage has attracted much interest because of its high energy efficiency and clean power systems. Batteries and supercapacitors are the most important electrochemical energy storage devices. Lithium-ion batteries (LIBs) with high energy density and low weight are widely used in mobile phones, computers, portable electronic devices, and environmentally friendly electric or hybrid electric vehicles. Sodium-ion batteries (SIBs) have similar chemistry to LIBs. More importantly, sodium sources are abundant in nature. Therefore, SIBs have been regarded as a low-cost alternative battery technology for promising electrical power systems. Moreover, supercapacitors have been paid significant attention and are widely applied in electric vehicles and aerospace systems due to their high power density, long cycle life, and competitive price. Electrode materials are critical and have become an active research area to further develop the energy storage devices mentioned above. LIBs and SIBs absorb and release energy by intercalation/deintercalation chemistry. Supercapacitors operate on the mechanism of adsorption and desorption of ions in an electrolyte. Therefore, the suitable electrode materials for LIBs, SIBs, and supercapacitors should have a high surface area, excellent electrical conductivity, and tailored pore size. Recently, metalorganic frameworks (MOFs) have been a research hotspot because of their controllable morphology, abundant pores, high specific surface area, and multifunctionalities. MOFs are composed of metal sites and organic linkers.

We provide the details of the synthesis and electrochemical properties of a new coordination polymers based on Fc-linkers. The study showed the unusual property of 2D platforms to form three-dimensional conglomerates with lithium sulfides.

This research was supported by the Russian Science Foundation, grant No. 18-73-10139

1-MORPHOLINO-2-CYANOETHYLENE IN THE SYNTHESIS OF AZOLO[5,1-*C*][1,2,4]TRIAZINES

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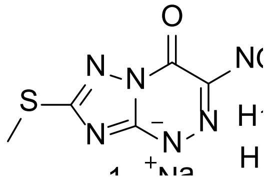
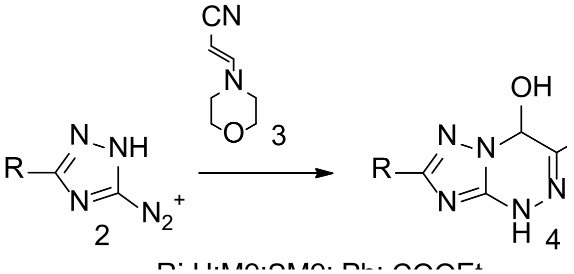
The antiviral drug “Triazavirin” (1) belongs to azolotriazine series - a class of compounds with a wide range of biological activity.

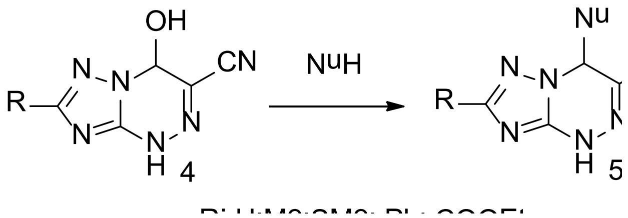


We have developed a new synthetic approach to the synthesis of cyanotriazolotriazines (4) [1].



Scheme 1.

Heterocycles 4 react with nucleophiles easily results in the formation of adducts 5.



Scheme 2.

Biological activity of the synthesized triazolotriazines was studied at the Saint-Petersburg Pasteur Institute.

The results obtained in the framework of the state order Ministry of Education of Russia (4.6351.2017/8.9)

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OLIGO- AND POLYDIMETHYLSILOXANE DERIVATIVES BASED ON RENEWABLE NATURAL RESOURCES

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Limonene is one of the most common monoterpenes. The annual world production of this compound exceed 300000 tons [1]. In this work, the commercially available natural terpenes — limonene and carvone — were chosen as the starting material for the synthesis of siloxane derivatives. Such type of the terpenes has a chemical potential due to the presence in its structure of two double bonds, which implies their further transformation into various derivatives. Recently, it has been found that limonene undergoes hydrosilylation reaction selectively on the terminal double bond [2]. The presence of the second double bond in difunctional siloxane derivatives of limonene allowed their further transformation by the hydrothiolation reaction. This approach allowed us to obtain a series of the copolymers with different alternation of siloxane and methylene units containing thiol and amide fragments in the polymer chain.

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SYNTHESIS AND PHOTOCHROMISM OF NAPHTHO[2,1-*B*]FURYL FULGIDES

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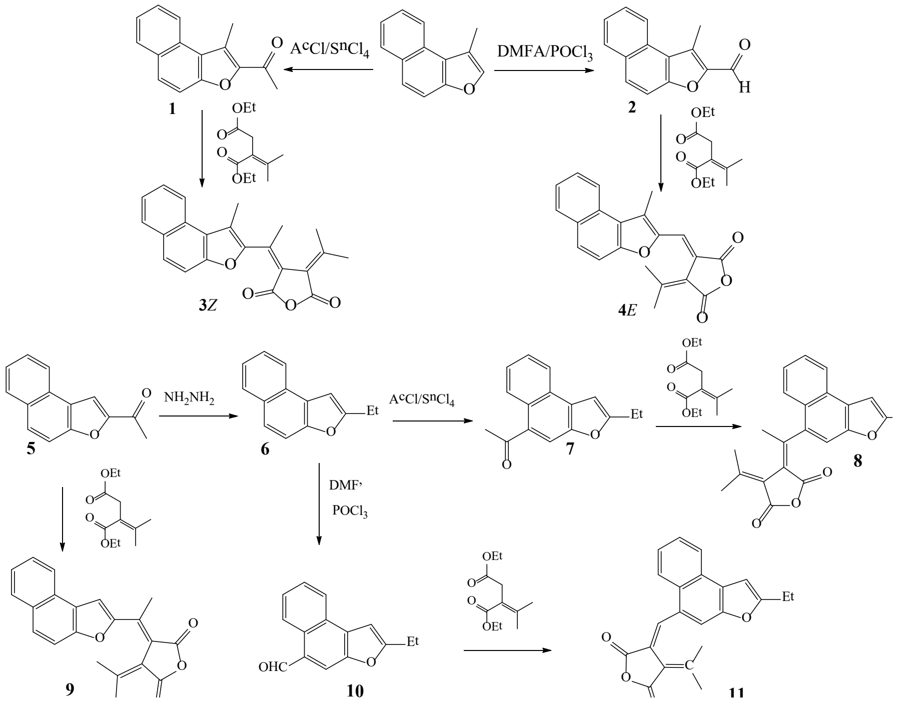
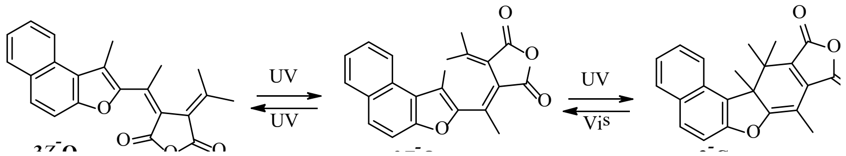
Photochromic fulgides are widely used as efficient molecular switches of fluorescent, chemosensor and complexing properties [1]. We have synthesized novel naphtho[2,1-*b*]furyl fulgides (Scheme 1).



Scheme 1.

Under irradiation fulgides **4**, **9**, **11** undergo reversible *Z/E*-photoisomerization. The compounds with a methyl group at the methylidene bridge **3**, **8** rearrange into the colored fluorescent ring-closed isomers **C**. Irradiation with visible light results in the backward isomerization into the initial ring-opened non-fluorescent form **O** (Scheme 2).



Scheme 2.

This work was carried out in the framework of the basic part of State task in the sphere of scientific activity (nos. 4.6497.2017/8.9 and 4.5593.2017/6.7) and State task of SSC RAS no. 01201354239.

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FUNCTIONALIZED NICOTINAMIDES: SYNTHESIS OF MULTICOMPONENT CONDENSATION AND SOME PROPERTIES

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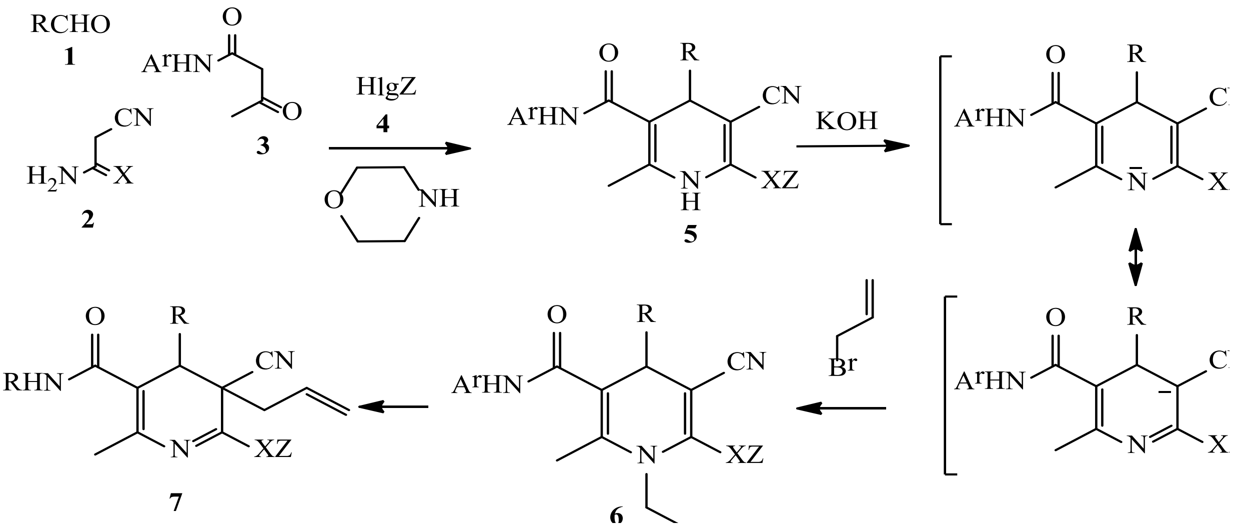
Substances with antitumor, anti-inflammatory, anti-atherosclerotic, fungicidal and herbicidal activity were found in a series of functionalized nicotinamides. In continuation of research in the chemistry of substituted nicotinamides [1], we developed a new method for synthesizing the above class of organic compounds consisting in the multicomponent condensation of aliphatic, aromatic and heteroaromatic aldehydes **1**, cyanothio(seleno)acetamides **2**, acetoacetanilides **3**, alkylating reagents **4** and morpholine. The reaction is carried out in ethanol at 20°C and leads to the formation of 6-alkylthio-4-alkyl(aryl, hetaryl)-*N*-aryl-2-methyl-5-cyano-1,4-dihydro-nicotinoamides **5**. Allylation of compounds **5** ends formation of derivatives **6**. During this reaction, [3,3]-sigmatropic rearrangement is realized, leading to the formation of substituted 4,5-dihydropyridines **7** (scheme 1).



Scheme 1.

The structure of the synthesized substances was confirmed by the data of mass-, IR-, ^{1}H NMR and ^{13}C-spectrometry. X-ray diffraction analysis is used for some compounds.

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3-SUBSTITUTED 2*H*-CHROMEN-2-ONES – PERSPECTIVE SEMI-PRODUCTS FOR OBTAINING BIOLOGICALLY ACTIVE SUBSTANCES

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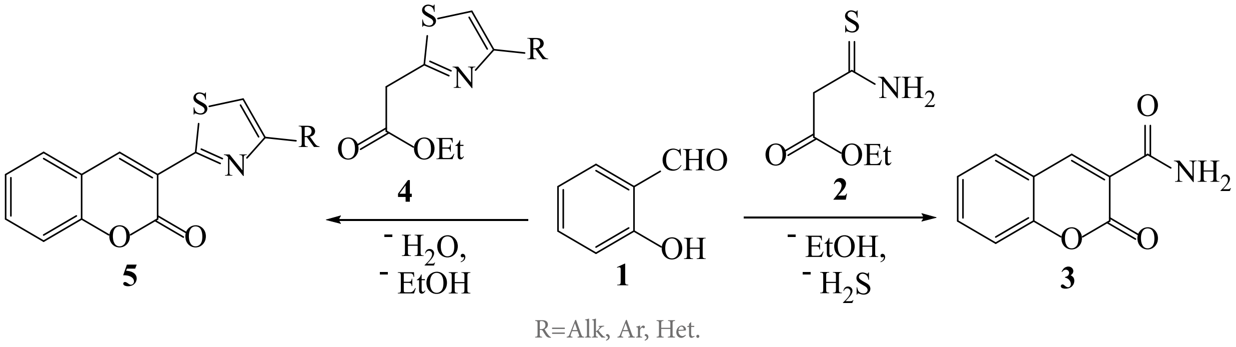
Derivatives of 2*H*-chromen-2-one (coumarin) possess various types of biological activity, among which we note fungicidal, antimicrobial, and antitumor.

In continuation of studies on the chemistry of 2H-chromen-2-ones [1], we studied the condensation of salicylic aldehyde **1** with CH-acids.

The introduction of ethyl 3-amino-3-thioxopropanoate **2** in ethanol to condensation at 20°C in the presence of an aqueous KOH solution leads to the formation of 2-oxo-2*H*-chromen-3-carboxamide **3**. The reaction proceeds through the Knoevenagel alkene formation stage, chemo-selective cyclizing to the final structure **3**. In this case, the thioamide group is hydrolyzed to the amide group.

The use of ethyl-2-[4-alkyl(aryl, hetaryl)thiazol-2-yl]acetates as the CH-acid component in condensation with salicylic aldehyde **1**, which is realized in ethanol at 20°C in the presence of KOH, does not fundamentally change the direction of the reaction – 3-thiazolyl-substituted 2*H*-chromen-2-ones **5** are obtained, respectively – convenient starting reagents for creating new potentially biologically active substances (scheme 1).



Scheme 1.

The structure of the synthesized compounds was confirmed by the data of mass-, IR-, ^{1}H NMR and ^{13}C-spectrometry, and the X-ray diffraction analysis was used for some compounds.

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SYNTHESIS AND PROPERTIES OF ETHYL [ADAMANTAN-1-YLALKYLENE (PHENYLENE) -AMINO] OXOACETATE AND BIS [ADAMANTANE-1-YLALKYLENE (PHENYLENE)] OXAMIDES

D'yachenko V.S., Burmistrov V.V., Butov G.M.

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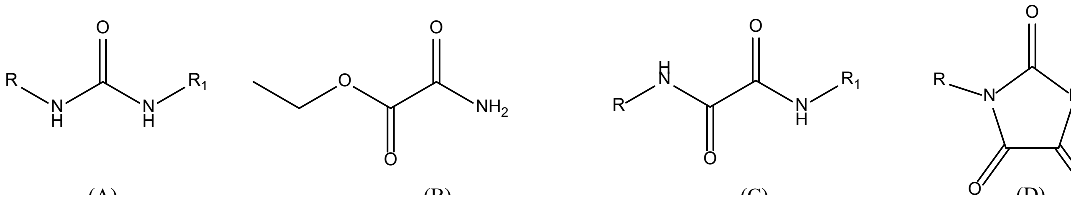
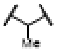
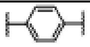
Adamantyl-containing 1,3-disubstituted ureas are effective inhibitors of human and mammalian soluble epoxide hydrolase (sEH) [1]. The inhibitor fragment, including the adamantyl radical and the ureid group (**A**), forms a pharmacophoric center capable of binding to the amino acid residues of the active site of the enzyme Tyr383, Tyr466 with ~C=O bonds and Asp335 with ~NH bonds [2]. However, recently we have shown that inhibitory activity is manifested not only by the ureid group, but also by imidazolidin-2,4,5-trione (**D**). The inhibitory activity against human sEH for this group was 1.6 - 650 nM [3]. In this regard, the search for new pharmacophore centers close to the ureid group (**A**) is relevant. In this work, 2-amino-2-oxoacetate (**B**) and oxamide (**C**) groups are considered as such a replacement.



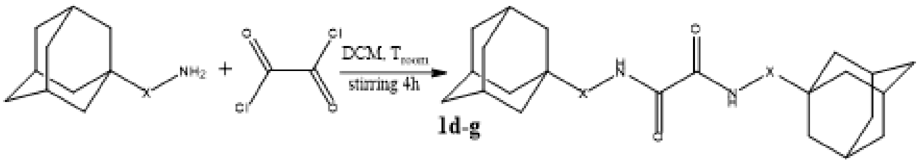
By the reaction of adamantyl-containing amines with ethyl chlorooxoacetate, a series of ethyl [(adamantan-1-yl)alkyl(aryl) amino]oxoacetate **1a-c** were obtained.

1a-c

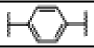
№	X	Yield, %
1a		72
1b		81
1c		82

The reaction was carried out in DCM with a reagent ratio of 1: 0.96 mol and 3 mol of triethylamine, for 12 hours at room temperature. Inhibitory activity against human sEH for this series was 3620 - 23630 nM.

By the reaction of adamantyl-containing amines with oxalyl chloride, a series of bis[adamantane-1-ylalkylene(phenylene)]oxamides **1d-g** were obtained



1d-g

№	X	Yield, %
1d	-	44
1e		52
1f		57
1g		61

The reaction was carried out in DCM with an equimolar ratio of the reactants, for 4 hours at room temperature.

Inhibitory activity against human and mammalian sEH was investigated at the University of California Davis Department of Entomology and Nematology, USA.

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SYNTHESIS OF Β-HYDROPEROXY-Β-PEROXYLACTONES

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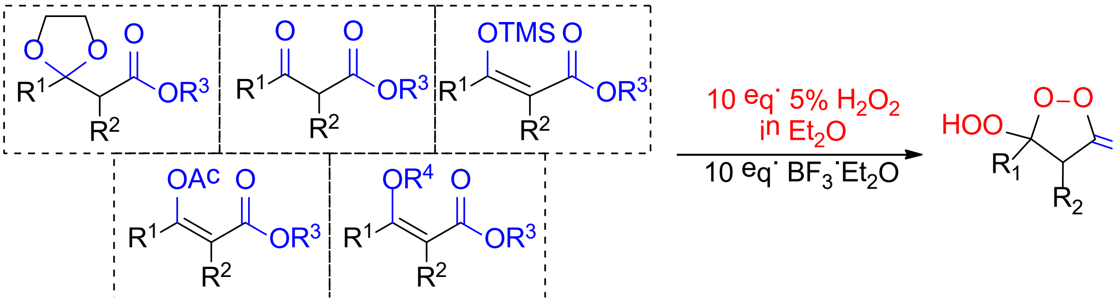
The discovery in 1971 of artemisinin (an effective antimalarial drug), was a powerful impetus to the development of medical chemistry of organic peroxides. In recent years, organic peroxides have been found to have cytotoxic, anthihelmintic, antiviral and fungicidal activity. It has been shown that many structurally simple peroxides exhibit antimalarial activity that is similar or superior to artemisinin. However, there are still no general approaches to obtaining both different classes and individual representatives of organic peroxides, due to the difficulties in preventing the formation of a complex mixture of oxidation products and rearrangements.

The fundamental property of β-ketoesters and their silyl enol ethers, alkyl enol ethers, enol acetates, and cyclic acetals was discovered - the formation of β-hydroperoxy-β-peroxolactones in the H_2O_2 / acid system (scheme 1). It was found that $BF_3{\cdot}Et_2O$ is the most effective catalyst for the process [1]. The synthesized peroxides are stable in the presence of water, oxygen, traces of acids. All of the above suggests that β-pydroperoxy-β-peroxolactones may be useful for further synthetic transformations.



Scheme 1. The formation of β-hydroperoxy-β-peroxolactones

This work was supported by Russian Science Foundation (Grant No. 18-13-00027).

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INTERFACIAL UPLOADING OF LUMINESCENT $[\{Mo_6I_8\}(L)_6]^{2-}$ CLUSTER UNITS ONTO AMINO-DECORATED SILICA NANOPARTICLES AS NEW DESIGN OF NANOMATERIAL FOR CELLULAR IMAGING AND PHOTODYNAMIC THERAPY.

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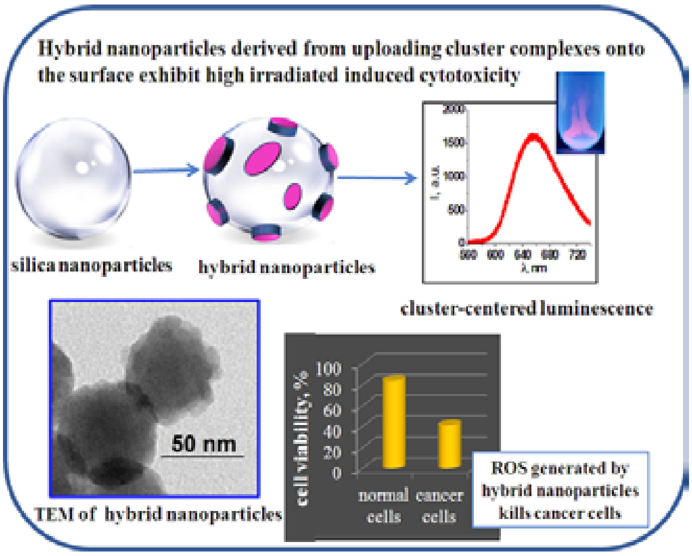
The present work introduces a facile synthetic route to embed phosphorescent $K_2[\{Mo_6I_8\}I_6]$ and $(nBu_4N)_2[\{Mo_6I_8\}(CH_3COO)_6]$ clusters (C) onto silica-water interface of amino-decorated silica nanoparticles (SNs, 60±6 nm) (Scheme 1).



Scheme 1. Schematic representation of self-assembly of the clusters complexes on silica surface; TEM images of the SNs and $[\{Mo_6I_8\}(L)_6]$-SNs.

The assembled C-SNs gain in the luminescence intensity, which remains stable within three months after their assembly. High uptake capacity of the clusters (8700 of $K_2[\{Mo_6I_8\}I_6]$ and 6500 of $(nBu_4N)_2[\{Mo_6I_8\}(CH_3COO)_6]$ per the each nanoparticle) derives from ionic self-assembly and coordination bonds between the cluster complexes and ionic (amino- and siloxy-) groups at the silica surface. The coordination *via* amino- or siloxy-groups restricts aquation and hydrolysis of the embedded clusters, in comparison with the parent $K_2[\{Mo_6I_8\}I_6]$ and $(nBu_4N)_2[\{Mo_6I_8\}(CH_3COO)_6$. High potential of the assembled nanoparticles in the ROS generation was revealed by EPR measurements facilitated by spin trapping. The high positive charge and convenient colloid stability of the assembled C-SNs hybrids are the prerequisite for their efficient cellular uptake, which is exemplified in the work by MCF-7 cell line. The measured dark and photoinduced cytotoxicity of the C-SNs hybrids reveals significant photodynamic therapy effect on the MCF-7 cancer cell line versus the normal cells. This effect is entirely due to the embedded clusters and is dependent on the chemical composition of the cluster.

NOVEL FERROCENE-CONTAINING STERICALLY HINDERED PHOSPHONIUM SALTS

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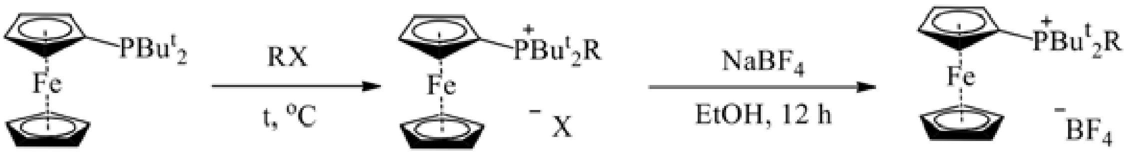
The chemistry of ferrocene and its derivatives has been widely developed over its long history. However, new opportunities and prospects for the use of ferrocene derivatives are currently opening up. The molecular and crystal structure of such materials allows to change their thermal, optical, electronic and magnetic characteristics. Ferrocene-based ionic liquids attract close attention due to its potential use in various fields of science and technology, such as electrochemistry, catalysis, the creation and study of photoactive materials.[1]

We have obtained phosphonium salts with a sterically hindered cation based on di-(*tert*-butyl) ferrocenylphosphine.[2]



R = CH_3, X = I;
R = C_3H_7, C_6H_{13}, $C_{10}H_{21}$, $C_{14}H_{29}$, X = Br

The obtained ferrocene-containing phosphonium salts were characterized with a several physicochemical methods, such as NMR spectroscopy (1H, 31P and 13C), ESI mass spectrometry. The melting and decomposition temperatures were determined by the TG-DSC method, the electrochemical properties were studied. It has been shown that with an increase of the length of the alkyl tail, the potential shifts to the anode region, which makes them promising for use in electrochemistry as redox oxidation mediators.

This work was supported by Russian Scientific Foundation (18-73-10139).

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COMPUTATIONAL REACTOR: GENERATION OF POSSIBLE PRODUCTS OF REACTIONS INVOLVING GIVEN CHEMICAL COMPOUND

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The key challenge in the computer planning of chemical synthesis is generation of new compounds from the set of available molecules.

We have developed an algorithm that generates new chemical structures from a given molecules, using transformation rules extracted from database of chemical reactions. Algorithm for extraction of rules based on chemical intuition was developed. Transformation rules were classified into one-, two- and multi-component based on number of molecules required to perform reaction transformation. Based on extracted transformation rules, functional groups that are subjected to transformations were identified.

List of possible reactants was extracted from databases of commercially available chemical building blocks, which were stored in reactant database based on our in-house Python-based CGR-DB cartridge. Chemical structures were indexed based on functional groups present in them.

At the stage of generation of products, for each reagent algorithm select only those transformations that can be applied to a given starting molecule. System identifies functional groups present in the initial molecule, and extracts from database only those transformation rules that can be applied to a given molecule. If selected transformation rule requires two or more reactants, the second reactant is also selected based on the list of functional groups. The groups absent in starting molecule but required for transformation rule is identified and corresponding molecules are extracted from the database. Having all required molecules reaction product is generated based on the transformation rule. In such a way, algorithm does not try to do unnecessary transformations with unsuitable molecules and it quickly generates new compounds and reactions.

Possibility to generate the whole reaction is also implemented.

Algorithm was tested on database of reactions. Speed and quality tests were performed.

This work was supported by a subsidy provided as part of government support for Kazan Federal University to make it more competitive with leading international scientific and educational centers, and to complete the government mission in the field of scientific activity (projects № 4.1493.2017/4.6 и № 4.5151.2017/6.7).

SUPERELECTROPHILIC REACTIVITY OF ISOXAZOLO[4,3-B]PYRIDINES

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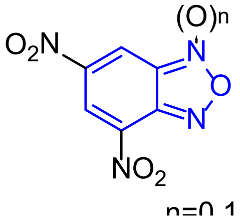
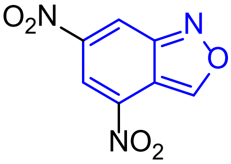
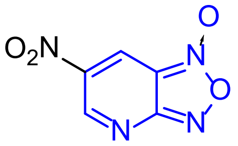
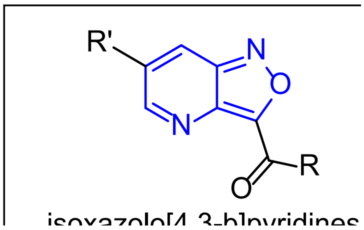
Heterocycles such as dinitrobenzofuroxan (furazan), dinitroanthranil, nitroazabenzofuroxan are known to exhibit superelectrophilic properties[1-3]. This is reflected in their ability to react with neutral nucleophiles (even H_2O). In addition, these heterocycles can be involved in Diels-Alder reactions as dienophiles as well as heterodyenes.

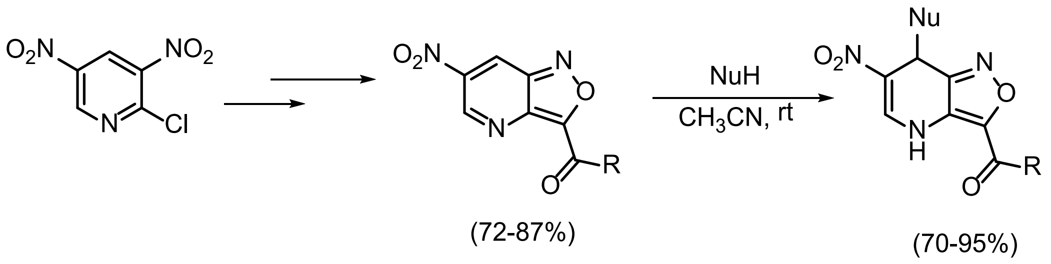






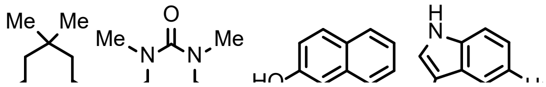


Exploring nitroazines we developed a new superelectrophilic system - isoxazolo[4,3-b]pyridines and studied its chemical properties. The route to these compounds is based on the sequence of Sonogashira reaction and ICl-promoted cycloisomerization [4]. High electrophilicity was demonstrated on example of reactions with various types of nucleophiles, such as alcohols, CH-acids, etc. Reactions of nitro-isoxazolo[4,3-b]pyridines with nucleophiles gave carbon-bonded 1,4-adducts – 1,4-dihydropyridines fused with isoxazole ring. It should be noted that all reactions proceed under mild conditions and in the abcence of a base.



R = Ph, 4-Me-C_6H_4, 4-F-C_6H_4, c-Pr

Nu = OAlk, $[MeC(O)]_2CH$, $(NC)_2CH$, $(EtO_2C)_2CH$, 4-NMe_2-C_6H_4,



Thus, a method for the synthesis of new derivatives of nitroisoxazolo[4,3-b]pyridines was developed and its behaviour as superelectrophiles was examined.

This work was supported by the Russian Foundation for Basic Research (grant № 17-03-00809_a).

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TRIAZOLO[1,5-*A*]PYRIMIDINES AS STRUCTURES FOR THE SYNTHESIS OF NON-NATURAL NUCLEOSIDES

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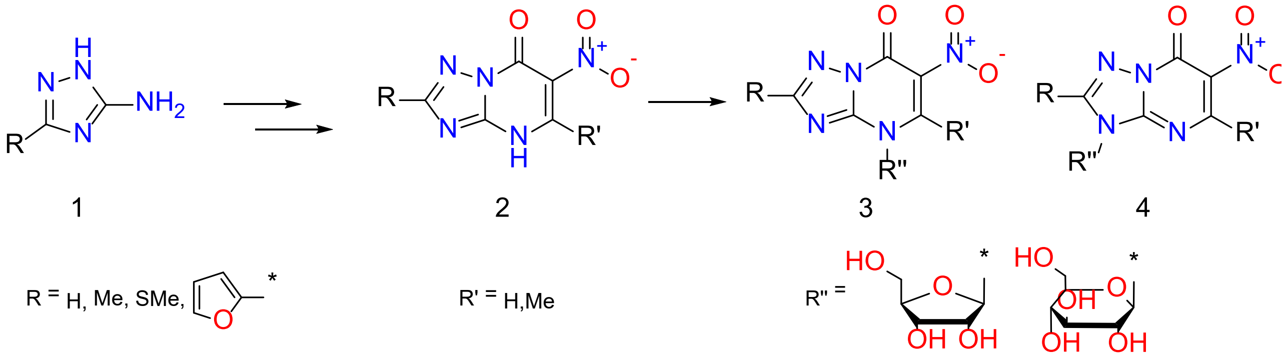
The importance of the development of the methods for synthesis of non-natural nucleosides is conditioned by the constant need to find new means of dealing with dangerous and infection diseases above all. Structural analogues of natural nucleosides are active against the simplex virus of herpes, varicella-zoster viruses, cytomegalovirus, hepatitis B viruses and human immunodeficiency viruses. In this respect, an interesting example of the synthesis of non-natural nucleosides is the use of the nitrogenous base in the form of triazolo[1,5-a]pyrimidines that proved themselves to be the structures of wide spectrum of beneficial biological effects.

Thus, the development of the methods of synthesis for triazolo[1,5-a]pyrimidine-based derivatives of nucleosides is an important scientific task.

To make the synthesis of nucleoside derivatives glycosylation by the method of Vorbruggen [1] was used in this paper. This approach involves the interaction of glycoside with a suitable silylated base in the presence of Lewis acids.



As a result, a method for synthesis of nucleosides 3, 4 in the presence of tin tetrachloride as Lewis acid and BSTFA as a silylation agent was developed and an approach to the synthesis of triazol [1,5-a]pyrimidines-based non-natural nucleosides was introduced.

The results were obtained within the framework of the state task of the Ministry of education and science of Russia (4.6351.2017/8.9).

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DONOR-ACCEPTOR SYSTEMS BASED ON CYANINE DYES WITH TERMINAL NITROGEN-CONTAINING GROUPS

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Self-assembled photoactive supramolecular systems formed by non-covalent interactions attract considerable attention. Cyanine dyes can be employed as light-sensitive components for the design of such supramolecular systems.

In order to elucidate the possibility to construct photoactive “host-guest” complexes based on cyanine dyes as a guest and the influence of their structure on the properties of supramolecular complexes, we synthesized cyanine dyes with ammonioalkyl substituents at the heterocyclic nitrogen atoms with yield up to 51%. Structure obtained dyes was determined by NMR-, IR-, UV spectroscopy, X-ray diffraction data, and elemental analysis [1].

The presence of primary ammonium groups capable of hydrogen bonding enables self-assembly of the dye with crown molecules containing electron-donating oxygen heteroatoms to form supramolecular complexes. This interaction may give rise to highly stable donor-acceptor complexes in which unusual photochemical processes may take place. Complexation was studied using absorbtion, luminescence and ^{1}H NMR spectroscopy.

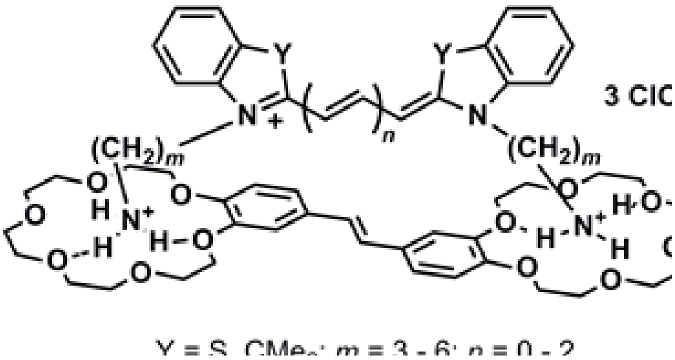

Fig. 1. The most probable structure of the bimolecular pseudocyclic complexes.

We demonstrated the possibility to construct the supramolecular systems based on cyanine dyes with two ammonioalkyl *N*-substituents using their complexes with bis(18-crown-6)stilbene as an example. It was shown that the components form highly stable bimolecular and relatively unstable trimolecular complexes in which the dye ammonium groups are hydrogen-bonded to the crown ether moieties of stilbene and their π-conjugated moieties are located one above the other. The stability constants for some of these complexes were determined, and the stability of the complexes was shown to depend on the dye structure, in particular, on the geometric matching of components, which is manifested as the distance between the ammonium groups of the dye and the stilbene binding sites.

The synthesized cyanine dyes and supramolecular systems based on them may be used as components of photoactive supramolecular devices, optical molecular sensors.

This work was supported by the Russian Science Foundation (project № 19-13-00020).

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AMPHIPHILIC DERIVATIVE OF IMIDAZOLE BEARING DECYL HYDROPHOBIC TAIL: AGGREGATION AND INTERACTION WITH BOVINE SERUM ALBUMIN

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In the framework of this investigation supramolecular systems based on imidazole-containing amphiphile bearing *n*-decyl hydrophobic radical (IA-10, fig.1) has been fabricated and its aggregation behavior in aqueous solutions has been studied. Using tensiometry technique critical aggregation concentration of IA-10 has been determined, which corresponds to 28 mM. Dynamic and electrophoretic light scattering data has demonstrated, that hydrodynamic diameter D_H of aggregates formed is in the range of 3-10 nm, and zeta potenial of aggregates ranges within +60 - +80 mV. The second step of this investigation has been dedicated to the study of complexation capability of IA-10 with natural polypeptide – bovine serum albumin (BSA). It has been exhibited, that BSA introduction to amphiphile solutions leads to the decrease of aggregation threshold of the system and to the appearance of additional inflection point at corresponding surface tension isotherm (17 mM). This point characterizes the initiation of IA-10/BSA complexes formation. It has been established, that hydrodynamic diameter of mixed surfactant/polypeptide complexes is 10-12 nm at low amounts of IA-n added (up to 0.1 mM of IA-n). Increase of surfactant concentration leads to the growth of D_H value to 700 nm and further precipitation, which corresponds to polypeptide denaturation and coagulation of the system. Electrophoretic titration of BSA solution by IA-n has shown, that compensation of BSA negative charge begins from 5 mM of surfactant concentration. However, full neutralization of the charge hasn't been reached up to 20 mM of surfactant concentration. Using synchronous fluorescence spectroscopy it has been revealed, that favorable binding site of components of IA-n/BSA binary system is tryptophan amino acid residue of polypeptide.

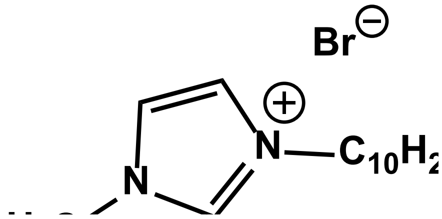

Fig. 1. Chemical structure of IA-10.

This work was supported by Russian Foundation of Basic Research (project № 18-33-00144).

N-HETEROCYCLIC TRANSITION METAL COMPLEXES BASED ON AMPHIPHILIC P-TERT-BUTILTHIACALIX[4]ARENE DERIVATIVES: SYNTHESIS AND CATALYTIC APPLICATIONS

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The idea of creating micellar catalysts that can solubilize water-insoluble substrates and conduct traditional organic transformations in water have attracts much attention of scientist. Macrocyclic compounds acting as ligands are able to arrange their functional groups in area in such a way that a finished chelate compound is formed in which a complexing ion is built in. So the combination of thiacalix[4]arene platform with NHC ligands will make it possible to creating palladium macrocyclic complexes used as catalysts. In addition, due to the structural features of the macrocyclic platform, it is possible to synthesize molecules with amphiphilic properties, which makes it possible to obtain various functional nanosystems used in micellar catalysis.

The fundamental goal of our research is to develop and synthesize new self-organizing catalytic systems based on amphiphilic macrocyclic platforms and d-metals nanoparticles stabilized by carbine forming macrocycles for catalysis of formation of C – C and CX (X = O, N, S) bonds and reduction.

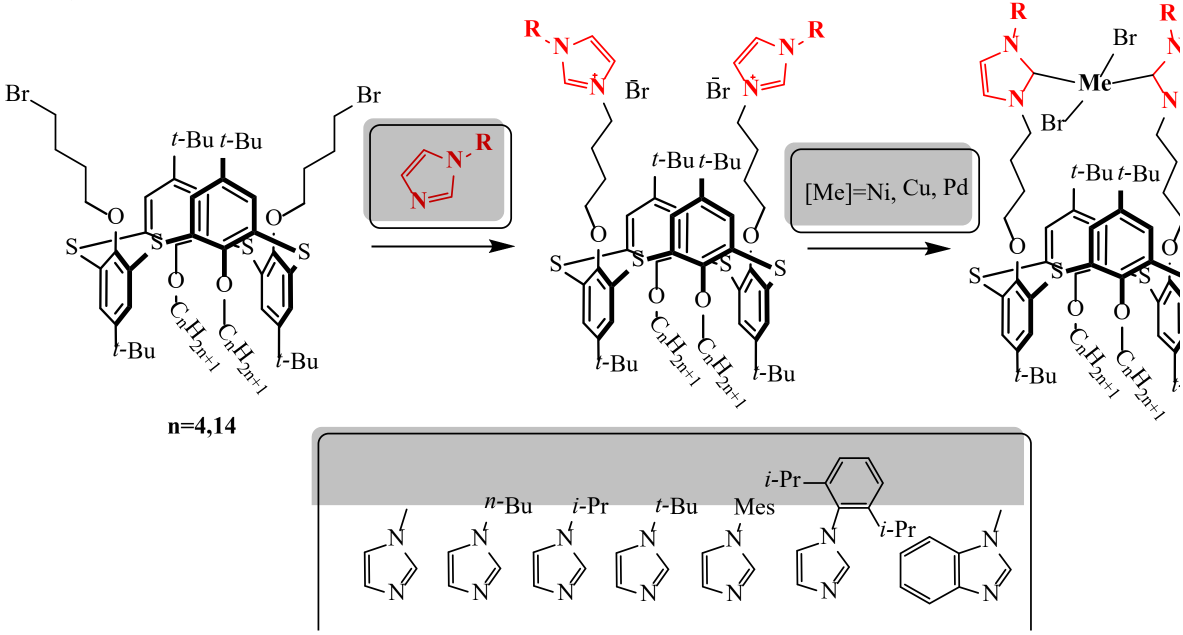

Fig. 1. The general scheme for the preparation of NHC palladium complexes with various substituents.

As a result of this work, an approach was proposed to the synthesis of new palladium complexes based on imidazolium derivatives of *p-tert*-butylthiacalix[4]arene in the stereoisomeric form of *1,3-alternate*, which makes it possible to obtain the target compounds with high yields. Palladium complexes showed high catalytic activity and selectivity in cross-coupling reactions, as well as in the reduction reaction in water-organic systems.

This work was supported by the Russian science Foundation (grant № 18-73-10033)

NOVEL SYNTHESIS OF 3-HYDROXY-4-ARYLQUINOLIN-2-ONES VIA A DARZENS CONDENSATION/FRIEDEL-CRAFTS ALKYLATION STRATEGY

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Shamil K. Latypov, Oleg G. Sinyashin, Vakhid A. Mamedov

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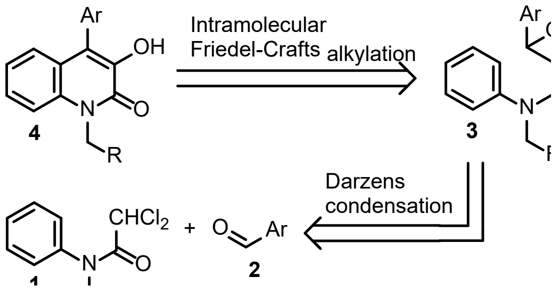
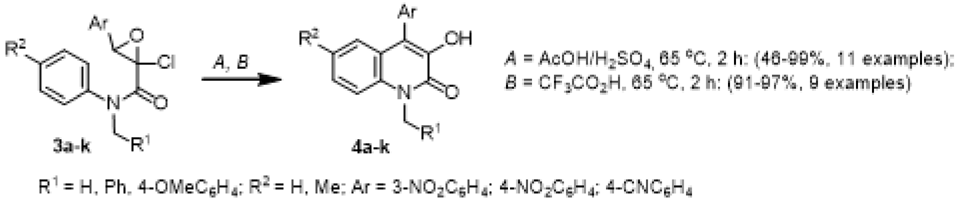
The new efficient synthesis of biologically important 3-hydroxy-4-arylquinolin-2-ones through the Darzens condensation (epoxidation) of dichloroacetanilides with aromatic aldehydes followed by one-pot dechlorative epoxide-arene cyclization is described. Our strategy for the synthesis of the 3-hydroxy-4-arylquinolin-2-ones is outlined in Scheme 1, where **4** are obtained from **3** via the intramolecular Friedel-Crafts alkylation. In turn, **3** can be prepared from dichloroacetanilides **1** and aromatic aldehydes **2** under the Darzens condensation conditions.



Scheme 1. Strategy for the synthesis of 3-Hydroxy-4-arylquinolin-2-ones **4**.

The desired 2-chloro-3-(3-aryl)-*N*-R-*N*-phenyloxirane-2-carboxamides **3** were obtained as the sole products when under the Darzens condensation aromatic aldehydes with the strong electron withdrawing groups **2** were used. Cyclization of epoxides **3i** took place smoothly to afford the desired quinolinones **4a-i** in 91-99% yields (Scheme 2).



Scheme 2. Intramolecular Friedel-Crafts alkylation.

In summary, we have demonstrated the new and efficient approach to the synthesis of the biologically active 3-hydroxy-4-arylquinolin-2-ones **4** by fully exploiting the chlorooxirane groups of the anilides of arylchloroglycidic acids **3**. Substrates for the reactions are widely available or can be readily prepared, thus greatly enhancing the synthetic potential of the method.

This work was supported by the Russian Science Foundation (RSF) (grant No 18-13-00315).

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CONVENIENT SYNTHESIS, STRUCTURE AND BIOLOGICAL ACTIVITY OF 6-CHLORO-4-(ALKYLTHIO(IMINIO)METHYLAMINO)-5,7-DINITROBENZOFUROXANS

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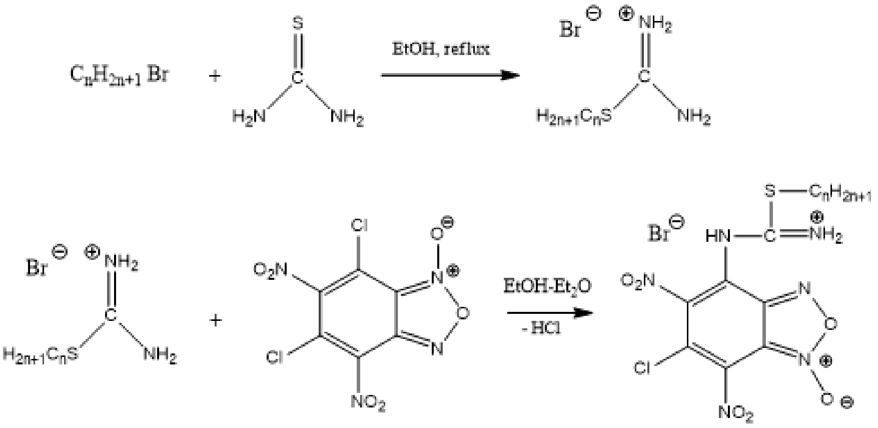
The interest of pharmaceutical chemists in the search for new approaches to structural modification of chloronitrobenzofuroxanes is explained by the high biological activity of such compounds, which is first of all associated by their ability to act as exogenous sources of nitric oxide, a regulator of biochemical processes in human body [1-3].

Earlier we showed that the reactions of 5,7-dichloro-4,6-dinitrobenzofuroxane with substituted phosphines and amines form stable mono- and disubstitution products with high antimicrobial activity [4,5]. Among many sulfur derivatives we choosed S-alkylisothiourea salts, which can be readily prepared from alkyl halides and thiourea. S-alkylisothiourea bromides were prepared by refluxing of higher alkyl bromides with thiourea in ethanol for 45 minutes.

By reacting 5,7-dichloro-4,6-dinitrobenzofuroxane with S-alkylisothiourea salts at a ratio of 1:1 and 1:2 in EtOH-Et_2O (1:3) we obtained yellow monosubstitution products, which were formed via nucleophile substitution at C7 of benzofuroxane system.



n = 10, 12, 14, 16, 18

The structure of the products obtained were established by chemical, physical, and physico-chemical methods and showed a high antibacterial and antimycotic activitiy against human and animal pathogenic microflora. The thermal stability was studied by synchronous thermogravimetry and differential scanning calorimetry (TG-DSC).

This work funded by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (№ 4.5888.2017/8.9).

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AMPHIPHILIC QUATERNARY *P-TERT*-BUTYLCALIX[4]ARENE DERIVATIVES WITH AZIDOALKYL FRAGMENTS ON THE UPPER RIM AS PROMISING BUILDING BLOKS FOR NHC POLYMERIC SUPPORTS USED FOR METAL CATALYSIS

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Cross-coupling reactions allow to form the C–C bonds under rather mild conditions. The tandem of nitrogen-containing heterocyclic carbene (NHC) ligands with transition metals is of great importance for the catalysis of this reactions. Particular interest to nitrogen-containing heterocyclic carbenes is due to their less sensitivity to air and moisture, high thermal stability of the metal-carbon bond and greater efficiency compared with the complexes of the corresponding phosphines [1].

The combination of calix[4]arenes with carbene NHC-ligands for the further preparation of transition metal complexes is a new and rapidly developing trend in catalysis. The possibility of selective modification of the upper and lower rims of the macrocyclic platform by various functional groups will significantly expand the potential of the resulting catalytic systems [2].

In present work we propose synthetic strategy for the synthesis of amphiphilic derivatives of *p-tert*-butylcalix[4]arene with imidazolium and azidoalkyl derivatives on the upper rim of the macrocycle as a promising building blocks for polydentate polymeric metal supports.

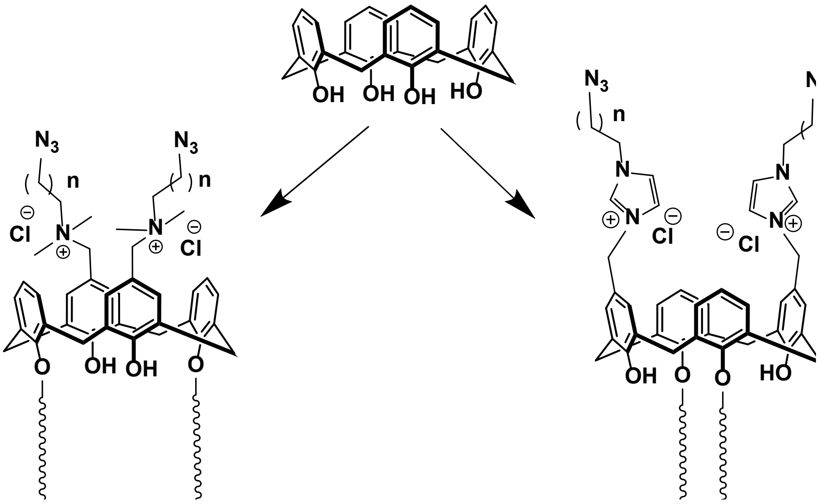

Fig. 1. The structures of synthesized calix[4]arene derivatives.

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REACTION OF THE DICHLOROMETHYLARENES WITH O-METHYL DIETHYLTHIOPHOSPINATE

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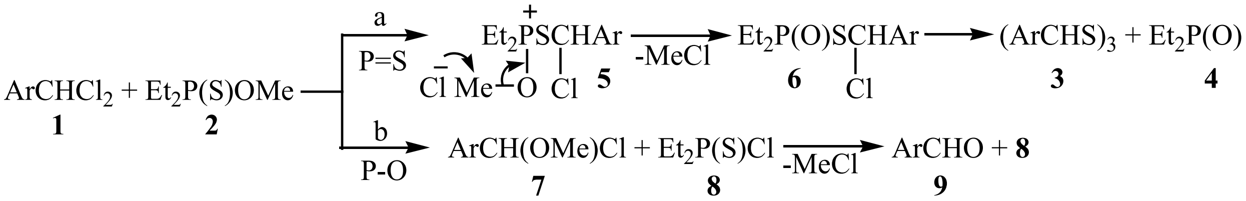
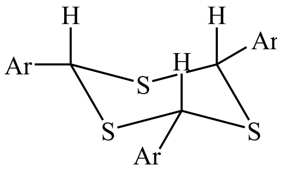
We have studied for the first time the reaction of the functionally substituted benzylidene chlorides **1** with O-methyl diethylthiophosphinate **2**, which is one of the ambident (P=S, P-O)-nucleophiles. The arenecarbthioaldehyde trimers **3** and diethylphosphinoyl chloride **4** were formed. This result suggests an initial attack of the thione sulfur (P=S) on the methyne carbon in **1**, i.e. the realization of route a. Intermediate phosphonium adduct **5** eliminates methyl chloride to produce the product of substitution of one chlorine atom in **1** by diethylphosphinothioyl group **6** (dechlorodiethylphosphinylthioylation). Intermediate **6**, like its oxygen analog [1, 2], is unstable and decomposes under the reaction conditions (100 °C), yielding diethylphosphinoyl chloride **4** and arenecarbthioaldehyde which exists exclusively as timer [3].



Scheme 1.

Arenecarbaldehyde **9** and diethylphosphinothioyl chloride **8** were not observed among the reaction products. It means that initial attack of the ester oxygen on the methyne carbon in **1** to form α-chlorether **7** (dechloromethoxylation, route b) is not realized.

The high melting points, as well as the ^{1}H NMR spectra (singlet signal of three axial CH protons) provide evidence showing that the trimers **3** synthesized exist in the β form. According to [3], the trithiane ring in the β form has a chair conformation and all three methine hydrogen atoms occupy axial positions and the aryl groups are in equatorial positions, i.e. the β form is (e,e,e)-cis, cis-2,4,6-triaryl-1,3,5-trithiane **3**.



This work was supported by the Ministry of Education and Science of Russian Federation in the framework of the basic part of the governmental contract in scientific area, progect № 4.5348.2017/8.9.

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TOWARDS THE DESIGN OF LUMINESCENT QUINOXALINONE THERMOMETERS BASED ON TEMPERATURE CONTROL OF THEIR PROTONATION

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The development of non-contact thermal sensors with submicron spatial resolution is a rapidly growing interdisciplinary scientific area. The most promising non-contact sensors are based on the analysis of temperature-induced changes in the optical properties of materials, among which luminescence is one of the most convenient for detecting. Luminescent thermometers, being highly sensitive, open the possibility for a fast contactless three-dimensional measurement of local temperature. The principles of luminescent thermometers are based on measuring of temperature-dependent luminescence parameters, such as intensity, lifetime, quantum yield, and luminescence wavelength. Efficient and convenient way is the use of ratiometric fluorescent thermometers. The principle of the latter is based on the use of systems exhibiting two emission bands, the intensity ratio of which depends on temperature and thus can serve as the indicator of the latter. Ratiometric approach can be achieved in various ways: by a combination of two emissive dyes (T-responsive probe and T-inert reference) or by a single dye displaying dual emission. In this work we present the approach based on the use of one compound (namely quinoxalinone **1**, [1,2] Fig. 1a) able to protonation with two forms (neutral and protonated) demonstrating different luminescent response.

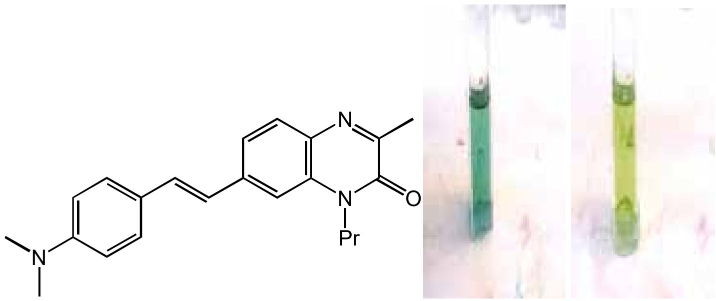

Fig. 1. Chemical structure of considered chromophor (a), solution of the sample in CH_2Cl_2 with addition of CCl_3COOH at 20°C and 80°C.

Variation of temperature leads to shift of equilibria between two forms changing color of the solution of samples (Fig. 1b,c) as well as emission features. It opens the perspectives for their use in luminescent thermometry . To get deeper insight into the observed features modern quantum chemistry tools are especially useful. In particular we present a convenient computational approaches relied on time-dependent density functional theory (TD-DFT) in prediction of important spectral characteristics: the electronic transitions energies for excited and ground states, spectral band shapes and their relative intensities, as well as nature of electronic transitions of neutral and protonated forms.

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RELIABLE QUANTUM CHEMICAL CHARACTERIZATION OF THE EXCITED-STATE PROPERTIES OF THE SERIES OF NOVEL DIAZINE CHROMOPHORES

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π-conjugated organic molecules demonstrate a great potential in a number of modern optoelectronic applications such as non-linear optical (NLO) materials, organic light-emitting diodes (OLEDs), pH/polarity sensors and photovoltaics. Novel recently synthesized diazines (Fig. 1) possessing a number of desirable properties including strong absorptivity in the visible/NIR spectral region, high thermal-/photo-stability, the reversibility of the oxidation/reduction reactions represent a valuable addition for such applications.

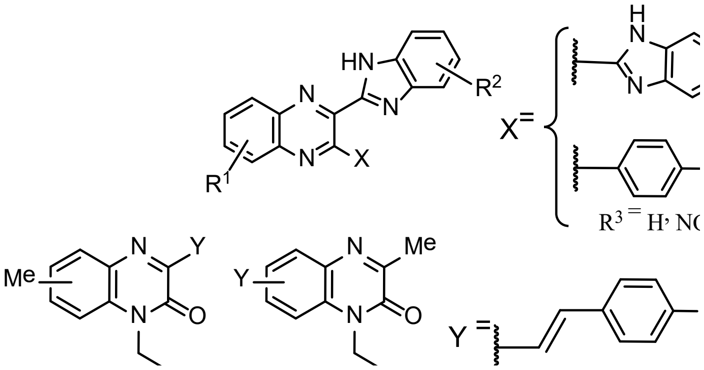

Fig. 1. Chemical structures of considered chormophores.

Their photophysical behavior is found to be highly sensitive toward even small environmental and structural modifications [1, 2]. To get deeper insight into the observed features modern quantum chemistry tools are especially useful. In particular we present a convenient computational approaches relied on time-dependent density functional theory (TD-DFT) in prediction of important spectral characteristics: the electronic transitions energies for excited and ground states, spectral band shapes and their relative intensities, as well as nature of electronic transitions. The latter could be effectively treated with the use of recently developed novel quantum-mechanical descriptors [3, 4] providing quantitative assessment of intramolecular charge-transfer character. Our results demonstrate that the TD-DFT approach represents a reliable theoretical tool allowing a rational design of the D-A chromophores based on diazines.

The reported study was funded by RFBR according to the research project № 18-33-00128 mol_a

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RARE-EARTH COORDINATION POLYMERS BASED ON 1,1'-FERROCENYL-BIS(METHYLPHOSPHINATES) AS MATERIALS WITH MAGNETIC AND LUMINESCENT PROPERTIES

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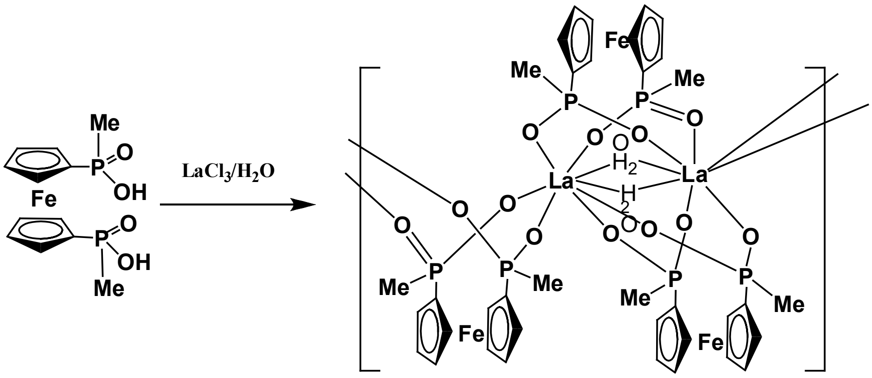
Ferrocene-containing acids are widely used to create coordination compounds and polymers with optical, magnetic and redox properties [1-2]. The possibility of rotation of the phosphinate groups around the P-C (Cp) bond in 1,1'-ferrocenediyl-bis(R-phosphinic acids) HOORP-Fc-PROOH results in an even greater number of coordination motifs depending on the reaction conditions. We have obtaned coordination polymers based on ferrocenylphosphinic acid with a wide range of rare-earth metals. [3]



In this study, it was shown that, in the presence of a ligand, lanthanum is capable of forming a one-dimensional chain with structurally repeating fragments. A comparative analysis of the formation of the polymer chain with varying substituent at the phosphorus atom was carried out. The fundamental importance of the hydrogen atom, which is the ability to form two-dimensional structures, is shown.

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THE SYNTHESIS OF NEW CHIRAL PHOSPHINIC ACIDS BASED ON N, N DIMETHYL-A-FERROCENYLETHYLAMINE AS POTENTIAL LIGANDS FOR SYNTHESIS OF (POROUS) COORDINATION POLYMERS (MOFS)

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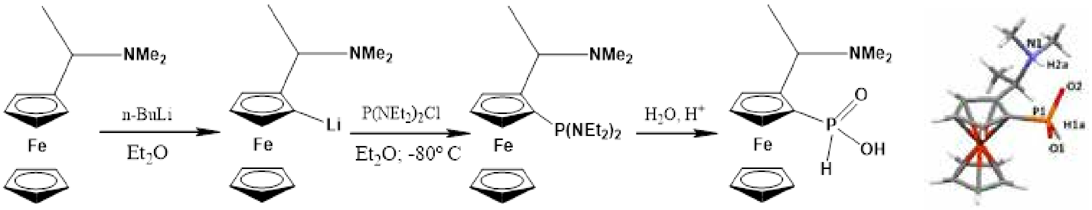
The properties of 1,2-disubstituted ferrocenylphosphinic acids, which are the logical continuation of the series of phosphines, phosphine oxides and phosphinous acids, phosphinic and phosphonic acids, remain completely unexplored. Chiral phosphinic acids have already successfully applied as ligands in asymmetric metallocatalysis [1] and can also be used to create optically active coordination polymers [2]. It is suspected that the chiral phosphine acids containing ferrocene moiety may act as effective ligands in metallocatalysis, and in the chemistry of chiral coordination polymers. And the possibility to influence the properties of acids by changing the substituent at the phosphinate group allows to adopt such ligands for a specific task.



This research was supported by the Russian Science Foundation No. 18-73-10139.

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REACTIONS OF 1,3-DEHYDROADAMANTANE WITH FLUORINATED HALOALKANES AND ALCOHOLS

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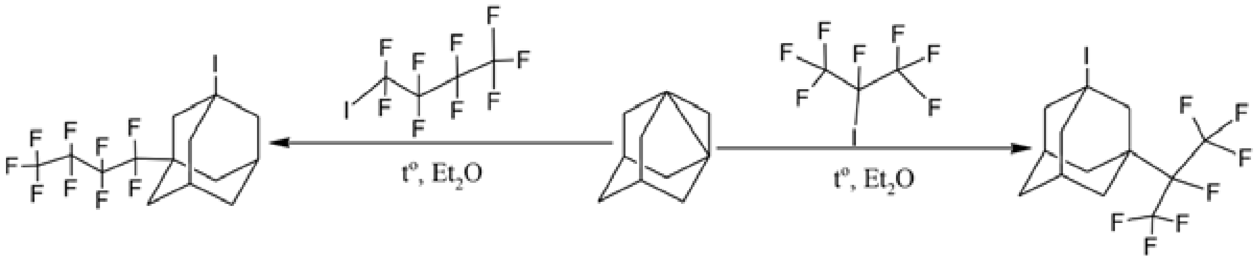
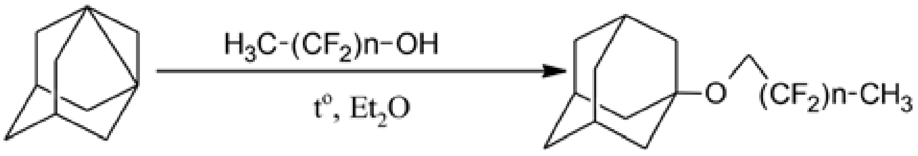
The introduction of an adamantyl fragment into various compounds attracts the attention of researchers in connection with the possibility of imparting to them various new properties (physicochemical, biological). Various adamantyl-containing derivatives are used to obtain synthetic lubricating oils, polymeric materials and others. Among them, a special place is occupied by adamantane derivatives containing perfluoroalkyl substituents. Adamantyl-containing fluorinated ethers and polyfluoroalkyl adamantane are poorly understood compounds and can be used as raw materials for the creation of new synthetic oils and lubricants. In this regard, the synthesis of adamantane derivatives containing polyfluoroalkyl substituents in the nodal position of adamantane, as well as the development of new methods for their preparation, is relevant.

The paper describes a simple method for obtaining polyfluoroalkylladamantanes by the reaction of 1,3-dehydroadamantane with polyfluoroalkanes in a polar solvent. Polyfluoroalkladanes containing both halogen atom and polyfluoroalkyl substituents, as well as a perfluorinated ester group, have been synthesized. Reactions of 1,3-dehydroadamantane with the corresponding halogenpolyfluoroalkanes were carried out in diethyl ether at a molar ratio of 1,3-dehydroadamantane : halogenopolyfluoroalkane : diethyl ether 1:3:6,5. To complete the reaction with halogenopolyfluoroalkanes, it was sufficient to hold the reaction mixture for 1 hour at a temperature of about 35°C. The product yield was more than 90%



Scheme 1. Scheme for the production of 3-iodine-1-polyfluoroalkyladamantane

Reactions of 1,3-dehydro-adamantane with the corresponding fluorinated alcohols were carried out in diethyl ether. The reaction time is 1 hour at a temperature of about 35°C. The product yield was more than 90%.



Scheme 2. The general scheme of obtaining the fluorinated esters of adamantane, where n = 4,6,8

The structure of the obtained compounds was confirmed using 1H NMR spectroscopy and chromatography-mass spectrometry.

SYNTHESIS OF CROWN ETHER-CONTAINING BIS-IMINES

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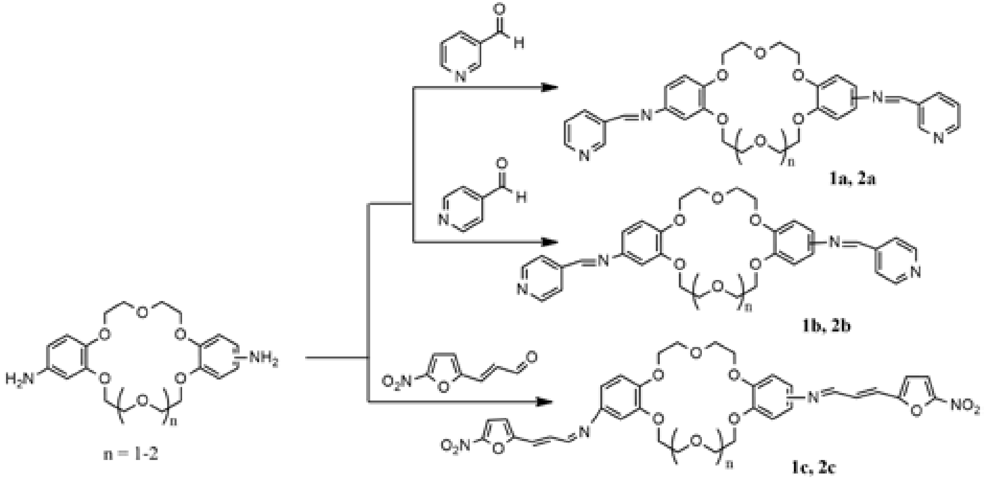
Crown ethers-containing imines are well-known ionophores and also represent promising highly sensitive sensors due to the presence of two coordination centers [1]. In addition, they can be used as luminescent and magneto dynamic materials and catalysts. Previously we found that their complexes are active as amphiphilic compounds for tumor chemotherapy [2].

We obtained and examined a number of azomethine derivatives of crown ethers by the interaction of diaminodibenzo-18-crown-6 (**1**) and diaminodibenzo-21-crown-7 (**2**) with 3’- (**a**) and 4’-pyridinecarboxaldehyde (**b**), and 5-nitro-2-furanacrolein (**c**).



Scheme 1. Preparation of azomethine derivatives of crown ethers

The UV spectra of the obtained products were taken on a Specord 250 Plus instrument in DMF.

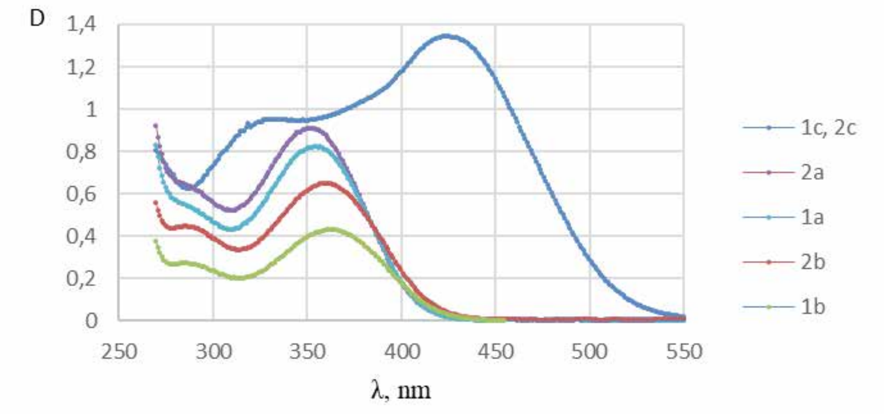


Fig. 1. UV spectra of azomethine derivatives of crown ethers

The resulting compounds were characterized by IR and NMR spectroscopy. Their melting points were also determined: **1a** – 160-162°C, **2a** – 161-163°C, **1b** – 168-170°C, 2b – 128-130°C, 1c - 172°C, 2c – 120-122°C.

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SYNTHESIS OF 5*H*-IMIDAZO[2,1-*B*][1,3]THIAZINS BASED ON ELECTROPHILIC-ACTIVATED ENYNES

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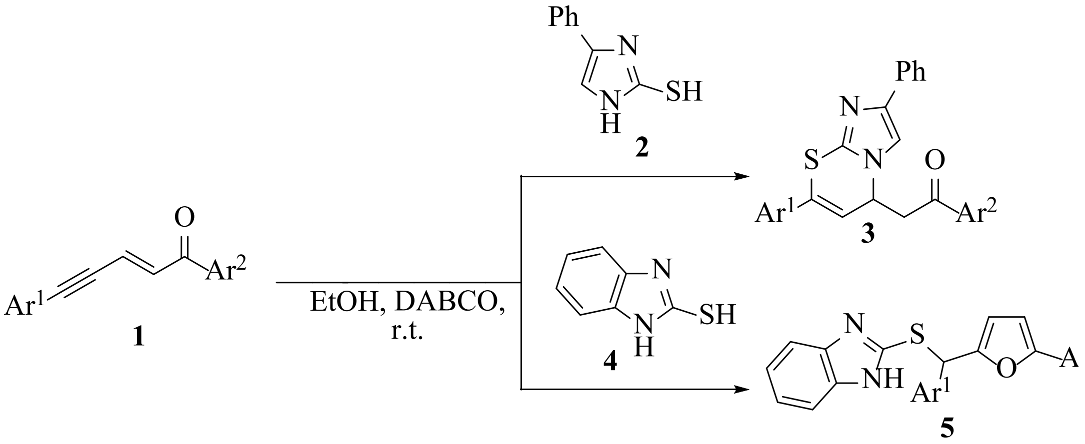
Linear-conjugated enyne ketones are successfully used in the synthesis of various derivatives of oxygen, nitrogen and sulfur containing heterocyclic compounds [1–3].

We have found that base catalyzed interacting of 1,5-diarylpent-2-en-4-yn-1-ones **1** and 2-mercapto-4-phenylimidazole **2** lead regioselective to 5*H*-imidazo[2,1-*b*][1,3]thiazines **3**. Obviously, the reaction begins with a nucleophilic attack of the SH-group on the triple bond of the substrate. The following intramolecular nucleophilic addition of the NH-group of the imidazole cycle at the 3-position of the intermediate adduct leads to the closure of 5*H*-imidazo[2,1-*b*][1,3]thiazine ring of compounds **3.**



Under identical conditions, the interaction of enynes **1** with 2-mercaptobenzimidazole **4** proceeds with the participation of ketone group oxygen and leads to the formation of furans **5** [4]. In this report discussed the possible causes of the different orientation of the reactions of thiols **2** and **4**.

This work was supported by the grant of the Russian Science Foundation No. 18-13-00008.

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A DOMINO ROUTE FROM IMIDAZOLINES AND ELECTRON-DEFICIENT ALKYNES TO POLYSUBSTITUTED PYRROLES AND TETRAHYDROPYRROLO[1,2-*A*]PYRAZINES

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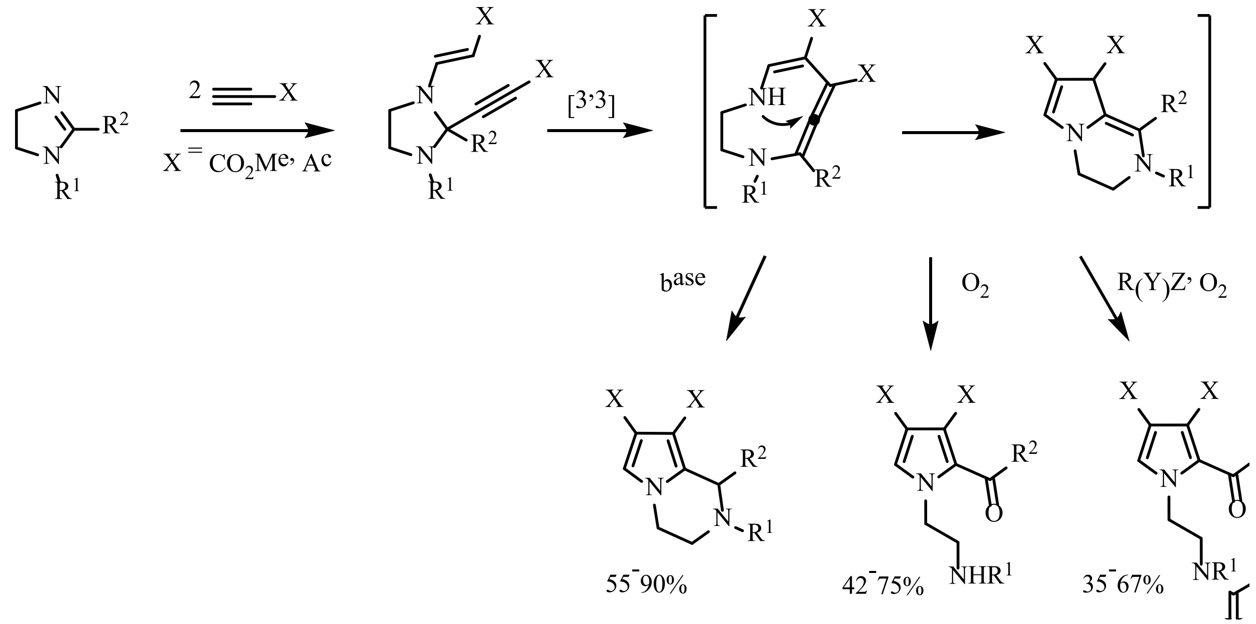
Nitrogen-containing compounds such as 1, 2, 3, 4-tetrahydropyrrolo[1, 2-a]pyrazines and N-substituted pyrroles are an important motifs due to their biological activities. In particular, polysubstituted pyrroles have anti-tumor activity and antibiotics while pyrrolo[1,2-a] pyrazine derivatives show neuropsychotropic properties. Thus, the synthesis of these widely exiting heterocyclic systems still attracts much attention of scientists.

The present work discloses our latest results, concerning pseudo three-component reaction of 2-imidazolines and electron-deficient terminal alkynes to form tetrasubstituted imidazolidines, which can undergo further transformations. As a convenient starting material, we consider 2-imidazolines which can be easily obtained by new preparative methods discovered in recent times.



Obtained tetrasubstituted imidazolidines have an amino-ester fragment, cyclic aminal fragment and an electron-deficient triple bond, such a concentrated set of reaction centers allows us to expect a high synthetic potential of these compounds. It can be interesting as for investigation a mechanism of the proceeding reactions as for synthesis aimed at expanding molecular diversity. It turned out that under microwave conditions imidazolidines can undergo 3,3-sigmatropic rearrangement with the formation of a 9-membered allene, followed intramolecular nucleophilic addition along the allene fragment with the formation of a bicyclic system and consequent oxidation of electron-enriched double bond by atmospheric oxygen furnishes pyrroles with aminoethyl moiety. At the same time under these conditions base addition leads to pyrrolo[1,2-a] pyrazine formation.

This work was supported by the Russian Foundation for Basic Research (grant № 19-03-00502 a).

NEW SYNTHETIC OPPORTUNITIES OF SALT DIBENZOPIRILIUM

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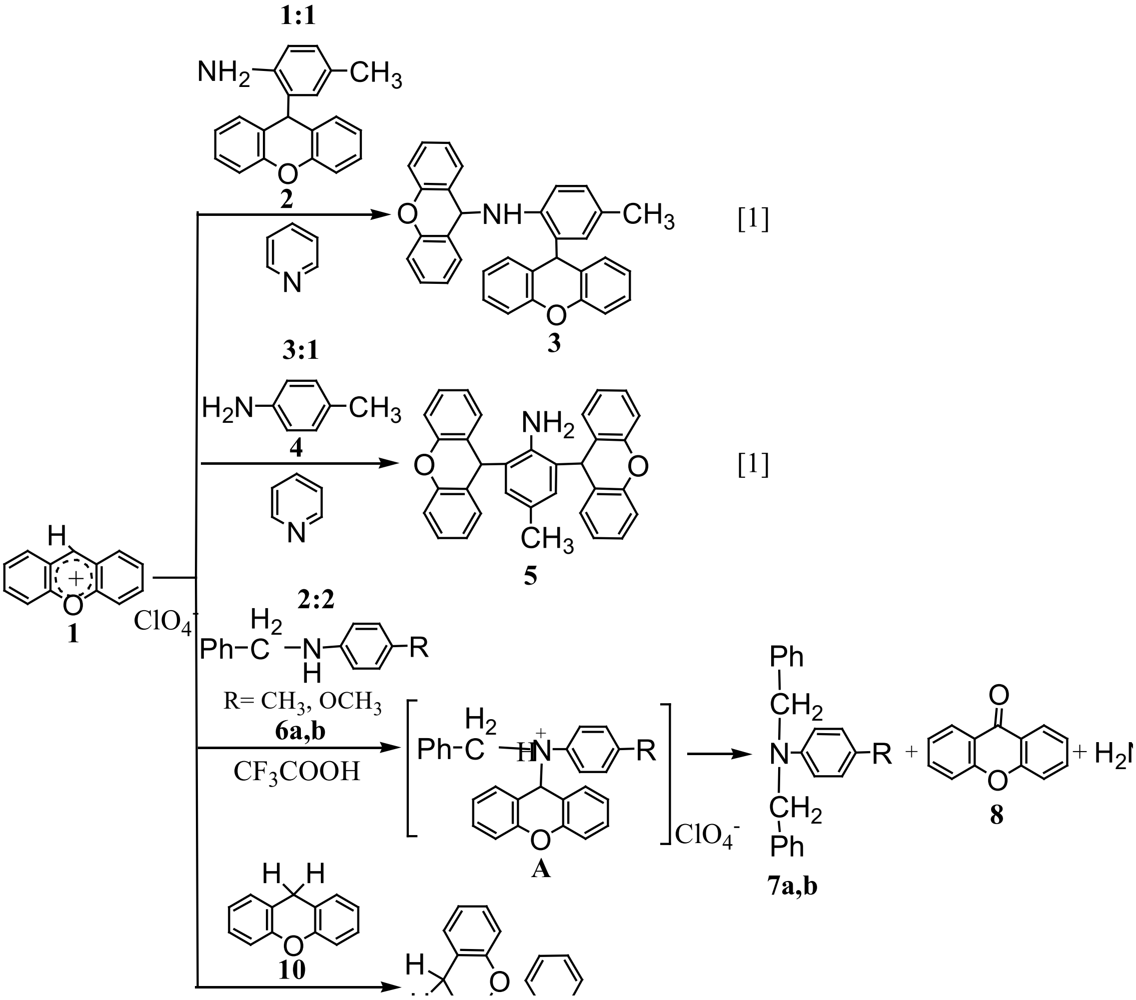
The high reactivity of dibenzopyrylium perchlorate (xanthilium) **1** in reactions with primary, secondary amines or dibenzopyrane has been established. So, by the interaction of salt **1** with 4-methyl-2-(9*H*-xanthen-9-yl)aniline **2**, spatial-obstructed 4-methyl-2,*N*-di(9*H*-xanthen-9-yl)aniline **3** was obtained, and the use of salt **1** in the reaction with *para*-toluidine **4** allowed in one stage to obtain a symmetric 4-methyl-2,6-di(9*H*-xanthen-9-yl)aniline **5** containing a free amino group.

A method has been developed for the synthesis of symmetric *N,N*-dibenzylanilines **7a,b** by the interaction of salt **1** with para-substituted N-benzylaniline **6a,b** through the stage of intermediate A. The latter, as a result of disproportionation, turns into **7a,b.**

An interesting result was obtained by the interaction of salt **1** with dibenzopyrane **10**, accompanied by the formation of 1-xanthen-9-yl-xanthene **11**.



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CARBAZOLYL SUBSTITUTED DYES: SYNTHESIS AND APPLICATION

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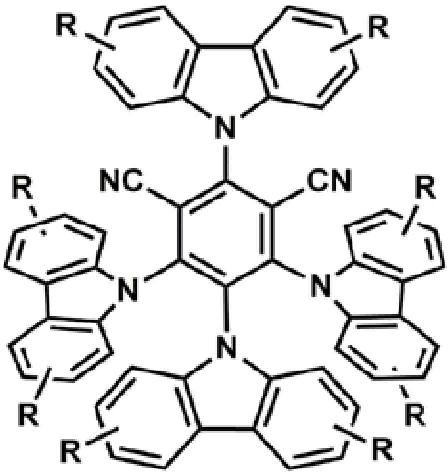
The 2,4,5,6-tetra(9H-carbazol-9-yl)isophthalonitrile (4CzIPN) are frequently utilized in OLED development[1] and photochemistry.[2] The carbazolyl substituted dyes as photosensitizers in photoredox catalysis has been well established in the last 5 years. These organic dyes offer cheap and sustainable alternatives for transition metal (Ru, Ir) photocatalysts.

In our work, we synthesized various 4-CzIPn dyes containing mono and disubstituted carbazole rings via one-step condensation or substitution reactions from commercially available starting materials.



Scheme 1. Carbazolyl substituted isophthalonitrile

After the synthesis of the target compounds their catalytic activity was studied in various photoredox transformations. The carbazolyl dyes were tested in a nickel co-catalyzed decarbonylative transformation and an arylation reactions. We optimized the photocatalytic conditions of this reaction and found that the simple organic photocatalyst the tetracarbazolyl substituted isophthalonitrile dyes (4CzIPN derivatives) under blue (445-450 nm) LED irradiation gave similar efficiency than $Ir[dF(CF_3)ppy]_2(bpy)PF_6$ photocatalyst under argon atmosphere at room temperature. However, their catalytic activity should be fine tuned to reach the same activity as the iridium complexes.

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SYNTHESIS OF NEW ALLOCOLCHICINOIDS – POTENTIAL COVALENT TUBULIN PROTEIN POLYMERIZATION INHIBITORS

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Several allocolchicinoids, containing Michael acceptor fragment, were synthesized from commercial colchicine. This agents are expected to capable of covalent binding to tubulin (Fig. 1, Scheme 1).

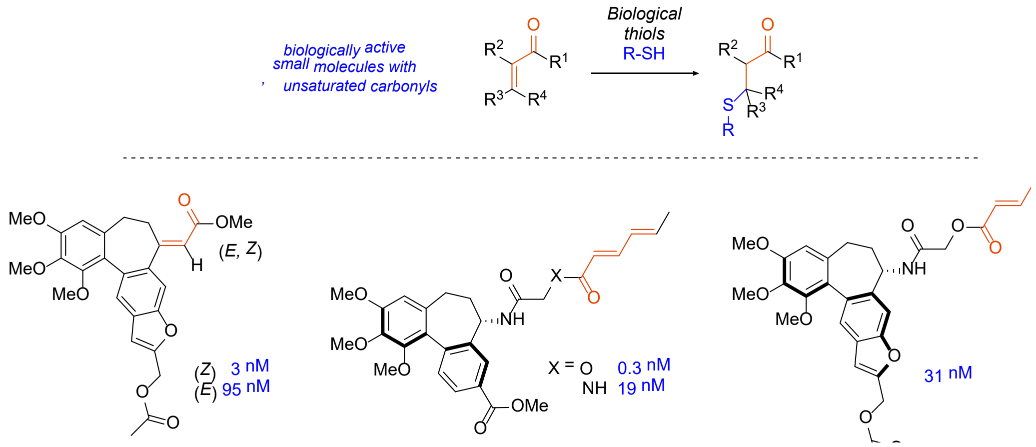
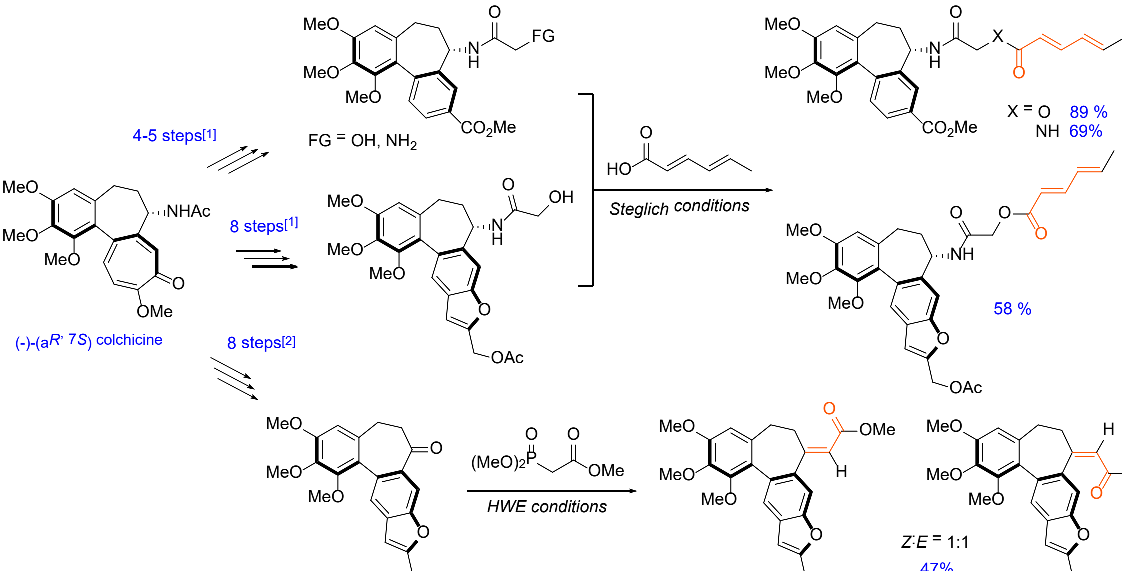


Fig 1. Structures of targeted allocolchicinoids and their *in vitro* cytotoxicity (IC_{50}, HaCaT cells).



Scheme. 1. Synthesis of allocolchicinoids capable of covalent binding with tubulin.

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ELECTROCATALYTIC TRIFLUOROMETHYLATION OF C-H BONDS OF AROMATIC COMPOUNDS

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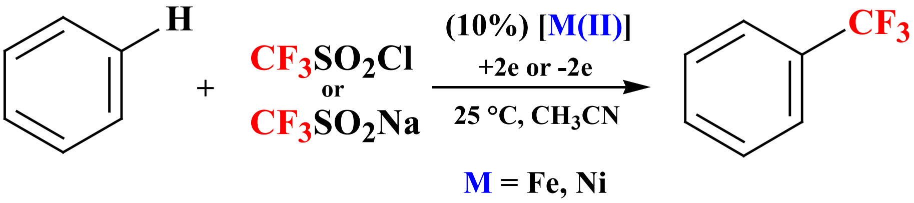
The introduction of the trifluoromethyl and perfluoroalkyl groups can dramatically affect the properties of organic molecules, thereby increasing the possibility of their use as drugs, agrochemicals or building blocks for the creation of new organic materials [1]. Today, there are many methods for introducing a fluoroalkyl group into an organic molecule, but little is known to introduce methods by direct C–H functionalization, although this method is most relevant, since it follows the principles of green chemistry, such as atom-economy, low waste, etc. [2].

The aim of our work is to create a convenient method for the synthesis of perfluoroalkylheteroaryls (benzene and its derivatives, caffeine, coumarins) through electrocatalytic activation of C–H bonds of aromatic substrates with Fe- and Ni-complexes in reaction with CF_3SO_2Cl or CF_3SO_2Na.



Scheme 1. Fe-catalyzed and Ni-catalysed trifluoromethylation of C-H bonds of aromatic and heteroaromatic compounds.

As a result of a series of experiments, the possibility of electrocatalytic fluoroalkylation of C–H bonds of aromatic and heteroaromatic compounds is shown. It is important to note that in these syntheses 100% conversion of the fluoroalkylating reagent is achieved, it does not remain in the reaction mixture after passing 2F. A distinctive feature of the reaction is that it is realized without the use of any additional reagents - bases, oxidizing agents or reducing agents [3].

This work was supported by the Russian Science Foundation, grant No. 19-13-00016.

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THE RELATIONSHIPS BETWEEN SELECTIVITY OF OXIDATION REACTION AND PROPERTIES OF “ALCOHOLS – C_3N_4 PHOTOCATALYST” COMPLEXES

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Oxidation of aromatic alcohols to the corresponding aldehydes assisted by the C_3N_4 catalysts is a promising approach in modern technology, especially for valorization of lignin wastes and for synthesis of pharmaceuticals. This problem is related to the oxidizing ability of C_3N_4 photocatalyst [1]. The aim of the work is to establish and analyze the relationships between selectivity and calculated descriptors of atomic and bound characteristics of the studied systems. The analyzed data are based on the binding energy and topological characteristics of the electron density at the bond critical points in complexes “substrate-catalyst”. Calculations were performed using FireFly, AIMAll and ISIDA programs. The objects of the research were 48 complexes consisting of 12 molecules of aromatic alcohols, C_3N_4 photocatalyst represented by dimelem and melon fragments and also H_2O_2 molecules for simulation of the modified catalyst. The reactivity, selectivity and conversion were determined experimentally [2].

The algorithm for constructing the regression models based on the calculated atomic and bond descriptors included the following steps: 1) divide of the array of calculated data for the studied complexes into 7 classes, taking into account the type of catalyst fragment, the influence of catalyst modification, the cross-use of descriptors; 2) make up of matrices of pair correlations with the subsequent exclusion of descriptors with small contributions to the considered properties; 3) multiple regression analysis of one-, two-, and three-factors models for selectivity of the oxidation using Statistica program. For obtained equations, we have estimated the contributions of the coefficients, controlled the stability and interpretability of models.

The best correlation coefficients for 3-factor models are not lower than 0.95. The correlations include descriptors responsible for atomic dipole moments $\mu(C)$, atomic charges $q(C)$, electron localization indices $\lambda(H)$, interaction energy in systems. Substructure molecular fragment (SMF) analysis [3] helped us to reveal the significant atoms and fragments of substrates that have high probability of interactions with the catalyst. It is shown that the oxidizing ability of the catalyst is linearly depended on the charges of aromatic carbons.

The result of our work is a series of electronic descriptors that correlate with the experimental data of oxidation of substrates bound with C_3N_4 photocatalyst. Combination of the best descriptors helped us to understand the most probable features of the aromatic alcohols binding on the photocatalyst surface.

This work was supported by the Ministry of Education and Science of the Russian Federation (grant No.4.1157.2017/4.6).

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LIQUID CRYSTALLINE POLY(PROPYLENE IMINE) DENDRIMER-BASED IRON OXIDE NANOPARTICLES

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Poly(propylene imine) dendromesogens (generations from 1 to 4) have been utilized for the synthesis and stabilization of ferrimagnetic iron oxide nanoparticles. Oxidation of Fe(II) at slightly elevated pH results in the formation of highly soluble nanocomposites of iron oxides into dendrimer, which are stable under a wide range of temperatures, figure 1. Size exclusion chromatography indicates aggregates in the 20-30-nm size regime, consistent with the oligomeric nature of the composite material. Transmission electron microscopy reveals small assemblies of mineral cores with electron diffraction and high-resolution TEM data, indicative of the mineral maghemite. All investigated poly(propylene imine) dendrimers-based iron oxide nanoparticles are liquid crystalline. The segregation of the polar core and the apolar alkoxy terminal chains in different domains is responsible for the appearance of mesophases, as is the case for the ligands. The PPI-Fe_2O_3 exhibit a hexagonal columnar (p6mm symmetry) mesophase.

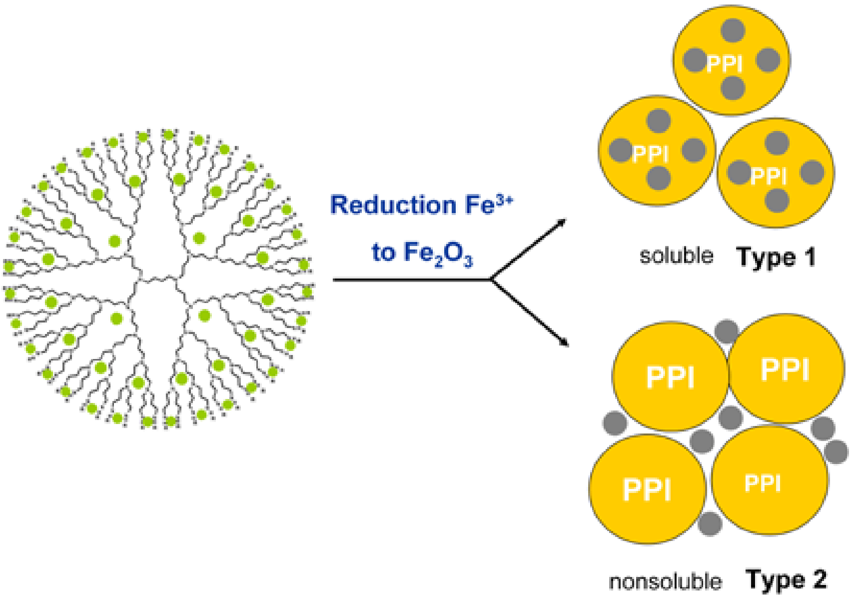

Figure 1. Schematic representation of stabilization of maghemite nanoparticles of two types of nanocomposites.

Photophysical properties of dendrimers were investigate in solution of THF. The absorption maxima compounds from 2-K2.10-$(Fe_2O_3)_2$ to 4-K2.10-$(Fe_2O_3)_{10}$ are significantly blue shifted compared with 1-K2.10-$(Fe_2O_3)_1$. An increase of the alkyl chain length (G1 to G4) leads to a decrease of the system polarization. This fact may be an explanation of the blue shift. The fluorescence quantum yields compounds in THF decreases from 16 to 2% with increasing of generation. These results should be attributed to an increase of the phenyl substituents number (G1 to G4). The phenyl substituents rotation leads to a fluorescence quenching of the system because of an increase of non-radiative losses.

The reported research was funded by Russian Foundation for Basic Research according to the research project № 18-29-04016_mk in the field of photophysical properties and magnetic behavior.

S_N^H-REACTION OF 5,6,7,8-TETRAFLUOROQUINOLINE-*N*-OXIDE WITH LITHIATED NITRONYL NITROXIDE

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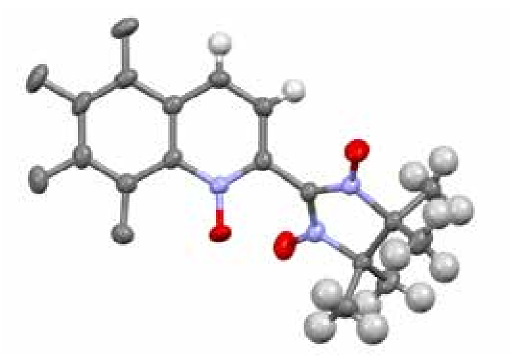
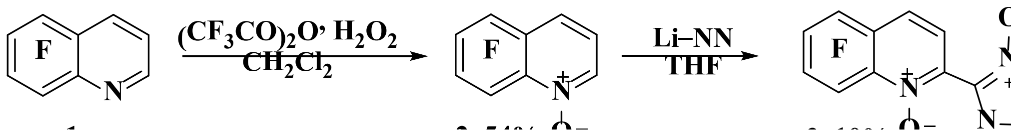


In the past few decades, substituted nitronyl nitroxides R–NN have been actively utilised as organic spin carriers that promoted fast development of their chemistry. It was shown that the paramagnetic lithium derivative Li–NN can substitute H [1] or F [2] atom in activated aromatic compounds to give a diverse range of functionalized nitronyl nitroxides R–NN.

In the present study, we investigated the interaction of Li–NN with 5,6,7,8-tetrafluoroquinoline **1** and its *N*-oxide derivative **2**. Among these studied compounds, the only *N*-oxide **2** was active enough and upon reaction with Li–NN gave the product of S_N^H-reaction, namely 2' -quinolinyl-substituted nitronyl nitroxide **3** with low yield.



New fluorinated nitronyl nitroxide **3** was completely characterized. The structure of **3** was solved by the monocrystal XRD, according to which the dihedral angle between planes of the nitronyl nitroxide and quinoline moiety was equal to 60°. The ESR spectra for oxygen free toluene solution (10^{-4} M) of **3** showed quintet-of-triplet patterns at $g = 2.0060$ with $A_{N1} = A_{N2} = 0.74$ mT and $A_{N3} = 0.08$ mT. Thus, quinoline **2** with polyfluorinated benzene part undergoes S_N^H-reaction with Li– NN at the position 2 of the pyridine moiety.

This work was supported by Russian Foundation for Basic Research (project 18-33-00203\18).

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SYNTHESIS OF 10-AMINOMETHYL DERIVATIVES OF PYRIDO[3',2':4,5] FURO(THIENO)[3,2-*D*]PYRIMIDINES

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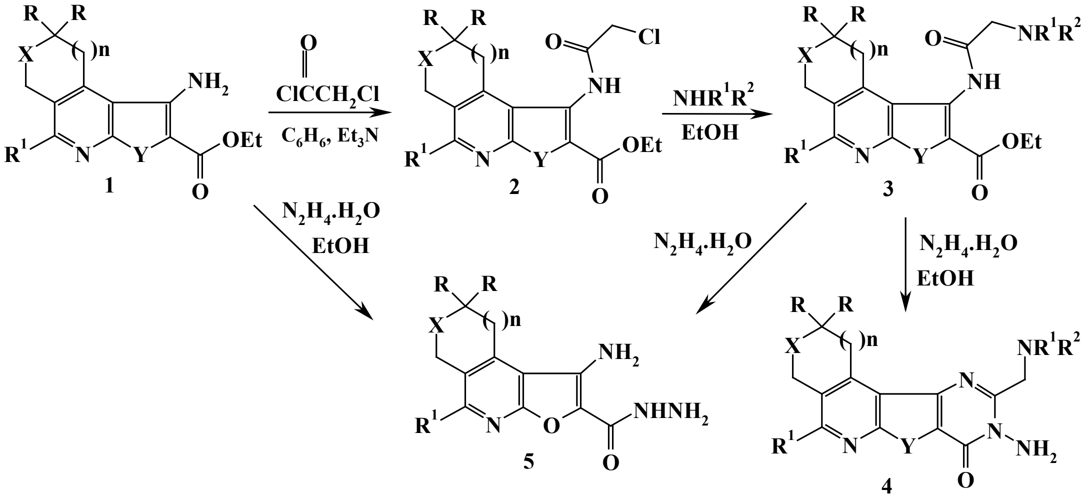
Annulated furo[2,3-*b*]- and thieno[2,3-*b*]pyridine derivatives attracted big interest of the scientific community due to their broad spectrum of biological activities [1–3]. As a continuation of our studies in the field of condensed furanes and thiophenes [4–6], herein we report the synthesis of new 9-amino-10-(aminomethyl)pyrido[3',2':4,5]furo(thieno)[3,2-*d*]pyrimidin-8-ones **4**. These compounds **4** were synthesized starting from the corresponding aminoesters of furo(thieno)[2,3-*b*]pyridines **1** as described in the scheme.

It was found out that, when carrying out the reaction in harsh experimental conditions: by refluxing in hydrazine hydrate, without any solvent, the hydrazinolysis and cleavage of the acyl group occurred with formation of furo[2,3-*b*]pyridine-2-carbohydrazides **5**. The structure of compounds **5** was also confirmed by the counter synthesis from the corresponding aminoesters of furo[2,3-*b*] pyridines **1**.



This work was supported by the RA MES State Committee of Science, in the frames of the research project № 18T-1D170.

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SYNTHESIS, STRUCTURE AND SPECTRAL PROPERTIES OF NOVEL D-Π-A CHROMOPHORES BASED ON QUIONXALINONE AND INDOLIZINE DERIVATIVES

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Organic molecules composed of electron-donating (D) and electron-withdrawing (A) motifs attract considerable attention of researchers due to numerous applications in the field of organic electronics such as solar cells, light-emitting diodes, sensory applications and non-linear optical materials. D-π-A dyes require balanced donor and acceptor strengths to avoid nonbeneficial energy loses and level perturbations. Search and development of stronger organic electron-donor materials matching with many of the common electron deficient π-bridge-acceptor motifs represent a challenging task. Most of the organic D-π-A systems utilize as donors triphenylamine (TPA), diphenylamine, or indoline moieties. However, their electron-donating strength is mitigated by such factors as, for example, non-optimal nitrogen lone pair orbital alignment relative to dye π-conjugated system due to sterically induced twisted angles. In contrast, indolizine unit shows an ideal planar nitrogen-substituent bond angle allowing productive delivery of the donated electron pair to the π-bridge that improves donor directionality. Limited reports on photophysical properties of the indolizine-based systems have been described to date [1-2].

At the same time D-π-A systems utilizing molecules with two nitrogen atoms like pyridazine, pyrazine, pyramidine and quinoxalines have been demonstrated as promising candidates in luminescent applications. Diazines, due to their π-deficient character effectively act as electron-withdrawing part in π-conjugated molecules. Intramolecular charge transfer (ICT) into the scaffold of the molecule can induce tunable luminescence. In particular such diazines as quinoxaline/quinoxalinone derivatives represent a valuable addition to the pool of NLO systems[3].

Herein we generalize recently developed novel convenient strategies allowing to obtain novel luminescent chromophores based on quinoxaline/quinoxalinone and indolizine systems. They have been systematically studied by combination of both an experimental methods of electronic spectroscopy and computational techniques based on time-dependent density functional theory (TD-DFT). The latter were successfully applied to reveal the peculiarities of their photophysical behavior. All the compounds demonstrate red/near-infrared absorption/emission. Structural modifications affect positions of luminescence bands revealing their potential in light-harvesting/emitting materials. Computational approaches provide convenient tools for rational design of the novel fluorophores of this family toward application in organic electronics.

The reported study was funded by RFBR according to the research project № 18-33-00128 mol_a

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SYNTHESIS AND ADDITION OF THE DIETHYLPHOSPHINYLMETHANEHYDRAZIDE TO THE 4-PHOSPHORYLATED METHYLENEQUINONES

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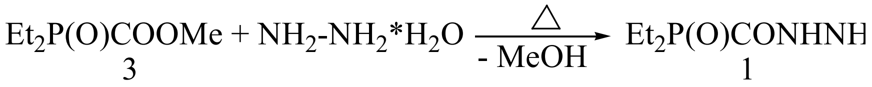
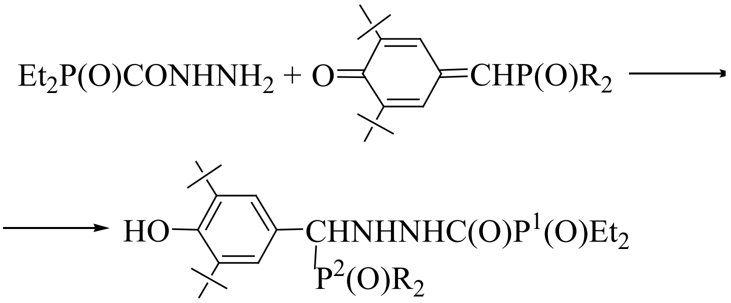
Diethylphosphinylmethanehydrazide $Et_2P(O)CONHNH_2$ **1** is a new analogue of psychotropic substance “phosenazid” $Ph_2P(O)CH_2CONHNH_2$ **2** [1]. It was synthesized by the reaction of methyldiethylphosphinylmethanoate with hydrazine-hydrate. A compound **1**, in contradistinction to “phosenazid”, is the formic acid derivative and being 30 times less toxic, possesses of moresedative properties.



$$\underset{3}{Et_2P(O)COOMe} + NH_2\text{-}NH_2{*}H_2O \xrightarrow[\text{- MeOH}]{\triangle} \underset{1}{Et_2P(O)CONHNH}$$

Scheme 1.

Hydrazide **1** was added to the 4-phosphorylated methylenequinones **5** to obtain the new biologically active compounds **4**.



4, R = MeO (a), Et (b), Ph (c)

Scheme 2.

Structure of the adducts **4** was confirmed by ^1H, ^{13}C, ^{31}P, $\{^1H,P^1\}$, $\{^1H,P^2\}$ and $\{^1H, P^1,P^2\}$ NMR spectra.

This work was supported by the Ministry of Education and Science of Russian Federation in the framework of the basic part of the governmental contract in scientific area, progect № 4.5348.2017/8.9.

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SYNTHESIS AND PROPERTIES OF ALKYNE HEXACARBONYLDICOBALT COMPLEXES OF SOME PGB ANALOGS

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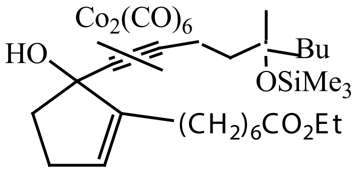
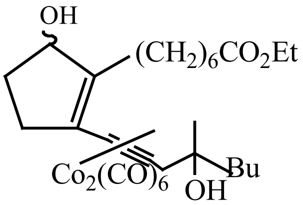
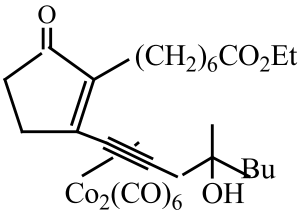
In biometallorganic chemistry alkyne complexes of many biologically active compounds and drugs with [$Co_2(CO)_6$] are among the most studied compounds due to their ease of preparation and stability [1]. In this paper we describe the synthesis and some properties of alkyne hexacarbonyldicobalt complexes of the 13-dehydro derivative PGB-analog of misoprostol **3** (Misoprostol, widely used in obstetrics and gynecology to stimulate the labor of mature pregnancy, and therapeutic abortion in early pregnancy, gastroenterology) [2] and its precursors **1**,**2**.



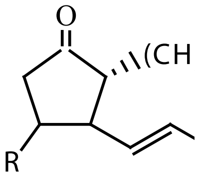
1, 85%



2, 65%

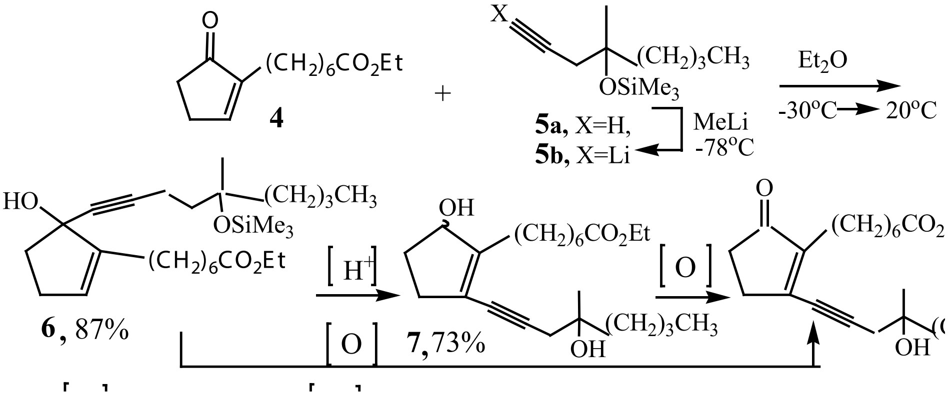


3, 95%



R=OH, miso

Compounds **6–8** used as ligands were obtained during the development of an alternative approach to the previously synthesized 11-deoxymisoprostol and comparable in activity to the prototype. The essence of the approach is the reaction of 1,2-condensation of cyclopentenone **4** with a lithium derivative of acetylene **5a**, the precursor of the omega-chain and the subsequent oxidative allyl rearrangement of the resulting tertiary alcohol **6**, leading to a key **8** with significant synthetic potential. Complex **3** was synthesized by its interaction with $Co_2(CO)_8$ showed cytotoxicity against cells HEK 293 and SH-SVSY, while the initial **8** does not. Since the activity of such complexes is largely determined by the structure of their ligants [3], to elucidate the "structure-activity" dependence, we have synthesized complexes **1** and **2** by analog reaction.



The work was done on the topic №AAAA-A17-117011910032-4 of state assignment.

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THE DONOR-ACCEPTOR CYCLOPROPANE LABYRINTH: ISOMERIZATION, DIMERIZATION AND RING EXPANSION

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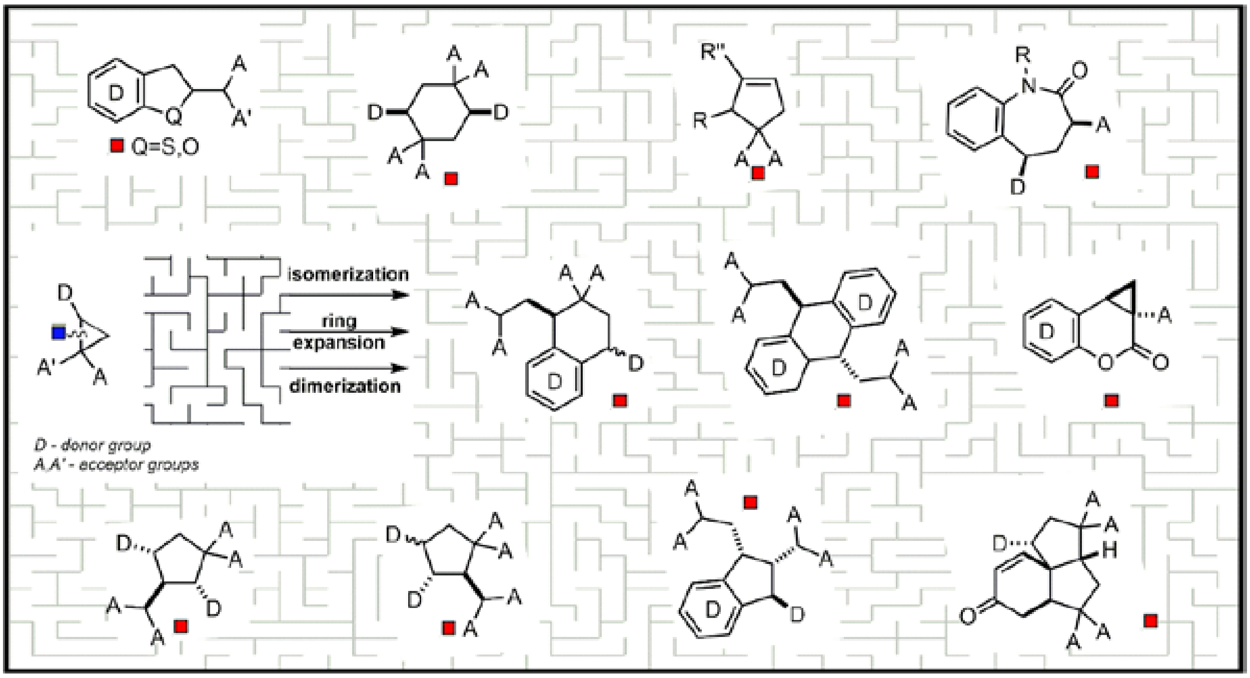
Donor–acceptor (D–A) cyclopropanes, being a unique class of substrates, have been proved to be useful building blocks for the synthesis of a broad diversity of cyclic systems [1]. Under the activation with Lewis or Brönsted acids, they undergo three-membered ring opening that can be accompanied by diverse 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 report several Lewis acid-induced transformations of D–A cyclopropanes ***without any reaction partner*** [1-3], namely, 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 represent promising synthetic approaches to various bioactive compounds. The chemo- and stereoselectivity of the processes is controlled by the reaction conditions, primarily by the Lewis acid applied, as well as by the nature of donor substituent.



This work was supported by Russian Foundation for Basic Research (grant 18-03-00954).

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[3] Ivanova, O. A.; Chagarovskiy, A. O., Shumskiy, A. N.; Krasnobrov, V. D.; Levina, I. I.; Trushkov, I. V. J. Org. Chem. 2018, 85 (2), 543.

NEW APPROACH TO 2-OXA-ADAMANTANES

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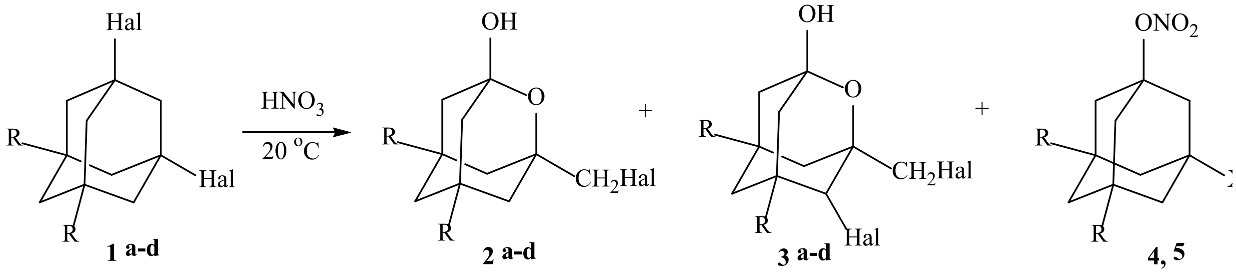
The derivatives of 2-oxa-adamantane are important for practical use as starting materials in the synthesis of new acetylholinesterase and NMDA-receptors inhibitors, as well as in preparation of conformationally rigid crown esters. Existing approach to the preparation of the 2-oxa-adamantane system are based on cyclization of the bicyclo[3.3.1]nonan-3,7-dione and 7-metylenebicyclo[3.3.1]nonan-3-one.

We have found a new approach to 2-oxa-adamantane derivatives. It consists in the oxidative transformations of 1,3-dihaloadamantanes (**1a-d**) in fuming nitric acid. The main products are 3-halomethyl-1-hydroxy-2-oxa-adamantanes (**2a-d**) and 3-halomethyl-4-halo-1-hydroxy-2-oxa-adamantanes (**3a-d**). The reaction proceeds through the formation of 1,3-dinitroxyadamantane (**4**) and 3-halo-1-nitroxyadamantanes (**5**), as evidenced by the presence of quaternary carbon atoms signals in the ^{13}NMR spectra.



R = H, Me
Hal = Cl, Br

X = ONO_2, Hal

Compounds **2 a-d** were isolated in 20-40% yields, **3a-d** – 7-20%. The structures of compounds **2 a-d** and **3 a-d** were verified by NMR 2D spectra and X-ray diffraction for compound **2a**.

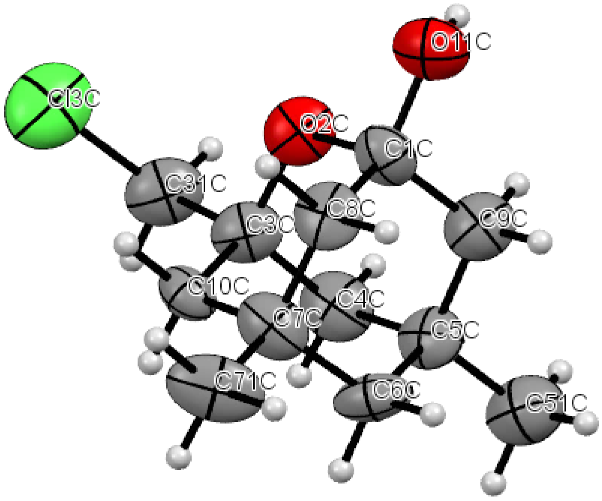


Fig. 1. The structure of compound **2a** (*CCDC 1833287*)

The reported study was funded by RFBR according to the research project № 19-03-00973

SYNTHESIS AND PHOTOPHYSICAL PROPERTIES OF 3,5-DIARYL-2-HETEROARYLTHIOPHENES

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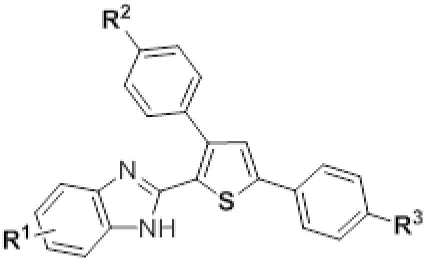
Thiophene is frequently observed as a core structure in pharmaceuticals [1] and optical materials [2]. Numerous reports on the optoelectronic applications of oligomeric and polymeric thiophene based materials are abundant in scientific References [3]. In contrast, the References on the optoelectronic properties of monomeric thiophenes is relatively scarce. We have decided to systematically explore the relationship between electronic and emissive properties of 2,3,5-trisubstituted thiophenes by the introduction of electron withdrawing groups or electron donating groups in aryl moieties (Sch. 1.). We were pleased to find that the proper choice of substituents in the R^1, R^2 and R^3 positions of 2,3,5-trisubstituted thiophenes allowed photoluminescence quantum yield of 83% to be achieved in solutions.



R^1 = -H, -Cl, -*di*-Cl
R^2 = -H, $-CF_3$, -OMe, $-OC_5H_{11}$
R^3 = -H, $-CF_3$, -OMe, $-OC_5H_{11}$

Scheme 1. General structure of studied 2,3,5-trisubstituted thiophenes.

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2-ZINCOETHYLZINCATION OF 2-ALKYNYLAMINES CATALYZED BY TITANIUM(IV) ISOPROPOXIDE AND ETHYLMAGNESIUM BROMIDE

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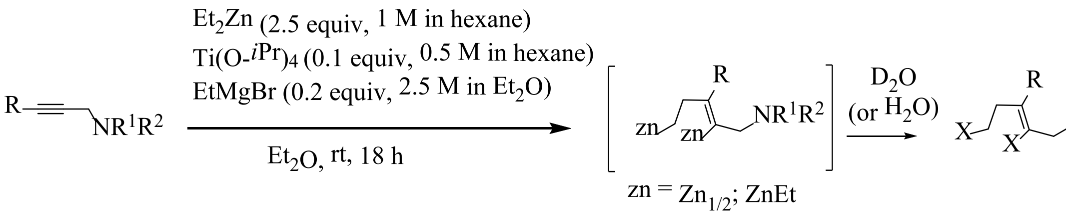
Carbometallation is an efficient method of regio- and stereocontrolled synthesis of olefins of various structure. The most widely encountered synthetic methods for alkynes carbometallation include Zr-catalyzed Negishi methylalumination of alkynes, carbocupration, carbostannylation, carboboration, and carbomagnesiation. The Rh- and Co-catalyzed carbozincation of ynamides can be used for selective synthesis of multisubstituted enamides and dienamides, and also 3-arylenamides. The number of known catalytic carbozincation reactions of alkynylamines is modest. For example, diastereoselective carbozincation of propargyl amine derivatives obtained from methylbenzylamine has been reported [1]. We found that 2-alkynylamines **1** react with 2.5 equivalents of Et_2Zn (1 M in hexanes) in the presence of 10 mol. % Ti(O-*i*Pr)$_4$, (0.5 M in hexanes) and 20 mol. % EtMgBr (2.5 M in Et_2O) in diethyl ether at room temperature for 18 hours to give, after deuterolysis, hydrolysis or iodinolysis substituted allylamines **3**,**4**,**5**. The structures of the resulting substituted allylamines were established using 1D and 2D NMR spectroscopy. This study demonstrates that the presence of the amine functional groups in the molecule of alkyne does not prevent but rather facilitates the 2-zincoethylzincation reaction. The strategy we developed opens up the way to the synthesis of heterofunctional alkenes of various structure via catalytic 2-zincoethylzincation of functionally substituted alkynes. In addition, the disclosed regio- and stereoselective transformation of 2-alkynylamines opens up new prospects for the synthesis of various polyfunctional compounds using a broad range of transformations of the functionally substituted organozinc intermediates formed in situ. These and other goals will be pursued in our subsequent studies.



1a: R = *n*-Bu, NR^1R^2 = NMe_2;
1b: R = *n*-Pent, NR^1R^2 = NMe_2;
1c: R = *n*-Hex, NR^1R^2 = NMe_2;
1d: R = *n*-Oct, NR^1R^2 = NMe_2;
1e: R = *c*-Pr, NR^1R^2 = $N(CH_2)_5$;
1f: R = *n*-Bu, NR^1R^2 = $N(CH_2)_5$;

3a : X = D, 88%

4a : X = H, 67%
4b: X = H, 70%
4c: X = H, 73%
4d: X = H, 79%
4e: X = H, 65%
4f: X = H, 81%

5b: X = I,
5c: X = I, 5
5f: X = I, 6
5g: X = I, 5

This work was supported by the Russian Foundation for Basic Research (grant no. 18-03-00817) and by Grant of the RF President (Sci. Sh.-6651.2016.3) which are gratefully acknowledged.

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REARRANGEMENT OF QUINOXALINONES WHEN EXPOSED TO 5,6-DIAMINO-2-MERCAPTO- AND 2,5,6-TRIAMINOPYRIMIDIN-4-OLS – AN EFFICIENT ONE-POT METHOD FOR THE SYNTHESIS OF SUBSTITUTED 7-(BENZIMIDAZOL-2-YL)(THIOXO)LUMAZINES

Kadyrova M.S., Nataliya A. Zhukova, Aidar T. Gubaidullin, Victor V. Syakaev, Anastasiya O. Isaeva, Tat'yana N. Beschastnova, Olga B. Bazanova, Ildar Kh. Rizvanov, Shamil K. Latypov, and Vakhid A. Mamedov

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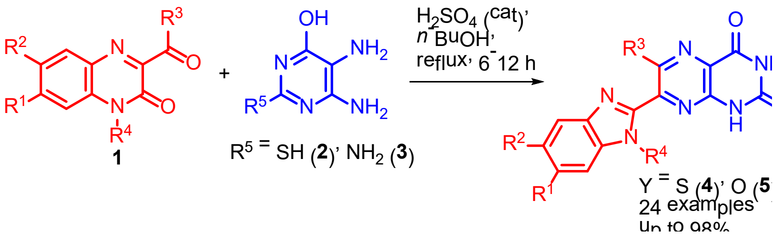
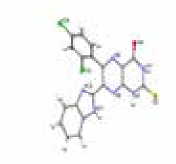
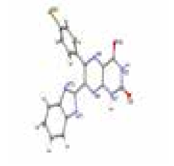
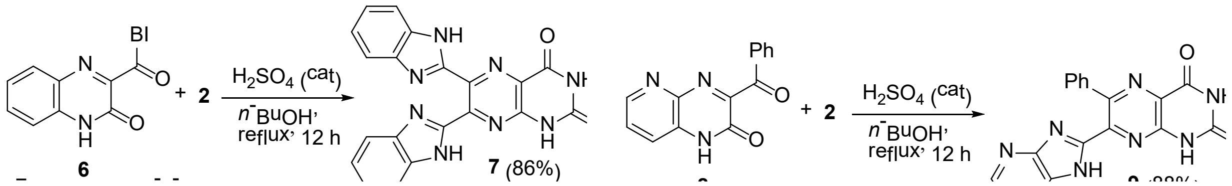
Pteridines are extensively distributed in nature, play an important role in vital processes, including metabolism of one-carbon units and are used as antitumor, antiviral, antibacterial and diuretic drugs in medicine. In this work, a facile approach to a range of substituted 7-(benzimidazol-2-yl)thioxolumazines (7-(benzimidazol-2-yl)-2-thioxo-2,3-dihydropteridin-4(1*H*)-ones) **4** and 7-(benzimidazol-2-yl)lumazines (7-(benzimidazol-2-yl)pteridine-2,4(1*H*,3*H*)-diones) **5** with use of the Mamedov Heterocyclic Rearrangement [1] is described [2]. The new bi-heterocyclic systems **4**, **5** are obtained *via* H_2SO_4-catalysed rearrangement of quinoxalin-2-ones when exposed to 5,6-diamino-2-mercapto- and 2,5,6-triaminopyrimidin-4-ols. Thus benzimidazole and pteridine rings are constructed in one synthetic step.




The X-Ray structure of **4**


The X-Ray structure of **5**

The use of 3-benzimidazoylquinoxalin-2(1*H*)-one in the reaction with 5,6-diamino-2-mercaptopyrimidin-4-ol **2** leads to synthesize pteridine **7** with two benzimidazole moieties. Applying the rearrangement to the aza-analogue of 3-benzoylquinoxalin-2(1*H*)-one – *i.e.* 3-benzoylpyrido[2,3-*b*]pyrazin-2(1*H*)-one – with **2** makes it possible to synthesize 7-(1*H*-imidazo[4,5-*b*]pyridin-2-yl)-6-phenyl-2-thioxo-2,3-dihydropteridin-4(1*H*)-one **9**, which is inaccessible by any other known methods for the synthesis of imidazopyridines and pteridines.



This work was supported by the Russian Science Foundation (grant No. 18-13-00315).

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SYNTHESIS OF HMF-BASED SELF-CLICKABLE MONOMER FOR CLICK-CHEMISTRY APPLICATIONS

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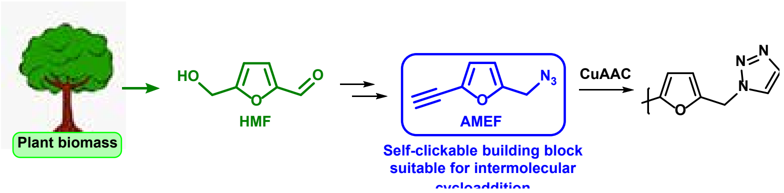
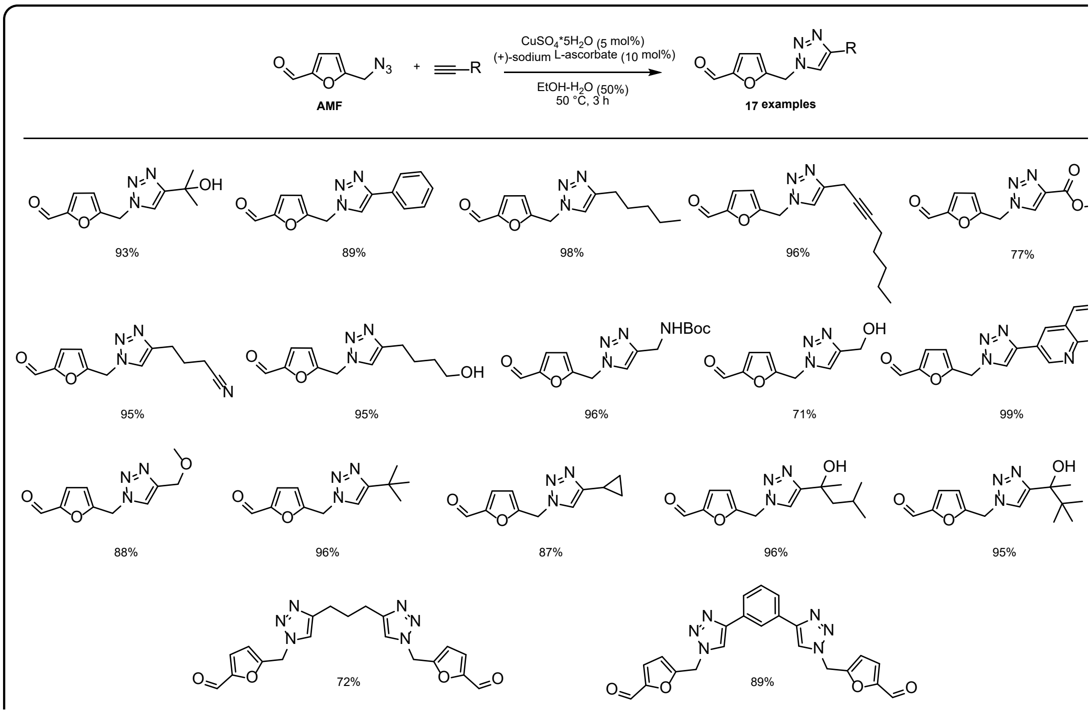
The biomass conversion is in the spotlight now, because it allows to obtain a plenty of valuable compounds, and 5-hydroxymethylfurfural (HMF) is one of the most studied among them. In this work we have synthesized a new HMF derivative that contains both an azide and alkyne substituents – 2-azidomethyl-5-ethynylfuran (AMEF). This duality allows to this molecule play both roles in azide-alkyne cycloaddition reactions, simultaneously acting as azide and acetylenic fragments and leading to formation of heterocyclic olygomers. Obtained materials were studied by FE-SEM, DSC, NMR- and IR-spectroscopy.

The reactivity of precursor of AMEF – 5-(azidomethyl)furfural (AMF) was also studied in series of Cu(I)-catalyzed “click” reactions, resulted in 17 new triazoles in good and excellent yields.





This work was supported by Russian Science Foundation 17-13-01176 grant.

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2-AMINOSPIROPYRAZOLYLAMMONIUM ARYLSULFONATES AS A PRODUCTS OF THE INTERACTION OF B-AMINOPROPIOAMIDOXIMES AND SUBSTITUTED ARYLSULFONYL CHLORIDES

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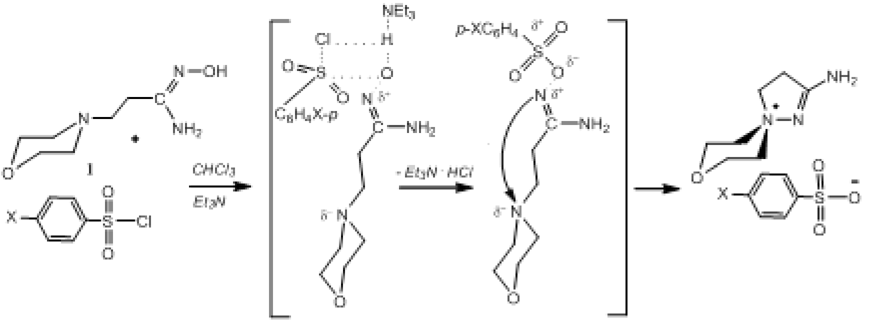
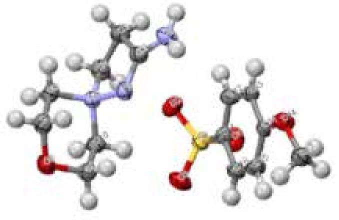
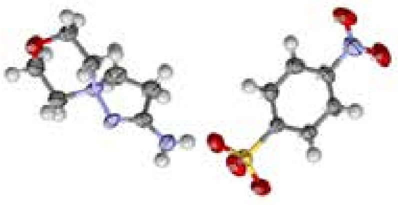
Stable aromatic and heteroaromatic O-sulfonylamidoximes – products of the interaction of substituted amidoximes and amidoximes of pyridine carboxylic acids with aromatic and aliphatic sulfonyl chlorides are known [1]. It is also known that this class of compounds can undergo rearrangements [2]. We have carried out the interaction of β-(morpholin-1-yl)propioamidoxime (**1**) with *para*-substituted phenylsulfonyl chlorides in $CHCl_3$ in the presence of Et_3N. Based on the data of elemental analysis, IR and NMR spectra, it was concluded that a series of O-(*para*-X-C_6H_4-sulfonyl)-β-(morpholin-1-yl)propioamidoximes (**2**–**7**) was obtained: X = CH_3O (**2**), CH_3 (**3**), H (**4**), Br (**5**), Cl (**6**), NO_2 (**7**) [3].

However, the X-ray diffraction data of the proposed products **2** and **7**, obtained later, testify in favor of the fact that the reaction results to the aryl sulfonates of 2-amino-4,5-dihydro-spiropyrazolyl ammonium.



This conclusion was obtained on the basis of extreme cases – for the sulfochlorination products with *para*-methoxy- and *para*-nitrosulfonyl chloride:





The easy formation of spirocompounds is consistent with the fact that O-arylsulfonyl-β- (morpholin-1-yl)propioamidoximes are obviously less thermodynamically stable than arylsulfonates of 2-amino-4,5-dihydropyropyrazolyl ammonium and the fact that arisulfonate anion is a good leaving group [4].

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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF OPTICALLY ACTIVE DERIVATIVES OF 2(5*H*)-FURANONE POSSESSING TERPENE MOIETY

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The 2(5*H*)-furanone subunit is found in several bioactive natural products and a number of drugs with diverse biological activities such as antifungal, antibacterial and anti-inflammatory. The wide range of biological properties and pharmaceutical applications of 2(5*H*)-furanone derivatives explains the increasing interest in the development of new methods for the synthesis of optically active 2(5*H*)-furanone based compounds. This work is devoted to the synthesis and study of biological properties of optically active thioethers, sulfones and sulfoxides of 2(5*H*)-furanone possessing terpene moiety at the carbon atom C(5) of the lactone ring.

At the first stage 5-menthyloxy- and 5-bornyloxy-2(5*H*)-furanones were synthesized by reactions of mucochloric and mucobromic acids with enantiopure *l*-menthol or *l*-borneol under acidic conditions. After the mixture of two diastereomers was obtained the *S*-stereoisomers were isolated by recrystallization from hexane. Reactions of the individual stereoisomers with aromatic thiols in the presence of triethylamine at room temperature afforded novel 4-substituted thioethers. At the next step 2(5*H*)-furanone thioethers were subjected to oxidation to the corresponding sulfones and sulfoxides. We have recently developed the selective methods of oxidation of mono- and dithioderivatives of 2(5*H*)-furanone. Hydrogen peroxide in acetic acid and *m*-chloroperbenzoic acid were successfully applied to the synthesis of optically pure sulfonyl and sulfinyl derivatives of 2(5*H*)-furanone, respectively. Novel compounds have been characterized in detail by IR, NMR spectroscopy, HRMS and single crystal X-ray diffraction.

The antimicrobial and biofilm-inhibiting activity of the synthesized compounds against various Gram-positive and Gram-negative bacteria was studied [1–3]. Some of furanone derivatives efficiently repressed the biofilm formation by *Bacilli*, *Staphylococci* and *Streptococci*, and also increased the antimicrobial efficacy of aminoglycosides (amikacin, gentamicin and kanamycin) and benzalkonium chloride against these bacteria suggesting their chemotype as attractive prototype as an alternative antimicrobials for the topical treatment option.

This work was supported by the Russian Government Program of Competitive Growth of Kazan Federal University and by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (4.1493.2017/4.6).

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REACTION OF THE ENAMINES WITH THE DIISOPROPOXYDITHIOPHOSPHORIC ACID

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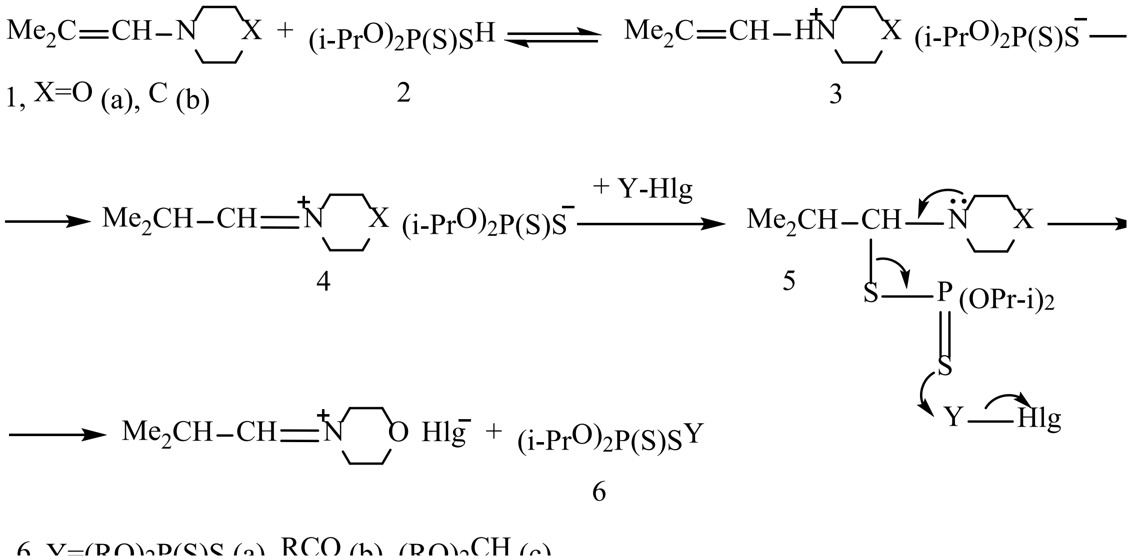
Earlier it was supposed [1] that an interaction of O,O-dialkyldithiophosphoric acids $(RO)_2P(S)SH$ with N-alkyl-2-haloimines $Me_2C(Hlg)CH{=}NR$ proceeds via the intermediate formation of enamine [1]. But the reactions of enamines with the P(IV) dithioacids were not studied. We found out, that enamines **1** react with the diisopropoxydithiophosphoric acid **2** to give iminium dithiophosphate **4.** Probably initial protonation of enamine nitrogen atom takes place with the formation of ammonium dithiophosphate **3** which transforms into the salt **4** owing to the prototropic process. When X=C the salt **4b** is stable and it was isolated as an individual substance. Salt **4a** is not stable and transforms into the product **5** of addition of acid **2** to enamine **1.** We also established that compound **5** react with organic halides (sulfenyl, acyl halides and α-chloroethes) to form substitution products **6**.



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IN SILICO SCREENING OF PYRAZOLE AND ISOXAZOLE DERIVATIVES AS POTENTIAL ANTIDIABETIC AGENTS

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Virtual screening methods are currently being actively used when searching for compounds of directional hits. In this paper, they are used to study the affinity of sulfanyl-substituted bis-3,5-dimethylpyrazole **1** and sulfanyl bis-3,5-dimethylisoxazole **2** with *Aspergillus niger* alpha-amylase. Recently [1], we have demonstrated the ability of these compounds to inhibit α-amylase by reducing the hydrolysis of carbohydrates in the intestine, which prevent the development of type 2 diabetes. To obtain water-soluble forms, hydrochloride adducts of **1•HCl** and **2•HCl** were obtained (Fig. 1). However, the question remains open about the details of the mechanism of interaction of these ligands with the protein under discussion.

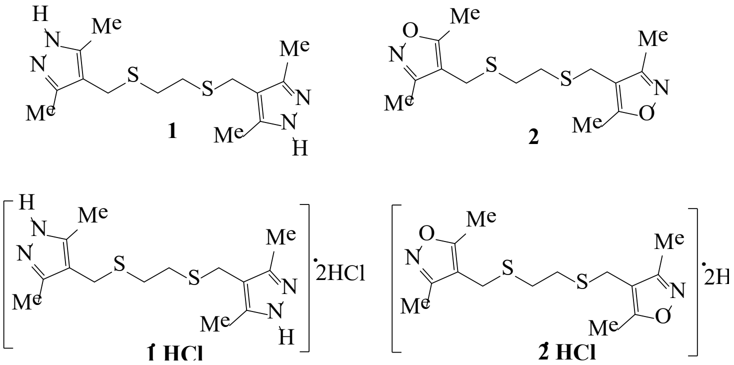

Fig 1. Stucture of ligands **1**, **2**, **1·HCl** и **2·HCl**

Using the LeadIT program, which implements the basic principles of flexible molecular docking, the positioning of the 4 ligands (Fig. 1) in the active sites of *Aspergillus niger* alpha-amylase has been studied. Molecular docking was performed with common default docking parameters. 50 conformations were automatically generated for each ligand, from which the best poses were selected using the FlexX evaluation function. The radius of the sphere in the simulation was 20 Å. Its centering was performed automatically in the center of mass of the reference ligand (maltose) (www.rcsb.org).

It was found that all 4 ligands **1**, **2**, **1·HCl** и **2·HCl** are able to effectively inhibit the catalytic activity of alpha-amylase. For all cases, bioactive conformations of simulated ligands were determined. The factors stabilizing their position in the active center of this enzyme are established.

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IR AND RAMAN SPECTROSCOPY STUDY OF DEHYDROACETYC ACID DERIVATIVE TAUTOMERS

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The study of dehydroacetic acid (DHA) derivatives is interesting and important because of their usage in the pharmaceutical, cosmetic and food industries. The DHA and its derivatives are biologically active substances used for the production of analgesics, anti-cancer drugs and to fight against HIV. DHA is the initial reagent in the synthesis of a large number of organic compounds.

The purpose of this work was to characterize the two lowest energy tautomeric forms of the DHA neopentyl homologs using IR and Raman spectroscopy methods and quantum chemistry calculations. We tried to follow the evolution of the acid structure, the strength of hydrogen bonds and its vibrational spectra during tautomeric transformations. The comparison of the tautomeric forms free energies in the gas phase and solution makes possible to estimate their population. According to DSC+TGA data, the melting and second crystallization did not show the tautomeric form changes.

The IR and Raman spectra of the dehydroacetic acid neopentyl derivative were studied. Acid tautomerizm was studied by the quantum-chemical calculation at the DFT/B3LYP/6-311G** level. The theoretical IR and Raman spectra of the enol tautomer are compatible with the experimental data. The intramolecular hydrogen bond was characterized by IR spectroscopy. The difference between the free energies of the tautomers and their populations was calculated for the gas phase and two different solvents.

HOMO and LUMO of DHA molecule are localized at the pyrone ring. During tautomeric transformations a significant delocalization of the charge occurs, which causes a change in the reactivity of the molecules.

The reactivity of the acid was characterized using descriptors. Turned out that form B has greater ionization energy, electron affinity, chemical potential and electrophilic index than form A. On the other hand, the dipole moment is higher for the form A. The softness of the two molecules is the same.

THE STRUCTURES OF NON-IPR FULLERENES: C_{40}, ISOMERS 29 (C_2), 31 (C_S), 38 (D_2) AND 39 (D_{5D}); C_{50}, ISOMERS 270 (D_3) AND 271 (D_{5H})

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The lower fullerenes C_n ($n < 60$) are highly unstable due to large strain energy and the violation of the isolated pentagon rule (IPR), making them extremely hard to obtain and study experimentally. However, they become stable as exohedral or endohedral derivatives. A good example is the successful production and characterization of the isomer 271 (D_{5h}) of small non-IPR fullerene C_{50} as its chlorine exohedral derivative $C_{50}Cl_{10}$ [1]. So, the purpose of this theoretical research is to expand the approach developed early by us for IPR fullerenes [2] to lower fullerenes to estimate their geometrical and electronic structure and possibility of their production. In this report, we investigated the molecular structures of non-IPR isomers 29 (C_2), 31 (C_s), 38 (D_2) and 39 (D_{5d}) of fullerene C_{40} and non-IPR isomers 270 (D_3) and 271 (D_{5h}) of fullerene C_{50}.

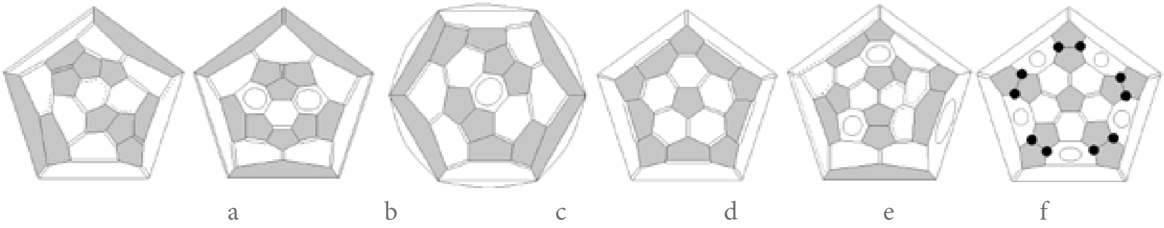

Fig. 1. Schlegel diagram of isomers 29 (C_2) (a), 31 (C_s) (b), 38 (D_2) (c) and 39 (D_{5d}) (d) of C_{40} and isomers 270 (D_3) (e) and 271 (D_{5h}) (f) of C_{50}: black points mark the positions of Cl in $C_{50}Cl_{10}$.

Quantum chemical calculations (DFT) show that isomers 31 (C_s), 38 (D_2) and 39 (D_{5d}) have closed electronic shells, whereas isomer 29 (C_2) has an open-shell electronic structure. Both researched isomers of fullerene C_{50} have closed electronic shells. The data about the distributions of single, double and delocalized π-bonds in the isomer molecules in question are presented for the first time as well as their molecular formulas (Fig. 1).

It is shown the chains of π-bonds delocalization passing through some cycles are appeared in the isomer 29 of C_{40} and isomer 270 of C_{50}, which to be unusual for higher fullerenes. It is shown that chlorine atoms in the exohedral derivative $C_{50}Cl_{10}$ [3] of isomer 271 (D_{5h}) are attached to the peculiar "indacene" substructures, where π-delocalized hexagon disposes between pair of pentalenes (see Fig.1f) confirming our recent conclusions about preference of π-bonds delocalized hexagons in radical addition reactions. Identified features in the structures of lower fullerene molecules can be predictive of the ability to their synthesis as derivatives and will assist in their structure determination.

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SYNTHESIS OF NEW [Dy12] CLUSTER SUPPORTED ON AZOPHENYL DERIVATIVE OF SALICYLIC ACID – A PROMISSING PHOTOSWITCHABLE SINGLE MOLECULAR MAGNET

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Contrary to conventional bulky magnets, single-molecule magnets or *SMMs* are a class of hybrid metal-organic materials, which show «superparamagnetic» behavior of purely molecular origin below a certain blocking temperature [1]. The molecules of *SMMs* contain a spin centers usually composed of metal ions (or metalloclasters), which are connected through bridging organic ligands. Lanthanide cations, such as Dy(III) and Tb(III), are attracting more and more attention when designing *SMMs* because of their large intrinsic magnetic anisotropy [2], electronic properties, including magnetism [3] and luminescence [4].The presence in the structure of binding organic ligands azo-groups it makes them attractive ligands for design of photoswitchable *SMMs* with controlled magnetic properties. Here we report the synthesis and crystal structure of new [Azo$_{10}$Dy$_{12}$] cluster (Figure 1).

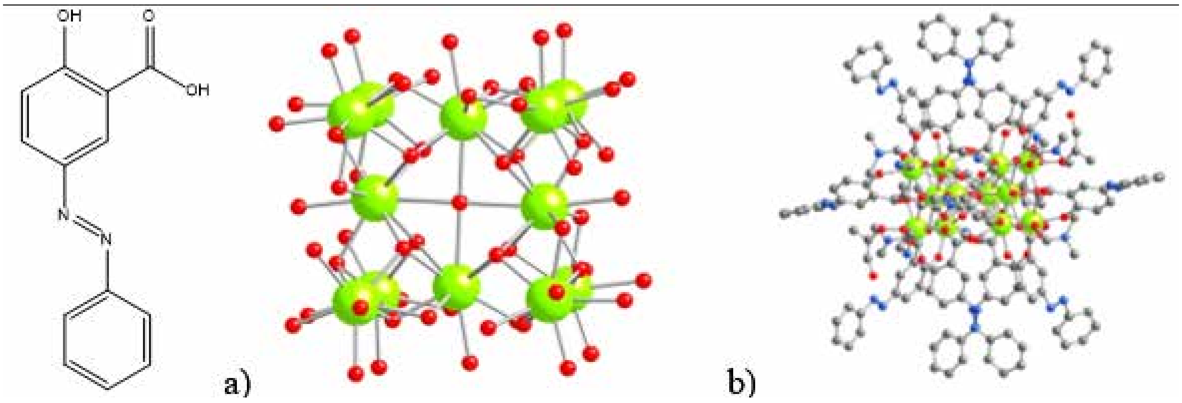

Figure 1.

This work was supported by RSF № 17-73-20117.

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ABOUT REACTION OF THE CHLOROANHYDRIDE A-BROMOPROPIONIC ACID WITH LITHIUM DERIVATIVES OF ETHYL ACETATE

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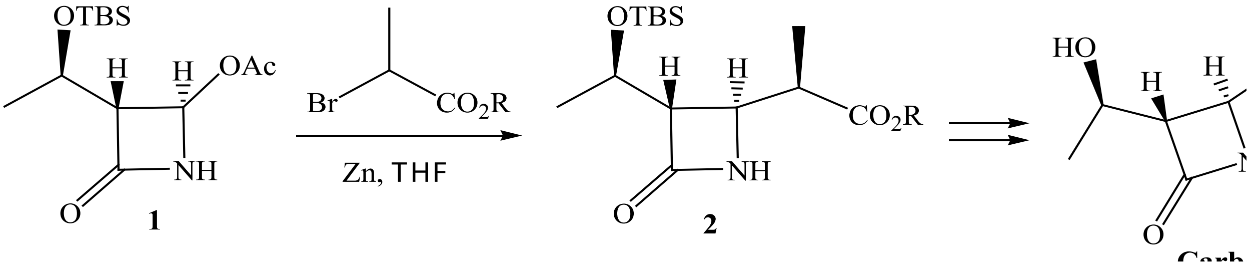
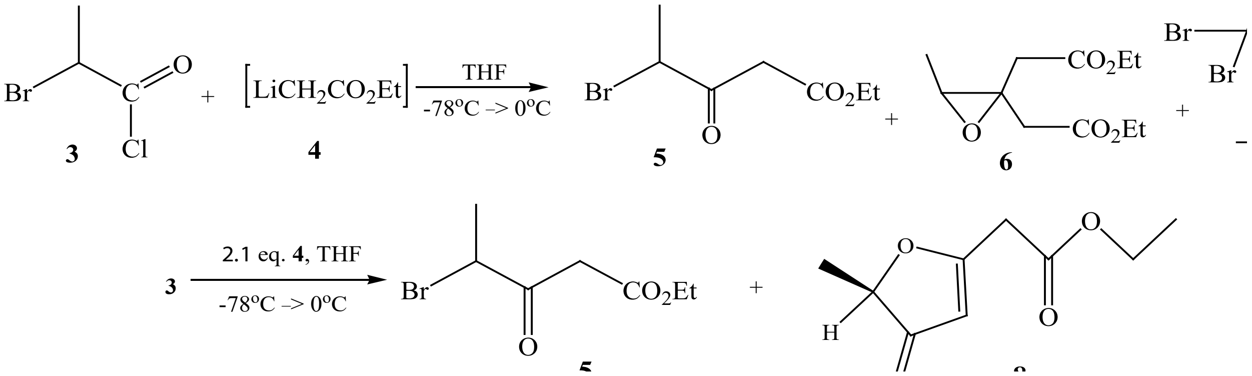
Derivatives of α-bromopropionic acids are used to alkylate the azetidinone **1** widely used in the synthesis of carbapenems [1] and to yield the precursors of carbapenems **2**. As is known, carbapenems are the most popular representatives of practically important β-lactam antibiotics [2].



Scheme 1

In order to obtain of more “prepared” bromo esters **5** for alkylation of **1** (Scheme 2), in this work, we investigated the reaction of α-bromopropionic acid chloride **3** with a lithium derivative of ethyl acetate **4** generated *in situ* from equimolar amounts of LDA and ethyl acetate in THF at -40°C. In reaction **3** with 1.3 eq. of **4** along with the formation of the expected acylation product **5**, unusual directions are also realized, leading to by-products **6** and **7**. With the use of 2.1 eq. of **4**, in addition to the above-mentioned α-bromo ketoester **5**, also isolated the vinyl lactone **8**, which is apparently formed by the addition of a second molecule $LiCH_2CO_2Et$ to the **5** and subsequent transformations.



Scheme 2

This work was supported by Russian Science Foundation (project no. 15-13-00039П).

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SYNTHESIS, CRYSTAL STRUCTURE OF THE NOVEL CAGE PHOSPHORANES BASED ON 2-(1-PHENYLETHENYLOXY)BENZO-1,3,2-DIOXAPHOSPHOLE

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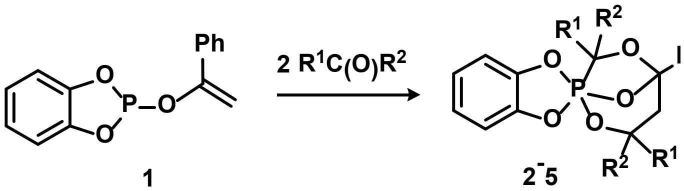
Vinyl esters of phosphorus (III) containing the PIII−O−C=C fragment are quite reactive compounds in nucleophilic reactions of P(III). M. I. Kabachnik, I. F. Lutsenko, and Yu. G. Gololobov made a great contribution into the development of synthesis methods and investigation of chemical properties of these compounds (Arbuzov, Perkow, Staudinger reactions, thionation, oxidation and others) [1–6]. Nevertheless, there are no papers considering the possibility of PIII−O−C=C systems participating in [4+2]-cycloaddition reactions (dihetero-Diels-Alder cycloaddition reaction) with activated carbonyl compounds, which might lead to the formation of cage derivatives of a pentacoordinate phosphorus atom.

The present research is dedicated to evaluation of the use of vinyl esters of P(III) acids in synthesis of cage phosphoranes on the example of readily available (1-phenylethenyloxy)benzo-1,3,2-dioxaphosphole **1** [7] and highly active carbonyl compounds (Scheme 1). The reactions proceed with formation of adducts **2**–**5** with the pentacoordinated phosphorus atom in the 1 : 2 ratio. Bonds P−C, P−O, C−C and C−O are formed under soft conditions. Cascade [4+2]- and [3+2]-cycloaddition reactions proceed with high regio- and stereoselectivities. The vinyl derivative of P(III) in this case plays the role of 1,4-diheterodien in which one of the double bonds is replaced by a saturated P−O fragment.



Scheme 1. Pathway of the formation of cage phosphoranes from phosphole **1** and activated carbonyl compounds

Soft hydrolysis of cage phosphoranes occurs with a high chemoselectivity level and results in formation of derivatives of phosphonic acid, as well as aldols. The proposed method of synthesis of cage phosphoranes can find the application for other types of phosphorous acid vinyl esters.

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UNUSUAL REARRANGEMENT OF C-C BOND IN MODIFIED PNP LIGAND BASED Ru COMPLEXES

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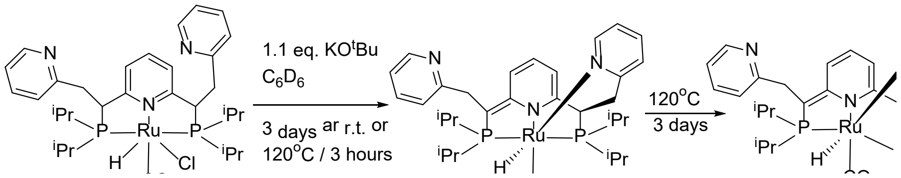
Metal complex catalyzed dehydrogenative coupling of alcohols to give esters [1] and the reverse hydrogenation of esters [2] is a relatively recent discovery currently of great industrial interest. [1] The initial mechanism proposed by Milstein suggested dearomatization of the central pyridine and utilization of the ligand arm in a metal/ligand cooperation framework to dehydrogenate the alcohol or split the H_2 bond. We modified the PNP pincer ligand by adding one or two picolyl arms to the ligand backbone in order to favor the dearomatized complex intermediate, and to test the ability of the species to activate alcohols.

After activation of the complex by base, we observed a very unusual rearrangement in the modified complexes resulting in increasing the chelate ring size of the pincer ligand and migration of the picolyl arm via C-C bond cleavage/formation reactions. This rearrangement results in a complete shutdown of catalytic activity in the dehydrogenation of alcohols. In the present study, we proposed the mechanism through an unusual spyrocycle cyclopropane transition state. A number of modified PNP pincer ligands with differing steric properties and number of picolyl groups were created in order to gain insight into whether the rearrangement pathway was general. Finally, the original parent PNP catalyst was tested with a number of substrates, where it proved to be a ‘living’ catalyst for simple alcohols, suggesting that the observed rearrangement for the modified complexes is not active in the original system.



Scheme 1.

This work was supported by an Okinawa Institute of Science and Technology start-up grant

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SYNTHESIS AND STRUCTURE OF EUROPIUM(III) COMPLEXES WITH AZOMETHINE LIGANDS

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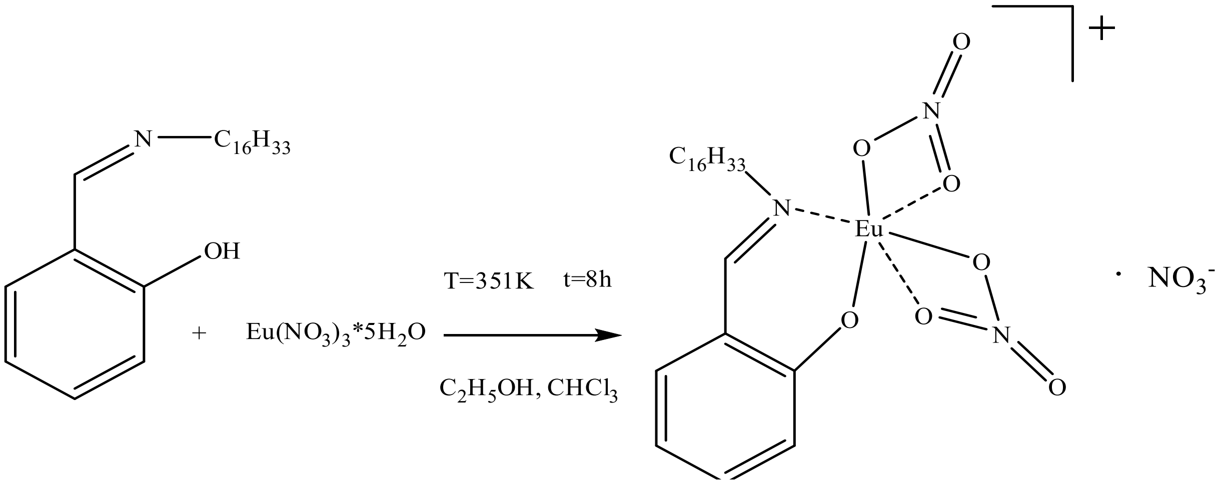
The Europium (III) complexes with organic ligands are of interest, since the Europium ion (Eu^{3+}) can interaction with a biomolecule such as RNA. It is not a trivial task to establish the structure of the Eu complexes, if the compound obtained does not form single crystals. In this work, the structure of the obtained europium complex with azomethine ligands was established using Mössbar spectroscopy, mass spectroscopy, X-ray powder diffraction and NMR spectroscopy.



Scheme 1. The synthesis scheme of europium complex with 2-((hexadecylimino)methyl)phenol

A CONCISE AND VERSATILE SYNTHESIS OF *VIRIDICATOL* FROM 3-HYDROXY-4-(3-NITROPHENYL)-*N*-(4-METHOXYBENZYL)QUINOLIN-2-ONE

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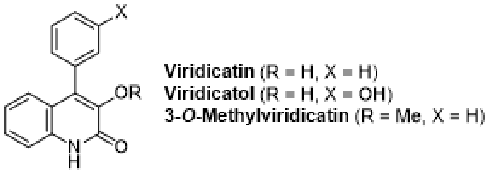
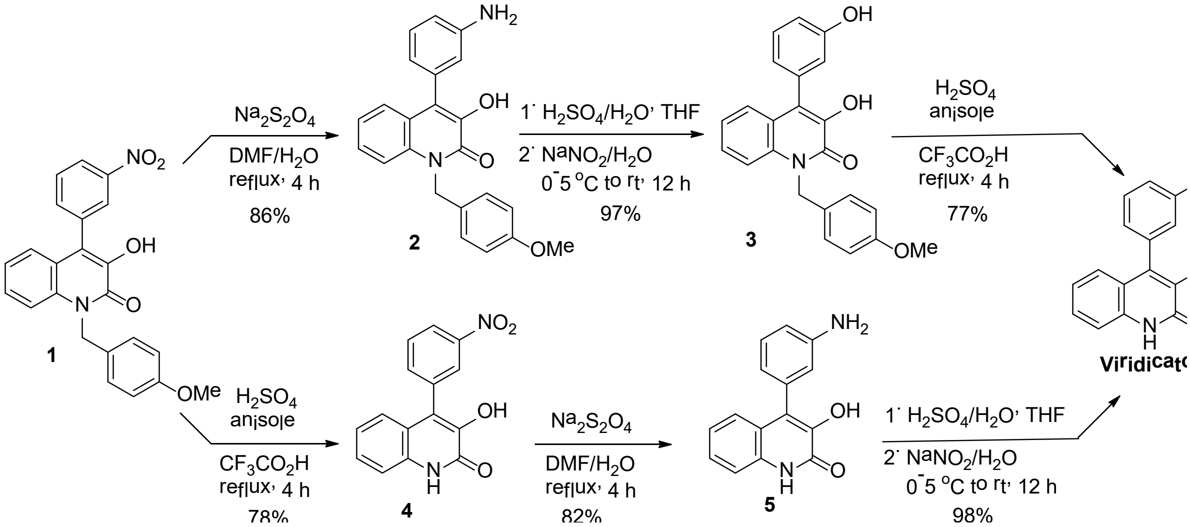
An alkaloid *viridicatol* is the fungal metabolite isolated from penicillium species. It is known that alkaloids of this series inhibit the replication of human immunodeficiency virus (HIV) [1],



We have previously developed a simple and effective method of synthesis of 3-hydroxy-4-aryl-*N*-(4-methoxybenzyl) quinolin-2-ones with acceptor groups in the aryl component, in particular 3-hydroxy-4-(3-nitrophenyl)-*N*-(4-methoxybenzyl)quinolin-2-one (**1**) [2]. In this report, we have developed two different sequences of three-step methods for converting **1** to *viridicatol*, which include the nitro group reduction, amine group diazotiation followed by replacement of the diazo group by hydroxy-group and 4-methoxybenzyl group removing. The overall yield of *viridicatol* was about 65% in both cases.



Physico-chemical studies were carried out in the spectral-analytical center for collective use CSF-SAC FRC KazSC RAS.

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This work was supported by the Russion Science Foundation (grant No 18-13-00315)

REACTIONS OF 2-HALOGENO-5-(A-ME$_3$SIO-TRIFLUOROALKYL)THIOPHENES WITH ARENES IN CF3SO3H

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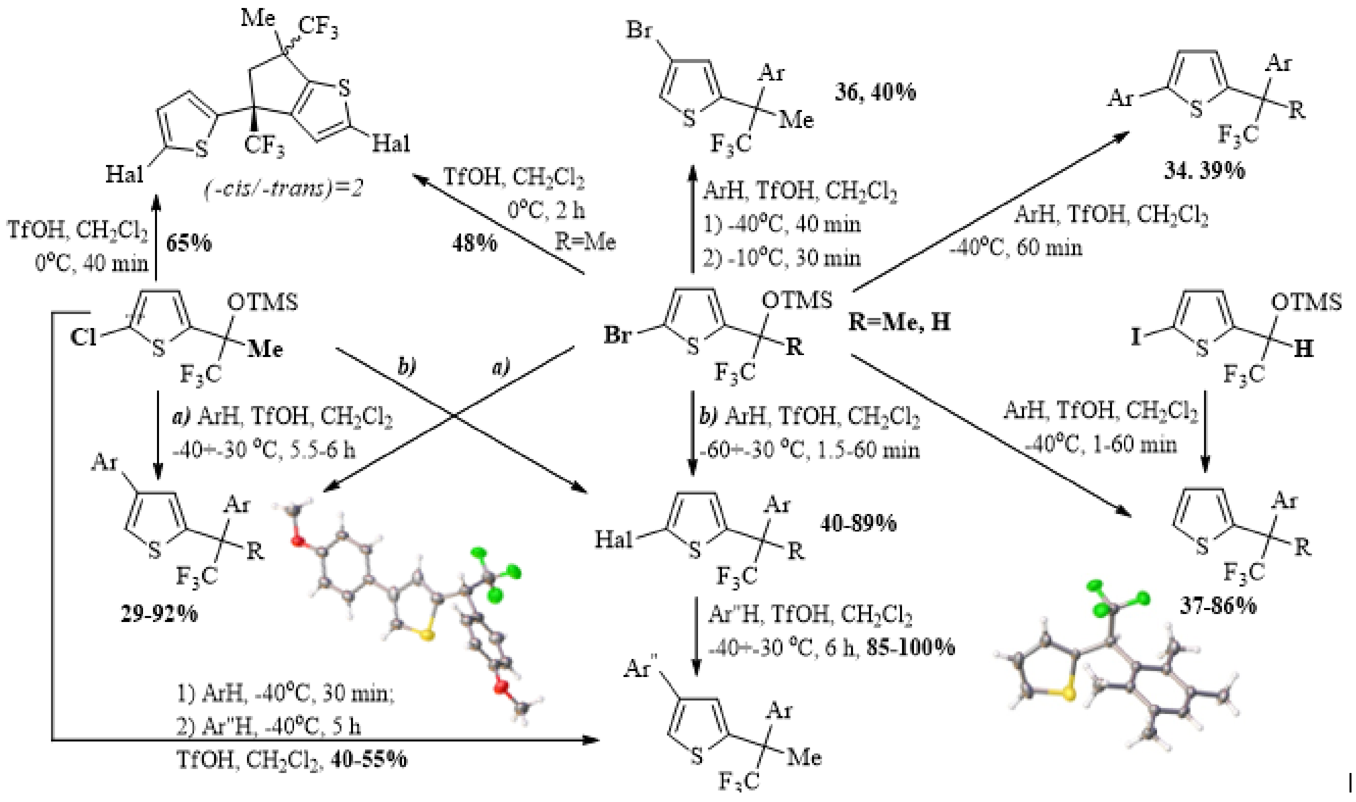
Thiophene derivatives are widely used to create photovoltaic cells [1], OLED [2] and drugs [3].

The reactions of 2-halogen-5-(α-Me$_3$SiO-trifluoroalkyl)thiophenes with arenes in CF$_3$SO$_3$H superacid (TfOH) lead to new compounds of the thiophene family, namely the products of the thiophene ring arylation and its side chain, halogen migration and hydrodehalogenation as well as dimerization (scheme 1).



Scheme 1. Reactions of 2-halogeno-5-(α-Me$_3$SiO-trifluoroalkyl)thiophenes in TfOH.

This work was supported by Russian Scientific Foundation (grant no. 18-13-00008).

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CURCUMIN AS A PROMISING AGENT AGAINST CANCER

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Compared to classical chemotherapy, chemoprophylaxis is a promising anticancer approach with reduced secondary effects. One of the most studied chemopreventive agents is curcumin, a natural compound extracted from Curcuma longa L. It is characterized as an anti-inflammatory, antitumor and antioxidant agent that promotes apoptosis in numerous cellular systems [1].

Turmeric is a perennial herb with a short stem, belonging to the family of Zingiberaceae. This plant is common in subtropical and tropical regions of the world, widely cultivated in Asian countries, mostly in India and China [2].

It was proved that curcumin is non-toxic to humans. By inhibiting a number of different molecules, which in turn play an important role in inflammation, curcumin has an anti-inflammatory effect and is effective in reducing postoperative inflammation. Turmeric inhibits the growth of Helicobacter pylori bacteria, which cause stomach ulcers and are associated with stomach cancer, and also helps prevent atherosclerosis by reducing the formation of blood. Another feature of curcumin is its ability to bind with heavy metals such as lead and cadmium, thereby reducing the toxicity of these metals. This property of curcumin explains its protective effect on the brain. In Ayurvedic medicine - combining the therapeutic properties of herbs with food, turmeric has been used for centuries [3].

Interest in curcumin, as an anti-cancer substance, appeared on the basis of the existence of a multitude of epidemiological data confirming the relationship between the low incidence of gastrointestinal mucous membrane cancer and turmeric. Based on a variety of experimental data, it was found that curcumin not only causes cell cycle arrest, but also induces apoptosis in human cancer cell lines derived from various tumors, including lung, colon, pancreas, breast and prostate cancer [4].

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HYBRID BATTERY/SUPERCAPACITOR ENERGY STORAGE SYSTEM BASED ON FERROCENE-CONTAINING POLYMERS WITH Co(II) NODES

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Although significant advancements have been made during the past decades to improve the battery performance, the main problem comes from the peak usage. Even in small electronic devices such as mobile phones and laptops, the battery damage occurs upon sudden usage of the battery's energy. This situation is constant in EVs, as different factors such as driving style, road, etc., cause rapid changes in the power consumption.

The batteries lose their performances over time for several reasons associated with the properties of the electroactive materials, conductivity and chemical stability of the current collectors, selection of the electrolytes compatible with the morphology of the electrodes, redox activities of the additives in electrodes or in electrolytes, as well as overcharging, internal and external environment and the application specifications. [1]

To store the generated power, it is necessary to convert it into other forms of energy, such as chemical or mechanical energy. As was presented by Gazarian[2], and based on the above definitions, energy storage consists of three different steps: charge: absorbing electrical energy from sources; storage: converting electrical energy to other types of energy and storing it and discharge: injecting the stored electrical energy back into the system. Moreover, storage systems can be divided into three different parts: central storage, the repository in which the energy is stored after conversion; power transformation, the interface between the central storage and the power system with bidirectional transfer; and control, which uses sensors and other measuring devices to determine the level of charge or discharge of the stored energy.

The fundamental search for new composite systems for energy storage devices is increasingly leading researchers to use coordination polymers, due to the possibility of adjusting the structure, as well as various physical properties. In our work, we present the directed synthesis of coordination polymers based on cobalt nodes and ferrocenyl linkers. It is shown that, in the composite, the polymers obtained are capable of intercalation/ deintercalation lithium ions. Quantum chemical, electrochemical and other properties are considered.

This research was supported by the Russian Science Foundation, grant No. 18-73-10139

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NEW SYNTHESIS OF [*1,2,4*]TRIAZOLO[*1,5-A*]HETEROCYCLES VIA ELECTROPHILIC ACTIVATION OF NITROALKANES

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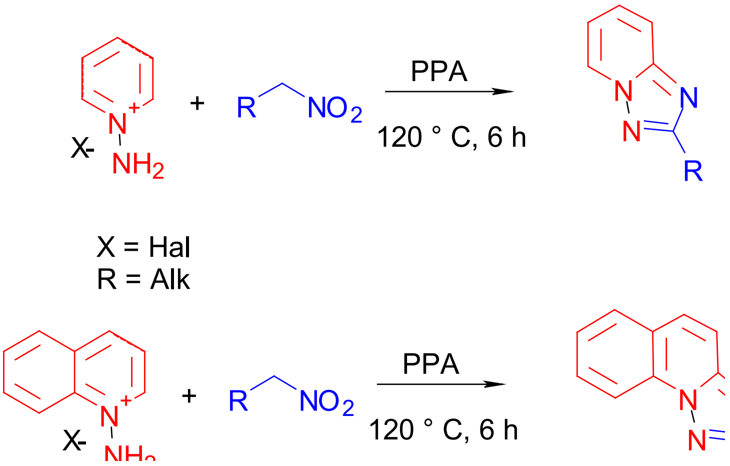
Quinoline containing fused *N*-heterocyclic compounds have also shown significant bioactivities and important representatives, such as lutonin A, dactolisib, pyronaridine. New efficient synthesis of [*1,2,4*]triazolo[*1,5-a*]heterocyclse, from different *N*-imino heterocyclse such as *N*-iminopyridine, *N*-iminoquinoline via electrophilic activation of nitroalkanes in polyphosphoric acid and further cyclocondensation is reported.

We wondered the way of employing 1-aminopyridin-1-ium salt and other heterocyclic imides en route to 2-ethyl[*1,2,4*]triazolo[*1,5-a*]pyridine scaffolds (Scheme 1). The reaction proceeds at 140°C with high yields (60-80%).



Scheme 1

Thus, a new reaction of heterocyclic *N*-imines was found in the PPA medium with activated nitroalkanes under mild conditions, including cyclocondensation.

This work was financed by the Russian Foundation for Basic Research (grant #№ 19-03-00308 a)

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SYNTHESIS OF NON-RACEMIC ADAMANTYL CONTAINING COMPOUNDS VIA Ni(II) CATALYZED ASYMMETRIC MICHAEL ADDITION

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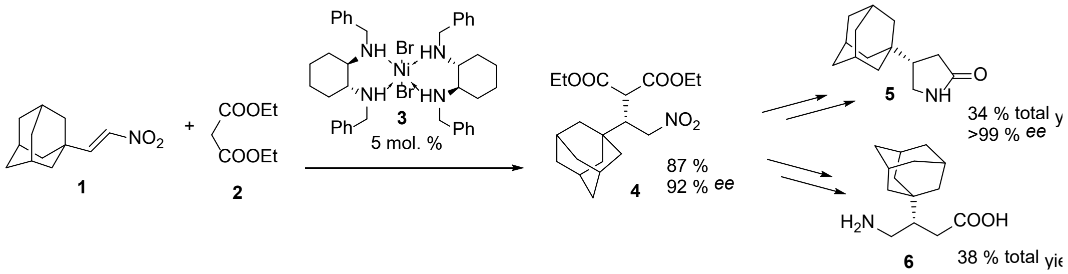
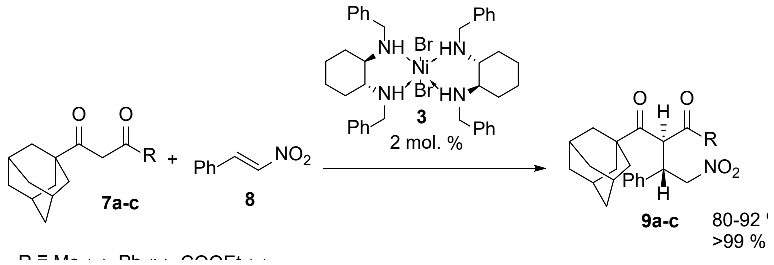
Adamantane derivatives have found numerous applications in the clinical practice, including treatment of viral diseases (influenza A, herpes, hepatitis C, HIV) and neurological disorders (Parkinson and Alzheimer diseases). The development of ways for the asymmetric synthesis of such compounds is of great importance, since the pharmacological activity of enantiomers may differ dramatically. In the present work we report the synthesis of enantiomerically pure adamantyl derivatives via asymmetric Michael addition of 1,3-dicarbonyl compounds to nitroalkenes in the presence of Ni(II) complexes with chiral vicinal diamines.

At first, we studied the Michael reaction of diethyl malonate **2** and 1-(1-adamantyl)-2-nitroethene **1** as model and showed that complex **3** is best to achieve the maximum enantioselectivity (**Scheme 1**).



Scheme 1. Asymmetric addition of diethyl malonate to (1-(1-adamantyl)-2-nitroethene

The addition of adamantyl containing 1,3-diketones **7a,b** and β-keto ester **7c** to ω-nitrostyrene **8** was carried out in the optimized conditions (**Scheme 2**).



Scheme 2. Asymmetric addition of 1,3-diketones and β-keto ester to ω-nitrostyrene

Subsequent hydrogenation of the Michael adduct **4** provides access to non-racemic 4-adamantyl pyrrolidine-2-one **5** and 4-amino-3-(1-adamantyl)butyric acid **6** (**Scheme 1**) [1]. These compounds are of interest because of their potential neurotropic activity.

This work was supported by Russian Science Foundation, grant 18-13-00447.

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DESIGN OF NEW CALIX[4]ARENE SUPPORTED MANGANESE CLUSTER COMPLEXES

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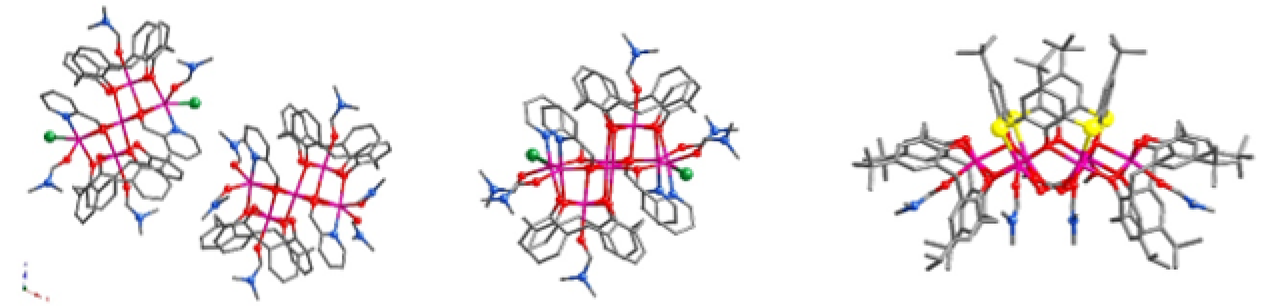
Calix[4]arenes are versatile ligands, capable of supporting the formation of a wide variety of polymetallic clusters comprising *3d* metal cations, especially, manganese cations displaying the single molecular magnet behavior. [1]. Moreover, the using of auxiliary organic ligands containing the chelate cavity in combination with calix[4]arene may improve the magnetic properties of obtained complexes.

In this report we present the synthesis and structure of new manganese based clusters supported on the calix[4]arene adopted in *cone* conformation, containing 5, 6 and 8 manganese cations in the metallic nodes involving the pyridine methanol and thiacalix[4]arene as co-ligands (Scheme 1).



$(C[4]A)_4$-Mn_{10}-$(PyMeOH)_4(DMF)_2$ $\{[Mn_8$-$CA_2(PyMeOH)_4DMF_6(O)_2]$ $[Mn_6$-$(TCA)(C[4]A)_2(DMF)_6(MeOH)_3]$

Scheme 1.

The work was supported by RSF № 19-73-20035

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SYNTHESIS, STRUCTURE AND COORDINATION ABILITY OF SALEN-TYPE SCHIFF BASES BASED ON CALIX[4]ARENE MOLECULAR PLATFORM

Kniazeva M.V.,[a] Ovsyannikov A.S.,[a] Mikhaylova I.A.,[b] Solovieva S.E.,[a,b] Dorovatovskii P.V., [c] Lazarenko V.[c] Antipin I.S.[a,b]

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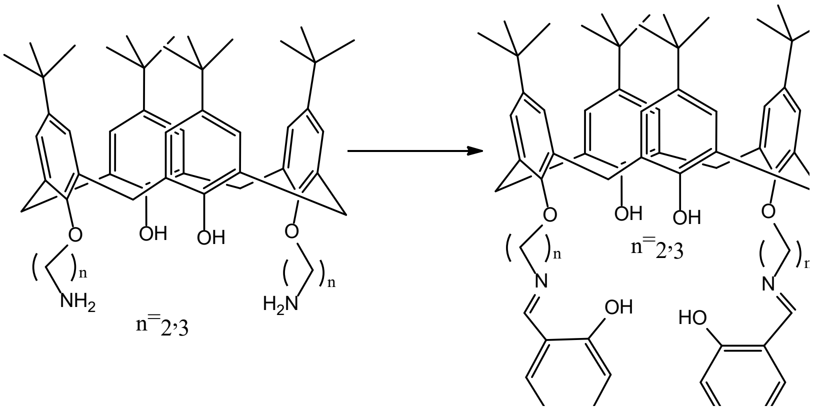
The actual problem in supramolecular chemistry is the establishment of regularities for the formation of crystalline structures with practical useful properties. It is known that salen-type compounds are capable of forming complexes with iron cations with spin-crossover properties which can be used for molecular magnetic devices, sensors and components in multifunctional materials. Moreover, the coordination environment of the ion and the presence of multiple supramolecular interactions play an important role in achieving a sharp spin transition. This fact and the possibility of functionalization of calix[4]arenes make them ideal candidates for the formation of SC complexes.

In this work we report synthesis of salen-type Schiff bases based on calix[4]arenes and their complexes with d/f cations (Scheme 1).



Scheme 1.

This work was supported by RFBR № 19-03-00519.

DESIGN AND SYNTHESIS OF HYDROXAMIC ACIDS WITH QUINAZOLINE FRAGMENT

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[c3] *"NMRC of oncology N. N. Blokhin" of the Health Ministry of Russia, 115478, Moscow, Kashirskoye Highway 23*

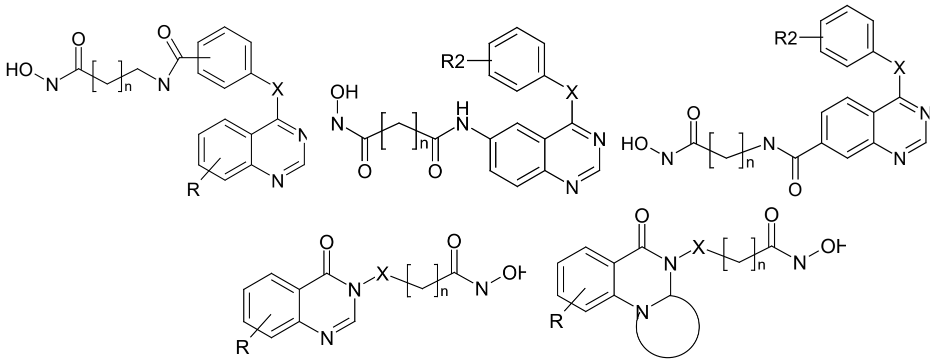
A promising strategy in the treatment of cancer at the present time is the design and synthesis of hybrid compounds consisting of two or more different bioactive fragments combined into one molecule and acting through the activation of multiple cell death mechanisms. Dual hybrids based on histone deacetylase inhibitors are becoming a new tool for anti-cancer therapy. [1].

In medicinal chemistry hydroxamic acid derivatives are considered the most part, as inhibitors of histone deacetylases [2].

The introduction of the pharmacophoric fragment of the histone deacetylase inhibitors into various natural and synthetic compounds, as well as into the known anti-cancer drugs [3,4] leads to a more pronounced synergistic therapeutic effect. There are known several successful examples of combining a hydroxamic acid with a quinazoline moiety.

The report discusses the strategy of creating bifunctional inhibitors using molecular docking of virtual conjugates in which hydroxamic acids are linked through a linker to the quinazoline fragment.

The results of the synthesis of new compounds containing hydroxamic acid and a heterocyclic fragment are presented.



The obtained compounds are potential dual targeting antitumor agents acting on histone deacetylase and various tyrosine kinases.

This work was supported by the Ministry of Education and Science of the Russian Federation, grant agreement № 075-11-2018-172 (RFMEFI62418X0051)

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TANDEM REACTIONS OF ELECTRON-DEFICIENT PROPARGYL ALCOHOLS WITH CYCLIC IMINES AND AMIDINES: DESIGN OF NEW POLYFUNCTIONAL HETEROCYCLIC SYSTEMS

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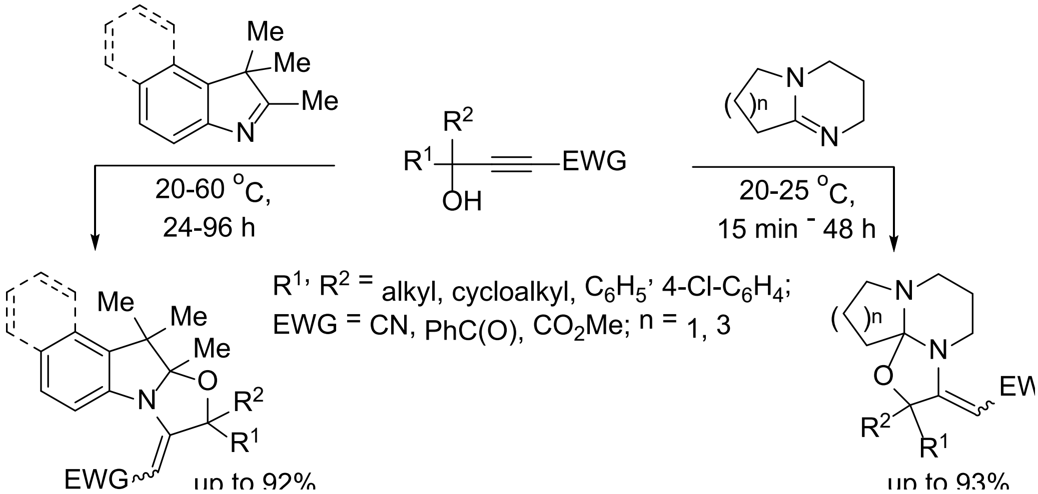
A new approach to the synthesis of fused heterocyclic systems with an angular nitrogen atom has been developed. The approach is based on annulation reaction of cyclic amidines and imines with electron-deficient propargyl alcohols having such electron-withdrawing substituents as cyano, benzoyl, alkoxycarbonyl functions.

It is found that the reactions of organic superbases, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and 3*H*-indoles with electron-deficient propargyl alcohols proceed regioselectively and, in most cases, stereoselectively under mild conditions (20-60 °C, without catalyst) to afford functionalized oxazolopyrrolohexahydropyrimidines, oxazolohexahydropyrimidoazepines and dihydrooxazolo[3,2-*a*]indoles in high yields.



The synthetic possibilities and fundamental regularities of the studied reactions have been elucidated. It is established that electrophilicity of the triple bond of propargyl alcohols depends on nature of the substituent and decreases in the order CN > PhC(O) ≥ CO_2Me.

It is shown that the reactions have general character and proceed *via* a cascade of zwitterionic intermediates generated by the nucleophilic addition of nitrogen atom of the cyclic fragment to the triple bond of propargyl alcohol to furnish annulated polycyclic adducts, highly reactive building blocks for fine organic synthesis, promising precursors of new generation drugs.

This work was supported by the Russian Foundation for Basic Research (grant no. 17-03-00927). The main results were obtained using the equipment of Baikal Analytical Center of Collective Using SB RAS.

ELECTROCHEMICAL STUDIES OF THE MULTI-ELECTRON REDOX PROCESS OF TRIFERROCENYL COMPLEXES

Khrizanforov M.N., Kononov A.I., Shekurov R.P., Islamov D.R., Kataeva O.N., Miluykov V.A., Budnikova Y.H.

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In the research field of organometallic chemistry, multiferrocene derivatives bridged by a π-conjugated spacer have received much attention from the viewpoint of the construction of a multi-step multi-electron redox system.[1]

This is because the electronic communication (charge delocalization) between the Fe(II) and Fe(III) sites across the π-conjugated spacer in the partial oxidation state (mixedvalent state) is capable of leading to the stepwise oneelectron oxidation process of the chemically equivalent ferrocene fragments in the multi-ferrocene system. The molecules of this kind are of significance because of their potential abilities to be used as conductive materials such as a molecular wire. The multi-step oxidation process derived from the multi-ferrocene system can be controlled by the π-conjugated spacer connecting ferrocene fragments due to the fact that the strength of the electronic communication between the mixed-valent metal centers strongly depends on the electronic nature and length of the linking π-conjugated spacer. Thus, there have been investigations of multi-ferrocene derivatives bridged by a wide variety of π-conjugated spacers such as aromatics.

In this work, we provide the details of the synthesis and electrochemical properties of a new types of multiferrocene complexes with copper salts.

Electrochemical properties were studied by cyclic voltammetry in solution and solid form. It is shown that the environment of the solvent and elecrolite strongly affects the redox transitions of individual components of the multiferrocene system.

The work was financially supported by the grant of President of the Russian Federation (MK--3375.2019.3)

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SYNTHESIS AND CHARACTERIZATION OF KETOACETYLENIC DERIVATIVES OF CALIX[4]ARENES

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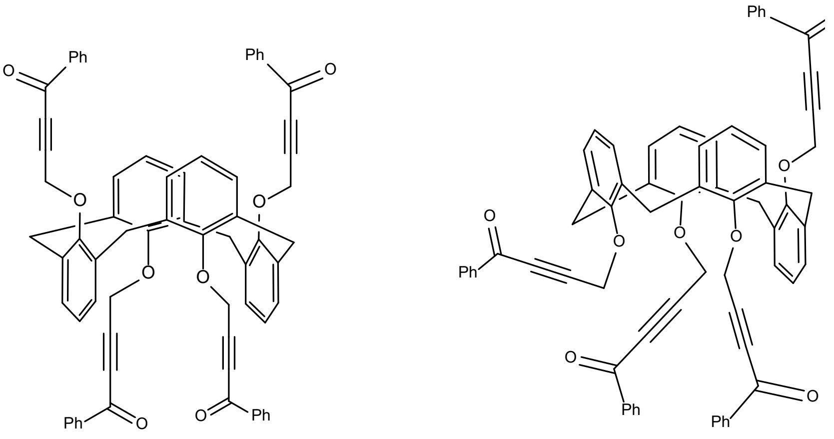
Development of new approaches to the synthesis of biologically active receptors on a calixarene scaffold is a relevant problem, because calixarene macrocycles not only offer several reaction centers for introduction of multiple fragments, but also represent a nontoxic scaffold. We previously suggested a facile approach towards heterocycle synthesis from ketoacetylenic precursors of *tert*-butyl(thia)calix[4]arenes, where stereisomeric form and the distance from receptor units to macrocyclic scaffold was varied [1]. However, no effect of the upper rim of macrocycle was considered.

Therefore, the aim of this work is to fully functionalize the lower rim of calix[4]arene scaffold without *tert*-butyl groups on the upper rim with arylketoacetylenic fragments.



1 **2**

Scheme 1.

As a result of this work, a number of phenylketoacetylene derivatives in *1,3-alternate* (**1**) and *partial cone* (**2**) configurations has been synthesized in almost quantitative yields from alkynyl precursors using palladium-catalyzed cross-coupling (91–95%). These products have been characterized using a number of NMR techniques (COSY, HSQC, HMBC).

This work was supported by the Russian Foundation for Basic Research (project nos. 17-53-10016-KO-A and 17-53-10016-KO-A).

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SYNTHESIS OF NEW HETEROCYCLIC SYSTEMS ON BASE OF FIVE-MEMBERED 2,3-DIOXOHETEROCYCLES

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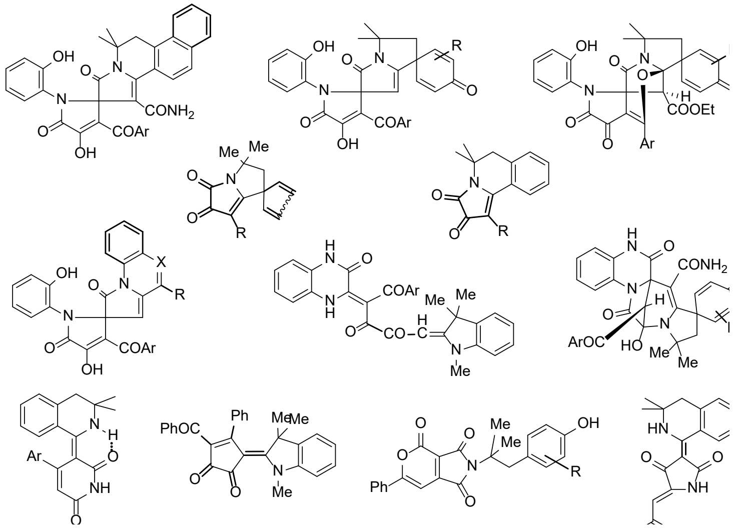
The nucleophilic transformations of the five-membered O- and N-2,3-dioxoheterocycles with a series of acyclic and heterocyclic enamines were investigated.

For example, 5-arylfuran-2,3-diones, and aroylketenes generated by thermal decomposition of dioxinones (via elimination of an acetone molecule), interacted with a series of acyclic (enamine ketones, α-enamine esters, β-enamine esters) and heterocyclic enamines (3,4-dihydroisoquinolines, spiropyrrolines, Fischer's base and 2-alkylazaarenes), resulting in the formation of aroylpyruvoyl [1] and aroylacetyl [2] derivatives of heterocyclic enamines and ensemble from two polyfunctional heterocyclic systems [3,4].

4-Benzoyl-5-phenylfuran-2,3-dione react with heterocyclic enamines of isoquinoline or spiropyrroline classes to produce analogs of pyrrolizidine alkaloids, substituted pyrrolo[2,1-a]isoquinolines and ensemble from two polyfunctional systems [5].

Nucleophilic transformations of of 1*H*-pyrrole-2,3-diones annulated with azaheterocycles on the [e] side by the action of heterocyclic enamines are convenient methods for the synthesis of products of addition [6], spiro-bis-heterocyclic [7], bis-spiro-heterocyclic [8] and bridged systems [9].



Scheme. New heterocyclic systems synthesized on base of five-membered 2,3-dioxoheterocycles

This work was supported by RFBR according to the research project № 18-03-00013.

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INTERACTION OF 3-ARYL-1,2,3,4-OXATRIAZOL-3-IUMOLATES-5 WITH NUCLEOPHILES

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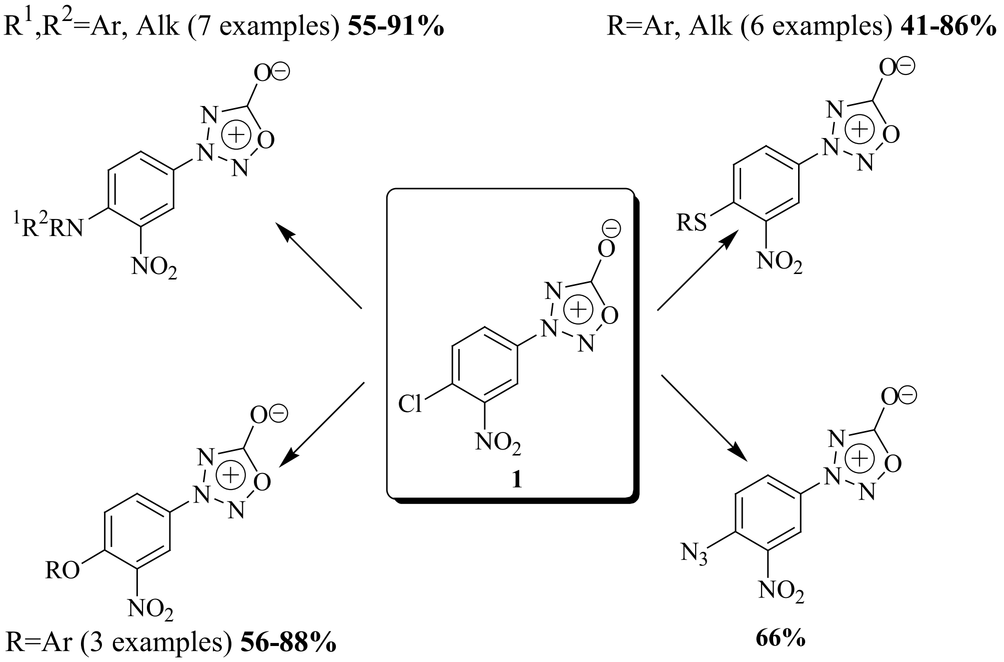
Mesoionic 3-aryl-1,2,3,4-oxatriazol-3-iumolates-5 (arylazasydnones) are a poorly known class of aromatic heterocyclic compounds. At the same time, few representatives of this class (about forty derivatives are known) exhibit hypotensive, antiplatelet, fibrinolytic, thrombolytic, and bronchiolytic activity. It has recently been shown that the azasydnone cycle is a new explosive group, and nitroarylazasydnones are of interest as a high energy compounds [1]. It should be noted that prior to our work, the reactivity of oxatriazoliumolates has not been studied, and the known methods for the synthesis of such compounds are entirely based on the formation of the azasydnones cycle at the last stage [2].

In the present work, nucleophilic substitution in the series of mesoionic 3-nitro substituted arylazasydnones was studied for the first time. As an example, 3-(4-chloro-3-nitrophenyl)-1,2,3,4-oxatriazol-3-iumolate-5 **1** was used, in which, under the action of various heteroatom-centered nucleophiles, the way and conditions of the reactions were studied (**Scheme 1**).



Scheme 1.

It was found that in all cases there is a selective substitution of the chlorine atom with preservation of the azasydnone cycle. Thus, for the first time, an effective method of targeted functionalization of arylazasydnones based on nucleophilic substitution has been developed.

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VIBRATIONAL SPECTROSCOPY STUDY OF HYDROGEN BONDING IN *P*-ALKYLCALIX[8]ARENES

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Calixarenes are able to effectively bind neutral molecules, ions and are used in ecology, medicine and nuclear power engineering. It has been shown that para-*tert*-butylcalixarenes are able to extract cesium from alkaline solutions. A characteristic feature of these compounds is their low solubility in organic solvents used in the extraction process. Therefore isononyl derivatives of calix[8]arene, which are better soluble in organic solvents and allow to extract Cs, Am, and Tc from alkaline solutions have been prepared. It turned out that n-isononylcalix[8]arene extracts cesium and americium in a much less effectively than the tert-butyl analogue due to the varying degree of aggregation in the organic phase. Isononyl derivative exists in monomeric form and tert-butylcalix[8]arene forms aggregates. To obtain a soluble and effective cesium and americium extractant, n-alkylcalix[8]arenes with various ratios of *tert*-butyl and isononyl groups on the upper rim of the calixarene platform were synthesized.

The FTIR and FT Raman spectra of p-alkylcalix[8]arenes (alkyl = *tert*-butyl, isononyl) were recorded. Analysis of IR spectra showed that the cyclic cooperative intramolecular hydrogen bond is realized in calix[8]arene. It was found that the strength of the cyclic cooperative intramolecular hydrogen bond in the series of alkyl derivatives of calix[8]arenes depends very little on the replacement of the p-*tert*-butyl groups by the more bulky isononyl group. From our data follows that the orientation of aromatic fragments in calixarene molecules depends on the type of alkyl substituent.

An analysis of the changes in the IR spectra with heating and dissolution shows that the conformation of the “pleated-loop” is retained in p-*tert*-butylcalix[8]arene. It turned out that the intramolecular hydrogen bond is a “probe” of the conformation of calixarene molecules and IR spectroscopy is a unique method that allows one to follow the slightest nuances of changes in the H-bound system of these supermolecules.

We thank the Russian Science Foundation for the financial support of this work (project №15-13-20017).

YTHRENE: RADICAL SUBSTRUCTURE IN FULLERENE MOLECULES

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Since discovery of fullerene in 1985 for the long time the isolated pentagon rule (IPR) was used as a criterion for fullerene stability. Now it is well known that among higher fullerenes C_n ($n > 60$), which are obeying IPR, there is appreciable part of molecules with open electron shells. Evidently such fullerene radicals are unstable as pristine fullerenes but they may be stabilized as endohedral or exohedral derivatives. Mainly, the molecules of such fullerenes contain phenalenyl radical substructures; some of them were discussed earlier [1].

Here for the first time we found and theoretically investigated a new radical substructure of fullerene molecules of IPR isomer 7 (C_{3v}) of C_{82} that bears two unpaired electrons and of IPR isomer 822 (D_{3d}) of C_{104} with two equivalent substructures (four unpaired electrons). The two were recently obtained, extracted and characterized by monocrystal X-ray diffractometry, their structures are in good accordance with our theoretical considerations [1,2].

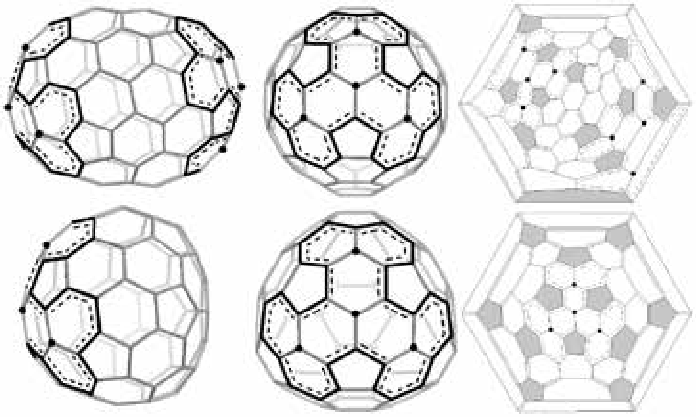

Fig. 1. 3D (two views) and Schlegel diagrams of the IPR fullerene molecules: C_{104}, isomer 822 (D_{3d}) (top), and C_{82}, isomer 7 (C_{3v}) (bottom).

According to our computations, two hypothetical polyaromatic radical molecules $C_{34}H_{18}$ and $C_{34}H_{12}$, which are the models of the fullerene substructure, have the same open-shell triplet ground states.

This work supported by Russian Foundation for Basic Research, research project No.18-29-19110mk and Portuguese "Fundação para a Ciência e a Tecnologia" (IF/00894/2015) and CICECO – Aveiro Institute of Materials (POCI-01-0145-FEDER007679 (UID/CTM/50011/2013)).

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Синтез аналога POPOP с использованием клик-реакции

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BASED ON CERTAIN AMIDINOTHIOUREAS METHOD OF OBTAINING 4-HETERYL-1-PHENYL-1,3,5-TRIAZINE-2 (1H)-THIONES

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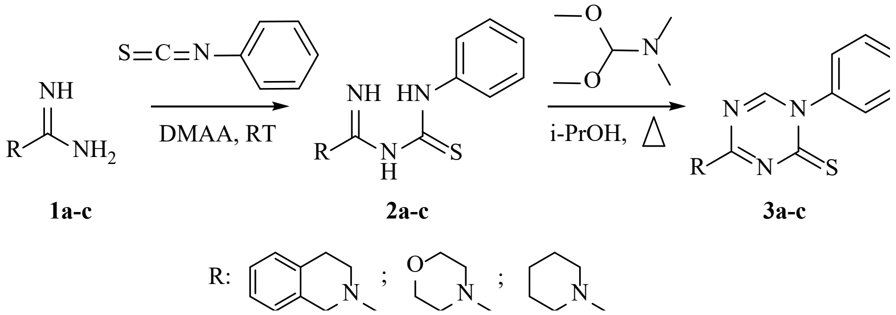
The undisputed leader among the diverse heterocyclic systems, both in theoretical and in the applied aspect, is nitrogen-containing heterocycles. So amidinothiourea and heterocyclic systems based on it show antirheumatoid and antihistamine activity and are widely used as antihypoxic drugs [1,2]. In addition, strong antimicrobial activity was found for some derivatives of 1,3,5-triazines [3].

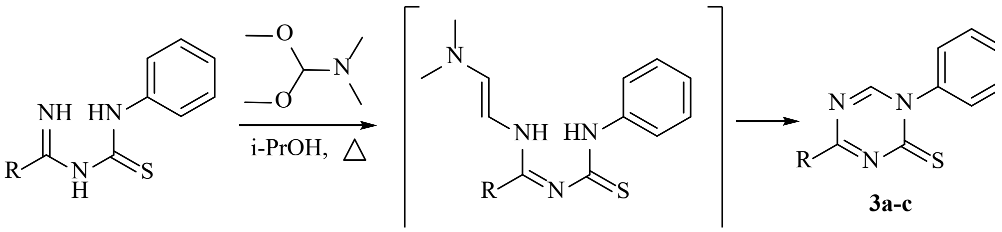
The method of obtaining 1,3,5-triazine derivatives based on synthesized by known methods substituted amidinothiourea derivatives **2a-c** [4] is investigated. By boiling a mixture of equimolar amounts of amidinothioureas **2a-c** with N, N-dimethylformamide dimethyl acetal in isopropyl alcohol, N2-N4 cyclization products of the starting compounds were obtained in good yields.



Scheme 1. Scheme of obtaining 4-hetaryl-1-phenyl-1,3,5-triazine-2 (1H) -thiones

The compounds obtained are white crystalline compounds, soluble in dimethylformamide, acetone, dioxane. The ^{1}H NMR spectra of 4-heteryl-1-phenyl-1,3,5-triazin-2(1H)-thiones **3a-c** contain signals of the CH-proton of the triazine cycle in the range of 8.40-8.50 ppm, the corresponding signals of the protons of the aromatic cycles in the region of 7.00-7.50 ppm. Peaks of heterocyclic CH_2 protons are presented in characteristic regions.

Apparently, the formation of 1,3,5-triazines in the considered cases can proceed by the following route (Scheme 2)



Scheme 2. Probable route of reaction

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THIACALIX[4]ARENE RECEPTORS WITH NITROGEN-CONTAINING FRAGMENTS ON THE UPPER RIM OF MACROCYCLE

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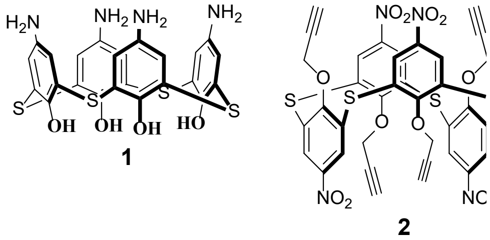
The design of (thia)calix[4]arenes substituted on the upper rim with nitrogen-containing fragments may lead to better binding of transition metal ions, such as silver, mercury, and copper due to their pre-organization on a macrocyclic scaffold also identified as multivalency concept in supramolecular chemistry. We recently suggested a convenient approach towards pyrazole ring formation from ketoacetylenic calix[4]arenes on the lower rim [1], which is new in macrocyclic chemistry. Alternatively, modification of the upper rim with functional fragments would contribute to higher binding ability of metal ions or introduce a new signal fragment.

The aim of this work is to address the role of upper rim and functionalize thiacalix[4]arene macrocycle on the upper rim with amino group (compound **1**) as a precursor for pyrazole ring formation, as well as nitro and propargyl groups on the upper and lower rims of thiacalix[4]arene (compound **2**).



Scheme 1.

To synthesize aminothiacalix[4]arene **1**, we reduced corresponding nitro-derivative with Sn/HCl reagent. Unlike References data, two weeks of heating at 80°C were necessary to achieve full conversion of the starting product. The nitrothiacalix[4]arene also reacted with propargyl bromide in acetonitrile at reflux to give propargyl derivative **2**; however, in spite of its full conversion and formation of tetrasubstituted product, a mixture of stereoisomers were identified according to NMR spectrum of the product, in addition to target *1,3-alternate* **2**, due to the small size of propargyl group and possibility of its through-the-annulus rotation.

This work was supported by the Russian Foundation for Basic Research (project no. 17-03-00389-a).

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CHALCOGENOPHOSPHORYL HYDROXYMETHYL PYRAZOLES *VIA* CATALYST-FREE ADDITION OF SECONDARY PHOSPHINE CHALCOGENIDES TO PYRAZOLECARBALDEHYDES

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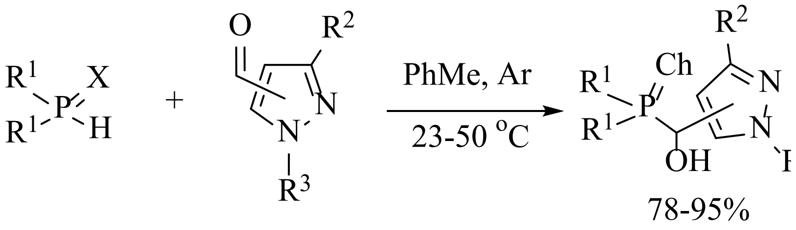
Pyrazole functions are widely used as the major fragments for a large number of compounds that have diverse applications, as catalysts, pharmaceuticals, agrochemicals, herbicides, fungicides, etc. Currently, many research papers are focused on the synthesis of organic ligands containing nitrogen donor atoms and other heteroatoms. In particular, the syntheses of nitrogen ligands bearing additional phosphine chalcogenide functions (N, P-hybrid ligands) and their complexes with transition metals become increasingly attractive in recent years due to their properties and structural diversity. In most of these complexes, the nitrogen atom contains pyridine or oxazoline groups, while compounds with bidentate pyrazole-phosphine-chalcogenide groups remain quite underutilized.

We have developed a one-pot atom-economic catalyst-free synthesis of a new family of pyrazole-phosphine chalcogenide ensembles separated by a one carbon functionalized (hydroxymethylene) spacer from available secondary phosphine chalcogenides and 4- and 5-pyrazolecarbaldehydes.



R^1 = Ph, $(CH_2)_2Ph$; R^2 = H, Me; R^3 =Me, *i*-Pr ;
Ch = O, S, Se

All synthesized compounds are characterized by NMR (^1H, ^{13}C, ^{31}P) technique.

The products obtained represent new promising ligands and precursors for drug design and advanced materials, particularly, for optoelectronic ones with extremely low energy consumption.

This work was supported by the Russian Foundation for Basic Research (grant no. 17-03-00739 and 18-02-00653). The main results were obtained using the equipment of Baikal Analytical Center of Collective Using SB RAS.

GEMINI SURFACTANTS WITH HETEROCYCLIC HEAD GROUPS: AGGREGATION AND SOLUBILIZATION PROPERTIES

Kushnazarova R.A., Mirgorodskaya A.B., Valeeva F.G., Lukashenko S.S., Zakharova L.Ya.

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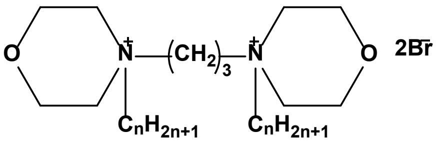
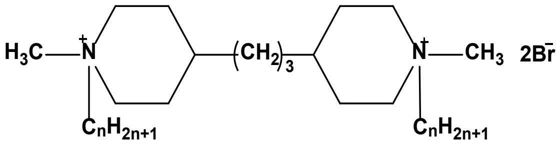
The unique property of gemini surfactants, which is the low value of the critical micelle concentration (CMC) enables them to function at low dose and therefore, they have become the object of many intensive studies. The combination of a large surface charge and a bulky hydrophobic domain allows these compounds to exhibit a high solubilizing effect.

In this study, comparative analysis of the aggregation properties and the solubilization effect of gemini surfactants containing heterocyclic head groups was carried out (morpholinium (1), piperidinium (2), imidazolium (3).



1



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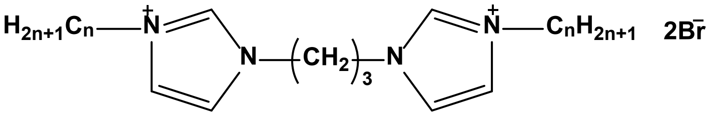

3

n=12; 14

The chemical structures of cationic surfactants

The physicochemical methods including tensiometry, conductometry, dynamic light scattering and spectrophotometry was used to determine CMC, the Krafft point, parameters of adsorption, the hydrodynamic diameter of the aggregates and the surface potential. A study showed that gemini surfactants are characterized by a CMC value, which is lower than their monocationic analogs. The spectrophotometry was used to quantitatively characterize the solubilization capacity of micellar solutions of gemini surfactants with respect to nonsteroidal anti-inflammatory drugs including ibuprofen and meloxicam. A study depicted that surfactants exhibit a high solubilizing effect, which allows a 5–8-fold increase in the solubility of these drugs in aqueous solutions.

Acknowledgements: This work is supported by the Russian Science Foundation (grant № 19-73-30012).

METAL COMPLEXES BASED ON N-SUBSTITUTED HYDRAZIDES OF 4-(HET)ARYL-4-OXOBUT-2-ENOIC ACIDS

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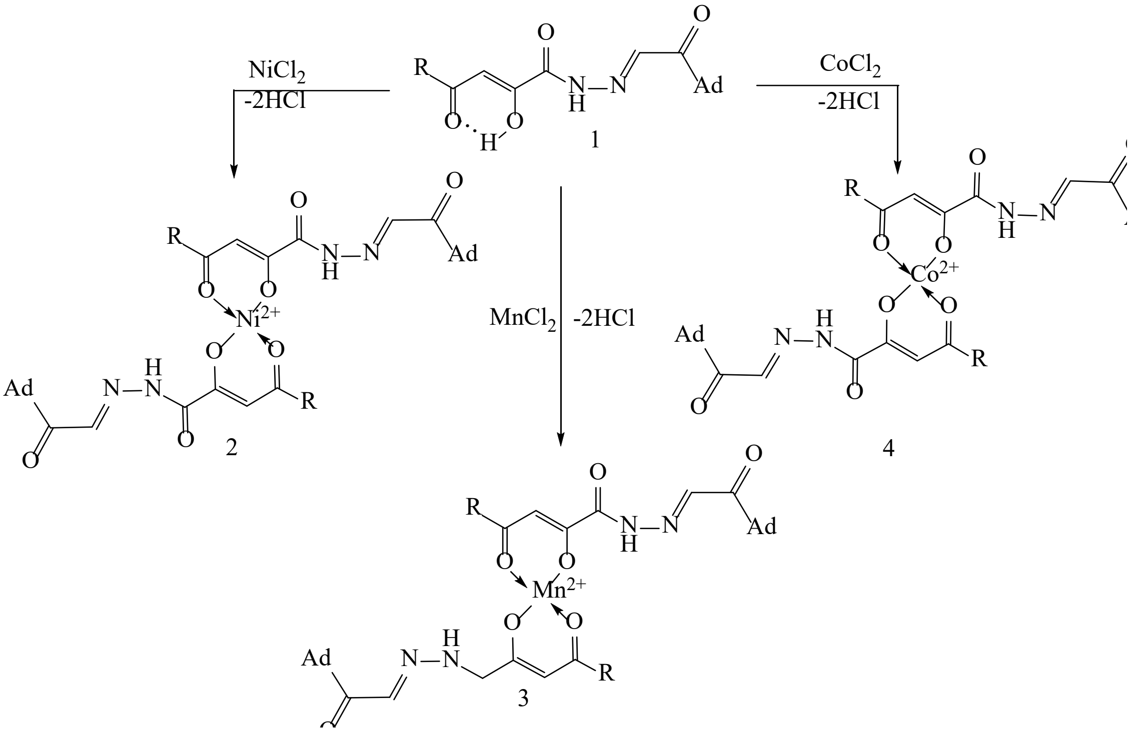
Adamantane-containing drugs with antiviral, neurotropic, immunostimulating activities are widely used in medicinal practice. It was previously found that metal complexes of Ni^{2+}, Mn^{2+}, Co^{2+}, Zn^{2+}, Cu^{2+} based on N-subtituted hydrazides of 4-aryl-4-oxobut-2-enoic acids exhibit various biological activities, including hypoglycemic, anti-inflammatory, antipyretic, antimicrobial ones [1,2]. Using available synthetic approaches we obtained N-[2-(adamantane-1-yl)-2-oxoethylidene]-2-hydroxy-4-oxo-4-(het)arylbut-2-enhydrazides (1) for the first time. When interacting with salts of bivalent metals in a ratio 2:1 they lead to formation of bis{3-((het) aryl)-1-N^2-[2-(adamantane-1-yl)-2-oxoethylidenehydrazido]-1,3-propanedionate}nickel, manganese, cobalt (2-4) (scheme 1):



Scheme 1.

The structure of the synthesized compounds was confirmed by physical and physico-chemical analysis. Complexes 2-4 were evaluated for their hypoglycemic and psychotropic activities on nonlinear white rats in alloxan-induced diabetic model together with black and white box, open field, marble burying tests. The compounds of cobalt-complexes 4 were found to exhibit the highest hypoglycemic activity. All low toxic complexes 2-4 show significant anti-stress activity. The relationship between the structure and biological activity is discussed.

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POLARITY AND STRUCTURE OF TRI(1-NAPHTYL)PHOSPHINE AND ITS CHALCOGENIDES

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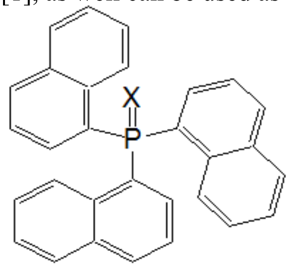
Trinaphthyl-substituted phosphines are widely used as ligands of organometallic complexes used in catalysis [1], they can have biological activity [2] and luminescent properties [1], as well can be used as building blocks for elementoorganic synthesis.



X = НЭП **1,** O **2,** S **3,** Se **4**

We determined polarities of tri(1-naphtyl)phosphine **1**, tri(1-naphtyl)phosphine oxide **2**, tri(1-naphtyl)phosphine sulfide **3**, and tri(1-naphtyl)phosphine selenide **4** in benzene and 1,4-dioxane solutions using second Debye method and carried out experimental and theoretical conformational analysis of phosphines **1-4** by the methods of dipole moments and quantum chemistry [DFT B3PW91/6-31G(df,p)].

From comparison of the experimental and theoretical dipole moments of compounds **1-4** (Table 1), we concluded that in solution tri(1-naphtyl)phosphine and its chalcogenides exist as an equilibrium of several conformers in which the naphthyl substituents are arranged in the form of *a propeller* and have *trans*- or *gauche*-orientation relative to the P=X (X = lone pair, O, S, Se) bond. In preferred conformers, the substituents at the phosphorus atom have *gauche*,*gauche*,*gauche*-orientation relative to the P=X (X = lone pair, O, S, Se) bond.

Table 1. Coefficients in the calculation equations, orientation polarizabilities, experimental and theoretical* dipole moments of **1-4**

Compound	Solvent	α	γ	$P_{or.}$, cm^3	μ_{exp}, D	μ_{theor},* D
1	Benzene	3.954	0.505	267.108	3.60	1.08
	Dioxane	6.306	0.773	372.600	4.25	
2	Dioxane	6.639	0.738	413.420	4.47	3.55
3	Benzene	6.883	0.490	533.999	5.08	4.54
	Dioxane	7.515	0.774	411.690	4.46	
4	Benzene	5.074	0.386	433.119	4.58	4.43
	Dioxane	6.871	0.547	510.105	4.97	

* μ_{theor} values are given for conformers with zero relative energy

According to the results of quantum chemical calculations for phosphines **2-4**, weak intramolecular interactions between one of the hydrogen atoms of the naphthyl substituent and the chalcogen atom of the corresponding group are possible: the distances are $P{=}O\cdots H{-}C_{sp2}$ 2.67 Å, $P{=}S\cdots H{-}C_{sp2}$ 2.74 Å, $P{=}Se\cdots H{-}C_{sp2}$ 2.73 Å (values are given for preferred conformers **2-4** with $\Delta E = 0.0$ kJ/mol).

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SELF-ASSEMBLING SYSTEMS BASED ON CATIONIC IMIDAZOLIUM SURFACTANTS BEARING CARBAMATE MOIETY AND BIOLOGICAL POLYANION

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In the framework of this study the capability of cationic imidazolium surfactants bearing carbamate moiety and different hydrophobic tails (the number of carbon atoms are 14,16,18 – IAC-n) to interact with bovine serum albumin (BSA) has been investigated by different physico-chemical methods (tensiometry, dynamic and electrophoretic light scattering, spectrophotometry, fluorescence spectroscopy, transmission electron microscopy (TEM)). All experiments were performed at a varied surfactant concentration and fixed concentrations of BSA (0.05% mass.). Using tensiometry it has been shown, that the addition of BSA does not affect the critical micelle concentration. For comparison, in the case of cationic imidazolium surfactants without carbamate moiety existence of two critical points at surface tension isotherms for surfactant-BSA binary systems has been shown.

Size and charge characteristics of the complexes formed have been estimated by dynamic and electrophoretic light scattering technique. It has been shown, that the formation of aggregates (surfactant-protein complexes) occurs at lower surfactant concentrations as compared to individual systems. The size of particles formed has bimodal distribution with populations in the range of 10-12 nm and 100-600 nm. The first one is responsible for the undenatured protein, the second one - for denatured macromolecules. Estimation of the zeta potential of surfactant-protein binary systems has showed that electrostatic mechanism of binding occurs for these systems, which is supported by the change of the zeta potential from the negative to positive values upon increase of surfactant concentration.

To visualize complexes of imidazole-containing surfactant bearing hexadecyl hydrophobic tail with bovine serum albumin TEM has been involved. Obtained data are in accordance with dynamic light scattering measurements: mean diameters of particles are15 nm and 100-400 nm.

Using synchronous fluorescence spectroscopy, it has been revealed, that the binding of the components occurs predominantly through the tryptophan amino acid residues of the protein. The degree of binding of surfactant and BSA through tyrosine amino acid fragment is much lower and occurs only beyond the critical concentration of association.

Solubilization ability of surfactant-BSA binary systems has been evaluated by spectrophotometry with the use of hydrophobic dye Orange OT. In the binary system there is no dissolution until critical micelle concentration value, after which sharp increase in the dye solubility occurs for all IAC-n/BSA binary systems. It has been established, that solubilizing capacity for surfactant/polypeptide systems are higher, than for individual surfactant solutions in all cases [1].

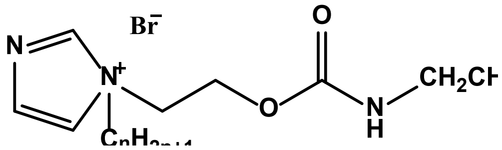

Fig. 1. Chemical structure of imidazolium surfactants IAC-n (n = 14, 16, 18).

This work was supported by Russian Science Foundation (project № 19-73-30012).

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SYNTHESIS AND STUDIES ON MULTI-LAYERED BIOMIMETICS OF LYTIC POLYSACCHARIDE MONOOXYGENASES

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Lytic polysaccharide monooxygenases (LPMO) are a class of copper-containing enzymes that catalyze oxidative cleavage of glycosidic bonds of recalcitrant polysaccharides.[1] Their active site consist of a copper ion coordinated in T-shaped geometry to one monodentate histidine residue and one bidentate *N*-methylated histidine through its imidazole side chain and *N*-terminal amine (Histidine brace). In certain types of LPMO (AA9/10s), either a tyrosine or phenylalanine is present in close proximity to the axial position. In order to gain a better understanding of the role of these structural elements in the catalytic oxidation mechanism, copper complexes with conformationally stable and predictable aromatic oligoamides have been designed to mimic the active site of LPMO. The effect of changes in the first coordination sphere groups such as the structure and sterics of the "histidine brace" on the catalytic activity will be examined. Complexes bearing longer aromatic olidgoamides that allows formation of a foldamer microenvironment will also be synthesized in order to study the effect of second coordination sphere groups on substrate binding and catalytic activity. The initial synthetic progress and perspectives of this work are described.

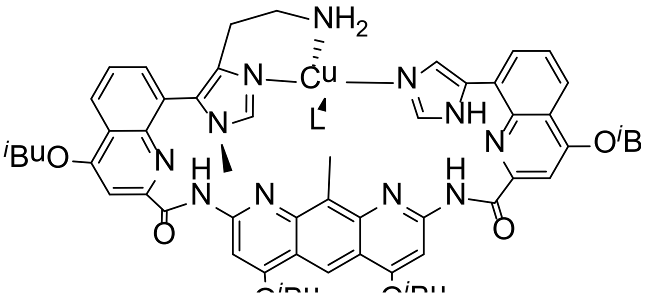

Fig. 1. Example of oligoamide based biomimetic of lytic polysaccharide monooxygenase

This work was supported by European Union through Marie Curie Actions.

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REGIOSELECTIVE SYNTHESIS OF FUROXANYLAZOLES BASED ON [3+2]-CYCLOADDITION OF 4-NITROFUROXANYLCARBONITRILE OXIDE TO VARIOUS DIPOLAROPHILES.

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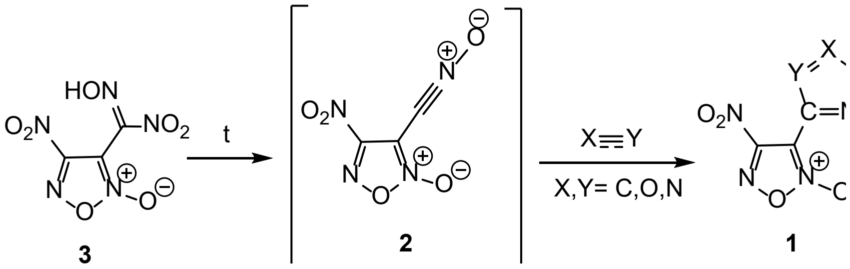
The main research area of our laboratory is devoted to the synthesis and reactivity of nitrogen-oxygen-containing heterocycles, especially 1,2,5-oxadiazole-2-oxides (furoxans).[1] Furoxan derivatives have a unique set of properties. On the one hand, they are exogenous nitric oxide donors, and on the other hand, heterocyclic ensembles incorporating a furoxan motif have a positive enthalpy of formation, which, along with high density and low volatility, enables the synthesis of high-energy structures.[2]

In present work we developed a new approach to the synthesis of hetarylfuroxans **1**, based on [3+2]-cycloaddition of various dipolarophiles to the 4-nitrofuroxanylcarbonitrile oxide **2**, generated *in situ* by thermolysis of 4-nitrofuroxannitrolic acid **3**. The reaction is an effective and regioselective method for the synthesis of polyheterocyclic ensembles containing furoxan ring (NO-donor) and azoles.



This work was supported by Russian Foundation for Basic Research (grants 18-33-00139).

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NEW SELECTIVE METHOD OF SYNTHESIS OF O-FLUORINATED BIPHENYLS

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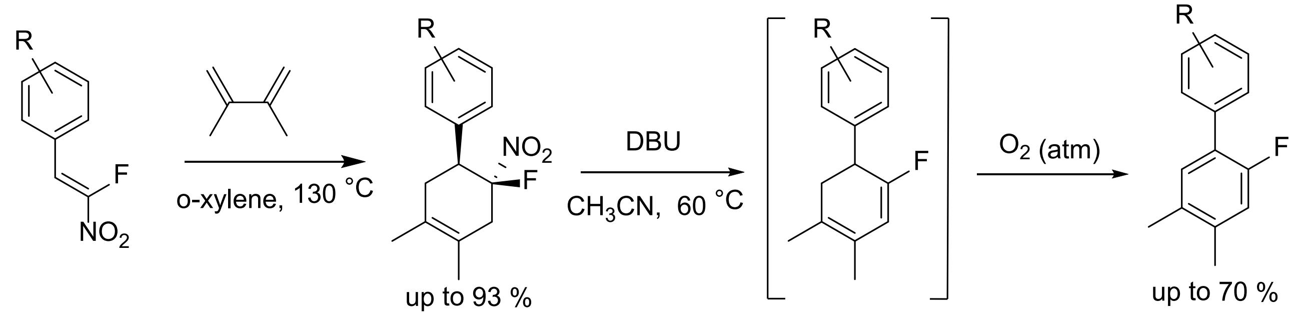
Biphenyl is an important intermediate in organic chemistry and a structural fragment of a wide range of compounds with high pharmacological activity. [1] Currently, one of the most effective methods for obtaining biphenyls are cross-coupling reactions [2]. In turn, all these methods require the use of expensive palladium compounds as a catalyst.

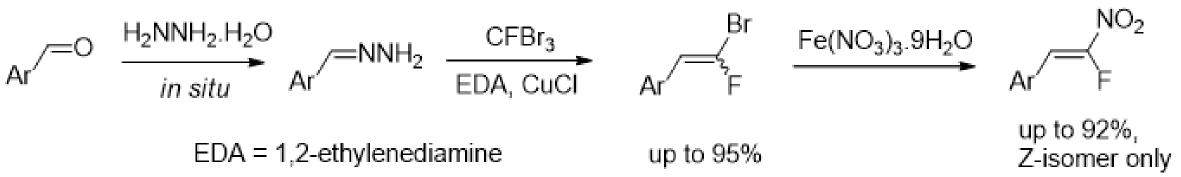
Fluorine-containing compounds are of an especial interest in organic and inorganic chemistry, chemistry of materials as well as in the production of drugs and agrochemicals. One of the key problems in the synthetic and medical chemistry is the design of structures with a strictly prescribed position of a fluorine atom. [3]

This work is devoted to the development of an alternative selective method for obtaining fluorine-containing biphenyls. This approach is based on the Diels-Alder reaction of β-fluoro-β-nitrostyrenes with 2,3-dimethyl-1,3-butadiene (Scheme 1). The subsequent elimination of HNO_2 from the resulting adducts with spontaneous oxidation of diene intermediate by air oxygen leads to the corresponding o-fluorinated biphenyl.



Scheme 1. Synthesis of o-fluorinated biphenyls

The starting β-fluoro-β-nitrostyrenes were prepared according to the previously developed method (Scheme 2), based on the radical nitration of 2-bromo-2-fluorostyrenes. [4] 2-Bromo-2-fluorostyrenes, in turn, were obtained by the reaction of catalytic olefenation from the corresponding aromatic aldehydes. [5]



Scheme 2. Preparation of starting β-fluoro-β-nitrostyrenes

This work was supported by the Russian Science Foundation (RSF) (Grant No. 17-73-10358).
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SYNTHESIS OF 2-SUBSTITUTED BENZIMIDAZOLES BY CYCLIZATION OF *O*-PHENYLENEDIAMINE WITH CARBOXYLIC ACIDS CATALYZED BY SNO

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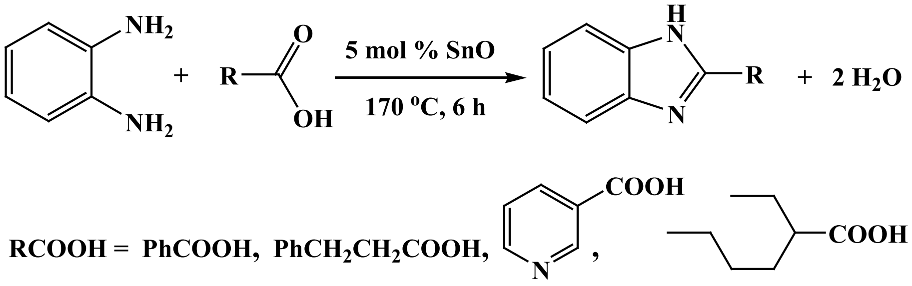
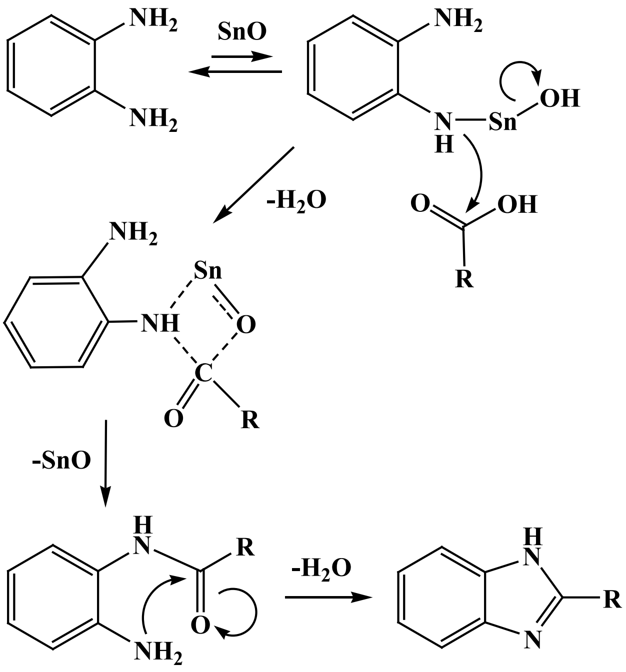
Benzimidazoles are an important class of heterocyclic compounds exhibiting biological activity, and are components of many drugs. Here we offer a convenient method for the synthesis of 2-substituted benzimidazoles by cyclization of *o*-phenylenediamine with carboxylic acids in the presence of SnO. (Scheme 1).



Scheme 1.

All reactions proceed without solvent in sealed evacuated glass ampoules. Substituted benzimidazoles were obtained in almost quantitative yield (*o*-phenylenediamine conversion was ~ 100%). Besides, we carried out the cyclization of *o*-phenylenediamine with benzoic acid using SnO, extracted from previous reactions. The catalyst was regenerated according to the procedure similar to that given in [1]. The conversion of *o*-phenylenediamine in this case was also quantitative.

A possible reaction mechanism including the reversible formation of an ArNH–SnOH adduct is presented in Scheme 2.



Scheme 2.

Thus, we have developed an efficient method for obtaining 2-substituted benzimidazoles from *o*-phenylenediamine and carboxylic acids using tin (II) oxide as a catalyst in almost quantitative yield. The reaction proceeds in a molten phase without a solvent, which is attractive from an environmental point of view. We have also shown that the regenerated catalyst can be used at least twice without loss of activity.

This work was supported by Russian Foundation for Basic Research (project no. 18-29-06010).

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SYNTHESIS OF NOVEL ISOXAZOLE-TRIAZOLE HYBRIDS

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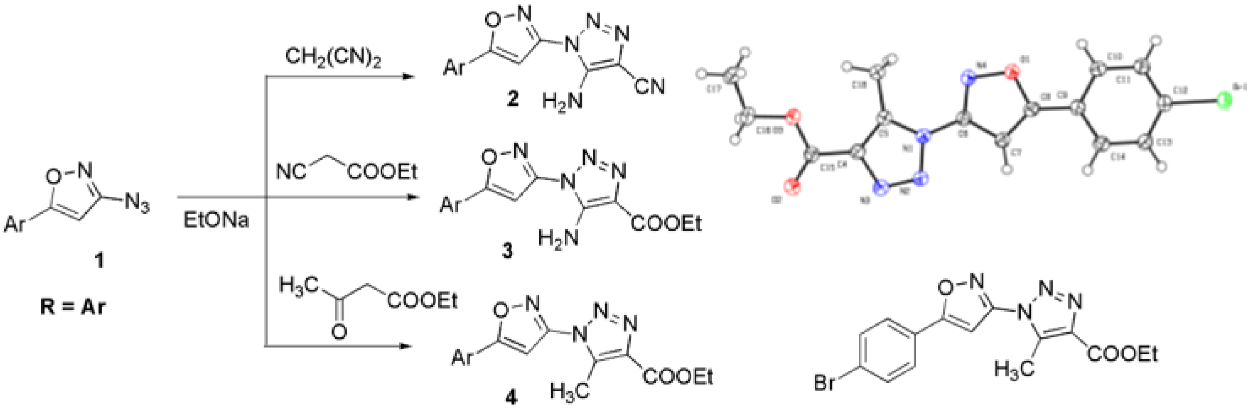
Biological and therapeutic properties of isoxazoles attract a lot of attention **[1]**. Nowadays many scientific groups are focused on synthesis of molecules containing both isoxazole and different heterocycle in their structure, e.g. 1,2,3-triazole scaffold **[2]**.

Recently we demonstrated the possibility of intramolecular cyclization of geminal diazido-vinylketones into azidoisoxazoles and revealed the chemistry of resulted azides **[3]**. SPAAC reactions of organic azides with cycloalkynes is a powerful instrument for many researches in this field. For instance, cyclooctyne and cyclooсynol **[4]** smoothly react with azidoisoxazole even at mild conditions.

However, the Dimroth cyclization remains one of the most efficient ways to create hybrid triazole systems. In this work we investigated the reaction of azidoisoxazoles **1** with various CH-acids such as dimethyl malonate, malonodinitrile, ethyl cyanoacetate and ethyl acetoacetate in the presence of strong organic bases.

The reaction with dimethyl malonate failed even under continuous reflux at 80°C, while the reactions with other abovementioned CH-acids in the presence of sodium ethoxide allowed us to obtain compounds of general formulas **2**, **3** and **4** in excellent yields (Scheme 1).



Scheme 1

Most of these products exist in different tautomeric forms what makes their NMR and IR spectra more complicated. Besides NMR and IR spectroscopy we used X-ray in order to have unambiguous confirmation of structure of obtained products.

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This work was partially supported by the Russian Federation President Grant for leading scientific schools № 4687.2018.3.

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SYNTHESIS OF SULFUR-CONTAINING GEMINAL VINYLDIAZIDES

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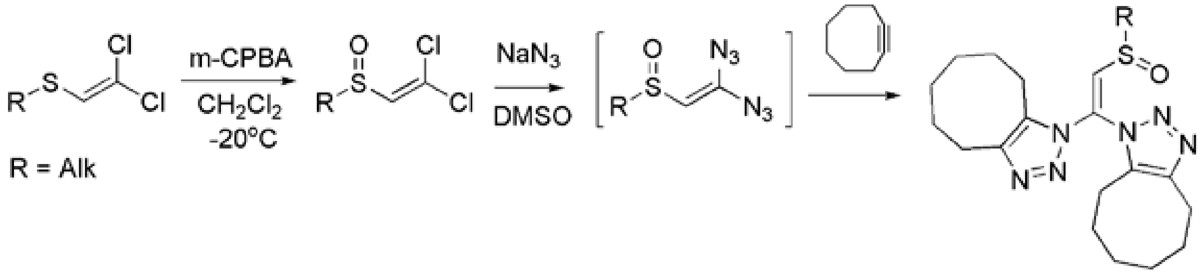
Alkenyldiazides are attractive compounds due to rich diversity of their reactivity. Recently we reported on the chemistry of 1,1-diazidoethenes [1, 2]. Therefore, vinyldiazides with functional group at β-position to C=C alkenyl bond may be considered as a perspective source to valuable heterocycles.

To the best of our knowledge, none of sulfur-containing geminal diazides are known so far.

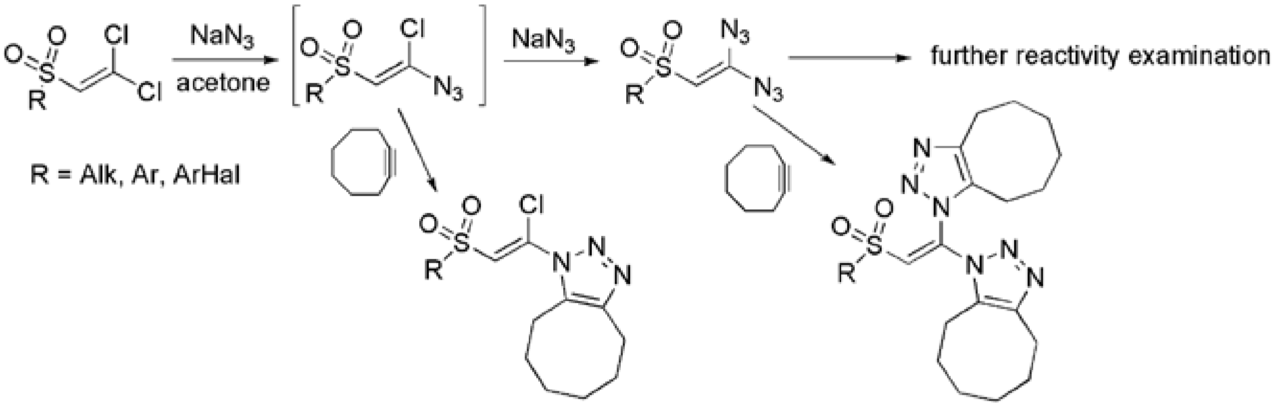
At first, we choose dichlorovinylsulfides as starting materials and attempted to conduct the reaction with sodium azide. However, the reaction did not proceed even at 120°C in DMSO.

In order to evaluate the reactivity of chosen substrates we developed a simple procedure of selective oxidation of dichlorovinylsulfides into dichlorovinylsulfoxides. The presence of more electronegative oxygen atom allows to conduct the substitution of the chlorine atoms by azido-group. Highly reactive diazidovinylsulfoxides were trapped with cyclooctyne (strain-promoted azide-alkyne cycloaddition) and have been isolated as individual *bis*-triazole derivatives (Scheme 1).



Scheme 1

As expected, dichlorovinylsulfones were found to be the most reactive substrates. Their reaction with sodium azide proceeds even at 0°C in acetone/water media to give corresponding diazidovinylsulfones. The last-mentioned species may be easily converted into *bis*-triazoles or may be isolated as individual compounds which are relatively stable at ambient temperature (Scheme 2).



Scheme 2

This fact allows someone to investigate the chemistry of that diazides in various transformations distinctive for organic azides.

Authors acknowledge support of Russian Foundation for Basic Research, grant №18-03-00791.
This work was partially supported by the Russian Federation President Grant for leading scientific schools № 4687.2018.3.

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THE REACTION OF N- AND C-TROPILIUM ADDITION TO MONO- AND DIAMINES OF PYRIDINE OR PYRIMIDINE SERIES

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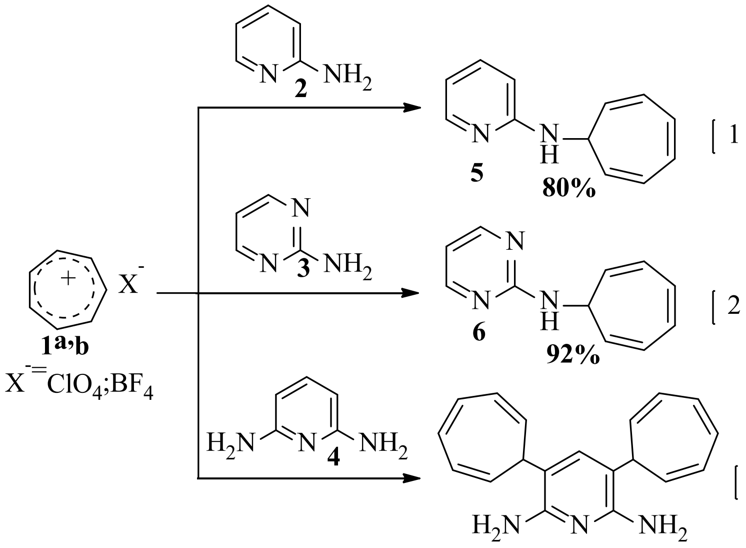
The interaction between 2-aminopyridine **2** and 2-aminopyrimidine **3** with tropylium salts **1a,b** proceeds selectively by the exocyclic nitrogen atom of amine group because of amine-imine tautomerism producing N-(cyclohepta-2,4,6-trien-1-yl)-2-aminopyridine **5** or N-(cyclohepta-2,4,6-trien-1-yl)-2-aminopyrimidine **6** respectively.



The interaction between tropylium tetrafluoroborate with 2,6-diaminopyridine **4** results in 3,5-di(cyclohepta-2,4,6-trien-1-yl) pyridine-2,6-diamine **7**, wherein two amine groups stay free, which can be attributable to strong orienting influence of two amine groups in pyridinic cycle.

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ELECTROCHEMICAL AMINATION OF SOME ANILINES

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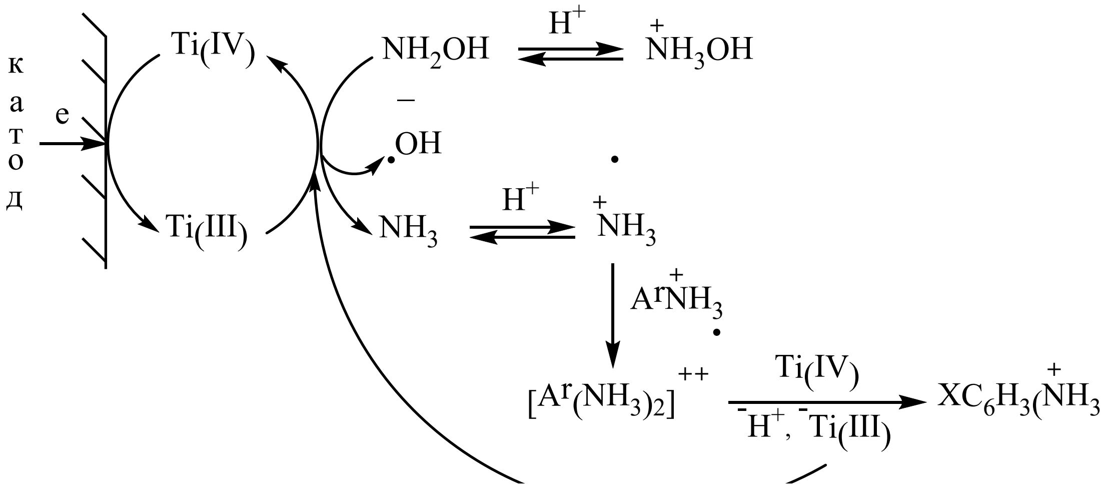
The processes of electrochemical amination of aniline, *ortho*-, *para*-anisidines and *ortho*-, *para*-, *meta*-chloroanilines by means of the Ti(IV) - NH_2OH system have been studied in aqueous solutions of 1–17 M H_2SO_4. The obtained results were interpreted from the standpoint of the state of monoamino compounds in these media. Aniline and its derivatives can exist in the form of both cations and associates that include the molecule or cation of the amino compound and the hydrosulfate ion. The amination process of the cations can be described by the following scheme:



Owing to an increase in the share of associated particles and a decrease in the reaction rate of reduction of aminyl radicals to ammonia by titanium(III), an increase in the concentration of H_2SO_4 is accompanied by an increase in the efficiency of cation-radical amination of anilines.

The ratio of the concentrations of the associates $ArNH_2{\cdot}HSO_4^-$ and $ArNH_3^+$, HSO_4^- and, therefore, the composition of the corresponding phenylenediamines are determined not only by the content of H_2SO_4 in the solution, but also by the nature of the substituent in the aromatic ring. The activating substituent enhances the strength of bonds in the $^+NH_3$-group, by donating electron density to the ring, and contributes to the existence of $ArNH_3^+$, HSO_4^- ion pairs in sulfuric acid media, while the deactivating substituent facilitates detachment of the proton from the ammonium group by sulfate ion, by withdrawing the electron density. That is, amines having a deactivating group in the ring are more prone to the formation of molecular associates $ArNH_2{\cdot}HSO_4^-$. Therefore, at a fixed concentration of H_2SO_4 in the absence of the sulfonation process, the selectivity of the amination of chloroanilines is lower than that of anisidines. An increase in temperature, acid content, and catholyte mixing speed leads to a decrease in the concentration of $ArNH_2{\cdot}HSO_4^-$ particles and an increase in the replacement regioselectivity. If the orienting influences of the substituent in the $ArNH_3^+$, HSO_4^- pair and the ammonium group in the $ArNH_3^+$ cation coincide, a highly selective synthesis of the corresponding isomeric diamino compound is possible.

4-Methoxy-1,3-phenylenediamine was obtained in 10 M H_2SO_4 with the weight fraction and current yield of 99.6 and 64%, respectively. And 4-chloro-1,3-phenylenediamine was obtained in 17 M H_2SO_4 with the weight fraction and current yield of 99.7 and 91%.

This work was supported by the Russian Foundation for Basic Research (project no. 16-03-01061) and performed according to the Russian Government Program of Competitive Growth of Kazan Federal University.

STYRYL BASES AND DYES: DIMERIZATION AND PHOTOREACTIONS IN DIFFERENT MICROENVIRONMENT

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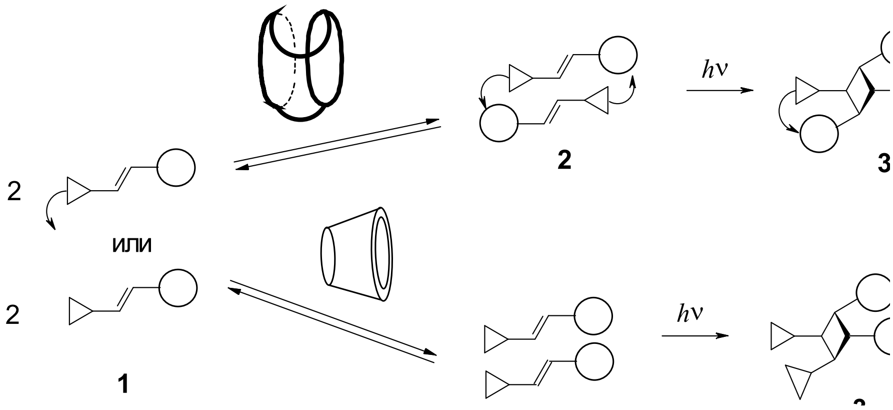
A number of styryl dyes **1** and their corresponding bases were synthesized. It was found that dyes **1** can spontaneously form dimers **2** in both the solid state and in solution (MeCN, CH_2Cl_2). The dimers have a head-to-tail pseudocyclic structure. The dimerization stability constants for dyes **1** were estimated by ^{1}H NMR titration in MeCN-d_3 (logK_d up to 8.0) [1, 2]. The complexation of styryl dyes and bases **1** with cucurbit[n]urils (CB[n], n = 7, 8) and β–, γ–cyclodextrins (CD) was studied by electron spectroscopy, NMR and X-ray [3, 4]. It was found that in aqueous solutions the addition of complementary cavitands (CB [7], β–CD) to compounds **1** lead to inclusion complexes of 1: 1 with a pseudorotaxane structure. For cavitands with a large cavity size (CB [8], γ–CD), the formation of complexes **2** of higher stoichiometry is also possible.



Scheme 1.

[2+2] photocycloaddition reaction generate cyclobutane derivatives **3**. For dyes the photocycloaddition quantum yield was varied between 0 and 0.38. The possibility of reaction passing depends on the nature of the compound **1** and the steric volume of its fragments. The structures of **1-3** were studied by X-ray diffraction and NMR spectroscopy. Dyes and bases **1** can be utilized in systems of optical registration and storage of information.

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α-AMINOPHOSPHORYL COMPOUNDS AS «HOSTS» FOR SUPRAMOLECULAR SYSTEMS

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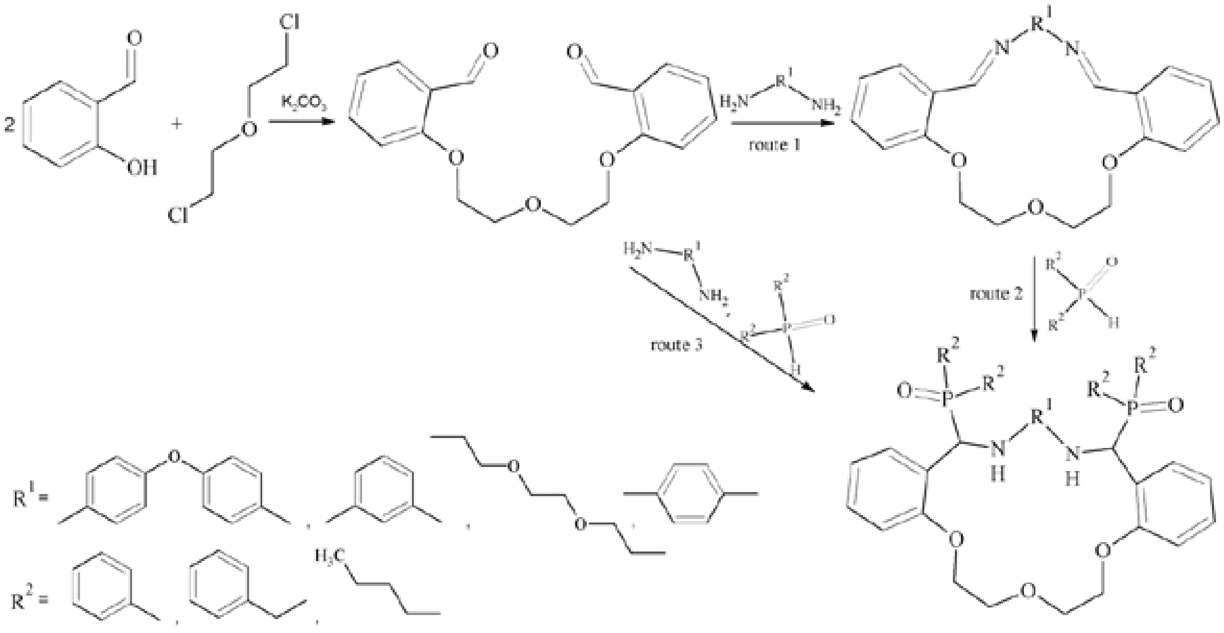
Supramolecular chemistry is a rapidly developing field of experimental chemistry. Novadays supramolecular systems are widely used in sorption, selective catalysis, and the development of new-generation drugs [1]. Thus, supramolecular systems can act as a carrier of medicinal substances, providing directional transport of the attached substrate to certain areas of the body [2].

We carried out the phosphorylation of new both nitrogen and oxygen containing macrocyclic Schiff bases with aromatic and aliphatic secondary phosphine oxides. The macrocycles were obtained by condensation of dialdehyde, synthesized on the basis of salicylic aldehyde, with different diamines (route 1). The resulted cyclic azomethines were phosphorylated by the reactions of Pudovik (route 2). Moreover we successfully carried out one-pot Kabachnik-Fields synthesis of the same α-aminophosphoryl compounds from the dialdehyde (route 3) (Scheme 1).



Scheme 1. Synthesis of α-aminophosphoryl compounds

The structure of the compounds obtained was confirmed by ^{1}H, ^{13}C, ^{31}P NMR, IR spectroscopy and ESI mass spectrometry.

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o-NITROBENZALACETOPHENONE OXIDES IN SYNTHESIS QUINOLINES

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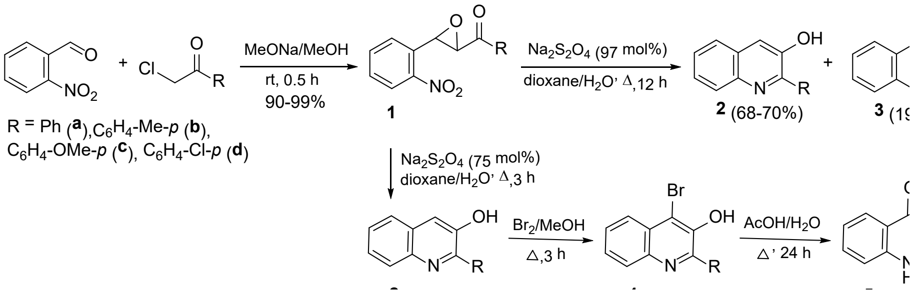
Quinoline derivatives continue to attract the attention chemists because of their wide range of pharmacological application. Among them are known antibacterial, antitumor, antimalarial, antiallergenic agents, immunostimulants, non-nucleoside HIV-1 inhibitors.

In this report, we propose new simple methods to obtain various quinolines from *o*-nitrobenzalacetophenone oxides (**1**), easily and quantitatively obtained under mild conditions of Darzens condensation from 2-nitrobenzaldehyde and chloroacetophenones.



3-Hydroxy-2-arylquinolines (**2**) were obtained mixed with 2-arylquinolines (**3**) from *o*-nitrobenzalacetophenone oxides (**1**) *via* the tandem Meinwald rearrangement/intramolecular reductive cyclization in the presence of sodium dithionite ($Na_2S_2O_4$) [1]. Compounds **2** and **3** were easily separated by column chromatography (eluent $CHCl_3$). The understanding of the reaction mechanism made it possible for us to develop the selective method for the synthesis of 3-hydroxy-2-arylquinolines (**2**) as sole product (see Scheme). As a result of bromination of **3**, 4-bromo-3-hydroxy-2-arylquinolines (4) were obtained, prolonged boiling of which in aqueous AcOH led to 3-hydroxy-2-arylquinolin-4-ones (**5**) (see Scheme).

The structure of compounds 1-5 was established by a complex of 2D NMR experiments (COZY, HSQC (^{1}H-^{13}C), HMBC (^{1}H-^{13}C), HSQC (^{1}H-^{15}N), HMBC (^{1}H-^{15}N) and confirmed by X-ray crystallographic analysis.

Physico-chemical studies were carried out in the spectral-analytical center for collective use CSF-SAC FRC KazSC RAS.

This work was supported by the Russion Science Foundation (grant No 18-13-00315)

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NOVEL CATIONIC AND ANIONIC AMPHIPHILIC CALIX[4]ARENE DERIVATIVES IN THE *CONE* CONFIGURATION: SYNTHESIS AND PHYSICOCHEMICAL PROPERTIES

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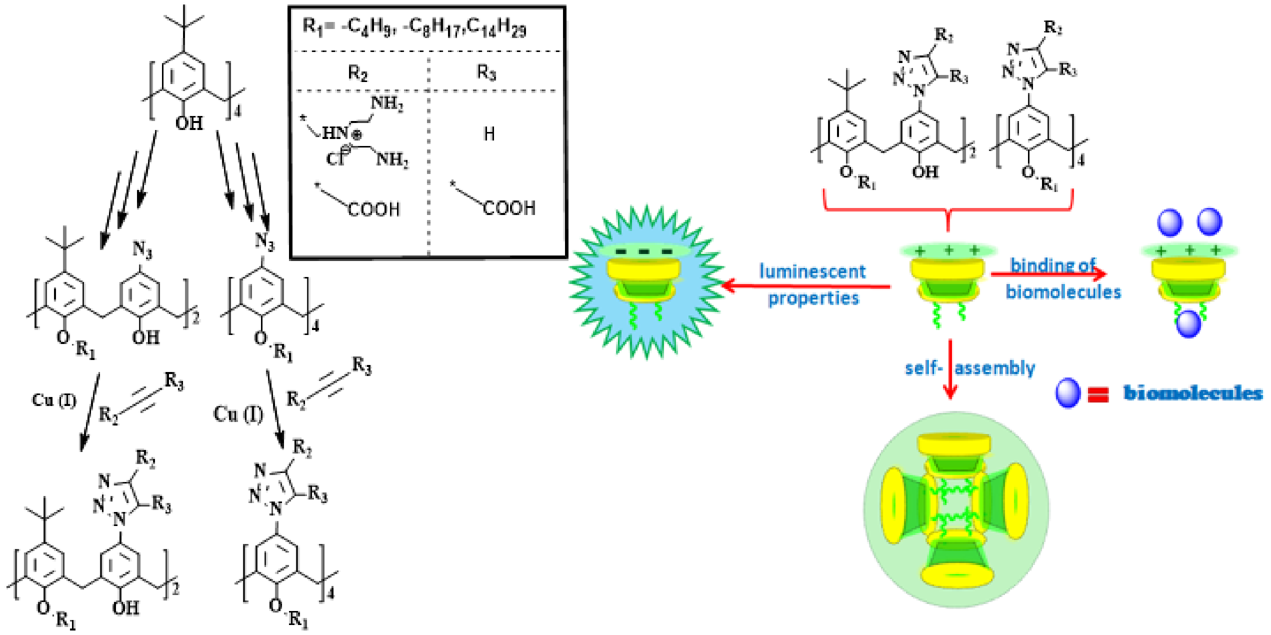
Calix[4]arenes are cyclic macromolecules consisting of four phenolic fragments linked to each other by methylene groups. Due to the ability to form guest-host complexes, calix[4]arene derivatives are successfully used in various fields of science. The presence of several reaction centers in the molecule allows finely adjusting the structure for a given substrate.

As a result of this work, a number of amphiphilic compounds with different functional groups in the *cone* configuration was obtained. It was found that calix[4]arenes containing polyammonium fragments can bind such biomolecules as adenosine diphosphate (ADP) and adenosine triphosphate (ATP). The selectivity of binding depends on the number of reaction centers. It has been established that calix[4]arene derivatives containing 4,5-carboxytriazolyl fragments on the upper rim can be used as a micellar environment in the Suzuki cross-coupling reaction; the efficiency of catalysis depends on the length of the lipophilic fragment.



REACTION OF B-ARYLETHYLAMINES WITH NITROALKANES IN PPA IN SYNTHESIS OF HETEROCYCLES.

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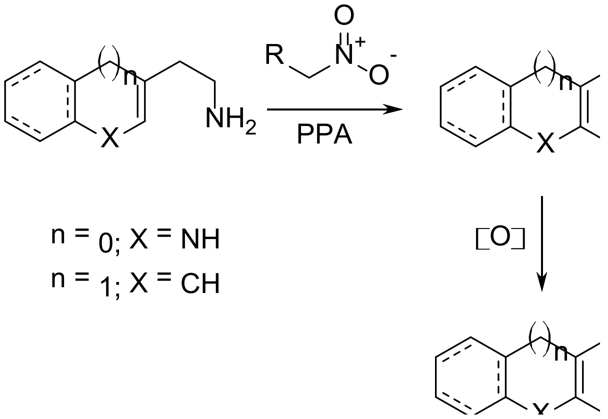
Usually, synthesis of 3,4-dihydro isoquinolines involves assembly of the pyridine nucleus — Bischler-Napiralski reaction. Many of these methods use carboxylic acid derivatives, which are not always available. In this paper, we report a new development, which is a very effective modification of the Bischler-Napiralski reaction that allows obtaining 3,4-dihydro isoquinolines using activated nitroalkanes instead of carboxylic acid derivatives.



Nitroalkanes form a very stable double-phosphorylated aci-form in polyphosphoric acid, which can act as an electrophilic component in many selective processes that proceed similarly to the Nef reaction involving C- and N-nucleophiles.

This work was financed by the Russian Foundation for Basic Research (grant #№ 19-03-00308 a)

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COPPER COORDINATION POLYMERS BASED ON *N*^{1}-(2-CARBOXYPHENYL)-*N*^{2}-(ARYL)OXALAMIDES

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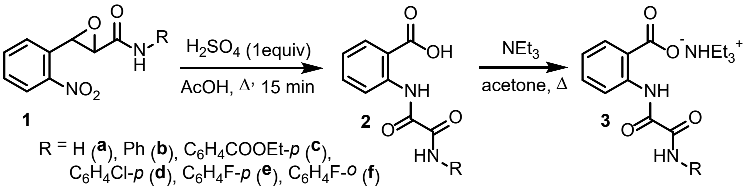
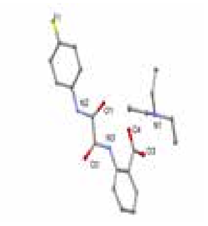
The synthesis and characterization of metal-organic frameworks (MOFs) is one of the most rapidly developing areas of chemical science. These materials have unquestionably enormous potential for many practical application and exceptionally beautiful structures. The carboxylates play important role in the construction of MOFs. The carboxylate anions easily form salts with metall. A versatile carboxylate anion can adopt a wide range of bonding modes, including monodentate, symmetric and asymmetric chelating, and bidentate and monodentate bridging.

In this work various complexes of *N*^{1}-(2-carboxyphenyl)oxalamides (**2**) with Cu(II) have been synthesized and structurally characterized. Multifunctional derivatives of antranilic acid **2** were synthesized *via* the new rearrangement of 3-(2-nitrophenyl) oxirane-2-carboxamides (**1**), and were converted to corresponding triethylammonium salts **3** for further transformations.

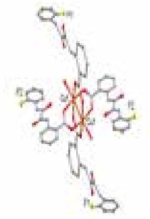


Copper(II) salts of 3-(2-nitrophenyl)oxirane-2-carboxamides (**4**) and copper(II) coordination polymers (CCPs) were synthesized as follows: copper(II) salts **4** were precipitated from the aqueous solution of triethylammonium salts **3** and $CuCl_2\cdot 2H_2O$ (1:5) at room temperature, CCPs were obtained from copper(II) salts **4** by dissolving them in DMSO and following slow evaporation DMSO at 180 °C.

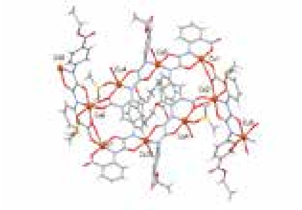
The structures of **3e**, **4f** and **5c** have been checked by single crystal X-ray analysis.



$C_{15}H_{10}FN_2O_4\cdot C_6H_{16}N$ (**3e**)



$C_{60}H_{36}Cu_2F_4N_8O_{18}$ (**4f**)



$C_{116}H_{102}Cu_{10}N_{12}O_{46}S_4\cdot 4DMSO$ (**5c**)

Additionally, the properties of CCP will be presented briefly.

Physico-chemical studies were carried out in the spectral-analytical center for collective use CSF-SAC FRC KazSC RAS.

This work was supported by the the Russion Science Foundation (grant No 18-13-00315) and partially (for X-ray analysis) by the Russian Foundation for Basic Research (grant No 18-33-00228).

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BIS(TOLUENE)CHROMIUM 1-((2-(2-METHOXYETHOXY)ETHOXY)METHYL)-1-HYDROFULLERIDE

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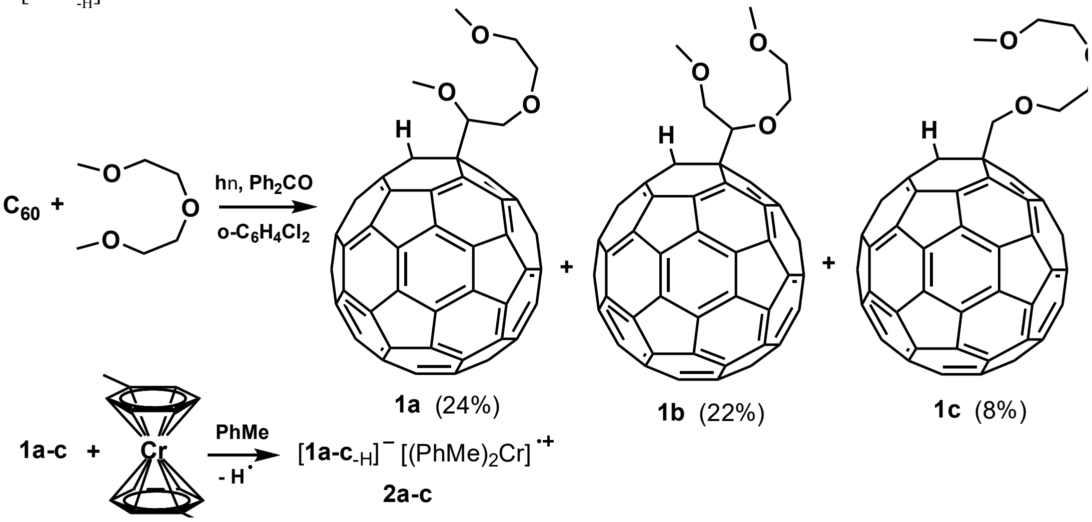
Bis(toluene)chromium reacts with 1-(1-methoxy-2-(2-methoxyethoxy)ethyl)-1,2-dihydrofullerene (**1a**), 1-(2-methoxy-1-(2-methoxyethoxy)ethyl)-1,2-dihydrofullerene (**1b**) and 1-((2-(2-methoxyethoxy)ethoxy)methyl)-1,2-dihydrofullerene (**1c**) in toluene at 293 K to form salts bis(toluene)chromium 1-(1-methoxy-2-(2-methoxyethoxy)ethyl)-1-hydrofulleride (**2a**), bis(toluene)chromium 1-(2-methoxy-1-(2-methoxyethoxy)ethyl)-1-hydrofulleride (**2b**) and bis(toluene)chromium 1-((2-(2-methoxyethoxy)ethoxy)methyl)-1-hydrofulleride (**2c**). Fullerides **2a-c** are stable at 333K. Fullerides **2a-c** are insoluble in hexane, sparingly soluble in PhMe, soluble in THF. NIR spectrum of fullerides **2a-c** in THF at 290 K indicates absorption bands in 985 -997 and 645 - 655 nm range typical for anions [**1a-c**$_{-H}$]$^-$.



Fullerenes **1a-c** were obtained by irradiation of fullerene C_{60}, diglyme and benzophenone in o-dichlorobenzene solution with 1:27:60 molar ratio and 3.3 mg/ml C_{60} concentration using luminescent UV lamp 370 nm 10x10w in an evacuated and sealed pyrex ampoule at 303 – 309 K for 207 minutes. After solvent evaporation in vacuo, fullerenes **1a-c** was extracted with $CHCl_3$, dried in vacuo, washed by hexane and acetone. Column chromatography over silica gel with toluene as eluent gave first unreacted [60]fullerene and then, consistently, fullerene **1a**, **1b** and **1c** as amorphous brown solids. Fullerenes **1a-c** are insoluble in hexane, soluble in CHCl3 and THF. The UV/vis spectra of **1a-c** in decaline at 290 K show absorption bands at typical for 1,2 [60]fullerene derivatives. All reactions were carried out under an inert atmosphere. The work was performed using the instrumental base of the Analytical Center of the G.A. Razuvaev Institute of Organometallic Chemistry, Russian Academy of Sciences and supported by RFBR ((№19-53-52001).

HETEROGENEOUS RADICAL STAGES IN MECHANISM OF GAS PHASE OXIDATION OF C_2H_5CHO

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The reaction of gas phase oxidation of C_2H_5CHO proceeds by chain degenerate branching mechanism [1], and the stage of branching at low temperatures (150-290°C) is the heterogeneous radical decay of $C_2H_5CO_3H$, while the leading active centers are $C_2H_5CO_3$ radicals. As the oxidation process advances the contribution of $C_2H_5O_2$ radicals, increases. Pathways of the formation of some compounds are:

$$\begin{aligned}
C_2H_5CO_3H &\rightarrow C_2H_5CO_2 + OH\\
C_2H_5CO_2 &\rightarrow C_2H_5 + CO_2\\
C_2H_5 + O_2 &\rightarrow C_2H_5O_2\\
C_2H_5O_2 + C_2H_5CHO &\rightarrow C_2H_5O_2H + C_2H_5CO\\
C_2H_5CO + O_2 &\rightarrow C_2H_5CO_3\\
C_2H_5 &\rightarrow C_2H_4 + H\\
C_2H_5 + O_2 &\rightarrow C_2H_4 + HO_2
\end{aligned}$$

During C_2H_5CHO oxidation it was discovered the effect of the nature of the reactor surface on the composition and the quantity of products, including also ethylene and hydroperoxide.

The possibility of heterogeneous interaction of $C_2H_5O_2$ radicals with C_2H_5CHO was shown in [2].

The analysis and discussion of the kinetic data obtained in reactors treated by H_3BO_3 and KCl at the C_2H_5CHO oxidation [1, 3] allowed us to find the experimental evidence for the heterogeneous formation of ethylene with the participation of C_2H_5 radicals.

So the mechanism of gas phase oxidation of C_2H_5CHO consists from heterogeneous and homogeneous stages of radicals. In connection with this, the elucidation of the possibility of heterogeneous reactions of $C_2H_5O_2$ and C_2H_5 radicals is important for the development of ideas on the oxidation and ignition reactions of aldehydes.

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SUPRAMOLECULAR DONOR–ACCEPTOR COMPLEX BETWEEN FUNCTIONALIZED DERIVATIVES OF STILBENE AND 4-(4-MERCAPTOSTYRYL) PYRIDINE:A PHOTOCHEMICAL STUDY

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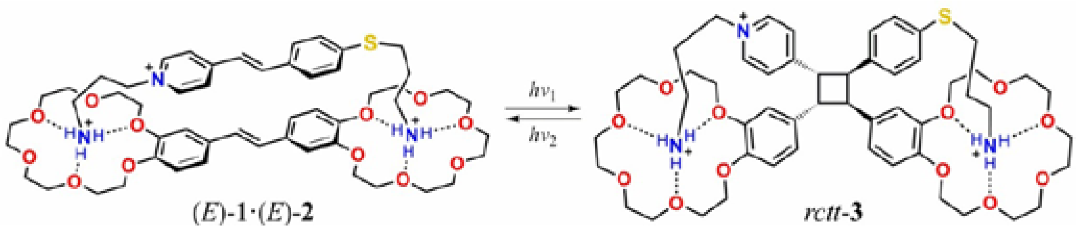
To date, a variety of supramolecular approaches have been developed to control the efficiency and selectivity of the [2+2] photocycloaddition (PCA) reaction both in solution and in the solid state [1],[2]. Most attention has been paid to auto-PCA, i.e. [2+2]-photodimerization, whereas supramolecular cross-PCA reactions remain less studied [3]. This especially concerns the reactions between electron-donor and electron-acceptor olefins, when photoinduced intermolecular electron transfer can be a competing process. In this case, it is rather difficult to predict the PCA efficiency, because both competing photoreactions are significantly dependent on the geometric properties of the supramolecular assemblies.

In this work, we have shown that styrylpyridinium dye (*E*)-**1**, which was synthesized for the first time, forms a highly stable bimolecular complex with bis(18-crown-6) stilbene (*E*)-**2** in solution owing to ditopic coordination via hydrogen bonds (Scheme 1). The complex formation results in much faster deactivation of the excited states of both compounds, which is explained by photoinduced electron transfer from the stilbene derivative to the styrylpyridinium dye. Despite this, the complexed olefins undergo [2+2] cross-photocycloaddition upon selective excitation of the dye to afford solely the *syn*-cycloadduct (*rctt*-**3**). The retro-photocycloaddition occurs readily upon UV irradiation of cyclobutane *rctt*-**3** and leads to the initial bimolecular complex.



Scheme 1. [2+2] Cross-photocycloaddition reaction.

To the best of our knowledge, compound *rctt*-**3** is the first representative of a 1-pyridyl-2,3,4-triphenyl cyclobutane derivative.

This work was supported by the Russian Science Foundation (grant No. 19-13-00020) and the Ministry of Science and Higher Education of the Russian Federation (State Assignment No. 0089-2019-0003).

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URACILS ANALOGS AS POTENTIAL ANTI-TUMOR AGENTS

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A quantitative analysis of relationships between structures of 5-benzyluracils and efficiency of inhibitors deoxyuridine triphosphatase (dUTPase) was made by the program GUSAR 2013 (General Unrestricted Structure Activity Relationships) [1-2]. Biological data from ChEMBL [3] were used for creation of QSAR models. In general 6 statistically significant QSAR-models ($R^2_{TrS}>$ 0.6, $R^2_{TS}>$ 0.5, $Q^2>$ 0.6) for prediction of IC_{50} values for various 5-benzyluracils for dUTPase were created based on MNA- and QNA-descriptors, as well as consensus of their combinations. The statistical characteristics of some of the models we constructed are presented in the Table1. These models can be used for quantitative prediction of potential anti-tumor drugs against dUTPase. Atoms and structural fragments of the studied structures influencing on increase and decrease of dUTPase inhibition were identified by GUSAR 2013 visualization of quantitative "structure-activity" relationships in the created models. The results of structural analysis of the contribution of the different functional groups in the activity of dUTPase inhibition can be considered in the molecular design of active substances of known anticancer drugs in order to enhance the efficiency of their inhibitory action dUTPase. As a result of the virtual screening of the ChEMBL database using consensus models M3 and M6, 10 potential dUTPase inhibitors have been identified.

Table 1. Characteristics and prediction accuracy of IC_{50} values for consensus-models M1-M6. pIC_{50} activity in TrS1 and TrS2 lies in the range-7.523 – -3.733.

Training set	Models	N	R^2_{TrS}	R^2_{TS}	F	S.D.	Q^2	V
QSAR model based on QNA-descriptors								
TrS1	M1	113	0.928	0.694	14.264	0.442	0.693	15
TrS2	M4	94	0.925	0.786	11.535	0.479	0.642	12
QSAR model based on MNA-descriptors								
TrS1	M2	113	0.941	0.6427	11.554	0.408	0.739	21
TrS2	M5	94	0.943	0.777	9.164	0.455	0.678	16
QSAR model based on QNA- and MNA-descriptors								
TrS1	M3	113	0.940	0.669	11.380	0.423	0.722	19
TrS2	M6	94	0.942	0.813	10.347	0.451	0.685	14

N – number of structuresinthe training set; R^2_{TrS} - a multiple coefficient of determination calculated for compounds from the training set; R^2_{TS} - a multiple coefficient of determination calculated for compounds from the test set; Q^2 – a cross-validated R^2 calculated during leave-one-out cross-validation procedure on data of the training set; F – Fisher's coefficient; SD –standard deviation; V- the number of variablesin the finalregression equation.

This work was supported by grant No. 19-73-20073 of the Russian Science Foundation.

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NEW 4-ARYL-SUBSTITUTED TETRAHYDROPYRIMIDIN-2-ONES CONTAINING A DIHEXYL PHOSPHINE OXIDE MOIETY

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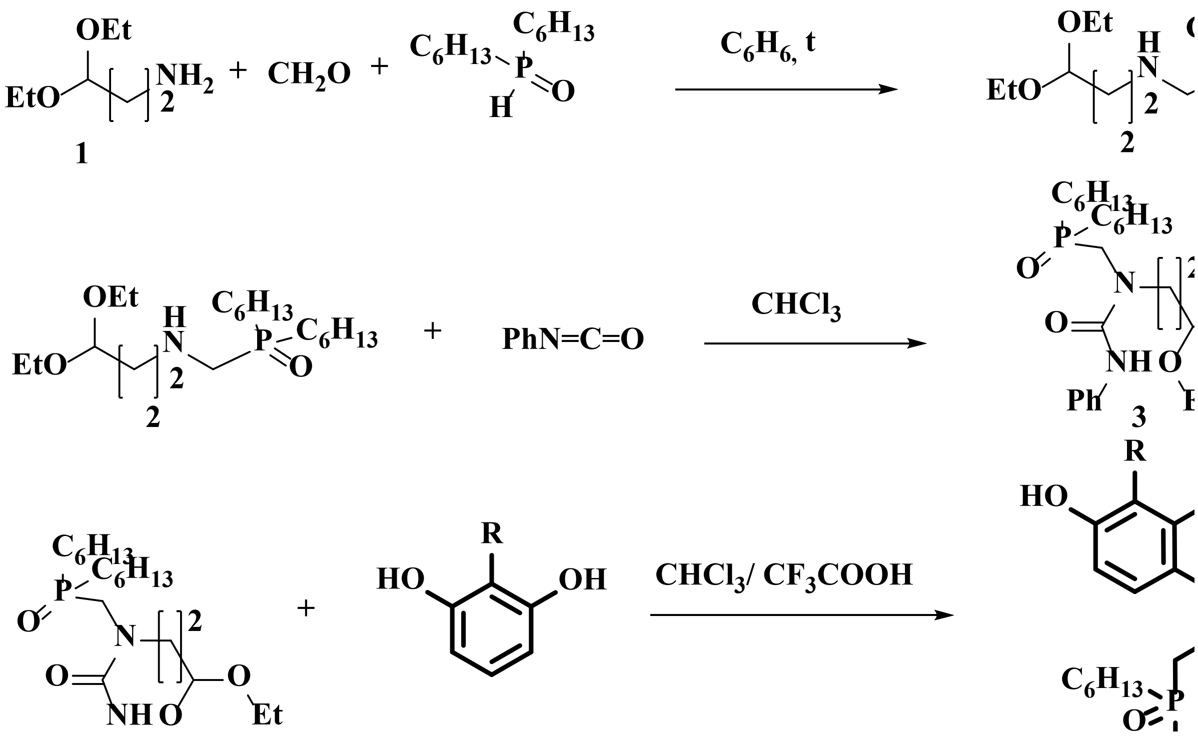
It is known that β-ureido acetals are building blocks in the synthesis of tetrahydropyrimidin-2-ones, which have diverse biological activity. However, to date, no data on the synthesis of 4-aryl-substituted tetrahydropyrimidin-2ones containing the phosphoryl fragment have been reported in the References. As a result of the reaction of β-aminoacetal **1** with formaldehyde and dihexylphosphinic acid, acetal **2** containing a phosphoryl fragment, was obtained for the first time by the Kabachnik-Fields reaction. Reaction of compound **2** with phenyl isocyanate a new β-ureido acetal **3** was obtained in quantitative yield. New 4-aryl-substituted tetrahydropyrimidine-2-on **4** were obtained in high yield by heterocyclization of ureido acetal **3**.



The reported study was funded by RFBR and Government of the Republic of Tatarstan according to the research project № 18-43-160004.

REACTIONS OF 1- (3,3-DIETHOXYPROPYL) UREA WITH PHENOLS - SYNTHESIS OF TETRAHYDROPYRIMIDINE-2(1H)-ONES AND DIBENZOXANTENES

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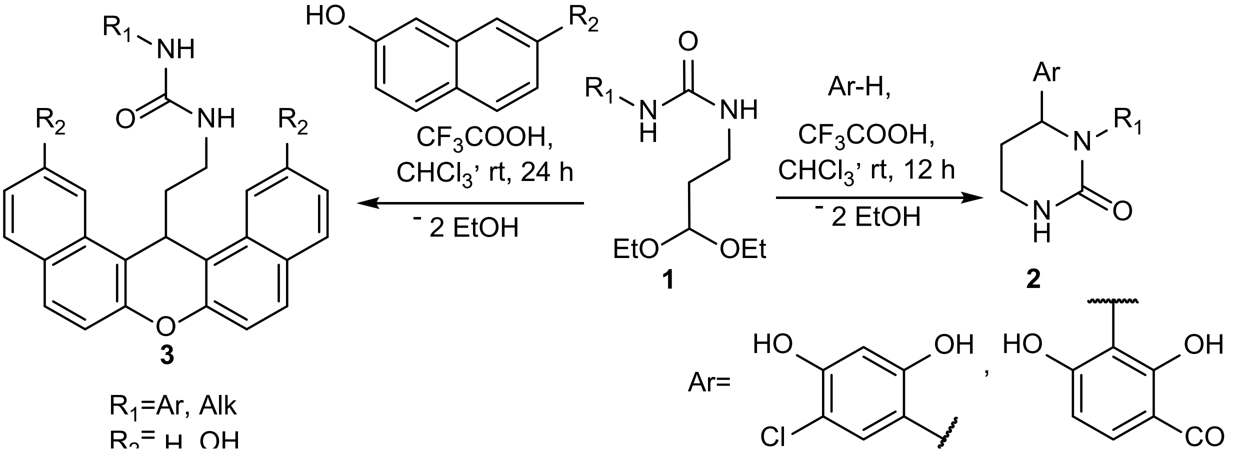
Cyclic urea derivatives – tetrahydropyrimidin-2(1*H*)-ones are known for their pharmacological activity. According to the References, some of these heterocyclic compounds are inhibitors of dihydroorosyase, HIV protease and topoisomerase. In this paper, a new approach to the synthesis of tetrahydropyrimidin-2(1H)-ones and dibenzoxantenes containing urea fragments has been proposed. The method is based on the reaction of 1-(3,3-diethoxypropyl) urea with phenols. Reaction of 1-(3,3-diethoxypropyl) urea **1** with phenols in the presence of an acid catalyst leads to the formation of new heterocyclic compounds - tetrahydropyrimidin-2(1H)-one derivatives **2**. Using 2-naphthol and 2,7-naphthalenediol as substrates leads to dibenzoxanthene derivatives **3**. The advantages of the method include the high yield of the target compounds, mild reaction conditions and the absence of the need to use expensive reagents.



The reported study was funded by RFBR according to the research project № 18-33-00206.

HYPERVALENCY AIDED ROUTE TO 3,3,3-TRIFLUOROPROPENYLATED HETEROCYCLES

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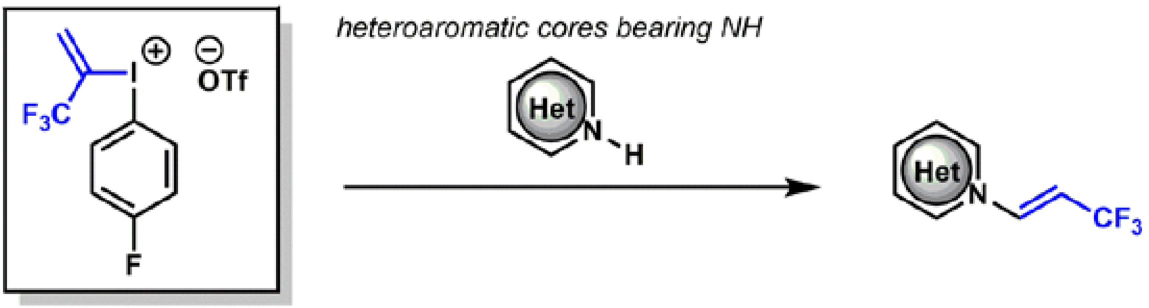
The synthesis of trifluoromethyl containing compounds are valuable transformations for organic and pharmaceutical chemistry. Despite of the wide range of their application, the efficient synthesis can be still challenging.

Previously, we designed a novel alkenyliodonium salt for synthesis of *N*-substituted-(2-trifluoromethyl)aziridines.[1] The iodonium salt is bench stable, nevertheless shows excellent reactivity towards *N*-nucleophiles without the need of transition metal catalysis under mild conditions.

Slightly changing the optimal parameters, we were succcessfully able to use our iodonium salt to form *N*-3,3,3-trilfuoropropenylated heteroaromatic compounds, methods often described through harsh and/or multistep reactions in recent References.

We explored the scope of reaction, and found to be a robust and simple tool for the incorporation of trifluoropropenyl group with a generally excellent stereochemical selectivity resulting (*Z*) configuration. Regarding the heteroaromatic compund, we found almost no steric and electronic limitation.



good functional group tolerance

mild and simple reaction conditions
catalyst free, cheap base

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SYNTHESIS AND USE OF MICROPOROUS OPTICALLY TRANSPARENT POLYMERS AS SORBENTS OF ORGANIC REAGENTS

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Quantitative determination of metal ions using test systems is required in medicine, ecology and food industry [1, 2]. In the most convenient form, they are solutions of organic reagents (OR) or solid carriers with fixed (immobilized) OR.

In this work, optically transparent microporous polymers were obtained as a substrate for immobilization of OR. Polymer synthesis is based on the sequential polyaddition of octamethyl-cyclotetrasiloxane and 2,4-toluene diisocyanate to macro-initiators of anionic nature, which are block copolymers of propylene oxide and ethylene oxide (PPEG), part of the hydroxyl groups of which are replaced by potassium alkoxide.

It has been established that the most favorable conditions for obtaining a polymer substrate with a high sorption activity are the conditions that promote the maximum involvement of octamethylcyclotetrasiloxane in the polyaddition process. This circumstance is due to the release of the flexible-chain polyether-polysiloxane component into a separate microphase capable of holding a large amount of sorbate-OR. It is shown that the flexible chain component, which is a block copolymer based on PPEG and polydimethylsiloxane, is located on the surface of microvoids.

The diffuse reflectance spectra of the Pb(II) complex with arsazen were obtained. In traditional chemical analysis, lead with arsazen in alkaline solutions forms strong coordination compounds extracted with butanol; in its spectrum there is a band with absorption at λ_{max}=480-485 nm. Impurities mask sulfosalicylic acid, thiourea, $K_4[Fe(CN)_6]$, NH_4F. Immobilization of the complex on the developed polymer substrate differs from the traditional method and does not require the use of organic solvents. For this system, there is a bathochromic shift of 75-80 nm. It is determined on films that the maximum absorption wavelength of the reagent is 400 nm, and that of the complex is 560 nm. There is also the effect of solvatochromia inherent in systems with carbonyl groups.

To understand the effect achieved, it should be noted that the block copolymers of propylene oxide and ethylene oxide are open-chain analogues of crown ethers, which are active complexing agents. This circumstance, together with the fact that a copolymer with polydimethylsiloxane is formed and located on the surface of the void, is the cause of the optical activity of the films. The presence of polydimethylsiloxane in the same microphase with the open-chain analog of crown ether, apparently, reduces the spatial interference with the ability to complex the latter.

This work was supported by Russian Foundation for Basic Research (RFBR), grant 19-03-00280.

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PREDICTION OF IC50 VALUE FOR GLUTAMATE RECEPTOR AND METHYLENE BLUE DERIVATIVES USING DIFFERENT MODELS

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Using methods of molecular modeling and available data on inhibitory activity of 23 compounds we have generated models predicting IC50 values for the rat NMDA-receptor. Three types of models were built: two ligand-based models and one target-based model.

The first type model was based on CoMFA. The molecules were aligned by ligand structure only. The second type also used CoMFA approach but alignment was obtained by docking procedure. The third type based on MM-PBSA (MM-GBSA) energy terms calculated for the complexes obtained after docking and molecular dynamics simulation. The quality and predictive ability was tested in leave-one-out cross-validating procedure.

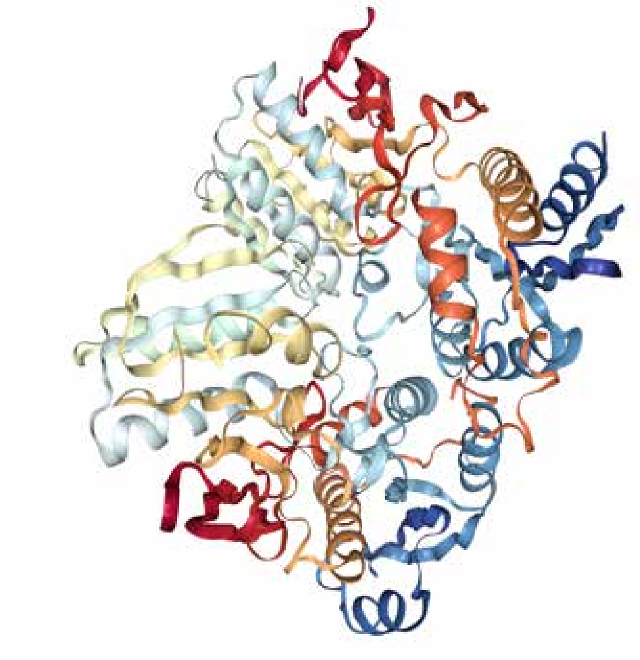

Fig. 1. Structure of rat NMDA-receptor.

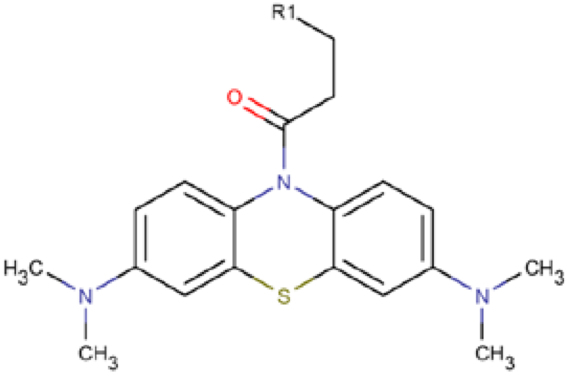

Fig. 2. The same part for 23 ligands derivatives of methylene blue.

P-TOLYLSILOXANES AS A PROMISING BUILDING BLOCKS FOR THE SYNTHESIS OF FUNCTIONAL ORGANOSILICON COMPOUNDS — *P*-CARBOXYPHENYLSILOXANES.

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In the present work, general synthetic approaches to the preparation of *p*-tolylsilanes and siloxanes are proposed as promising precursors for the synthesis of functionalized organosilicon compounds [1, 2]. To obtain siloxy, ethoxy- and hydride-silanes and siloxanes various, specially developed, synthetic approaches were used.

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COMPARISON OF DIFFERENT WAYS TO DESCRIPTION METHODS FOR CHEMICAL REACTIONS IN THE MODELING “ STRUCTURE - REACTIVITY ”

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Currently, more and more attention is drawn to chemical reactions as objects of QSAR/QSPR modeling. One of the problems in this area is the search of optimal representations for reactions that could describe the correlation between the structure of the reaction and the reactivity for various data sets.

In this work, comparison of methods for characterization of chemical reactions by using different descriptors was carried out. Following approaches for reaction’s representations were compared: (1) condensed graphs of reactions (CGR) descriptors, (2) only reactants or (3) only reaction products descriptors, (4) concatenation of descriptors of reactants and products, (5) differential descriptors (the descriptors difference of reactants and products). ISIDA fragment descriptors [1] were used in our study. Moreover, differential fingerprints from RDKit, presented in previous works [2-4] were applied for representation of reaction.

Four data sets of reactions (bimolecular nucleophilic substitution (SN2), bimolecular elimination (E2), Diels-Alder (DA) rate constants and tautomerization (Tautomer) equilibrium constants) which used by us in previously published articles were used for benchmarking study (Fig. 1).

Based on obtained results, we concluded, that each of the considered methods of representing reactions can be used to model the relationship structure - reactivity. Moreover, models based on condensed graphs of reactions show, on average, better quality of results than other methods of representing reactions.

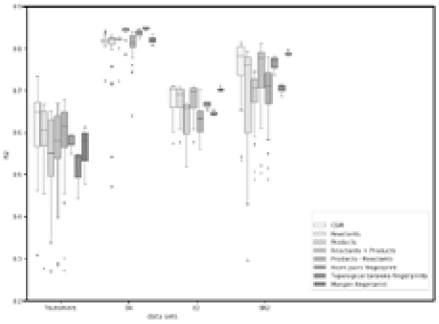

Fig. 1. The distribution coefficient of determination values after cross-validation model.

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OBTAINING OF WATER-SOLUBLE METAL COMPLEXES BASED ON SODIUM PECTINATE

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Mironov V.F., Milyukov V.A.

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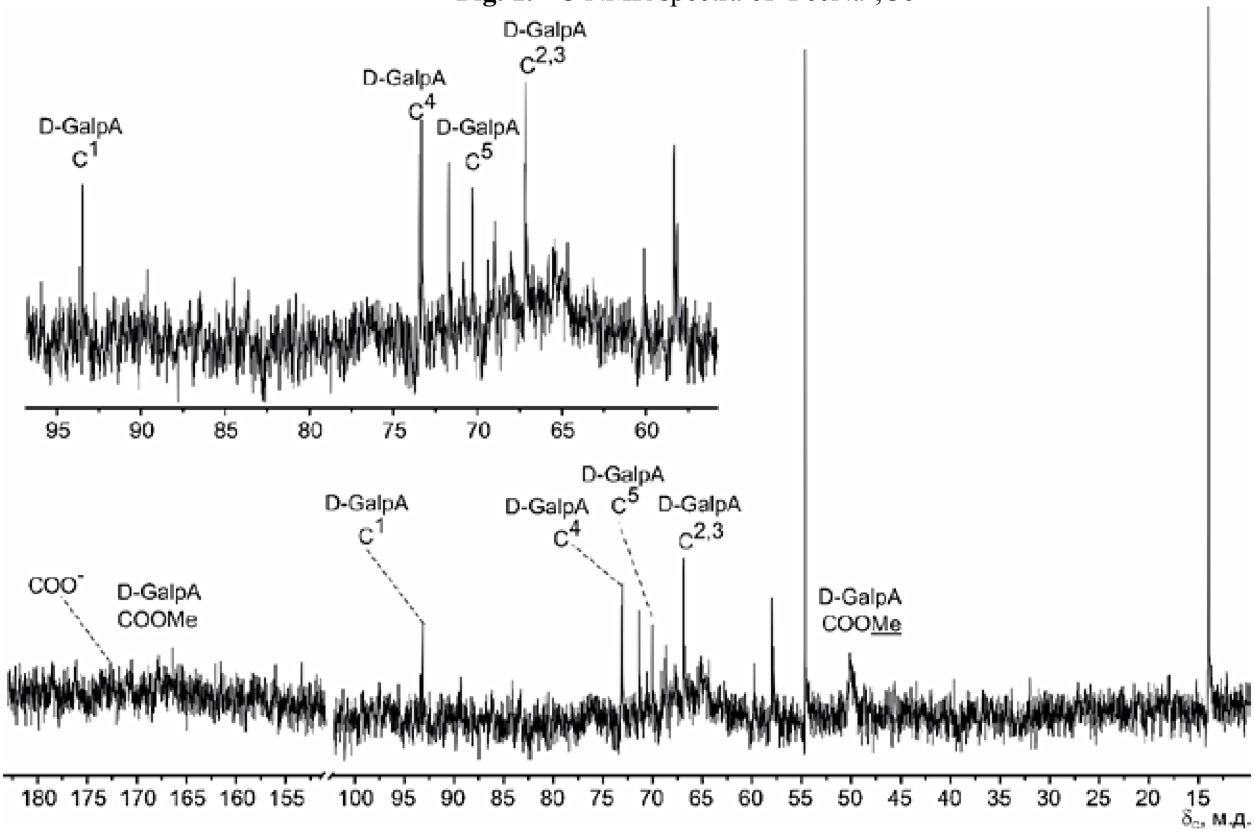
Based on sodium pectinate, the new water-soluble complexes, containing assimilable bivalent ions of biogenic metals (Ca, Mg, Co, Ni, Cu, Fe, Zn) were synthesized [1]. The obtained compounds are promising, since they contain trace elements, necessary for many vital processes in the organism, in biologically available form, and are synthesized on the basis of matrix- carrier close to pectin. It is known that pectin polysaccharides have a wide spectrum of physiological activity, increase therapeutic efficacy and reduce the toxicity of drugs. IR spectroscopy was used to monitor the state of carboxyl groups in the region of stretching vibrations of the COO^- group (1500-1800 cm^{-1}). The obtained compounds were studied by a complex of physicochemical methods (NMR and UV spectroscopy, TGA / DSC, DLS, AFM). Figure 1 shows the ^{13}C NMR spectrum of sodium, cobalt pectinate (PecNa-,Co), which has antimicrobial activity.

Fig. 1. ^{13}C NMR spectra of PecNa-,Co



This work was supported by RFBR, № 18-03-00310.

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NEW CALIX[4]ARENE DERIVATIVES CONTAINING TRIAZOLYL AND ALKYL FRAGMENTS: USE IN MICELLAR CATALYSIS

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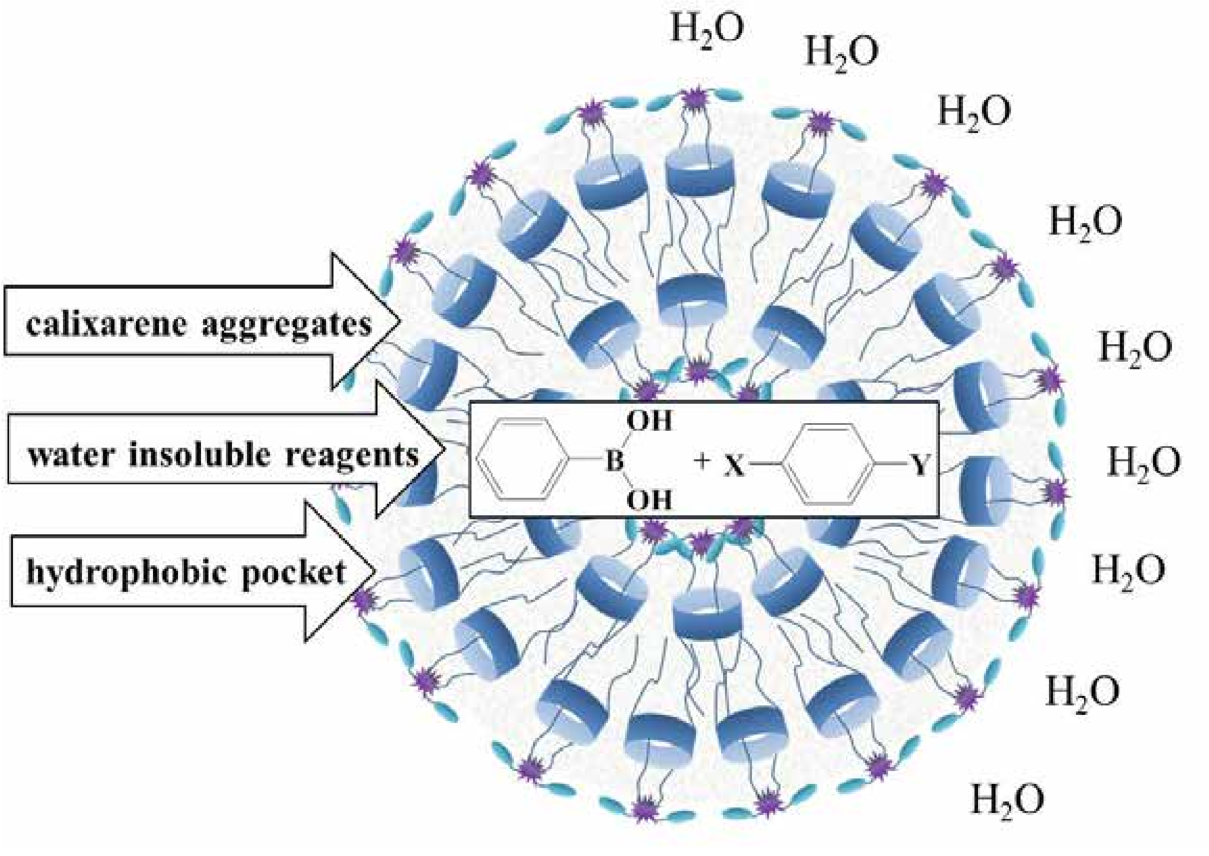
A series of amphiphilic calixarenes containing four 4,5-dicarboxytriazolyl fragments on the upper rim in the *"cone"* stereoisomeric form with different lipophilicity were obtained using azide-alkyne cycloaddition reaction. It has been shown that amphiphilic macrocycles containing four octyl or tetradecyl fragments on the lower rim forms monodisperse nanoaggregates in aqueous solutions. It was found that all obtained macrocycles have intensive blue fluorescence with a bathofluoric shift of the emission maximum upon increase of the concentration, which is consistent with the formation of aggregates. The resulting macrocycles were successfully used as a micellar environment for the Suzuki *coupling* reaction. Experiments demonstrated quantitative yields of the products of *coupling* between iodine and bromarenes with phenylboronic acid in an aqueous solution at room temperature.



We thank the Russian Science Foundation for the financial support of this work (grant No. 18-73-10033).

STRUCTURE AND REACTIVITY OF POWERFUL WATER-SOLUBLE OXIDIZING HYPERVALENT IODINE REAGENTS

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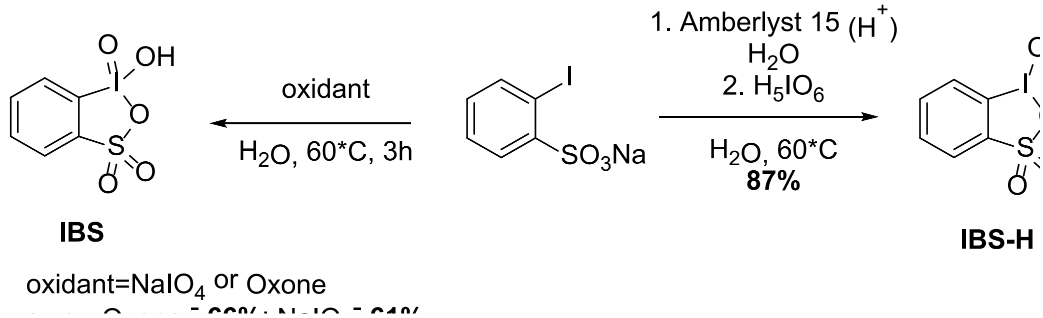
Hypervalent iodine reagents are versatile and eco-friendly reagents for different oxidative transformations of organic substrates. 2-Iodoxybenzenesulfonic acid (IBS) is a thia analogue of 2-iodoxybenzoic acid (IBX) with strong oxidative properties. IBS was not previously isolated in individual form because of its extremely high solubility in water and high reactivity towards organic solvents. [1]

We have developed a new procedure for the preparation and isolation of IBX and investigated its structure by X-ray analysis (Fig. 1). Furthermore, we have developed a new method for the preparation of the IBS reduced form, 2-iodosylbenzenesulfonic acid (IBS-H), with the use of periodic acid as an oxidant.



Scheme 1. Synthesis of 2-iodoxybenzenesulfonic acid (IBS) and 2-iodosylbenzenesulfonic acid (IBS-H)

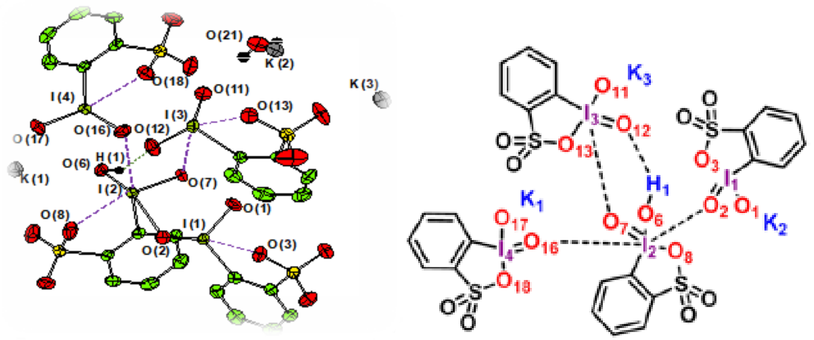


Fig. 1. X-ray structure and its representation in ChemDraw

We have shown that iodine (V) compound is formed under neutral conditions, while iodine (III) one, 2-iodosylbenzenesulfonic acid (IBS-H), which was previously described in [1], is formed in acidic media.

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REACTIONS OF 2-ALKOXYETHENYLTRYCLORPHOSPHONY HEXACHLOROPHOSPHATES WITH SULFUR ACID HYDROXYLAMINE

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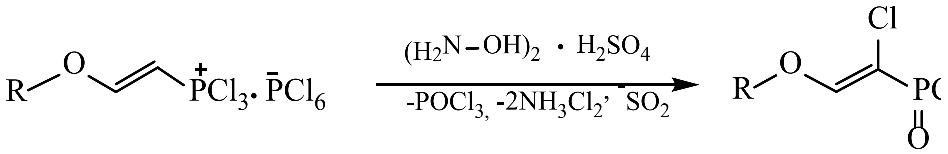
As is known, reactions of phosphorus pentachloride with various C-, O-, S- and N-nucleophiles (alkenes, alkadienes, alkynes, ethers and esters, acetals, sulfides, tertiary amines, amides, etc.) are one of the common methods for obtaining unsaturated compounds with a phosphorus-carbon bond. The structure of the formed compounds substantially depends on the method of transformation of intermediate adducts. We have previously shown that when dimethyl sulfate is used as a transformer, the formation of a phosphoryl group is accompanied by chlorination of a double bond [1]. Sulfuryl chloride effects on the adducts in a similar manner [2].

In continuation of works [1-3], we have studied the interaction between 2-alkoxyethenyl-trichlorophosphonium hexachlorophosphates (**1a, b**) and hydroxylamine sulfate. We have been shown that adducts (**1a, b**) easily react with hydroxylamine sulfate at room temperature with the formation of 2-alkoxy-1-chloroethenylphosphonic acid dichloroanhydrides (**2a, b**):



$$\xrightarrow[-POCl_3,\ -2NH_3Cl_2,\ SO_2]{(H_2N-OH)_2\ \cdot\ H_2SO_4}$$

1a,b **2a,b**

R=C_2H_5 (a), C_4H_9 (b)

This process can be explained by the fact that during the formation of the phosphoryl group, the formation of a by-product of sulfuryl chloride is possible, which further act as a chlorinating agent.

The structure of dichloroanhydrides (**2a, b**) was confirmed according to the data of the IR, NMR ^{1}H and ^{31}P spectroscopy, and the composition was confirmed by elemental analysis.

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AN ABNORMALSODIUM NITRITE INDUCED NEF REACTION OF β-SUBSTITUTED β-NITROSTYRENES

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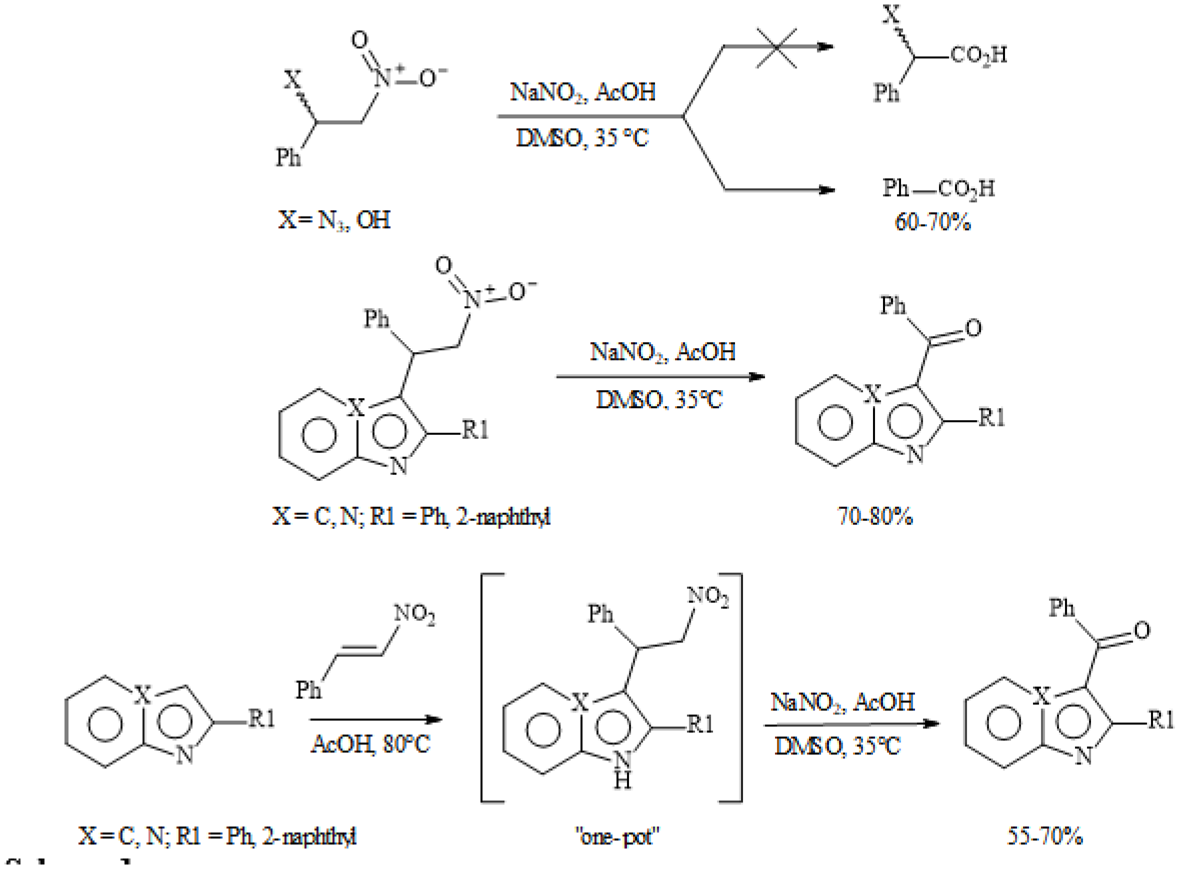
An improved mild method for the conversion of primary and secondary nitro compounds to their corresponding carboxylic acids and ketones in the presence of $NaNO_2$/AcOH [1,2] is shown to be an important extension of the Nef reaction, especially in cases of unstable or sensitive molecules such as, for example, protected β-nitroamines [3]. However, our attempts to apply this procedure to β-hydroxy- or β-azido-β-nitrostyrenes led to benzoic acid as the only product instead of expected carboxylic acid derivatives (Scheme 1). In turn, atypical products as well —phenyl heterocyclic ketones — were obtained in this reaction if the 3-(2-nitro-1-phenylethyl) indole and imidazopyridine derivatives were used as starting materials (Scheme 1). The latter observation led us to the development of "one-pot" synthesis of above-mentioned ketones through the nitrostyrene Michael addition followed by the discussed $NaNO_2$ induced nitro to carbonyl conversion (Scheme 1). Presumably, this kind of domino process could serve as a synthetic equivalent of Friedel Crafts acylation of electron-rich heterocycles — an assumptionwhich is currently under our evaluation.



Scheme 1.

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SYNTHESIS, STRUCTURE AND PROPERTIES OF CARBOXYLATE PHOSPHABETAINES BASED ON 3- (DIPHENYLPHOSPHINO) PROPIONIC ACID AND UNSATURATED AMIDES

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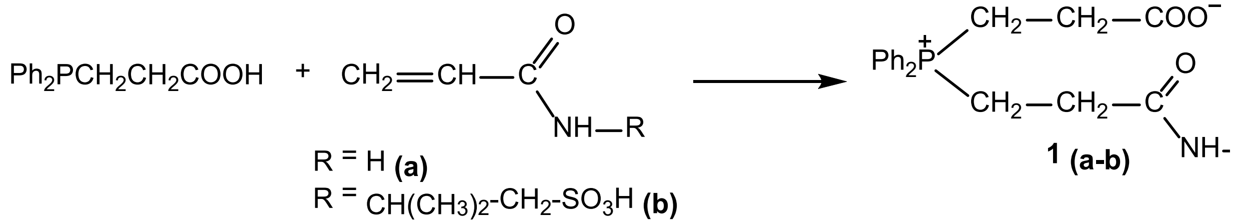
The interaction of 3- (diphenylphosphino) propionic acid with unsaturated amides (acrylamide, 2-acrylamido-2-methylpropanesulfonic acid) leads to formation of corresponding stable phosphabetaines **1(a-b)**. The betaines structure was confirmed by a set of physical, chemical and physicochemical methods (IR, NMR, elemental analysis)



In the interaction of obtained phosphabetaine **1a** with bromoalkanes (the length of hydrocarbon radical of bromoalkanes varies from 10 to 16 carbon atoms), the corresponding phosphonium salts **2(a-d)** are formed:

The antimicrobial, antimycotic and bactericidal activity of the synthesized phosphonium salts **2(a-d)** was studied. The highest biological activity of synthesized compounds shows the substance **2a** (contains C10 alkyl chain).

Antimicrobal activity (growth inhibition zone, mm) of compoumds **2(a-d)** (c = 100 µg/0.1 mL)

Compounds	***E. coli***	***B.cereus***	***Ps. aeruginosa***	***S. aureus***	***Candida albicans***
2a	19	20	10	17	23
2b	8	16	-	14	16
2c	15	10	-	15	14
2d	-	8	-	-	12
1a	-	-	-	-	-

Antifungal and bactericidal (growth inhibition zone, mm) of compoumds **2(a-d)** (c = 100 µg/0.1 mL)

Compounds	**Shigella**	**Salmonella**	**Klebsiella**	**Acinetobacter**	**Enterococcus**
1	10	12	15	16	10
2	10	8	10	10	-
3	10	8	8	10	-
4	-	-	-	-	-
5	-	-	-	-	-

This work is performed according to the Russian Government Program of Competitive Growth of Kazan Federal University.

GENERATE BIOISOSTERIC SUBSTITUTIONS USING THE CONDENSED GRAPH OF REACTION APPROACH.

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Creating a drug begins with a search for a hit with the desired pharmacological activity. However, the hit may have undesirable side effects or may have poor pharmacokinetic characteristics. Therefore, it is necessary to modify the structure of the hit in order to increase its solubility, reduce toxicity and improve the selectivity of action. To solve these problems, one can apply the approach of bioisosteric substitutions.

In most cases, it is not known which replacement will lead to a change in biological activity and which one will not. The goal of this work was to propose a model was that could recommend such modifications and would not lead to a loss of the biological activity of the substance.

The development of the model was based on condensed graph of reaction (CGR) approach. CGR is a representation of the reaction as a pseudomolecule , which has additional features, which show changes in the transformation process. This representation simplifies the extraction of substituted and replacement groups. These groups can be used as a template to generate all possible bioisosteric replacements that can be extracted from the original data set.

The CGR approach was used to represent matched molecular pairs (MMP) in such a way that each MMP turned into a transformation of one compound into another. Thus, for the ligands with known IC50 activity for 16 biotargets from the ChEMBL database, 149890 MMP were generated. These MMP were used to construct classification models using the Random Forest machine learning method for bioisosteric replacements of each target.

The approach was tested on a sodium-dependent serotonin transporter biological target, and fluvoxamine was used as template for bioisosteric replacement. The model suggested 79 bioisosteric substitutions. Among them clovoxamine, which was not annotated in the training set from ChEMBL, but has inhibitory activity against the target was detected.

As a result, a model that can predict bioisosteric substitutions was obtained. The developed algorithm can successfully predict new bioisosteric substitutions for molecules. The models for 16 biological targets were built.

The approach was developed as part of a project supported by the Ministry of Education of Youth and Sports of the Czech Republic, agreement MSMT-5727 / 2018-2, as well as the Ministry of Higher Education and Science of the Russian Federation, agreement 14.587.21.0049 (unique project identifier RFMEFI58718X0049).

REDOX-RESPONSIVE POLYMER NANOCONTAYNERS BASED ON SULFONATED VIOLOGEN CAVITANDS

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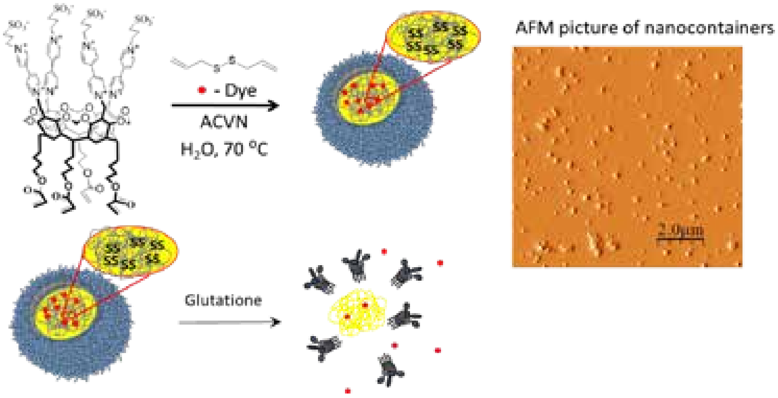
Creation of systems for controlled drug delivery is actual goal of modern research. The necessarily in such systems is caused by low stability some drugs, their low solubility, non-specific distribution in cells and tissues, fast metabolism and quick removal from the body. Nanocarriers are important components in modern drug delivery systems. They increase bioavailability of the drugs, protect and stabilize sensitive substrates (e.g. proteins), minimize side effects of the drugs and provide target delivery.



We present new redox-responsive polymer nanocontainers, which can be used as nanocarriers for controlled drug delivery. The carrier consists of a redox-sensitive hydrophobic core and a multiply charged shell. The core can be destroyed by the thiol-containing reducing agents such as glutathione. The use of sulfonated viologen-cavitand promotes to the targeted delivery of the substrate to cancer cells. Polymer nanocontainers have been used for glutathione-controlled release of dyes.

This work was funded by Russian Foundation for Basic Research (RFBR № 19-03-00429) and the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (4.1493.2017/4.6 and 4.5151.2017/6.7).

DISPERSE SYSTEMS BASED ON THE PESTICIDE ROUNDAP AND SUCCINIC ACID IN A WIDE RANGE OF CONCENTRATIONS: THE RELATIONSHIP OF SELF-ORGANIZATION, PROPERTIES AND BIOEFFECTS

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Recently, ecotoxicologists have been concerned about the negative effect of the pesticide Roundap **(R),** active ingredients of which are glyphosate and surfactant polyethoxylated tallow amine, on the condition of humans and aquatic animals [1]**.** Reducing the toxicity of pesticides, designed to ensure the safety of their effects on the body and the environment with comparable efficiency, can be achieved by reducing the concentrations or combining with a nutrient. To implement these approaches, we chose succinic acid **(SA),** which is a plant growth stimulator and antioxidant. Presently [2–4]**,** it has been established that the appearance of a bioeffect in the region of low concentrations is due to the formation and rearrangement of nanoassociates. The aim of the work is a comparative study of the physicochemical methods of self-organization, physicochemical properties and spectral characteristics of aqueous systems based on **R** ($1\cdot10^{-1}$-$1\cdot10^{-19}$g/l), in the absence and presence of **SA** ($1\cdot10^{-3}$-$1\cdot10^{-13}$ g/l), in a wide range of concentrations of both components. A comparative study of the influence of **R, SA** and **R + SA** systems on the growth and development of plant and animal organisms (*Triticum vulgare* wheat roots, *Ceriodaphnia affinis cladocerants* and *Chlorella vulgaris* unicellular algae) was also conducted.

A study of DLS and UV**-**spectroscopy **R, SA** and **R + SA** in a wide range of concentration revealed the ratios of components at which the formation of a mixed aqueous-organic dispersed phase with a size of hundreds of nm with a characteristic absorption band in the UV spectrum is observed, similarly to [5]**.** It is shown that the **R + SA** systems in which a mixed dispersed phase is formed differ significantly from individual **R** and **SA** in the degree and sign of the effect on plant and animal organisms.

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CONSTRUCTION OF BIOLOGICAL ACTIVE AZOLOAZINES ON METALLOCENES MATRIX

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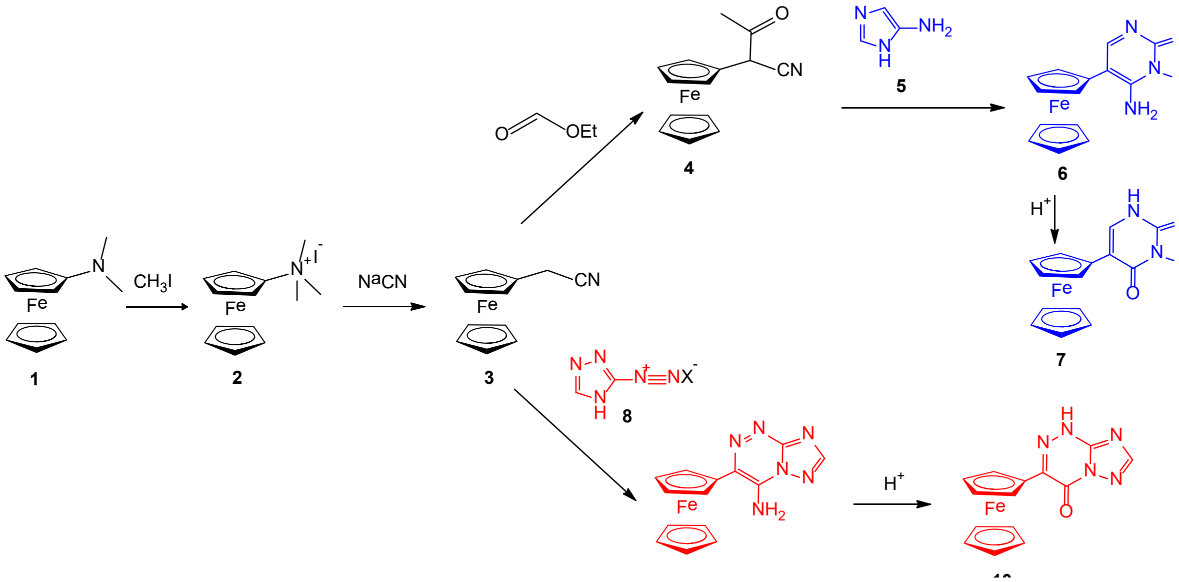
It is known that the introduction of the ferrocenes fragment into the structure of a physiologically active compound allows modulating the properties of the resulting compound, as a rule, enhancing them. The most relevant in this regard are derivatives of the azoloazines series due to the fact that their structure is close to be structure of nitrogenous bases. Azoloazines have a wide range of physiological activities, including antifungal agents (Fluconazole, Hexaconazole), antiviral (Ribavirin, Triazavirin) or antibacterial activities, drugs of triazolobenzodiazepines range (Estazolam, Triazolam, Alprazolam) and other [1].



Scheme 1. Synthesis of ferrocene containing azoloazines.

The new ferrocenes derivatives have been obtained by the construction of azines fragment on the metallocenes matrix (Scheme 1) for the new physiologically active compounds design including ferrocene containing derivative of Triazavirin.

This work was supported by the Ministry of Education and Science of the Russian Federation (Project № 4.6351.2017/8.9) and Foundation Act 211 Government of the Russian Federation, contract № 02.A03.21.0006.

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AMINOMETHYLATION OF THE HELIOMYCIN ANTIBIOTIC

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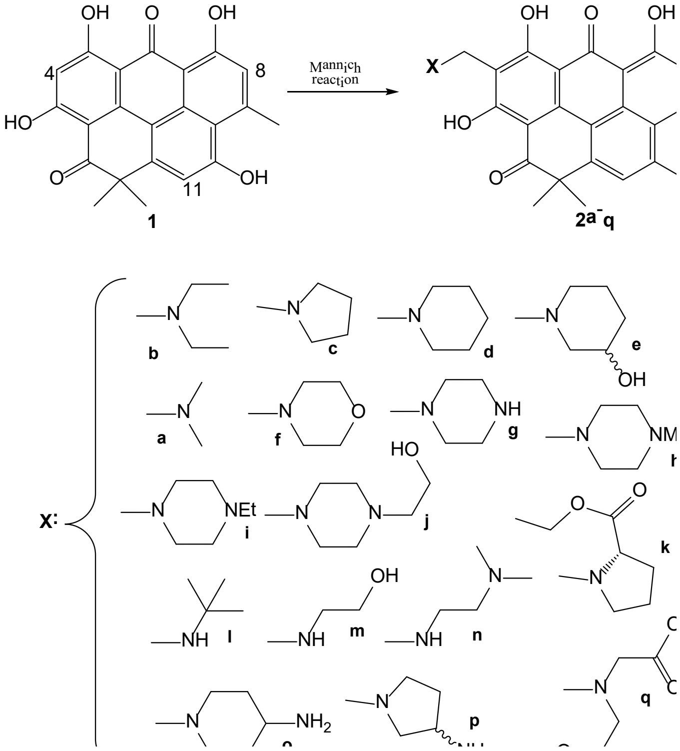
Heliomycin (**1**) is a secondary metabolite produced by some *Streptomyces* bacteria. This antibiotic possesses some important properties such as antiviral, antibacterial and antiproliferative activity make it extremely promising to modify its structure. However, poor solubility of the antibiotic severely limits its researching [1]. Conditions for the selective aminomethylation of the benzopyrene nucleus in the 4-position by the Mannich reaction were found (Scheme 1). It is important to note that transformation proceeds just in 4 position of the structure due to the presence of two electron-withdrawing substituent nearby.



Scheme 1. Modification of heliomycin by Mannich method

A series of new derivatives was obtained by two different methods - for **2a**: by reaction of heliomycin with N,N-dimethyl(methylene)ammonium chloride in DMF at 75 ºC and for **2b-q** by reaction of **1** with an aqueous solution of formaldehyde with the corresponding amine in acetic acid at 40 ºC. Synthesized structures were confirmed by NMR and HRMS. Synthesized derivatives **2a-q** possess cytotoxicity, which evaluated on a panel of mammalian tumor cells including colon adenocarcinoma HCT116 and K562 with its MDR sublines, murine leukemia L1210, human T-cell leukemia CEM and cervical carcinoma HeLa. The majority of new derivatives **2a-q** effectively killed tumor cells (IC$_{50}$ values in the low micromolar to submicromolar range) [1].

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SYNTHESIS OF FUNCTIONALIZED PHOSPHACOUMARINS

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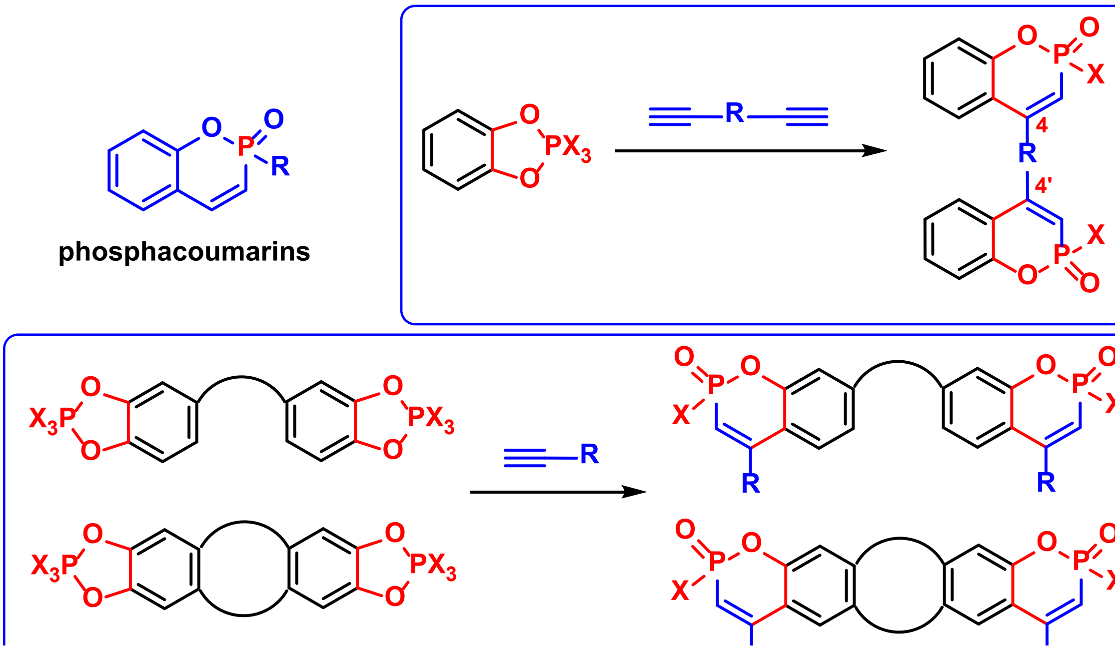
Phosphacumarins (areno[*e*]-1,2-oxaphosphinins) are an interesting heteroatom derivatives of the natural compounds. The presence of inhibitory activity against HIV protease and protein tyrosine phosphatase has been established for phosphacoumarins [1]. One of the most convenient ways to produce 4-substituted areno-1,2-oxaphosphinins is the reaction of areno-1,3,2-dioxaphospholes with acetylenes [2,3]. Herein the data on the development of approaches to the synthesis of functionalized areno-1,2-oxaphosphinins, in which two oxaphosphinin fragments are conjugated at position 4 or in an arene moiety, are presented (Scheme 1).



Scheme 1.

Two approaches to conjugated oxaphosphinins have been implemented: the first is based on the reaction of areno-1,3,2-dioxaphospholes with aromatic or aliphatic diacetylenes, the second – on the reaction of bridged diphospholes with acetylenes.

This work was funded by RFBR (grant №19-03-00730) and by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (4.5151.2017/6.7).

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NOVEL STRAIGHTFORWARD APPROACH OF SYNTHESIS OF BIARYL N,O-LIGANDS

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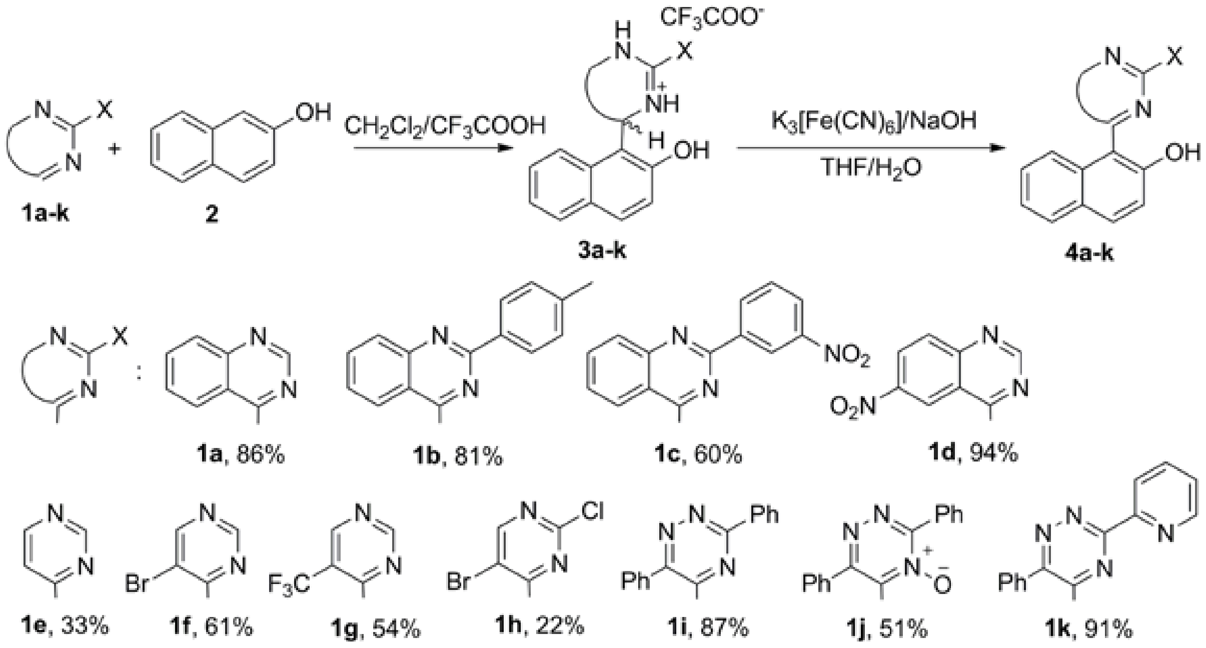
QUINAP is first example of successful azinyl-naphthyl atropoisomeric ligand for asymmetric synthesis. (*R*)- or (*S*)-4-(2-Diphenylphosphino-1-naphthyl)quinazolines (QUINAZOLINAPs) are analogs of QUINAP.

Key step of synthesis azine containing biaryls is formation of C-C bond between initial (hetero)arenes. There are known a few approaches to obtain precursor of QUINAZOLINAP. The first method based on Pd-catalyzed Suzuki cross-coupling reaction of 4-chloroquinazoline with 2-methoxy-1-naphthylboronic acid [1].

The direct C-H/C-H-coupling of quinazoline and 2-hydroxynaphthalene can be carried out based on the reaction of nucleophilic aromatic substitution of hydrogen (S_N^H reaction). S_N^H reactions don't require preliminary functionalization of initial reagents and the use of metal catalysts.

We have found that synthesis of **4a**-**k** is easily implemented by the direct coupling azines **1a**-**k** and 2-naphthol in absence of metal catalysis (Scheme 1). The process proceeds in two steps. The first step involves an addition of nucleophile to electron-deficient arenes **1a**-**k** to give the σ^H-adducts **3a**-**k** followed by oxidation into the corresponding compounds **4a**-**k**.



Scheme 1. Synthesis of biaryl N,O-ligands

S_N^H reaction of azines **1a**-**k** with 2-naphthol can proceed both with isolation of adducts **3a**-**k** and *one-pot*.

The research was financially supported by the Russian Foundation for Basic Research (18-33-00927).

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SEQUENTIAL ONE-POT FOUR-COMPONENT REACTION OF INDOLES, AROMATIC ALDEHYDES, ISOCYANIDES AND ALCOHOLS

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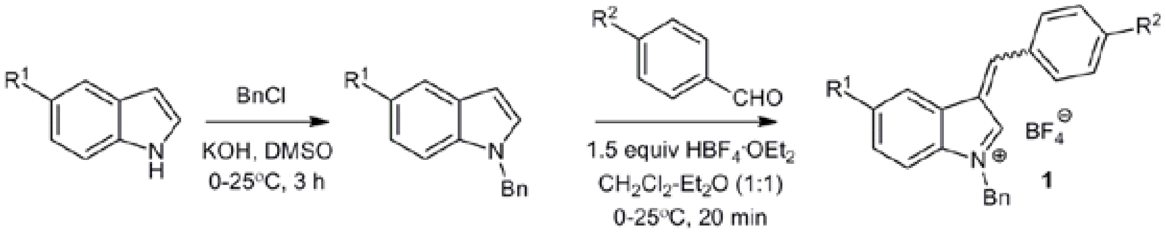
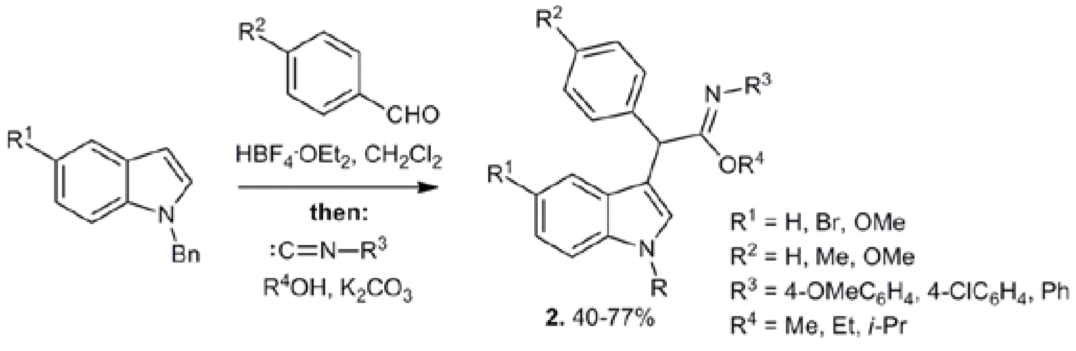
Multicomponent reactions (MCR) serve as a powerful and widely used instrument in organic synthesis [1]. A special place among them is occupied by transformations with the participation of isocyanides, unique reagents where nucleophiles and electrophiles attack the same atom [2].

To the best of our knowledge, reactions of alkylideneindolenines or the corresponding salts with isocyanides have not been published yet. 3-Arylidene-3*H*-indolium salts **1** were obtained by alkylation of corresponding indoles followed by reaction with aromatic aldehydes in conditions similar to a previously published procedure [3].



Herein, we report the possibility of imidate synthesis from the indole and the aldehyde by a sequential one-pot four-component process, without isolation of the corresponding 3-arylidene-3*H*-indolium salt. After acid-catalyzed condensation of the aldehyde with 1-alkylindole, an excess of K_2CO_3 and a solution of isocyanide in the appropriate alcohol were added to the reaction mixture. As a result imidates **2** were obtained in moderate to high yields.



The structure of synthesized compounds was confirmed by IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectra.

This work was supported by the Russian Science Foundation (grant 18-73-10099)

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DESIGN AND INVESTIGATION OF THE SUPRAMOLECULAR COMPLEXES BASED ON CYANINE DYES CONTAINING TERMINAL AMMONIUM GROUPS WITH MACROHETEROCYCLIC MOLECULES

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The "host-guest" complexes of macrocycles with organic molecules, in which the guest molecule has a chromophoric moiety, are of particular interest for supramolecular photochemistry.

In order to elucidate the possibility to construct photoactive "host-guest" complexes based on cyanine dyes as a guest and the influence of their structure on the properties of supramolecular complexes, we synthesized cyanine dyes with terminal ammonium groups in the *N*-substituents of heterocyclic residues [1]. The presence of primary ammonium groups capable of hydrogen bonding enables self-assembly of the dye with macroheterocyclic molecules containing electron-donating oxygen heteroatoms to form supramolecular complexes.

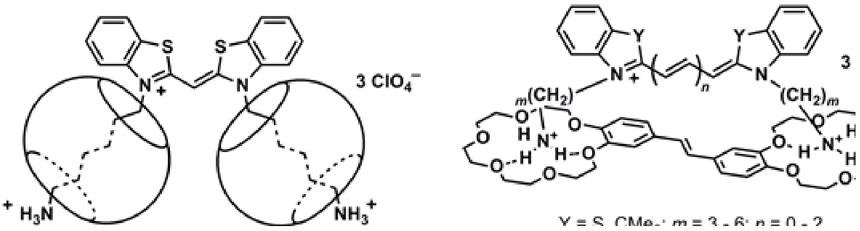

Fig. 1. The "host-guest" complexes of cyanine dyes with macrocycles.

We demonstrated the possibility to construct the supramolecular systems based on cyanine dyes with two ammonioalkyl *N*-substituents using their complexes with cucurbit[7]uril and bis(18-crown-6)stilbene as an example.

Supramolecular complexes with cucurbit[7]uril were investigated. It was shown that inclusion of the dye molecule into cucurbituril cavity highly influence dye fluorescence spectra.

It was also shown that stilbene form highly stable bimolecular and relatively unstable trimolecular complexes in which the dye ammonium groups are hydrogen-bonded to the crown ether moieties of stilbene and their □

THE ADDITION REACTIONS ON DOUBLE BONDS OF FLUORODINITROALKYLOLEFINS.

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Starting with fluorodinitroalkanols new series of fluorodinitroalkylolefins have been synthesized by dehidration (P_2O_5 in absolute benzene) according the scheme:

$F(NO_2)_2C\text{-}CH_2\text{-}CH_2\text{-}CH(OH)\text{-}R \; > \; F(NO_2)_2C\text{-}CH_2\text{-}CH{=}CH\text{-}R.$

If R are different alkyls (methyl, ethyl etc.) the products are mixture of olefinic isomers, for example 5-fluoro-5,5-dinitropent-en-1 and 5-fluoro-5,5-dinitropen-ten-2. When R are aryls (phenyl, tolyl xylyls etc.) we have only one product, for example, 4-fluoro-4,4-dinitro-1-phenylbutene. The olefins in question were used in reactions of chlorination, bromination, nitration with nitrogen tetroxide, and *cis*-hydroxylation with $KMnO_4$ according Wagner. Spectral data and properties of the reaction products were studied.

TRANSITION STATE OF A RADICAL DECOMPOSITION OF CN BOND IN NITROBENZENE ACCORDING TO QUANTUM CHEMICAL CALCULATION

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Structure determination of the transition state (TS) reaction radical decomposition of nitro compounds is a very difficult problem. Generally, radical-recombination reactions, formed at the homolytic breaking of a bond are non-activated. Its potential energy surface profile along coordinate reaction does not have pronounced maximum corresponding to the TS. This makes it impossible to use the classical version of the TS theory to determine the rate constant and Arrhenius reaction parameters. At the same time, there are various alternative options for calculating the kinetic parameters of the homolytic bond break in a molecule. In our work, we used Gibbs free energy equation, in order to calculate the structure of the TS reaction of the homolytic breaking of the CN bond in nitrobenzene (on the curves, there are changes of electronic energy and enthalpy in the course of the reaction, there is no maximum, Fig. 1). Calculation of oscillation frequencies, orthogonal reaction paths has been performed at each point of descent along the coordinate reaction of the formation of the CN bond at the interaction of nitroxyl and phenyl radicals (the reverse reaction of the breaking of the CN bond). The maximum structure found was taken as the TS structure of the indicated reaction. According to the B3LYP/6-31G (d,p), geometrics of the TS are shown on the Fig. 2. Similar geometric values are predicted by other calculation methods used in the work.

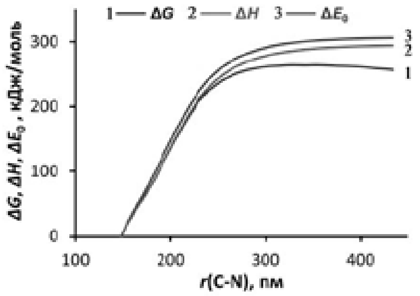

Fig. 1 – Calculated data on the change in Gibbs free energy (1), enthalpy (2) and electronic energy (3) of the reaction of the homolytic breaking of the CN bond in nitrobenzene, obtained using the B3LYP/6-31G(d,p) method. Values corresponding to the nitrobenzene molecule are taken as zero on the coordinate axis.

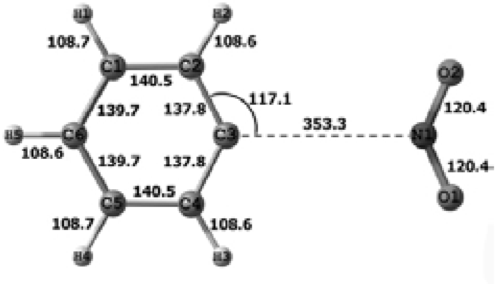

Fig. 2 – Geometrics of the TS reaction's homolytic breaking of the CN bond in nitrobenzene, found using the Gibbs free energy equation using the B3LYP/6-31G(d,p) method (bond length pm, angles in degrees).

REACTIVITY OF 3,5-DINITROPYRIDINE TOWARDS C-NUCLEOPHILES

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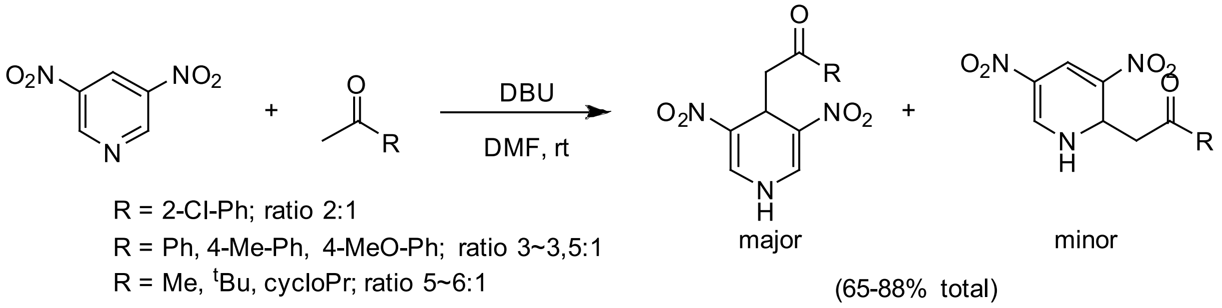
Nucleophilic substitution of aromatic nitro group is a well-known reaction, which is extensively used to introduce various O,N,S-substituents into aromatic and heteroaromatic systems[1]. This reaction doesn't have specific demands and can be applied to wide range of nitroarenes. On the other hand, nucleophilic addition is less common reaction in chemistry of nitroarenes and generally occures with C-nucleophiles and strongly electron-defficient hetarenes. Here we report a facile addition of various C-nucleophiles to 3,5-dinitropyridine.

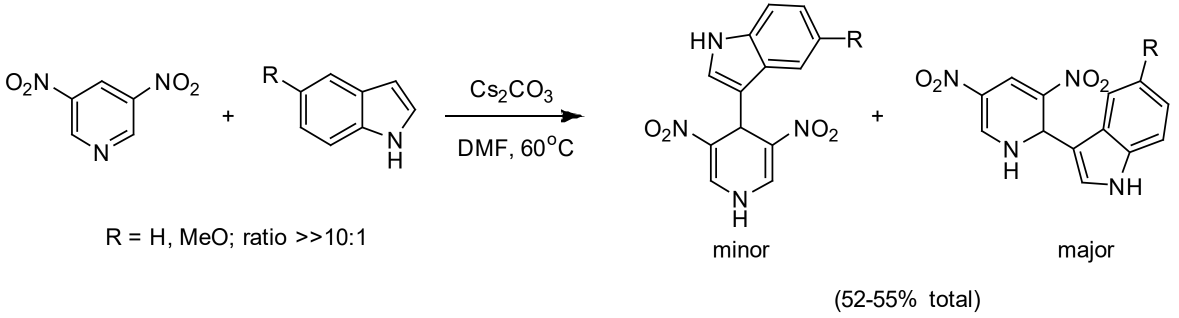
Methylketones readily react with 3,5-dinitropyridine under mild conditions, furnishing substituted 1,4-dihydropyridines as major products with variable amounts of isomeric 1,2-dihydropyridine. This reaction was shown to be general for both aliphatic and aromatic methylketones, although electron effects of substituent seem to have significant impact on product distribution. These compounds can be used to synthesize indole derivatives[2].



Scheme 1. Reaction of 3,5-dinitropyridine with methylketones

Chloroform can also be used under the same conditions with similar regioselectivity, allowing to directly introduce tricholoromethyl group.

Indoles show lower reactivity towards 3,5-dinitropyridine and require higher temperature for addition, but give 1,2-dihydropyridines as main products with very minor amounts of 1,4-isomer.



Scheme 2. Addition of indoles

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SYNTHESIS OF 2-AMINOPROPANE-1,2,3-TRICARBOXYLIC ACID.

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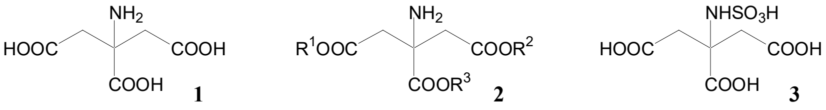
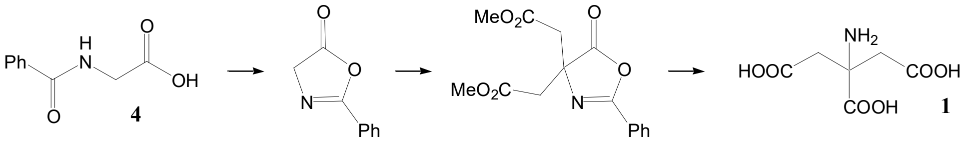
2-Aminopropane-1,2,3-carboxylic acid **1** is unnatural nitrogen equivalent of citric acid (Scheme 1). The biological properties of **1** and its derivatives are not well investigated. It is known that the acid itself and its calcium salts almost do not inhibit β-lactamases, while lipophilic esters **2** of the acid in some cases are quite effective inhibitors [1]. Also it was found that the sulfoderivative **3** acts as an inhibitor of calcification [2]. Our interest to the acid has appeared while we were looking for the symmetrical highly hindered α-aminoacid with hydrophilic substituent and devoid of biological properties.



Scheme 1.

The acid **1** is known since 1905 when it was firstly synthesized and characterized in the form of silver salts by means of Strecker reaction but only with poor yield [3]. Fifty years later the method was improved via Bucherer reaction but the utilization of highly toxic compounds has remained as the negative side of the synthesis [4]. Nonetheless the method was used in a number of works for the future thirty years. Two other major strategies that were applied for the acid **1** and its derivatives synthesis are alkylation of nitroacetic acid esters [5] and imine derivatives of glycine esters [1a, 1b]. They have different inconvenient features such as multistep process, expensive starting materials, column chromatography and work under high pressure of hydrogen. These shortcomings limit the use of the above methods large-scale synthesis.

We have developed new, convenient, cheap and laboratory friendly synthesis of 2-aminopropane-1,2,3-carboxylic acid **1** from commercially available hippuric acid **4** in three steps (Scheme 2) without application of toxic reagents, elevated pressure or high temperature reactions.



Scheme 2.

This work was funded by the Russian Foundation for Basic Research. Project № 19-03-00477

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REACTIONS OF 3,6-DI(*TERT*-BUTYL)-4,5-DICHLORO-1,2-BENZOQUINONE WITH DIFFERENT 1,1-DITHIOLATES. SYNTHESIS NEW BIFUNCTIONAL O-QUINONES.

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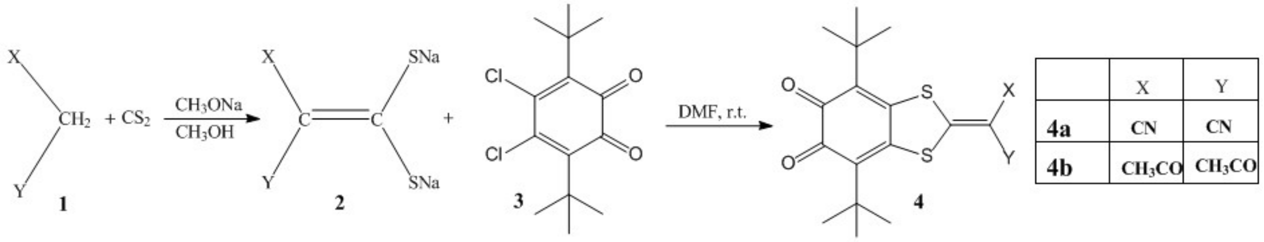
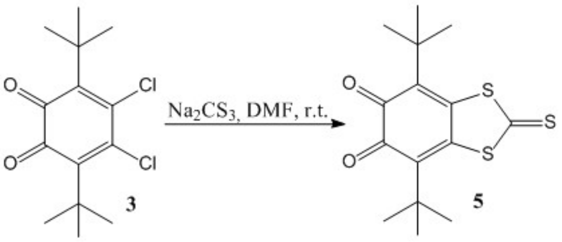
o-Quinones are both well-studied and promising redox-active chelating ligands. The functionalization of o-quinones is able to solve the problems of introducing additional coordination-capable fragments, free radical bearing groups into the molecule, as well as expand the range of redox properties. Functionalized o-quinones have prospects for use as building blocks in the construction of polyspin ordered systems with controlled switching between different magnetic states.

3,6-di(*tert*-butyl)-4,5-dichloro-1,2-benzoquinone **3** reacts with 1,1-dithiolates **2**, prepared from the reaction of CH-acids and carbon disulfide, to give 4,7-di(*tert*-butyl)-5,6-dihydroxy-1,3-benzodithioles **4**. The similar reactions of **3** with sodium trithiocarbonate gives **5**. The synthesized compounds were isolated and characterized by IR, NMR, ESR spectroscopy and X-ray crystallography.

To the best of our knowledge the dichlorinated o-quinone **3** [1] was first used to obtain a 1,3-dithiol derivative in the reaction with 1,1-dithiolates. The conditions for this reaction were optimized by selecting the solvent, reaction time and temperature.



	X	Y
4a	CN	CN
4b	CH_3CO	CH_3CO



The synthesized compounds obtained has been tested as bifunctional ligands for the preparation of redox-active transition metal complexes.

This work was supported by Russian Foundation for Basic Research (grant № 18-43-520025 r_a)

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CGRTOOLS: PYTHON LIBRARY FOR MOLECULE, REACTION AND CONDENSED GRAPH OF REACTION PROCESSING

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Chemical reactions are important objects in chemoinformatics which have been attracting the attention of researchers in last years. Many different tasks emerging in chemical synthesis were solved using chemoinformatics technologies. Computer representation of reaction is an important part of modeling workflow, in large extent determining the modeling performance. Among many various methodologies of reaction encoding, the Condensed Graph of Reaction (CGR) approach recently demonstrated its efficiency in structure-reactivity modeling, reaction condition prediction, metabolic reaction products ranking, atom-to-atom mapping error identification, substructure and reaction similarity search. There exist several universal tools that were developed for handling molecular information, both open-source and commercial, such as: OpenEye Toolkits, ChemAxon JChem, Indigo Toolkit, RDKit, CDK, Open Babel, CACTVS. Existing tools provide with relatively weak support of reactions. Only some simple operations for reaction are possible: extraction of reactants and products, some simple operations. To our knowledge, no public tool supporting CGR was developed so far.

Rise in interest to chemical reactions in last two-three years, as well as growing incorporation of Python-based libraries, motivated us to develop native Python based library CGRtools.

CGRtools is an open-source Python library aimed to handle molecular and reaction information. It is a sole library developed so far which can handle Condensed Graph of Reaction (CGR) handling. CGR provides the possibility for advanced operations with reaction information, and could be used for reaction descriptor calculation, structure-reactivity modeling, atom-to-atom mapping comparison and correction, reaction center extraction, reaction balancing and some other related tasks. Unlike other popular libraries, CGRtools is fully written in Python with minor dependencies on other libraries and cross-platform. Reaction, molecule and CGR objects in CGRtools support native Python methods and are comparable with the help of operations “equal to”, “less than”, “bigger than”. CGRtools supports common structural formats. CGRtools is distributed via L-GPL license and available on https://github.com/cimm-kzn/CGRtools.

This work was supported by Foundation the the Ministry of education, youth and sport of Czech Republic, agreement number MSMT-5727/2018-2 and by the Ministry of Education and Science of the Russian Federation, agreement No 14.587.21.0049 (unique identifier RFMEFI58718X0049).

PHOTOACTIVE SET OF THE CROSS-CONJUGATED α, α’-DIARYLIDENECYCLOALKANONES

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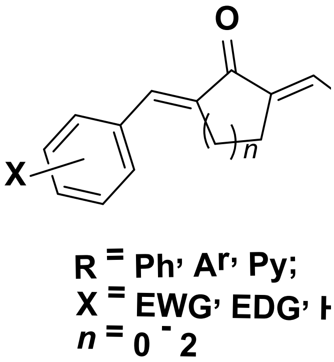
Cross-conjugated dienones of cyclic ketones are easy available compounds, therefore they are widely used as precursors for synthesis of carbo- and heterocycles. These substrates can be readily involved into photochemical reactions and might be served as photosensitizers and as featured ligands of light-sensitive coordination polymers build.[1] Moreover, changes of the aryl-substituent electron nature and insertion of various receptors allow to perform fine tuning of structure-spectrum mutual response.



Most promising examples of the wide library compiled from unsymmetrical dienones of the rather perspective planar C_4 and C_5 families. All substances were obtained in the best synthetic route and comprehensively described by spectral and analytical data. The most of all fascinating results were demonstrated via photocontrolled isomerization and solid state photochromic behavior.

This work was supported by the Russian Science Foundation.

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NEW COPPER-PALLADIUM CATALYSTS BASED ON FUNCTIONALIZED SILICAGEL FOR SELECTIVE HYDROGENATION OF BIFUNCTIONAL NITROARENES IN A FLOW MICROREACTOR

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Bimetallic nanoparticles, composed of two different metal, are of great interest, from both the scientific and technological views, for the improvement of the catalytic properties of metal particles. This is because bimetallization can improve catalytic properties of the original metallic catalysts and create a new property, which may not be achieved by monometallic catalysts. These effects of the added metal component can often be explained in terms of an ensemble and/or a ligand effect in catalysis.

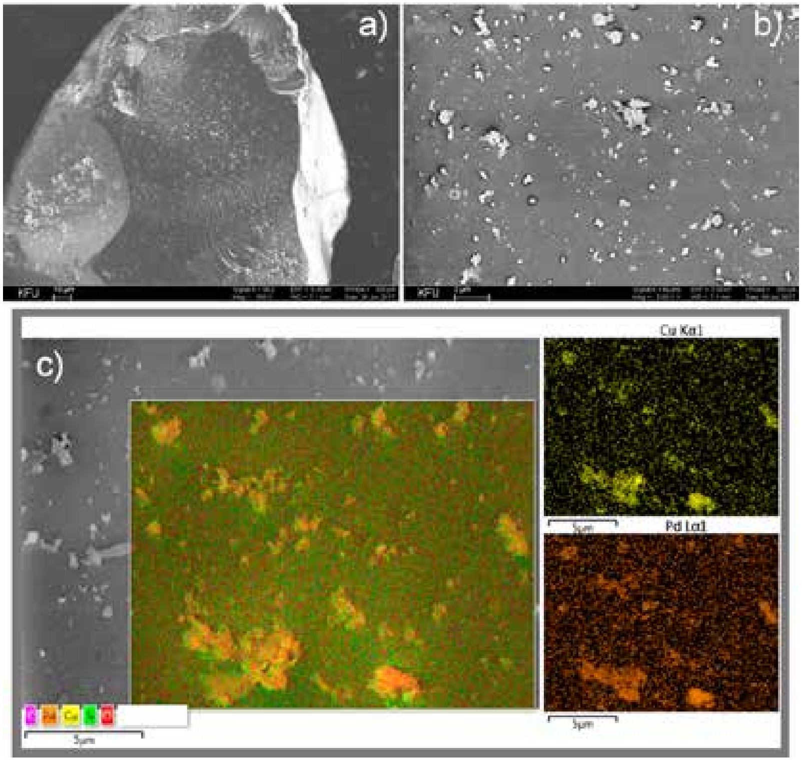

Fig. 1. SEM image of CuPd/SiO_2@$NaBH_4$ (a) scale 10μm; (b) scale 2μm; (c) multi-layer EDS map with Cu and Pd distribution maps.

In this work we have obtained new heterogeneous copper-palladium catalysts based on silica gel with nitrogen including precursors on the surface by chemical reduction method. The resulting bimetallic particles were characterized by X-ray diffraction (XRD), scanning electron microscopy (SEM), energy-dispersive X-ray spectroscopy (EDX), X-ray photoelectron spectroscopy (XPS) and Auger electron spectroscopy (AES). The resulting catalysts showed excellent activity in selective hydrogenation of bifunctional nitroarenes in a flow microreactor.

THE BIOLOGICAL EVALUATION, MODE OF ACTION AND CRYSTAL STRUCTURE OF SOME [1,2,3]TRIAZOLO[5,1-*B*][1,3,4]THIADIAZINES

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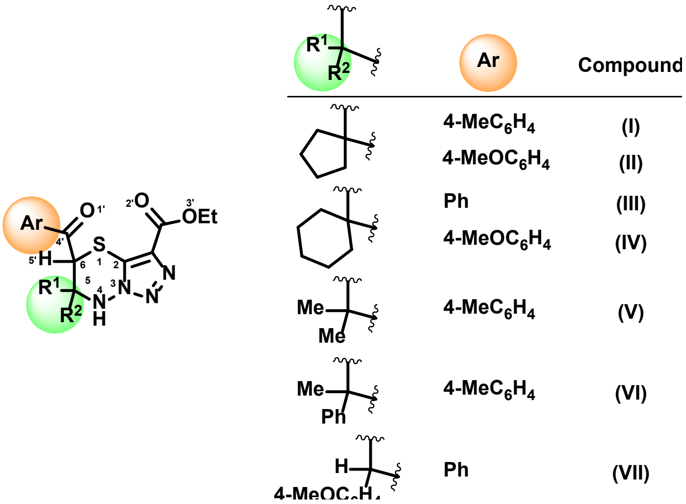
The triazolothiadiazines have been of interest since many of these derivatives produce useful applications as biological active compounds [1]. A great attention is paid to their antiproliferative activities against cancer cells [2], antibacterial activities are paid attention [3]. Recently, we have shown that *as*-triazolothiadiazines affect the proliferative activity of such cells as transformed fibroblasts K-22, human embryonic kidney cells (HEK-293), rhabdomyosarcoma tumor cells (RD) and normal human fibroblasts (HF) [4]. In this work, for seven related [1,2,3]triazolo[5,1-b][1,3,4]thiadiazines the crystals were grown and their cellular activity has been evaluated. For establishment of their action mode and molecular target the investigation of a correlation between structure and antiproliferative activity have been done.



We compare the biological activity profile of the componds (**I-VII**) with their antiproliferative activity against HeLa, HEK293, RD. The biological activity profile these compounds was got by means of Prediction of activity spectra for substances online service (PASS). It was found, that there is correlation (R^2=0.66) between predicted lipoxygenase inhibition activity and Hela half maximal inhibitory concentration (IC_{50}). For the molecules, we have assumed there are major molecular interactions that determine binding with target and packing together in crystal therefore an analysis of the molecules crystal structure has been accomplished.

This research was supported by the Russian Foundation for Basic Research (grant № 18-316-20018).

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SELF-ASSEMBLY OF NOVEL AZACROWN DIENONES WITH ALKANEDIAMMONIUM IONS

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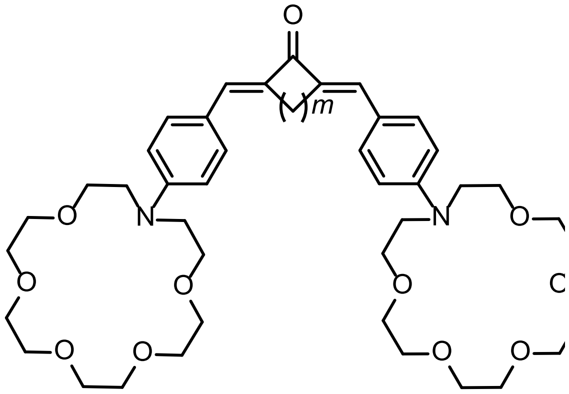
During the last two decades, considerable research interest has been devoted to the design of crown ether substituted chromophores. These compounds were mainly studied for their photochromic and fluorescence properties. In order to elucidate the possibility to construct photoactive supramolecular systems based on dienones we synthesized symmetrical dienones **1a-c** substituted with two azacrown ethers moieties. The behavior of dienones in acetonitrile in the presence of alkanediammonium ions $^+NH_3(CH_2)_nNH_3^+$ (n = 1-12) was studied by UV/vis absorption spectroscopy, fluorescence and NMR ^1H spectroscopy.



1: m = 1(**a**), 2(**b**), 3(**c**)

2: $^+H_3N(CH_2)_nNH_3^+$ $2ClO_4^-$: n =1-12

Scheme 1. Structure formulas of dienones **1a-c** and salts **2**

The formation of complexes **1a–c** with alkanediammonium ions **2** is caused by interaction of the ammonium groups of **2** with the crown ether moieties. Spectra of the dienones undergo significant changes in the presence of alkanediammonium ions. The stability constants of the formed complexes were determined.

It was shown that in a dilute solution bis(azacrown)dienones **1a–c** forms stable 1:1 and 1:2 complexes with alkanediammonium ions. The stoichiometry and the stability constants of the complexes the dienone with alkanediammonium ions depends on the geometric matching of components, which is manifested as the distance between the terminal ammonium groups of alkanediammonium ions and the dienones binding sites. The dienones form 1:2 complexes with short alkanediammonium ions and high stable 1:1 complexes with long ions. Protonation of azacrown moieties, which competes with complexation, takes place in some cases. Influence of rigidity of central cycle on complexation was also demonstrated.

The results of this study can be used for directional design of photoactive supramolecular assemblies and optical molecular sensors.

This work was supported by the Russian Science Foundation (project № 19-13-00020).

DESIGN OF NEW COORDINATION CAGES SUPPOTED ON THIACALIX[4]ARENE

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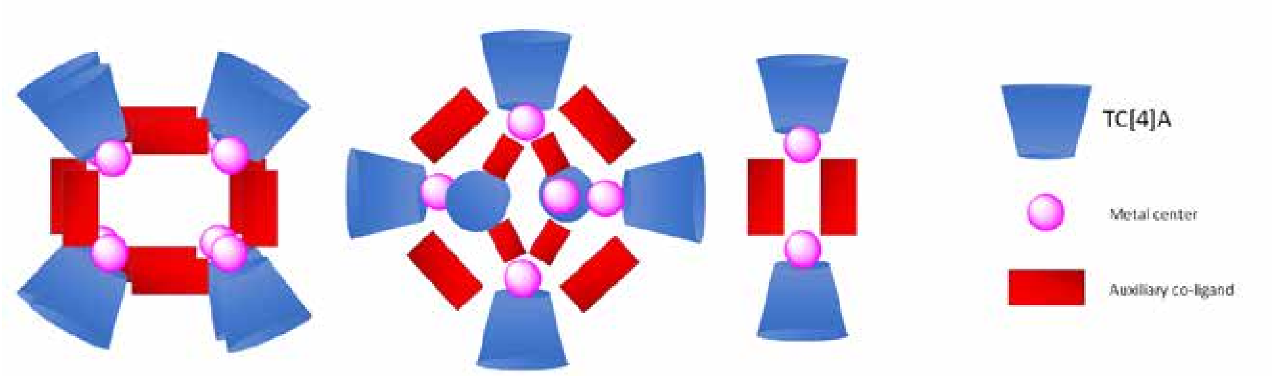
In nowadays metal based clusters and complexes expand for their widely potential applications as molecule-based materials in magnetic materials, catalysis, encapsulating guest molecules, gas separation and storage, and electrochemical applications. (Thia) calix[4]arenes containing phenolic and S/SO_2 bridging groups and pre-organization structure in *cone* conformation are attractive multidentant organic ligands for binding with metal cations and forming polynuclear coordination compounds (cages). In particular, when combined with transition metal salts and auxiliary carboxylic co-ligands it affords a great variety of supramolecular coordination cages which are promising to exhibit catalytic activity [1].

Here we report synthesis and structure of new octahedral and hexahedral coordination cages formed by using *tert*-butylsulfonylcalix[4]arene as molecular building block with different dicarboxylic acids as co-ligands and nickel (II), cobalt (II) or zinc (II) cations (Scheme 1). Structures of obtained coordination compound has been characterized by X-ray spectroscopy.



Scheme 1.

The work was supported by RSF № 17-73-20117.

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ANTIRADICAL ACTIVITY OF PHOSPHORYLATED PHENOLS

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The initial reactive oxygen spices (ROS) in living organism is the superoxide anion radical $O_2^{\bullet -}$, which plays an important role in the initiation of different biotic or pathologic processes. The antioxidative action of the different compounds determined by their antiradical activity toward ROS, in particular toward the $O_2^{\bullet -}$. The antiradical activity of phosphorylated phenols (3,5-di-*tert*-butyl-4-hydroxyphenyl)methylenediphosphonic acid **1**, 3,5-di-*tert*-butyl-4-hydroxyphenyl)hydroxymethylenediphosphonic acid **2**, tetraethyl (3,5-di-*tert*-butyl-4-hydroxyphenyl)-methylenediphosphonate **3**) and trolox **4** toward $O_2^{\bullet -}$ was studied using the superoxide producing reaction of adrenaline autooxidation in an alkaline medium (pH = 10.65), and the formation of adrenochrome was detected at a wavelength of 347 nm [1]. Superoxide dismutase is the metalloenzyme involved in the antioxidant protection of cell membranes from the damaging effect of highly toxic ROS. Therefore the effect of the compounds **1-4** on the SOD activity of a biological product, the liver of the Russian sturgeon, was also studied. It was found that compounds **1-4** exhibited antiradical activity (Fig.).

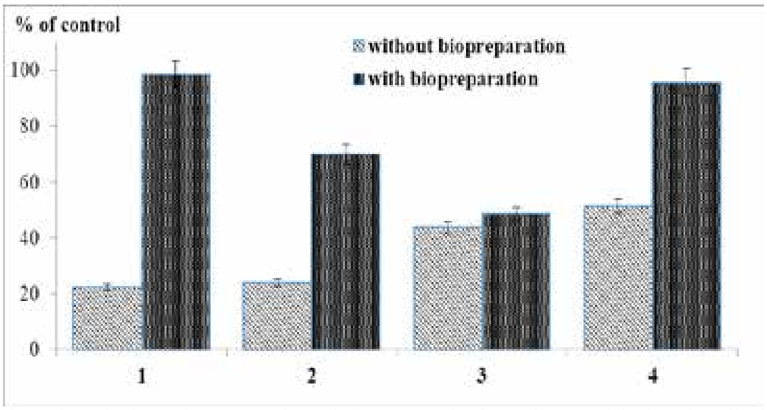

Fig. The effect of compounds **1-4** on the rate of accumulation of the auto-oxidation products of adrenaline without a biological product and in the presence of the liver homogenate (biopreparation) of Russian sturgeon ($C_{(1-4)}$=25 µM, λ=347 nm, $C_{adrenalin}$=5.46 mM). The rate of accumulation of the products of auto-oxidation of adrenaline in bicarbonate buffer in the presence of a biopreparation, was taken as 100% (control).

Phosphorylated phenols **1–3** reduced the rate of adrenaline oxidation in alkaline bicarbonate buffer by 78, 76 and 56%, respectively, and trolox by 48%. Compound **2** and **3** showed the highest SOD activity at the presence of the Russian sturgeon liver homogenate, reducing the $O_2^{\bullet -}$ generation rate by 30-51%. The addition of the homogenate of sturgeon liver don`t leads to inhibition of adrenaline oxidation in the presence of compounds **1** and **4**. The interaction of compounds with an electrochemically generated $O_2^{\bullet -}$ in CH_3CN on a platinum electrode also was studied [2]. The form of cyclic voltammograms of the electroreduction of O_2 were changed in the presence of compound **1-2**. The cathode peak increase of oxygen reduction were established. Decline anodic peak of current $O_2^{\bullet -}$ indicates that the compound react irreversibly with superoxide anion-radical. Based on the obtained voltammetric data, the rate constants of the interaction (k) of compound **1** (k=31.58 L/mol•s) and **2** (k=217.27 L/mol•s) with $O_2^{\bullet -}$ were calculated. Thus, the antiradical activity of phosphorylated phenols toward $O_2^{\bullet -}$ has been revealed. The ability of compounds to increase the superoxide dismutase activity of the biopreparation from of Russian sturgeon liver has been demonstrated.

This work was supported by the Russian Foundation for Basic Research (grant № 17-03-00434).

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EVALUATION OF ANTIOXIDANT ACTIVITY A NEW HETEROCYCLIC COMPOUNDS *IN SILICO* AND *IN VITRO*

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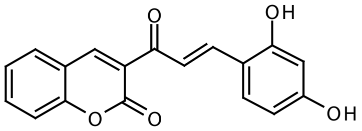
The new heterocyclyc compounds **I-VI** were obtained and the spectrum of biological activity of compounds was predicted *in silico* using PASS (PharmaExpert.ru ©2011 - 2017 • Version 2.0). The spectrum of biological activity for substances is presented in the form of a list of types of biological activity, for which the probability of presence (P_a) and probability of lack of activity (P_i) are calculated. P_a and P_i values are independent and their values vary from 0 to 1.



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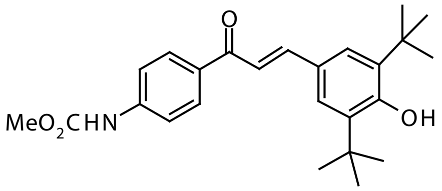
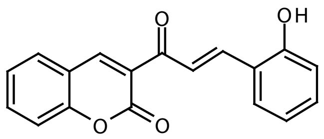


II



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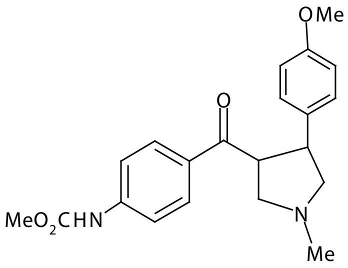
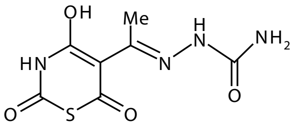
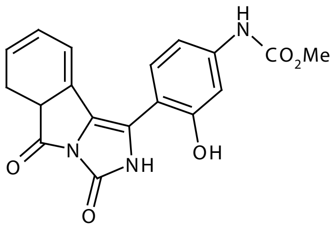


IV



V



VI

Among the large number of predicted types of bioactivity of compound **I-VI** we have identified those that were closely related to antioxidant properties. For compounds **I-IV** the ability to act as antioxidants (P_a=0.138÷0.477) and «traps» of reactive oxygen species initiating oxidative processes (P_a=0.446÷0.710), and antidotes (P_a=0.204÷0.295) only for compounds **I-III**.

To confirm the forecast the effect of compounds on the rate of superoxide anion-radical generation in the auto-oxidation reaction of adrenaline in an alkaline medium was investigated and on the SOD-protector activity of a biological product, the liver of the Russian sturgeon. It was found that all compounds exhibited antiradical and SOD-protector activity. The results of computer screening were confirmed by the data of the experimental studies *in vitro* on model system auto-oxidation reaction of adrenaline in an alkaline medium. Compounds **I-VI** increased the SOD-protector activity of the Russian sturgeon liver homogenate.

Thus antioxidant activity was predicted *in silico* and correlated with the data obtained from *in vitro* experiments. The results of the prediction of the biological activity can be used in planning of further experimental studies of biological and pharmaceutical activity *in vitro* and *in vivo* systems.

This work was supported by the Russian Foundation for Basic Research (grant № 19-03-00006).

REACTIONS OF *O*-QUINONE METHIDES WITH 4*H*-CHROMENES: SYNTHESIS OF CHROMENO[2,3-*B*]CHROMENES

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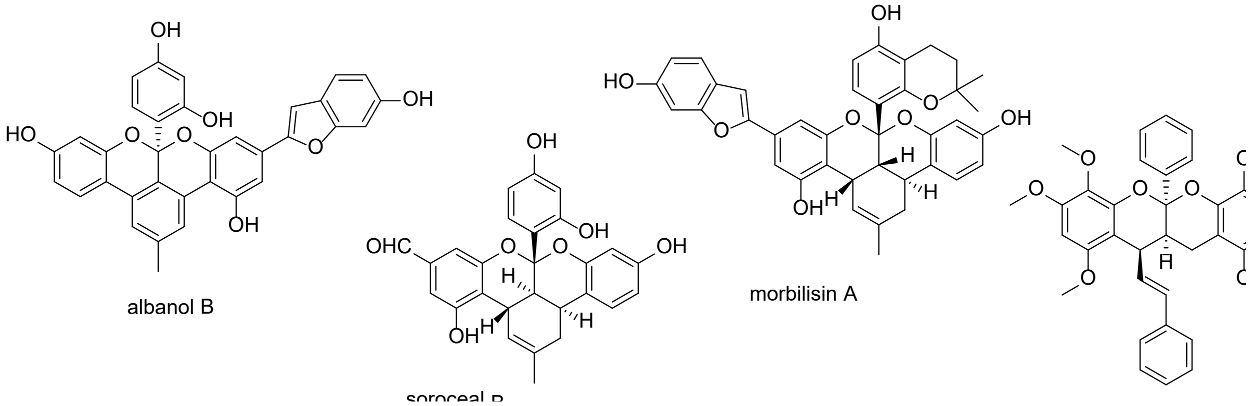
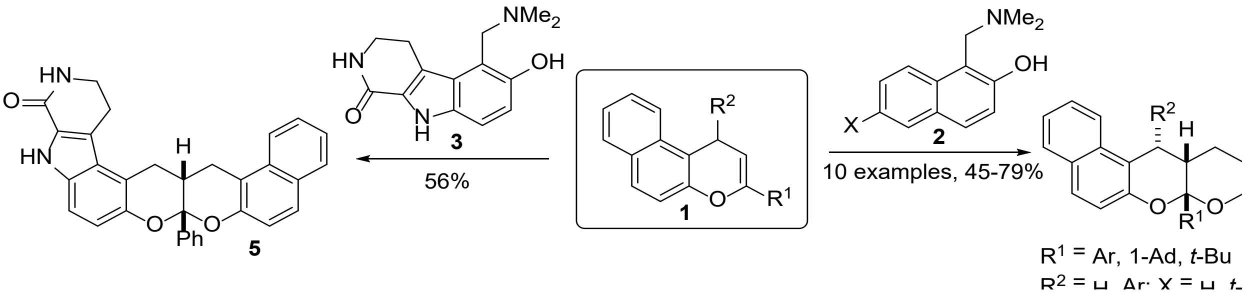
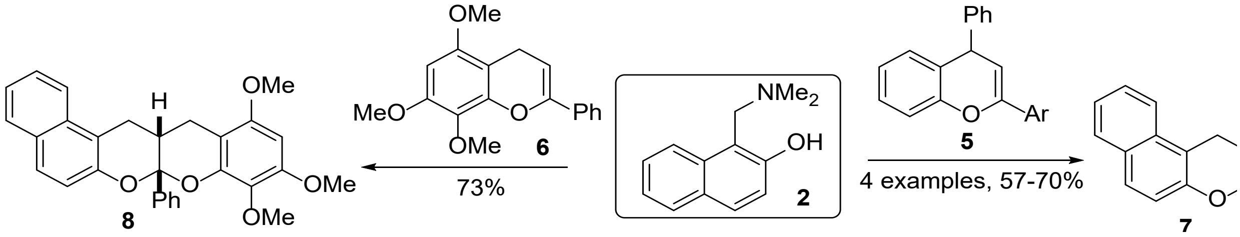
Pyrano- and chromeno[2,3-b]chromenes are of interest due to a wide spectrum of their biological action, including anti-plasmoid, anticancer and anti-inflammatory activity, as well as neuroprotective properties. In addition, chromeno[2,3-b]chromen fragment is found in a number of natural compounds. Examples include albanol B, soroceal B, morbilisin A and 8”,9”-dihydrowelwitschin H.



We have shown that the reaction of 1*H*-benzo[*f*]chromenes **1** with Mannich bases of naphthalene **2** or carboline **3** series with moderate to good yields results in arenocondensed chromeno[2,3-*b*]chromenes **4**, **5**. The reaction proceeds diastereoselectively with the formation of *trans*-isomers in the case of 1,3-disubstituted 1*H*-benzo[*f*]chromenes.



4*H*-Chromenes **5** and **6** can also be introduced into this reaction. The reaction mechanism apparently includes the generation of electron-deficient *o*-naphthoquinone methides, which act as heterodienes in the inverse electron demand Diels-Alder reaction. It should be noted that the 1-aryl-substituted Mannich bases on the basis of 2-naphthol do not give the corresponding cycloadducts.



This work was supported by the Russian Foundation for Basic Research (grant 17-03-01156 A) and the Ministry of Education and Science of the Russian Federation within the framework of State Assignment (project N 4.5628.2017/6.7).

DESIGN OF NEW COORDINATION CAGES SUPPOTED ON THIACALIX[4]ARENE

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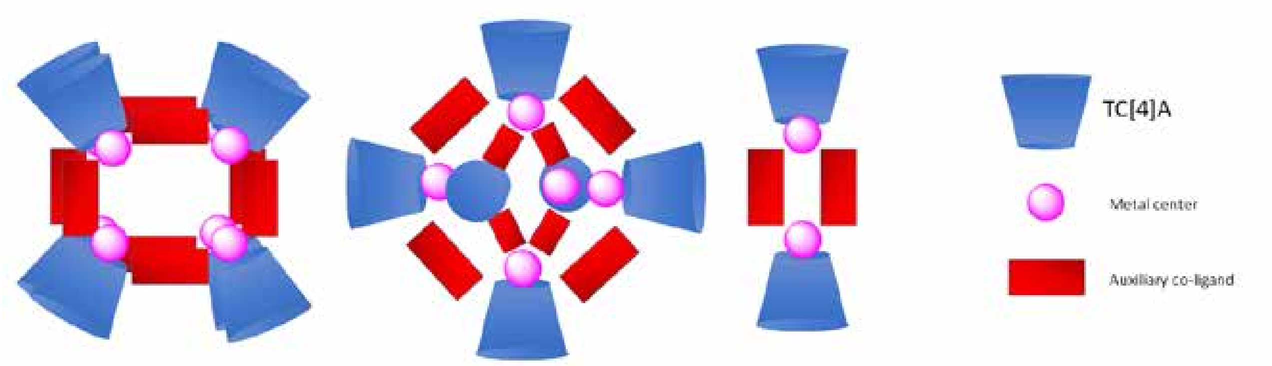
In nowadays metal based clusters and complexes expand for their widely potential applications as molecule-based materials in magnetic materials, catalysis, encapsulating guest molecules, gas separation and storage, and electrochemical applications. (Thia) calix[4]arenes containing phenolic and S/SO_2 bridging groups and pre-organization structure in *cone* conformation are attractive multidentant organic ligands for binding with metal cations and forming polynuclear coordination compounds (cages). In particular, when combined with transition metal salts and auxiliary carboxylic co-ligands it affords a great variety of supramolecular coordination cages which are promising to exhibit catalytic activity [1].

Here we report synthesis and structure of new octahedral and hexahedral coordination cages formed by using *tert*-butylsulfonylcalix[4]arene as molecular building block with different dicarboxylic acids as co-ligands and nickel (II), cobalt (II) or zinc (II) cations (Scheme 1). Structures of obtained coordination compound has been characterized by X-ray spectroscopy.



Scheme 1.

The work was supported by RSF № 17-73-20117.

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INTRODUCTION OF THE PHOTOACTIVE FRAGMENTS INTO THE STRUCTURE OF BIOLOGICALLY ACTIVE MOLECULES

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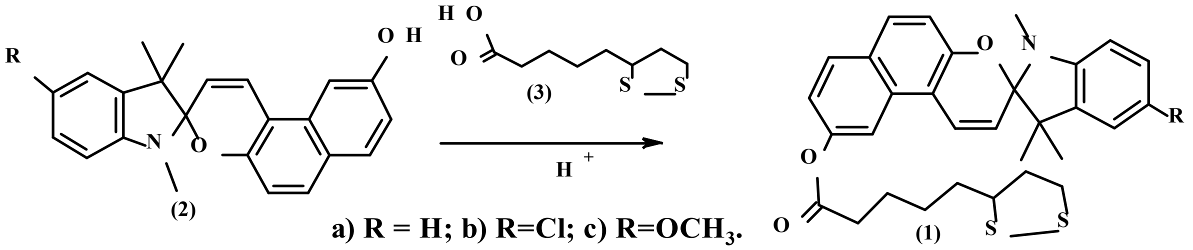
Earlier there were attempts to obtain antitumor drugs containing photocontrolled fragments in their structure. Some photoactive compounds based on azobenzenes, whose structure was similar to alkaloid colchicine, were obtained and studied. This modification of the colchicine molecule gave a possibility to control the resistant properties of the drug with the help of visible light and to conduct a targeted attack of cancer cells [1]. However, most of the existing methods for introducing photo-switching centers into biologically active molecules are not universal, and limit the possibilities for using of photodynamic systems in biomedical applications.

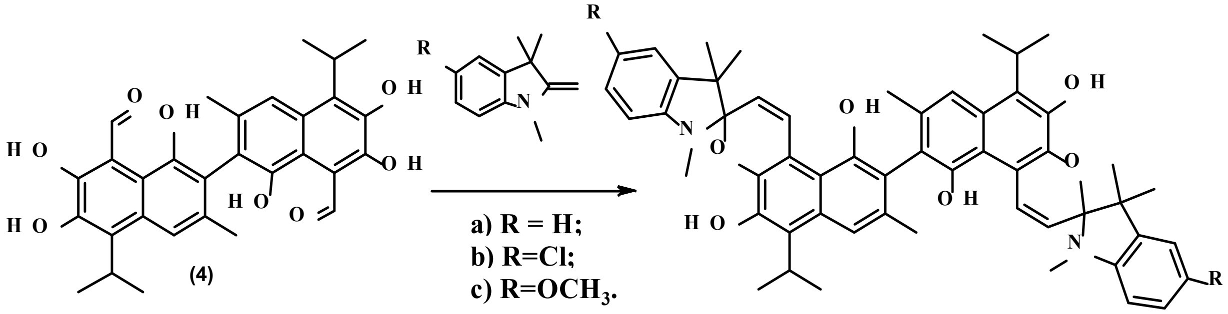
The aim of this work was to develop the universal methods for combining photochromic spirocyclic centers with biologically active molecules. To solve this problem we have chosen two directions. The first one was to obtain a hybrid compound (1) based on indoline spiropyran (2) and lipoic acid (3) using the esterification reaction:



(2) (3) (1)

a) R = H; b) R=Cl; c) R=OCH_3.

The second direction was based on the introduction of a spirocyclic fragment directly into the structure of a gossypol molecule (4) through the cyclocondensation reaction due to the presence of *ortho*-located hydroxy and aldehyde groups in it [2]:



(4)

a) R = H;
b) R=Cl;
c) R=OCH_3.

This work was supported by the Russian President Grant MK-1721.2019.3.

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THIOPHENYLOXAZOLES THROUGH AZIRIDINES: EASY AND FAST

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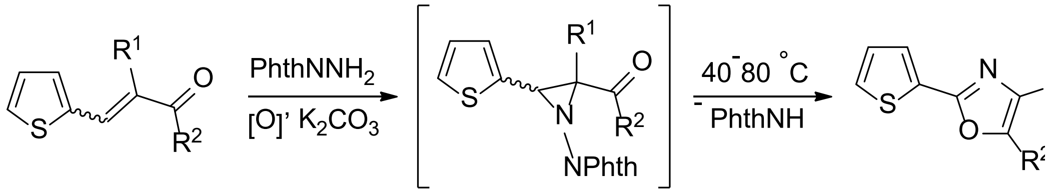
A direct access to thiophenyl-substituted oxazoles has been developed using buildup-cleavage of an aziridine ring as key transformations. Versatility of the Knoevenagel reaction allows getting a wide range of alkenes bearing a thiophene ring and a carbonyl moiety on the opposite sides. Aziridine ring can arised from the alkene via an oxidative addition of *N*-aminophthalimide ($PhthNNH_2$) to the double bond as it is a well known general method for the preparation of aziridine derivatives [1]. Further, thermal cleavage of the C–C bond of 2-acylaziridine can give oxazole as a result of the 1,5-electrocyclization of the azomethine ylide thus generated [2, 3]. Merging these two reactions in a sequence opens a short pathway to structures with thiophene and oxazole rings linked directly. Three substituents in the starting alkene grant a double advantage for the whole transformation: weak heating is enough to cleavage a trisubstituted aziridine, and target oxazole gets three different groups at once.



R^1 = CO_2Me, CN, Ac, Ar, COAr; R^2 = OMe, Me, Ar

50-75%

The two-step procedure can be performed without isolation of intermediate aziridines only by the simplest workup of the initial reaction mixtures followed by heating. Operational convenience and minimum of reagents are the main advantages of this synthetic protocol. Moreover, it can be successfully expanded to thiophen-3-yl- and benzothiophenyl-substituted analogues thus making this sequence a general pathway to various functionalized thiophenyloxazoles.

This work was supported by Russian Science Foundation (grant No. 18-73-00089).

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SIMPLE METHOD FOR OBTAINING OF SUBSTITUTED 5-HYDROXYPYRAZOLO[1,5-A]QUINOXALIN-4-ONES

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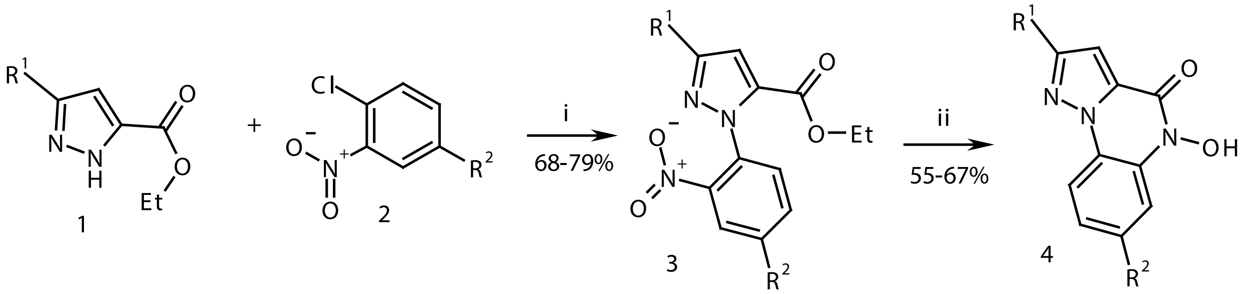
Recently much attention has been given to the syntheses of various pyrazole derivatives, including heterocyclic fused systems [1]. Pyrazolo[1,5-a]quinoxalines that manifest different types of biological activity as inhibitors of various human enzymes are interesting representatives of this class of compounds.



Scheme 1 *Reagents and conditions*: i, K_2CO_3, DMF, 50–80°C, 3–6 h;
ii, $SnCl_2$, HCl, EtOH, 50 °C, 3–4 h.

Analysis of reported data has shown that there is a limited choice of methods for synthesizing pyrazolo[1,5-a]quinoxalin-4-ones and no methods to synthesize 5-hydroxypyrazolo[1,5-a]quinoxalin-4-ones. Therefore we have been developed a two-step synthesis of substituted 5-hydroxypyrazolo [1,5-a] quinoxalin-4-ones **4** based on N-arylation pyrazolcarboxylates **1** with o-halogennitroarenes **2** followed by reductive cyclization of the resulting nitro compounds in target products [2] (Scheme 1**)**.

The reaction on first stady afforded mainly 3-arylpyrazole-5-carboxylates **3** (above 95%, NMR data), apparently due to negative charge localization on the nitrogen atom adjacent to the carboxy group. At the second stage, nitroarylpyrazoles **3** were reduced with divalent tin by a known technique [3]. The presence of the second electron-withdrawing substituent (R^2= CF3, CN, NO_2, COOEt) in the nitroaryl fragment of N-arylation pyrazoles **3** caused intramolecular selective condensation into 5-hydroxypyrazolo[1,5-a]quinoxalin-4-ones **4** in up to 67% yield (one-pot reaction). In the case of compounds **3** (R^2 = NO2), reduction of the second nitro group occurred due to application of two-fold excess $SnCl_2$ thus giving amino derivatives **4** ($R^2 = NH_2$). The structures of compounds 3 and 4 were confirmed by acombination of IR and NMR spectroscopic and mass spectrometric data.

The resulting new compounds can to be of interest to medical chemistry

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SUPRAMOLECULAR MULTITARGET SYSTEMS BASED ON FUNCTIONALIZED DERIVATIVES OF STERICALLY HINDERED PHENOLS: CHOLINESTERASE INHIBITION AND ANTIOXIDANT ACTIVITY

Burilova E.A.[a], Pashirova T.N. [a], Tagasheva R.G.[b], Starodubtseva R.R.[a], Zueva I.V.[a], Nizameev I.R.[a,b], Sudakov I.A.[a], Vishtakalyk A.B.[a], Kadirov M.K.[a,b], Petrov K.A.[a], Burilov A.R.[a], Bukharov S.V.[b], Zakharova L.Ya. [a]

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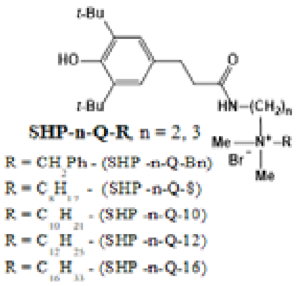
The development of low-molecular compounds with multifunctional effects, targetting the different pathways is one the most promising pharmacological approach for the treatment of complex neurodegenerative diseases and other diseases [1]. The derivatives of sterically hindered phenols display an antioxidant activity like α-tocopherol and butylated hydroxytoluene (BHT) [2,3]. Sterically hindered phenols show antiviral, antitumor, antibacterial and anti-inflammatory activities [4,5]. In addition, the sterically hindered phenols to be considered as promising drugs against Alzheimer's disease [6]. In this study, multitarget compounds based on amphiphilic hindered phenols and containing quaternary ammonium moiety (SHP-n-Q-R) were synthesized. These compounds are inhibitors of cholinesterases with antioxidant properties. The inhibitory selectivity for BuChE was observed. For water soluble SHP-n-Q-R derivatives the self-assembly was studied by tensiometry, conductometry, spectrophotometry, fluorimetry and dynamic light scattering. The quantitative characteristics of self-assemblies: critical association concentration (CAC), solubilization capacity, aggregation numbers, and size were determined. The CAC of SHP-n-Q-8 is 0.005 M. The CAC decreases with increasing the length of alkyl chains of SHP-n-Q-R from octyl to octadecyl homologues by 2 orders. The best solubilizing ability was possessed by SHP-n-Q-16. The sizes of SHP-n-Q self-assemblies depend on the structure (length of the alkyl chains) and their concentration. For short-chain analogues (SHP-n-Q-8 and SHP-n-Q-10) the particle sizes are in the range from 50 to 80 nm. For long-chain analogs (SHP-n-Q-12 and SHP-n-Q-16) two types of particles (30 nm and 100 nm) are observed. The nanotechnological approach was used to increase the bioavailability of SHP-n-Q-R derivatives and to overcome or circumvent the blood brain barrier. Mixed cationic liposomes based on L-α-phosphatidylcholine and SHP-n-Q-R with the size of 100 nm were prepared. The stability, encapsulation efficacy and release from liposomes of a model drug, Rhodamine B, depend on the structure of SHP-n-Q-R. Cationic liposome based on L-α-phosphatidylcholine and SHP-n-Q-R show a good stability in time (1year) and a sustained release (> 65 hours). SHP-n-Q-R and SHP-n-Q-R-loaded liposomes exhibit more pronounced antioxidant properties than the BHT. It was shown that SHP-n-Q-R are promising templates for the development of anti-Alzheimer multitarget-drug delivery systems.



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MIXED SELF-ORGANIZING SURFACTANT — HYDROTROPIC DICATIONIC SALT — WATER SYSTEMS

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Hydrotropes are compounds which enhance solubility of organic substances, as well as surfactants, in water. Hydrotropes can affect aggregation and solubilization parameters of amphiphilic compounds. Alcohols, amines, salts of aromatic sulfonic acids refer to hydrotropes. A dicationic hydrotropic salt propanedyl-α,β-bis(dimethylammonium bromide), *2-3-2,* has been synthesized by our group. The purpose of this work was to investigate effects produced by the dicationic hydrotropic salt on critical micelle concentration (CMC), solubilizing abilities of classic nonionic surfactants (Triton X-100, Tween, Bridge-35) and an anionic surfactant (sodium dodecyl sulphate, SDS), as well as their mixed composition.

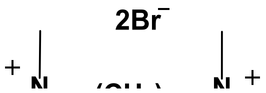

Fig. 1. Chemical structure of hydrotropic dicationic salt 2-3-2.

With use of tensiometry, dynamic and electrophoretic scattering, aggregate and thermodynamic parameters of micelle formation and adsorption of anionic and nonionic surfactants in the presence of 1 mM and 3 mM of hydrotropic additive 2-3-2 have been evaluated. It was shown that the hydrotropic dicationic salt does not influence CMC's of nonionic surfactants, however in presence of 1 mM of 2-3-2 the CMC of SDS is 5 times lower, and in the presence of 3 mM – 20 times lower. In case of a 1:1 mixed system with SDS and Tween-80 addition of 3 mM of the hydrotrope lowers their CMC 5 times. The sizes of micellar aggregates with and without the hydrotropic additive have been evaluated. Absorbance spectroscopy measurements with chloramphinecol as a model antibiotic have shown that 2-3-2 helps to achieve thrice the solubilisation capacity (S) in case of Tween-20. For Bridge-35 the S value is lowered when the hydrotrope is added.

This work was supported by Russian Foundation of Basic Research (project № 18-43-160015).

COPPER-CATALYZED INSERTION OF DIAZO COMPOUNDS INTO VINYL HYPERVALENT IODINE REAGENTS TO GENERATE ALLYLIC ESTERS[1]

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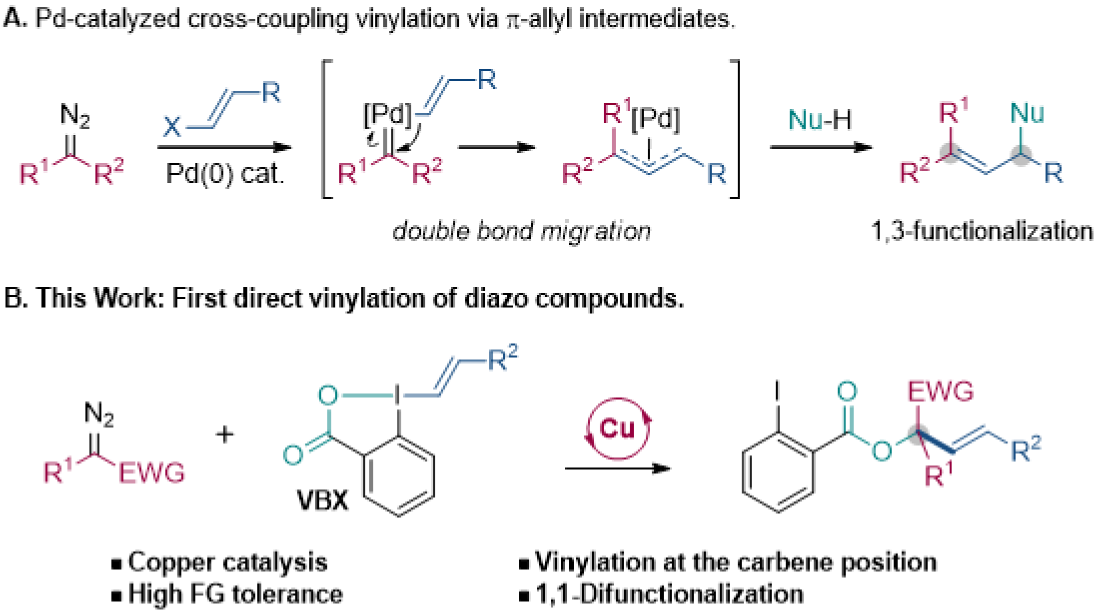
Metal carbenes are highly versatile intermediates, easily generated from diazo compounds, which have been extensively used in synthetic chemistry (cyclopropanation, Nu-H insertion, ylide chemistry).[2] Recently, metal carbenes have emerged as a new type of cross-coupling partners for the formation of C–C bonds.[3] In this context, the generation of palladium carbene intermediates for the cross-coupling with vinyl halides has been highly successful for the synthesis of functionalized olefins, but resulted in the formation of isomerized 1,3-alkene products through double bond migration (Scheme 1A).[4]



Scheme 1. Cu-catalyzed vinylation of diazo compounds with VBX reagents.

To develop the first direct vinylation of diazo compounds (Scheme 1B), we identified vinylbenziodoxolone (VBX) reagents as ideal coupling partners:[5] The hypervalent bond confers a highly electrophilic character to the vinyl motif and the benzoate group can act as a nucleophilic oxygen source. VBX reagents have been much less used than the more established EBXs (ethynylbenziodoxolones).[6] The use of inexpensive and earth-abundant copper associated to the high atom-efficiency of the reaction are notable advantages of the methodology. The transformation is tolerant to a wide range of functional groups and provides ready access to a broad scope of allylic esters in very high yields.

This work was supported by ERC (Starting Grant iTools4MC, number 334840).

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SYNTHESIS OF 10R-PYRIDO[2,3-A]PHENAZINES

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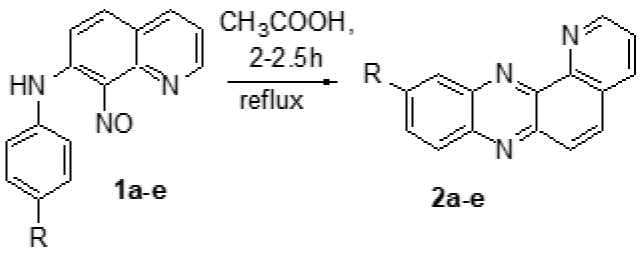
Phenazines exhibit significant biological activity [1,2], which attract understandable attention. There is continued interest in both developing new methods for the synthesis of phenazine derivatives and the design of potentially valuable analogs.

Recently [3] we have been demonstrated that the reaction of nitroquinolines with anilines, performed in the presence of excess sodium hydride in DMSO at room temperature, gives rise to nitro and nitroso derivatives of arylaminoquinolines. It is known that one of the methods for constructing the phenazine core is the cyclization of the N-aryl-2-nitrosoanilines which can be performed under both acidic and basic conditions [4]. The transformation of 7-arylamino-8-nitrosoquinolines to pyrido[2,3-a]phenazines was carried out by boiling in acetic acid. This simple procedure allows to obtain the desired products **2a-e** with up 53 to 73% yields.



1a-e

2a-e

R	Product (yield after chromatographic separation, %)
H	**2a** (73)
Me	**2b** (73)
MeO	**2c** (64)
Br	**2d** (53)
F	**2e** (69)

Scheme 1.

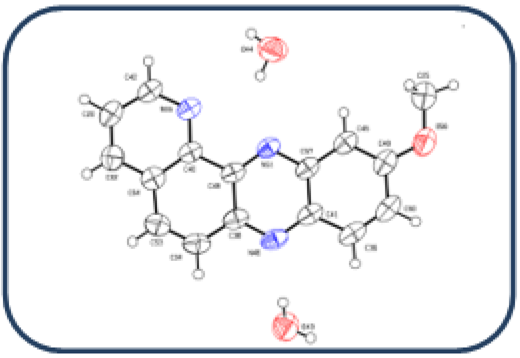


Fig. 1. The molecular structure of compound **2c** with atoms represented by thermal vibration ellipsoids of 50% probability

A characteristic feature in ^1H NMR spectra of pyrido[2,3-a]phenazines **2a–e** that were acquired in $CDCl_3$ solutions was the pronounced downfield shift of 2-H proton signals (9.24– 9.28 ppm). The structure of pyrido[2,3-a]phenazine **2c** was confirmed by X-ray structural analysis (Fig. 1)

This work was performed with financial support from the Ministry of Education and Science of the Russian Federation within the framework of State Assignment (project No. 4.6306.2017/8.9)

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CYCLIC KETONES AS IMPORTANT PRECURSORS FOR CREATIONING RADIOPHARMACEUTICALS

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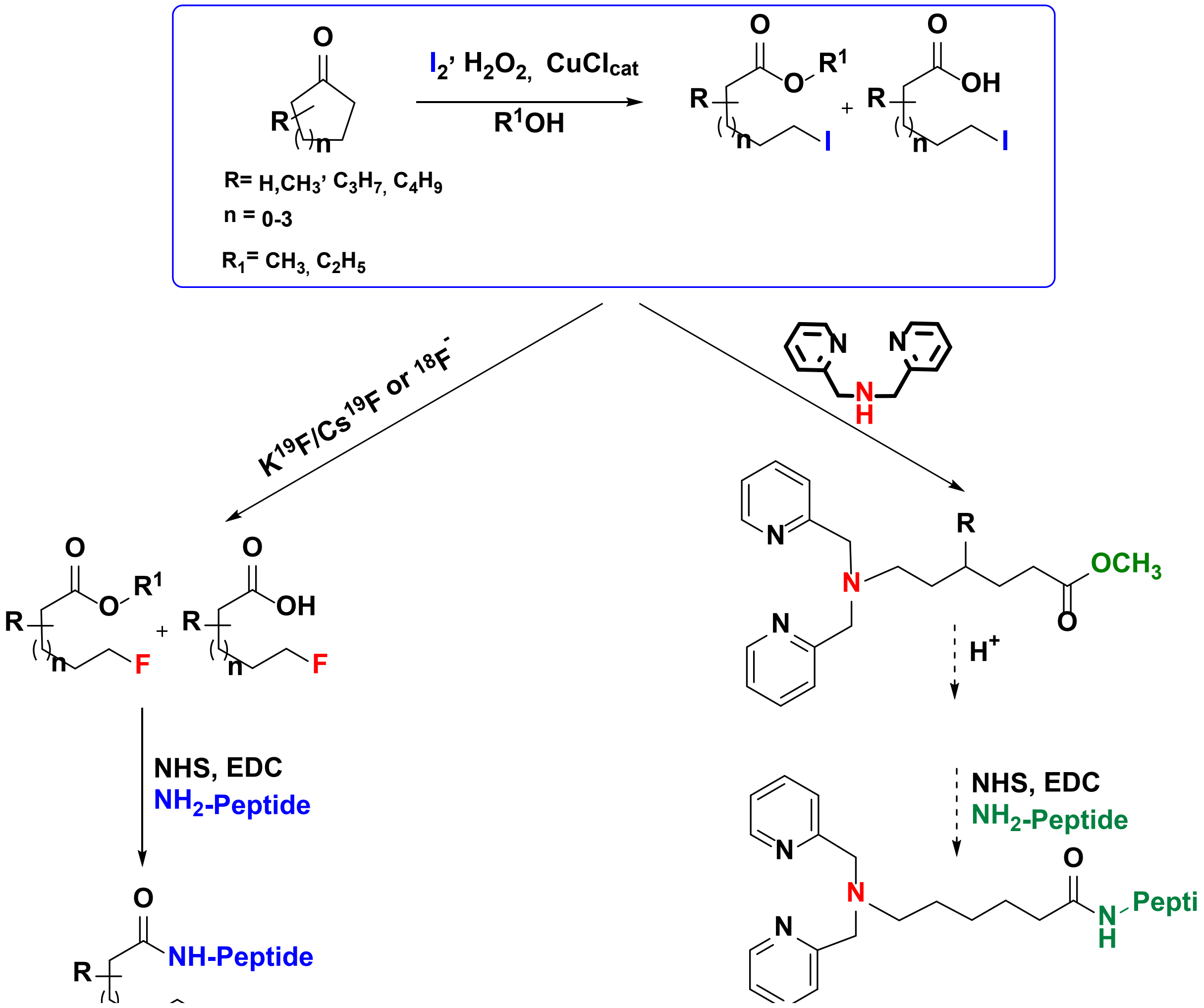
At the present time, it is of interest to use cyclic ketones to produce ω-derivatives (iodine, fluoro, amino, mercapto) carboxylic aliphatic acids and their esters, which are used as precursors for the synthesis of drugs and radiopharmaceuticals. The aim of this work was to develop a new method for the preparation of ω-derived carboxylic acids and their esters containing chelate centers.



Scheme 1 - General design bioconjugates based on cyclic ketones

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PHOTOCHROMIC MALEIMIDES CONTAINING AMINO ACID FRAGMENTS IN THE PYRROLE-2,5-DIONE BRIDGE

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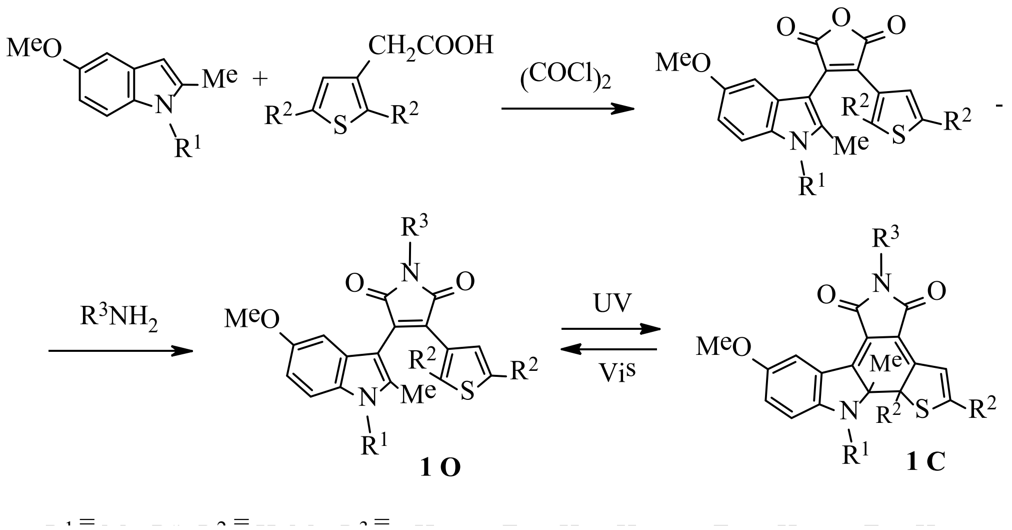
Photochromic compounds capable of reversible transformation between two stable isomeric forms are widely used in the design of materials for molecular electronics, optical data storage, optical switching, molecular logic devices, photo pharmacology, biovisualization, chemo- and biosensors [1]. We have synthesized a series of novel maleimides **1** containing fragments of ethyl amino acid ethers in the pyrrole-2,5-dione bridge (Scheme 1). According to ^{1}H and ^{13}C NMR spectroscopy data the obtained compounds exist in a ring-opened form **O** and display emission at 530 nm.



Scheme 1

Upon irradiation with light of 436 nm all maleimides rearrange into colored ring-closed non-fluorescent isomers **C**. Irradiation of photoinduced forms with visible light of 546 nm induces the reverse reaction. Transformations **1O**/**1C** can be carried out repeatedly, which makes these compounds molecular switches of fluorescent properties.

This work was carried out in the framework of the basic part of State task in the sphere of scientific activity (nos. 4.6497.2017/8.9 and 4.5593.2017/6.7) and State task of SSC RAS no. 01201354239.

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SYNTHESIS OF MONO-FLUORINATED NORBORNENES AND NORBORNADIENES

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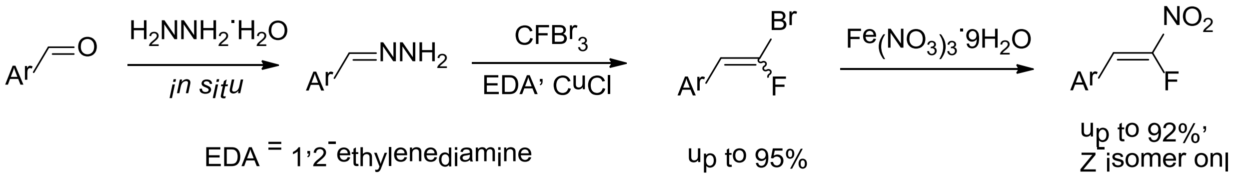
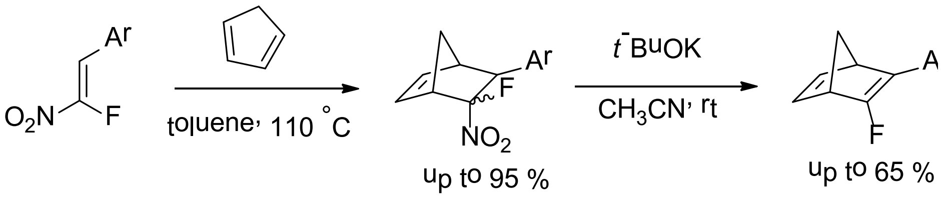
Norbornene, norbornadiene and their derivatives have become important objects of modern chemistry and chemical engineering. These compounds have found wide application in medicine, agriculture, microelectronics, rocket technology and in the production of polymeric materials with unique properties, as well as solar energy converters and efficient gas separation membranes.[1] The incorporation of fluorine into the target molecule changes some of its important features: lipophilicity, solubility, receptor binding, metabolism, membrane permeability, acid-base characteristics aconformational properties. All of these features are considered in the design of new drugs and materials. [2]

This work is devoted to the synthesis of novel fluorine-containing norbornenes and subsequent transformation them into the corresponding mono-fluorinated norbornadienes. The starting β-fluoro-β-nitrostyrenes were prepared according to the previously developed method (Scheme 1), based on the radical nitration of 2-bromo-2-fluorostyrenes. [3] 2-Bromo-2-fluorostyrenes, in turn, were obtained by the reaction of catalytic olefination from the corresponding aromatic aldehydes. [4]



Scheme 1. Preparation of starting β-fluoro-β-nitrostyrenes

The Diels-Alder reaction of β-fluoro-β-nitrostyrenes with cyclopentadiene results in monofluorinated norbornenes (Scheme 2). The subsequent eliminations of HNO_2 from the resulting adducts by *t*-BuOK give the corresponding norbornadienes.



Scheme 2. Synthesis of mono-fluorinated norbornenes and norbornadienes

This work was supported by the Russian Science Foundation (RSF) (Grant No. 17-73-10358).
This work was partially supported by the Russian Federation President Grant for leading scientific schools № 4687.2018.3.

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SYNTHESIS OF 3-POLYFLUOROALKOXY-1-PROPANOLES

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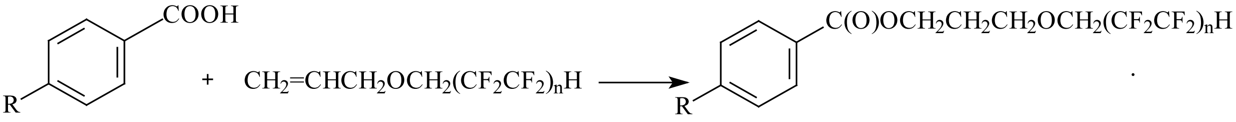
The synthesis of new linear fluorinated primary alcohols opens up the prospects for the creation water and oil repellents based thereon for treatment of fabrics, surfactants and surface modifiers. The possibility of obtaining primary linear alcohols containing a polyfluoroalkyl fragment from the corresponding polyfluoroalkoxypropenes has been studied in this research. It is a well-known fact that the introduction of a hydroxyl group in a position "1" of similar structures can be carried out according to the Brown method by means of oxidative hydroxylation of the corresponding trialkylboranes.

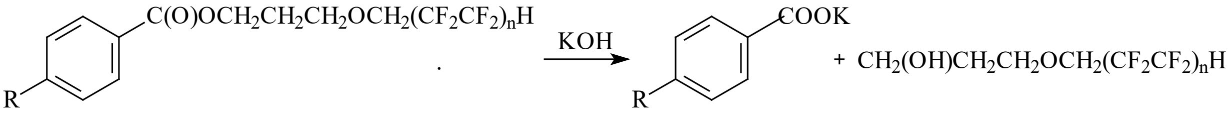
We have determined that the end 3-polyfluoroalkoxypropanols can be obtained from polyfluoroalkoxypropenes as a result of their interaction with benzoic and *p*-toluic acids and the subsequent hydrolysis of esters. Allyl ethers – 3-(2,2,3,3,4,4,5,5-octafluoropentoxy)-prop-1-ene and 3-(2,2,3,3,4,4,5,5,6,6,7,7-dodecafluorohexoxy)-prop-1-ene were synthesized by a known method [1] from polyfluoroalkyl alcohols and allyl halides (Hlg = Br and Cl) in the presence of aqueous alkali (yields 80-87%). Then, they were used in the alkylation reaction of benzoic and *p*-toluic acids. The analysis of the NMR ^{1}H spectroscopic data indicates that the addition proceeds against the Markovnikov rule and 3-(polyfluoroalkoxy)propyl benzoates and –toluylates (Sheme 1) are formed (yields 75-85%). The similar regularities are observed in the case of alkylation of rosin acids [2].



R = H, CH_3; n = 2, 3..

Sheme 1

The alkaline hydrolysis of the synthesized (polyfluoroalkoxy)propyl benzoates and toluylates has been carried out at a molar ratio of reagents 1: 2 in the presence of methanol at heating (40-60°C) for 1 h and at ambient temperature for another 24 h (Sheme 2) according to the method [4]. The primary (polyfluoroalkoxy)propanoles have been obtained in the form of light yellow mobile oily liquids with a characteristic smell (yields 73-80%).



R = H, CH_3; n = 2, 3.

Sheme 2

The composition and structure of the synthesized compounds were confirmed by UV, IR, ^{1}H and ^{19}F NMR spectroscopy data and analytical characteristics.

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DIRECTED SYNTHESES BASED ON THE REACTIONS OF FURAN ALDEHYDES WITH H_2O_2

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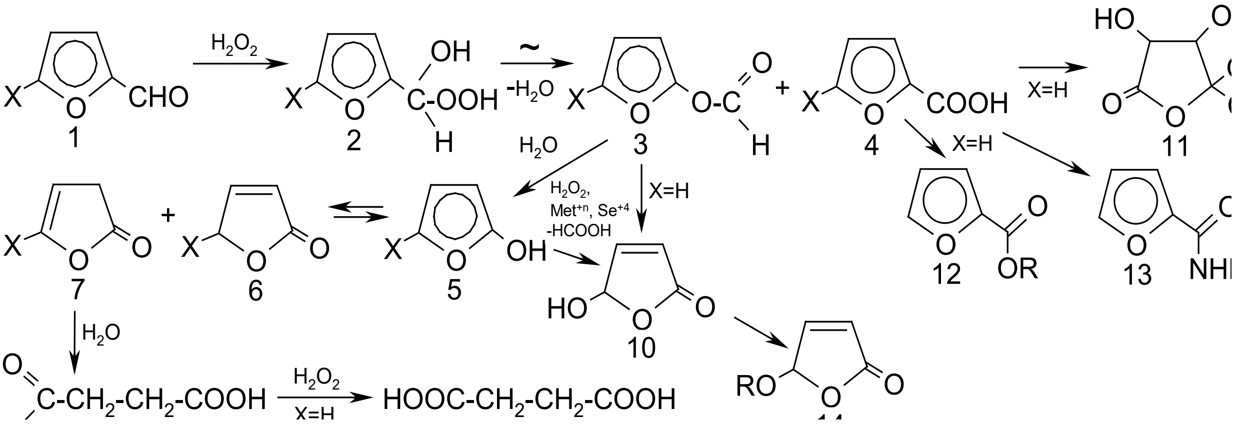
We have established a multifactorial effect on the processes in the reaction system «furan aldehyde – H_2O_2 – solvent». The reactions occurring in the system are multidirectional and are described by Scheme 1.



Scheme 1.

Their key stages are the rearrangement of peroxides 2 into furancarboxylic acids 4 or enoloesters 3 and subsequent transformations of these esters. The influence of substituents in the furan cycle, the nature of the solvent, the pH of the medium, the catalyst, the temperature and the molar ratio of the reagents on these stages was revealed. This made it possible to direct the oxidation process in the required directions [1].

A number of corresponding furancarboxylic acids were obtained by oxidation of furan aldehydes with electron acceptor substituents in a cycle in an aqueous dioxane medium at 70 ^{0}C. Oxidation of furfural and 5-methylfurfural in the media with increased basicity (water – triethylamine or in water at pH>5) at 25 ^{0}C was allowed to synthesize 2-furancarboxylic or 5-methyl-2-furancarboxylic acids 4. Esters of 2-furancarboxylic acid 12 were obtained by oxidation of furfural with 5% alcohol solution of H_2O_2 in the presence of SeO_2 at 50 ^{0}C. Oxidation in an aqueous alcohol medium in the presence of primary aromatic amines led to amides 13. The reaction in water at pH>8 allowed to synthesize previously unknown polysubstituted furanone 11.

Oxidation of furfural and 5-methylfurfural with hydrogen peroxide at 50-60 ^{0}C allowed to simultaneously synthesize hydrofuranone 6 and the products of hydroxyfuranones 7 conversion – levulinic acid 8 (from 5-methylfurfural) and succinic acid 9 (from furfural). Hydrofuranone 6 also obtained with quantitative yield by oxidation of furfural in the presence of niobium compounds.

Formic acid, formed from ester 3 during its hydrolysis, acts as a catalyst for the subsequent stages of the process.

Cyclic form of *cis*-β-formylacrylic acid 10 was synthesized by the oxidation of furfural with aqueous H_2O_2 in the presence of d-metals of V and VI groups compounds or SeO_2. Pseudo ethyl ester 14 was obtained in water-ethanol medium.

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NEW EXAMPLES OF THE APPLICATION OF THE MICHAEL'S REACTION IN A SERIES OF NITROGEN-CONTAINING HETEROCYCLES

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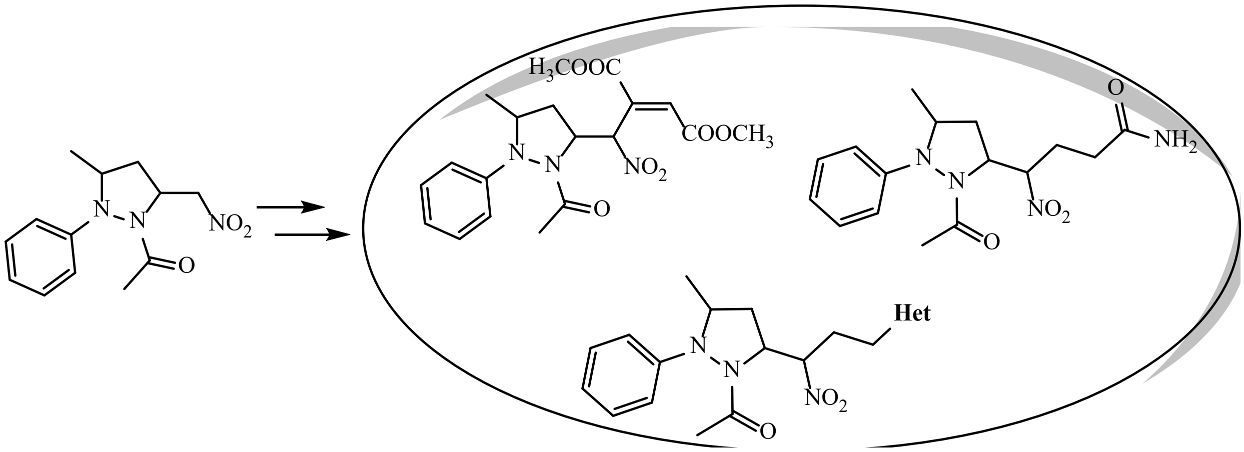
The Michael reaction has been used widely in organic synthesis for its C–C bond-forming ability. Conjugate addition of nitoalkyl group to electron deficient olefins is a highly useful reaction as basic strategy for organic synthesis, including the synthesis of polyfunctional heterocyclic compounds.

Previously was found that 3-nitromethylpyrazolidine **1** is the useful donor toward Michael addition, but the synthetic application this compound as nitronate anion have been limited a few examples [1].

Here we present synthetic utility of **1** by Michael reaction with vinyl pyridine, acrylamide and acetylenedicarboxylic acid (**Scheme 1**) it turns out that the reaction **1** with conjugated olefin proceeds best of all at room temperature on basic aluminum oxide containing 20% adsorbed KF.



Scheme 1

The structure of all obtained compounds was confirmed by data of IR, ^{1}H NMR, and mass spectroscopy.

Thus there are possible to synthesize new polyfunctional derivatives of pyrazolidines from nitromethyl pyrazolidines by their further functionalization.

This work was supported by Russian Foundation For Basic Research 18-03-00680\18

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SYNTHESIS OF NEW POTENTIALLY BIOLOGICAL ACTIVE PYRANOPYRIDONES WITH TRYPTAMINE FRAGMENT

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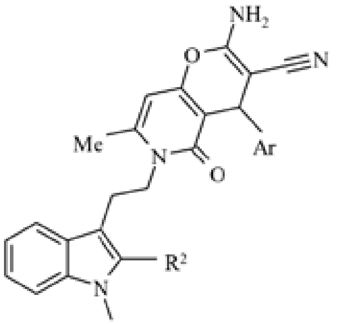
Continuing research on the use of multicomponent reactions in the synthesis of potentially biologically active compounds,[1,2] we obtained a number of new pyranopyridone derivatives with a tryptamine fragment **1**.



1

1 R^1=H, CH_2Ph; R^2=H, Me; Ar= C_6H_5, 2-ClC_6H_4, 4-MeSC_6H_4, 2,5-$(MeO)_2C_6H_3$,
4-(2-furyl)C_6H_4, 2-EtOC_6H_4, 4-Py, 4-(4-morpholinyl)C_6H_4, 3,4-$Cl_2C_6H_3$, 3-$NO_2C_6H_4$,
4-MeC_6H_4, 4-*i*-PrC_6H_4, 3-BrC_6H_4

Compounds **1** are formed with a yield of 55-90% by heating equimolar amounts of pyridonotryptamines, malononitrile and aromatic aldehydes in alcohol in the presence of Et_3N for 1-3 hours. Pyridonotriptamines were obtained by the interaction of tryptamines synthesized by the Grandberg reaction[3] and 4-hydroxypyranone-2. The choice of compounds **1** is determined by the intention to trace the influence of the substituents in the aromatic core of the pyranopyridone fragment on the cytotoxic activity, which is predicted by PASS calculations. Primary tests of compounds **1** on the course of mitosis in seeds of *Allium cepa L.* plants were carried out.

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SYNTHESIS OF CYCLIC ACETALS OF THE FURANE SERIES

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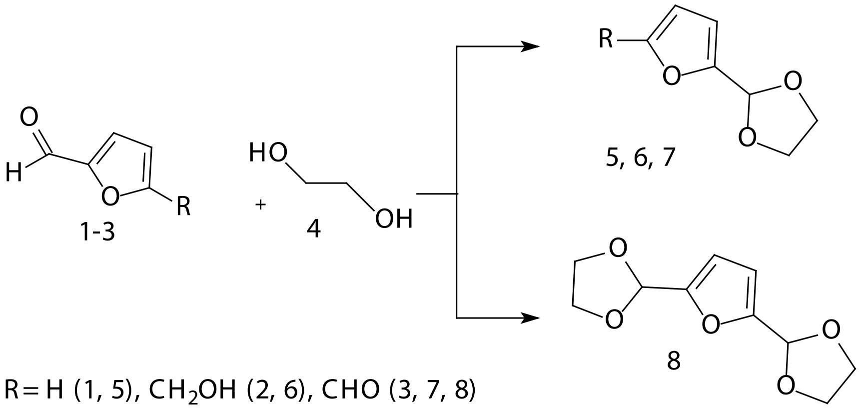
Abstract: The preparation of acetals of ethylene glycol and furan aldehydes is described.

We have previously studied the acetalization of diols and triols — ethylene glycol, glycerol, 1,2,3-butanetriol, and 1,2,4 butantriol [1-3]. The acetals obtained were used for the synthesis of biologically active ethers and esters [4-6].

Continuing these studies, acetals based on furfural **1** and its analogs, 5-hydroxymethylfurfural **2** and diformylfuran 3 (scheme), were obtained.



Ethylene glycol acetals **5-8** are formed with a quantitative yield in the presence of benzene in 3-5 hours. For dialdehyde **3**, mono-**7** and diacetal **8** were isolated, the formation of which is mainly influenced by the ratio of reagents. Thus, in 4 hours, with a 3-fold excess of diol **4**, only diacetal **8** is observed, whereas with a 3-fold deficiency of diol **4**, only mono acetal is predominantly formed **7** in the reaction mass.

This work was supported by the Russian Foundation for Basic Research (grant № 19-33-80002\19).

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SUPERAMPHIPHILES BASED ON CALIX[4]RESORCINOLS AND SURFACTANTS IN DRUG NANOCONTAINER DESIGN

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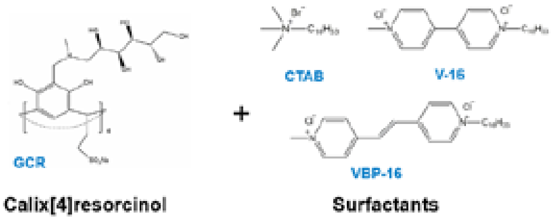
Nanoscale aggregates formed through noncovalent interactions are of great interest in drug delivery field. The supramolecular amphiphiles (super-amphiphiles) based on macrocycles and surfactants have a great potential for creating materials with fundamentally new properties and functions, primarily due to the relative simplicity of their creation, as well as a wide range of their possible applications: controlled self-assembly, creation of sensitive surfaces (capable of selectively binding molecules), nanocontainers, etc. In this regard, the present work is aimed at the creation of super-amphiphiles based on calix[4]resorcinols with N-methyl-D-glucamine groups on the upper rim (GCR) and surfactants (CTAB, V-16, VBP-16) (Scheme 1). Aggregation and solubilization properties of mixed systems were studied by set of physicochemical methods. Presence of GCR in surfactant solutions leads to decrease of critical aggregation concentration and solubilization capacity toward hydrophobic substrate that testifies about morphological changes, namely, micelle-to-vesicle phase transition due to host-guest interaction. Capability of these vesicles to encapsulate of hydrophilic Rhodamine B was investigated. Macrocycle-surfactant ratios with maximum encapsulation efficiency were found and structures of these amphiphiles was determined. The encapsulation efficiency of vesicles depends not only on the component ratio, but also on the concentration of the super-amphiphilic system as a whole. The results obtained show the possibility of spontaneous vesicles formation in the mixing of macrocycle with surfactant. At the same time, the composition of this system influences on the encapsulation capability of formed aggregates. Our results are an important step towards the development of controlled-release nanocontainers.



Scheme 1. Chemical formulas of studied substances

This work was supported by Russian Science Foundation, grant no. 17-73-20253.

SYNTHESIS OF LINEAR AND CYCLIC UREAS BASED ON THE REACTION OF 1-(3,3-DIETOXIPROPYL)UREA WITH PHENOLS

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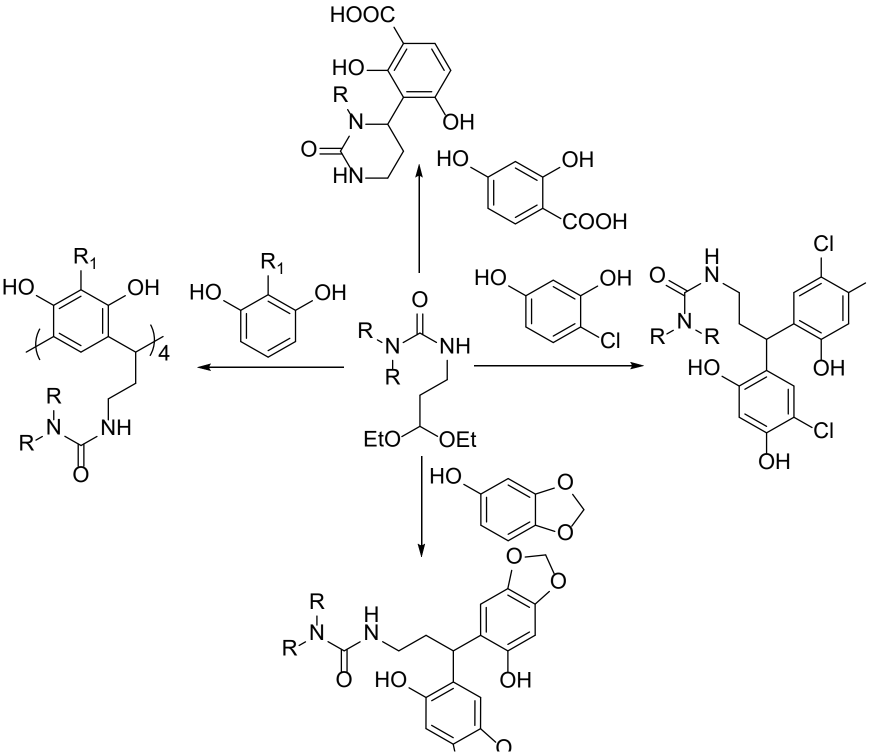
Substituted linear and cyclic ureas are widely used in medicine, agriculture and technology. Ureas containing alkyl aromatic fragments - derivatives of diarylpropane, calixarene and tetrahydropyrimidine-2(1*H*)-ones - are an important class of organic compounds due to their high pharmacological activity. However, at the moment there is no common and simple method for the synthesis of these classes of compounds. Therefore, in the present work, a new approach to the synthesis of substituted ureas containing alkylaromatic substituents on the nitrogen atom is proposed.

Our proposed approach to the synthesis of linear and cyclic ureas is based on the acid-catalyzed reaction of (3,3-diethoxypropyl) ureas with various phenols. Varying the structure of the (3,3-diethoxypropyl)ureas and phenols used allows to obtain either diarylpropanes, calix[4]resorcinols or tetrahydropyrimidin-2(1*H*)-ones.



The reported study was funded by RFBR according to the research project № 18-33-00206.

NEW QUATERNARY PHOSPHONIUM SALTS BASED ON TERTIARY PHOSPHINES AND UNSATURATED CARBOXYLIC ACIDS

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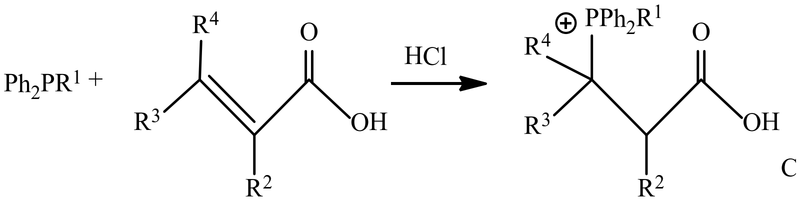
In recent years, reactions of tertiary phosphines with *α,β*-unsaturated electrophilic substrates have received considerable attention in organic chemistry. Stable products of these transformations, quaternary phosphonium salts, attract interest as potential Lewis acidic catalysts and phase-transfer catalysts.

Herein we report synthesis new stable quaternary phosphonium salts on the basis of unsaturated carboxylic acids containing electron donating groups at double bond.



1-3 (a-d)

	1a	1b	1c	1d	2a	2b	2c	2d	3a	3b	3c
R^1	Ph	Ph	Ph	Ph	CH_3	CH_3	CH_3	CH_3	$(CH_2)_2COOH$	$(CH_2)_2COOH$	$(CH_2)_2COOH$
R^2	H	H	H	CH_3	H	H	H	CH_3	H	H	CH_3
R^3	H	H	CH_3	CH_3	H	H	CH_3	CH_3	H	CH_3	CH_3
R^4	py	SC_4H_3	CH_3	H	py	SC_4H_3	CH_3	H	py	CH_3	H

Scheme 1

The reactions we carried out by boiling starting compounds in chloroform with adding two drops of hydrochloric acid at 100˚C during 6-10 h.

Table 1. Physical data for phosphonium salts **1-3** **(a-d)**

№	mp, ˚C	ν(C=O), cm^{-1}	NMR ^{31}P, δ_p ppm	Yield, %
1a	197	1698	26.33	38
1b	199	1736	24.75	49
1c	179	1712	35.95	55
1d	oil	1713	27.79	40
2a	177	1700	40.11	37
2b	179	1720	24.90	41
2c	175	1712	31.90	55
2d	168	1690	40.00	40
3a	143	1713	34.01	64
3b	180	1714	37.96	75
3c	85	1714	34.45	69

All phosphorylated derivatives were synthesized in good yield, characterized by different spectral studies and analyses.

This work was funded by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (№. 4.5888.2017/8.9).

ASYMMETRIC PROPARGYLATION OF ALDEHYDES CATALYZED BY NEW CHIRAL LEWIS BASES

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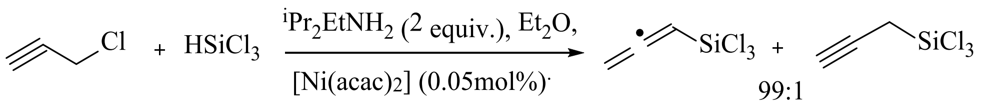
Optically active homopropagrylic alcohols are rare type of organic compounds due to the synthetic potential of acetylene group. They can be highly functional building blocks which found an application in the total synthesis of some biologically active compounds[1]. But the direct catalytic synthesis of this class of compounds appears to be challenging. Nowadays several methods of enantioselective propargylation have been developed. Some of these methods include using highly toxic reagents, such as tin compounds, some protocols requires an expensive reagents such as propargyl borolane. At this point using an allenylsilane as the propargylation agent is the most promising.



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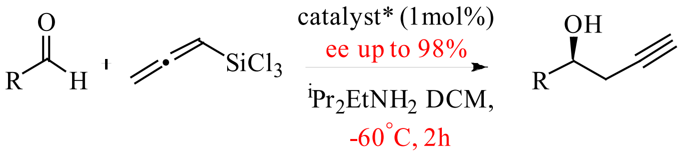
Scheme 1.

However, the development of catalysts for asymmetric propargylations using allenyltrichlorosilanes has proved much more challenging[2]. To our knowledge there are only two examples of using this reagent in asymmetric catalysis[2, 3].

In this work we've designed a series of new chiral Lewis Bases and show their excellent catalytic ability in the reaction of asymmetric propargylation of aromatic and α-unsaturated aldehydes.



*Structure of catalysts, their synthesis, optimization of reaction conditions and possible mechanisms will be discussed.

The authors thank the Russian Science Foundation for Grant 18-73-10156

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A NEW SYNTHESIS OF ETHYL 1-AZOLYL-1*H*-1,2,4-TRIAZOLE-3-CARBOXYLATES

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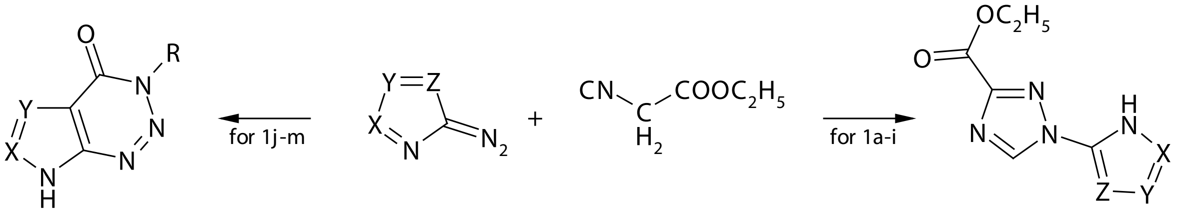
Depending on the nature of the substituents at the aromatic ring, the the reaction of arenediazonium salts with derivatives of isocyanoacetic acid leads to either 1-aryl-3-*R*-triazoles or products of dediazoniation [1, 2]. Nevertheless, there aren't any examples in which the heterocyclic diazo compounds are used in the same interactions.

In the other hands the reactions of 5-diazoazoles and their diazonium salts with aliphatic methylene active reagents, such as □□ketonitriles, nitrilesters and dinitriles, affords corresponding azol-5-ylhydrazones. Depending on the nature of the reactants and on the pH of the medium, these coupling products can either be isolated in good yields or can directly cyclize to azolo[5,1-c][1,2,4] triazine derivatives [3].

In the present work, we investigated the synthetic routes to interaction of 5-diazoazoles **1a–m** with ethyl isocyanoacetate **2** (scheme 1). Coupling were carried out in acetone in the presence of sodium acetate and ethyl 1-azolyl-1*H*-1,2,4-triazole-3-carboxylates **3a–i** were obtained with 72–90 % yields. However when the reaction was performed with 5-diazoazoles **1j–m** containing carboxamide groups in position 4, only azolo[4,5-*d*][1,2,3]triazine-4-(3*H*)-ones **4a–d** were isolated in a high yields.



4a-d 1a-m 2 3a-i

1,3a-d X = N, Z = CH, a Y = C-C_6H_5, b Y = C-C_6H_4-CH_3-p, c Y = C-C_6H_4-OCH_3-p, d C-C_6H_4-Cl-p,
1,3e X = N, Y = CH, Z = C-$COOC_2H_5$; 1,3f-i X = CH, Y = N, f Z = C-$COOC_2H_5$;
g Z = C-Morpholinocarbonyl, h Z = C-Piperidinocarbonyl, i Z = C-Pyrrolidinocarbonyl;
1j,k X = N, Y = CH, j Z = $CONH_2$, k Z = $CONHCH_3$, 1l,m X = CH, Y = N, l Z = $CONH_2$, m Z = $CONHCH_3$;
4a,b X = N, Y = CH, a R = H, b R = CH_3; 4c,d X = CH, Y = N, c R = H, d R = CH_3

Scheme 1.

As a results of research we have developed a new method of synthesis of ethyl 1-azolyl-1*H*-1,2,4-triazole-3-carboxylates **3a–i**, which based on the reaction of 5-diazoazoles **1a–m** with ethyl isocyanoacetate **2**.

The structure of the synthesized compounds was confirmed by ^1H NMR, ^{13}C NMR, IR spectroscopy and mass spectrometry.

This work was partially supported by the Russian Federation President Grant for leading scientific schools № 4687.2018.3.

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SYNTHESIS AND CHARACTERIZATION OF MONO-, DI- AND TETRASUBSTITUTED ITEROMERS OF THIACALIX[4]ARENE WITH AMINO GROUPS ON THE LOWER RIM

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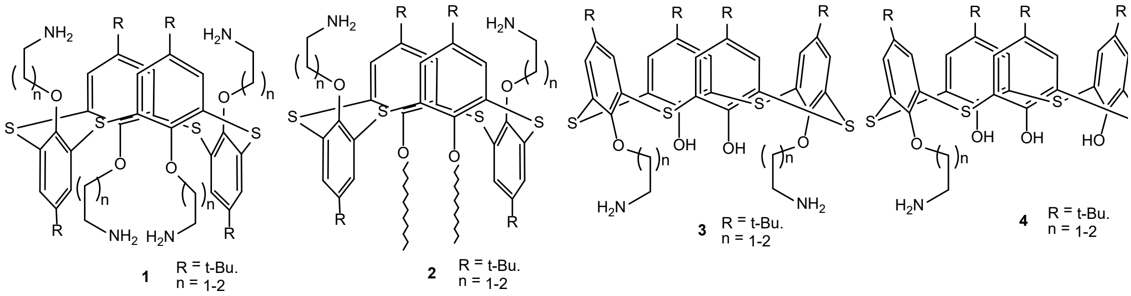
The compounds possessing amino fragments are characterized by a number of pharmacological effects, such as antitumor, anti-inflammatory, antibacterial, and antiarythmic activity. A convenient approach to decrease the therapeutic dose of these pharmacophores is to employ a calixarene scaffold, which allows one to attach several amino groups on the lower rim of the macrocycle. This macrocycle is also readily accessible and nontoxic. In addition to the pharmacological activity of amino derivatives, these groups can also be modified to prepare diverse heterocycles.

The aim of this work is to synthesize and elucidate the structure of di- and tetrasubstituted iteromers of thiacalix[4]arene possessing amino groups on the lower rim.



Scheme 1.

In this work, a number of amino derivatives of thiacalix[4]arene in *1,3-alternate* (**1**, **2**) and *cone* (**3**, **4**) stereoisomeric forms has been synthesized in high yields from phthalimide precursors (55–72%). These products have been characterized using a number of NMR techniques (COSY, HSQC, HMBC) and MALDI mass spectrometry. Amino derivatives **1**–**4** have been converted into ammonium salts using methyl iodide and their preliminary toxicity towards microorganisms has been evaluated.

This work was supported by the Russian Foundation for Basic Research (project no. 17-53-10016-KO-A).

CATALYTIC REGIOSELECTIVE SYNTHESIS OF CYCLOPROPYL VINYL SULFIDES AND POSSIBLE PRACTICAL APPLICATIONS

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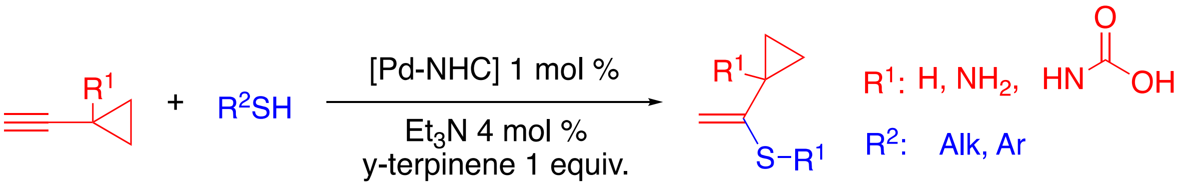
Vinyl sulfides represent an important class of compounds in organic chemistry and materials science. They are utilized in synthesis of biologically active compounds, polymer chemistry and radical reactions [1-3]. Today chemistry of radicals actively develops, and another often – used substrate in this field is cyclopropane. Interaction of cyclopropane derivatives with different radicals can lead to rearrangement into five- and six-membered rings. Because of this property, the cyclopropane ring is used in organic chemistry as a radical clock for investigation of reaction mechanisms. In our work we combined the two fragments: vinylsulfide and cyclopropane ring in one molecule. Such structures are promising monomers for radical chemistry due to the presence of a cyclopropane ring and the availability of sulfur atom, which is a good stabilizer of radicals.

To achieve this goal, we studied functionalization of cyclopropyl acetylene with thiophenol in various catalytic systems based on nickel, palladium and platinum. Among many candidate catalysts, a palladium complex with N-heterocyclic carbene ligand (IMes)Pd(acac)Cl was found to be the most effective. This complex was subsequently used for optimization of the reaction conditions. The developed catalytic system is active for a wide range of thiols (Scheme 1). The structure and composition of products have been confirmed by NMR and MS in the isolated individual state.



1 2 3

Scheme 1. The developed thiol-yne click catalytic system provides an atom-economic access to vinyl(cyclopropyl) sulfides.

Vinylated derivatives of cyclopropane are highly reactive, due to the presence of double carbon-carbon bond next to the strained three-membered ring. These compounds can react with different radicals. It should be noted that, depending on the nature of the radical which was generated during the reaction, we observed different reactivity of vinylated derivatives of cyclopropane. Thus, we propose application of these compounds for radical recognition.

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THE EFFECT OF HYDROGEN BONDS ON THE REACTIVITY, MECHANISM AND THERMODYNAMIC PARAMETERS OF REACTIONS

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Complexes with hydrogen bonds form a wide range of compounds. Considering their role in chemistry, first of all, they focus on their structuring role. Hydrogen bonds determine the secondary, tertiary structure of both natural (proteins, DNA, RNA, cellulose, chitosan, etc.) and synthetic (polyurethanes, polyamides, polyureas, polyacids, polyamines, polyvinyl alcohol, etc.) high molecular weight compounds . Hydrogen bonds ensure the existence of a double helix of DNA, matrix synthesis on it. Compounds with a mobile hydrogen atom (water, alcohols, carboxylic acids, mercaptans, amines, phenols, etc.) are examples of compounds that are structured by the type of hydrogen bonds.

The main consideration when considering the role of complexes with hydrogen bonds in chemical reactions is given to the fact that in many cases they form a pre-reaction complexes. However, there are many reactions when complexes with hydrogen bonds (dimers, trimers, etc.) enter into transformations as reagents. In this regard, the question arises whether there are assumptions that suggest the different reactivity of monomers and their associates in chemical transformations? How do the thermodynamic parameters of activation and reactions involving monomers and their associates differ? What is the difference between the mechanisms of reactions occurring with the participation of monomers and complexes with hydrogen bonds?

We have studied change in acid-base and donor-acceptor properties of a number of organic compounds during the formation of hydrogen-bonded complexes. Our calculations have shown that complexes with hydrogen bonds possess enhanced electron donor-acceptor and acid-base properties as compared with their monomers, which is a premise for predicting the increased reactivity of hydrogen-bound associates. Further, we studied the effect of hydrogen-bonded complexes on the mechanism and thermodynamics of the reactions.

It has been shown that the reactions of isocyanates with hydrogen-bonded homocomplexes of alcohols, phenols, amines, mixed complexes of phenols with alcohols, amines with alcohols flowing through consistent late asymmetric transition states are kinetically and thermodynamically more preferable than interactions involving monomers as in a gas, and in the liquid phases. Reactions on the N = C bond of isocyanates are much more preferable than the interaction on the C = O bond. The autocatalytic nature of the reactions of isocyanates with alcohols is due to the fact that complexes with hydrogen bonds of carbamates with alcohols have higher electron donor properties as compared to monomers of alcohols.

The influence of the nature of the hydroxyl-containing compound and the type of its associate on the electronic character of attachment to isocyanates has been established. These interactions can occur as a reaction of nucleophilic and electrophilic addition to hetero-fold bond.

The catalytic effect of phenols in the reactions of isocyanates with alcohols has been found. The targeted formation in the mass of polyurethanes of complexes with hydrogen bonds of phenols with hydroxyl groups resulting from the thermal decomposition of carbamate fragments is a method of increasing the heat resistance of polyurethanes.

It is shown that the transesterification of cyclic carbonates with alcohols, the formation of carbamates in the interaction of organic carbonates with amines with associates of alcohols and amines, are kinetically and thermodynamically more preferable than interactions with their monomeric forms.

CHAIN AND NON-CHAIN RADICAL PATHWAYS IN REACTIONS OF CARBONYLMETALLATE ANIONS WITH ALKENYL AND ARYL HALIDES

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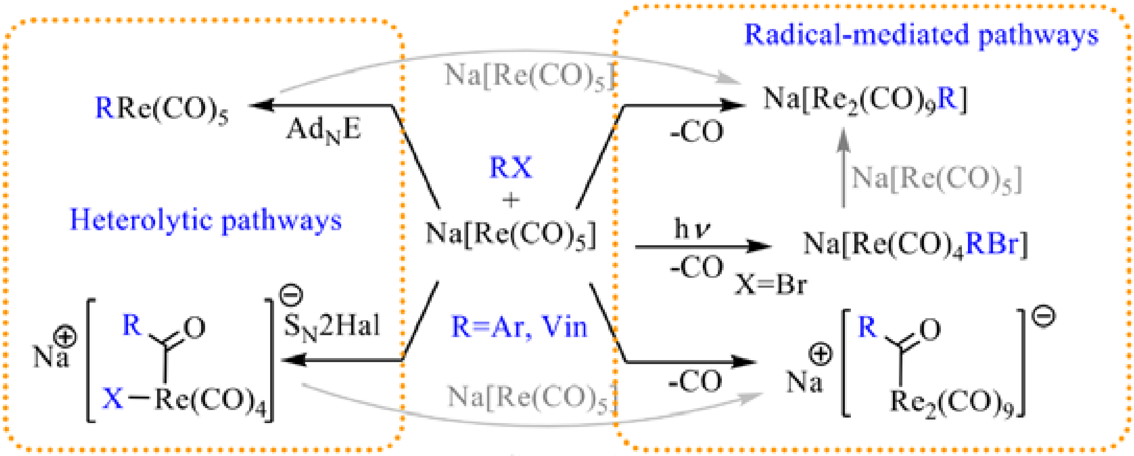
Free radicals, both organic and metal-centered ones, are much more reactive than closed-shell molecules, but can be generated from the latter by single electron transfer process (SET). Generation of radicals may in turn trigger new reaction pathways and significantly change reactivity and selectivity of reaction. First realized in $S_{RN}1$ nucleophilic aromatic substitution [1] this kind of activation is now attracting increasing interest in the form of redox-catalysis [2].

Metal carbonyl anions are good one-electron donors, and in this communication we show that SET-mediated reactions of carbonylate anions with alkenyl and aryl halides can lead to unexpected and otherwise inaccessible products. Binuclear [R-Re$_2$(CO)$_9$]$^-$ complexes are the first and most frequent type of such products. Radical-chain reactions of [Re(CO)$_5$]$^-$ with bromostilbene and 3-bromocyclohexen-2-one furnish another type of products, [R-Re(CO)$_4$Br]$^-$ which can subsequently convert into binuclear complexes. Binuclear acyl complexes [R(CO)Re$_2$(CO)$_9$]$^-$ are formed in slow halogenophilic (S_N2Hal) reactions of RX (X=Cl,Br) with [Re(CO)$_5$]$^-$ by CO-ligand substitution in initially generated halo(acyl)rhenates (Scheme). In all these cases mechanistic tests (light-stimulation, effect of radical-traps and initiators) suggest the involvement of odd-electron species in CO substitution step and possibly in the main nucleophilic substitution/oxidative addition reaction of RX with [Re(CO)$_5$]$^-$.



Scheme 1.

The 3-halocyclohexen-2-one reaction with Na[Re(CO)$_5$] turned out to be unique in providing the possibility to observe the transition from polar addition-elimination pathway to radical-chain oxidative addition and further to S_N2Hal process. The mechanistic switch can be triggered by visible light or by steric hindrance in 5,5-substituted cyclohexenone. Radical traps also inhibit the reactions of the same alkenyl halides with [CpFe(CO)$_2$]$^-$ and [Mn(CO)$_5$]$^-$, which give normal nucleophilic substitution products, yet turn out to proceed by way of free radical intermediates.

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ORGANOIODINE(III) MEDIATED INTRAMOLECULAR OXIDATIVE CYCLIZATION OF AZINYLHYDRAZONES

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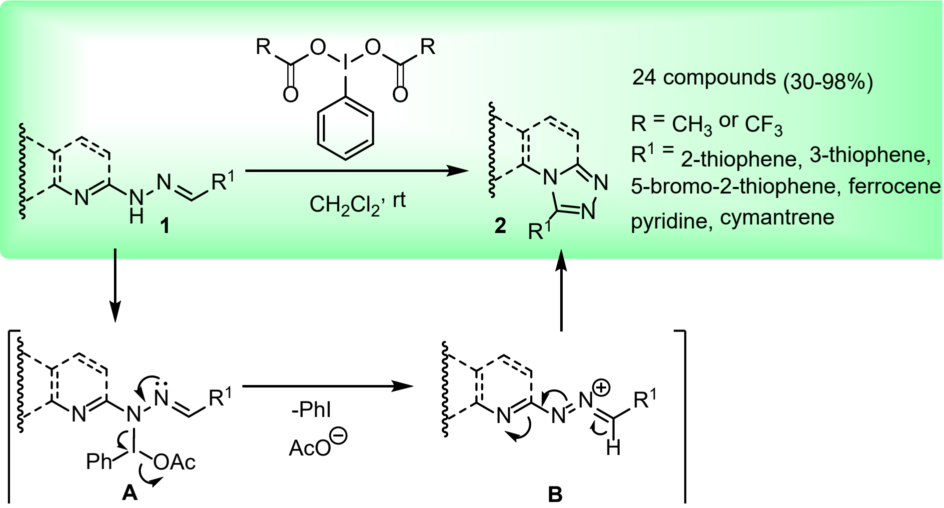
Most of the compounds derived 1,2,4-triazoles have been shown to display a wide spectrum of biological activities. It is known that the synthesis of triazolopyridines, triazoloquinolines and so on has been based on oxidative cyclization from their respective hydrazones. The reactions proceeding in the presence of hypervalent iodine is taking special place among oxidative cross-dehydrogenative cyclization. The unique properties of hypervalent iodine make it possible to refuse not only catalysis by transition metals, but also “hard” synthetic methods in the synthesis of heterocyclic compounds.

In this work, the oxidative cross-dehydrogenative cyclization was developed for the synthesis of 1,2,4-triazolo[4,3-*a*]azines, containing both heterocyclic (thiophene, pyridine) and metallocenyl (ferrocene, cymantrene) fragments (Scheme 1). The reaction condition depends on selected substrates. The cyclization reactions are carry out in the presence of [bis(trifluoroacetoxy)iodo]benzene (for hydrazones that contain the pyrimidine and ferrocene fragments) and (diacetoxyiodo)benzene (for hydrazones that contain the pyridine, quinoline, quinoxaline and cymantrene fragments) under mild conditions.



Scheme 1. The oxidative cross-dehydrogenative cyclization of azinylhydrazones

Thus, it was shown that the reaction of oxidative cross-dehydrogenative cyclization in the presence of hypervalent iodine (III) is a convenient method for the synthesis of new potential biologically active compounds.

The research was financially supported by the Russian Foundation for Basic Research (18-33-00927), the Ministry of Education and Science of the Russian Federation grant number 4.6351.2017/8.9.

DICHLORO-SUBSTITUTED 1,2-DIAZABUTA-1,3-DIENES AS HIGHLY REACTIVE ELECTROPHILES IN THE REACTIONS WITH C-NUCLEOPHILES

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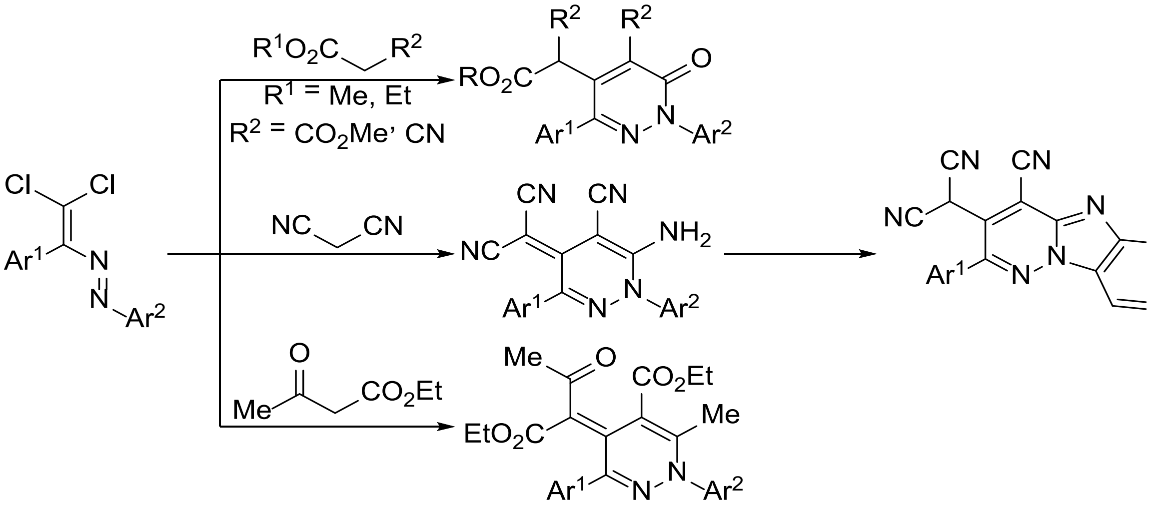
4,4-Dichloro-1,2-diazabuta-1,3-dienes are convenient synthons for preparation of various organic compounds. Their effective application in the synthesis of nitrogen-containing heterocyclic compounds makes especially important the development of new effective approaches to obtaining various potentially promising structures. Recently, we showed that 4,4-dichloro-1,2-diazabuta-1,3-dienes can react with different nucleophiles [1],[2].

This work is devoted to detailed investigation of 4,4-dichloro-1,2-diazabuta-1,3-dienes as electrophiles in reactions with dimethylmalonate, cyanoacetic esters, malononitrile, ethyl acetoacetate (Scheme 1). The selectivity of pyridazine-ring closure for different electron-withdrawing groups in 1,3-dicarbonyl compounds was shown. A number of benzo[4,5]imidazo[1,2-*b*]pyridazine derivatives was obtained from the synthesized aminopyridazines. Also, the spectral and fluorescent characteristics of new compounds were investigated.



Scheme 1.

This work was partially supported by the Russian Federation President Grant for leading scientific schools № 4687.2018.3.

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SUPRAMOLECULAR AND POLYMERIC NANOSTRUCTURES BASED ON CARBOXYLATE DERIVATIVES OF RESORCINARENES

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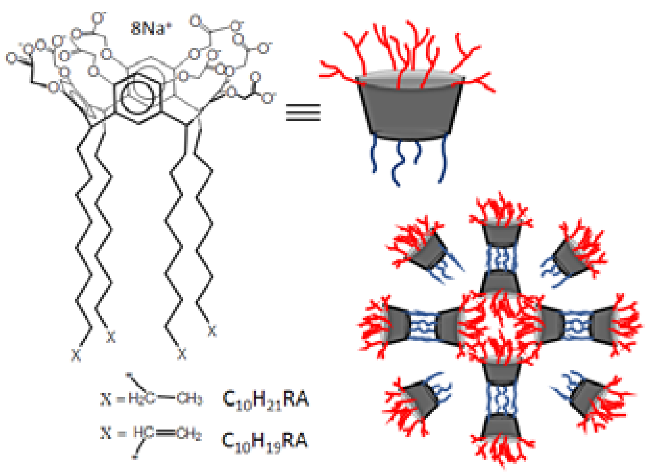
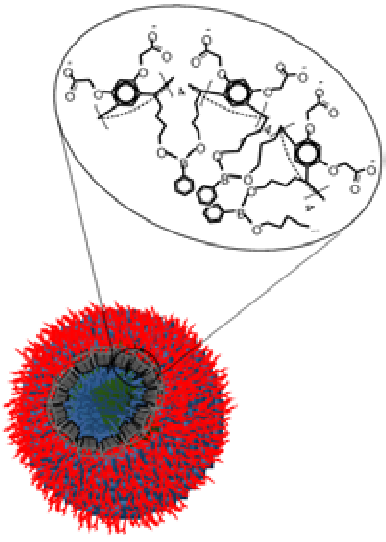
Synthesis of nanostructures is one of the most important research areas. Different strategies for the creation of nanocomposites using of supramolecular and polymeric matrix have been applied. Protection of organic and inorganic substrates is one of the areas of applications of nanocomposites. Supramolecular and polymeric nanocontainers have advantages and disadvantages in the use as carriers of organic substrates and a catalytically active particle.





We studied supramolecular and polymeric nanocontainers based on carboxylate derivatives of resorcinarenes. Nanocontainers were investigated in binding og organic substrates and in creation of catalytically active nanocomposites.

The results obtained show that supramolecular nanocontainers are effective in synthesis of catalytically active nanocomposites. Polymer nanocontainers have better inclusive characteristics.

This work was supported by Russian Foundation for Basic Research (RFBR № 19-03-00429) and the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (4.1493.2017/4.6 and 4.5151.2017/6.7

TANDEM ONE-POT ASSEMBLY OF DIHYDROPYRROLO[2,1-*B*]OXAZOLES FROM 1-CYANO-3-HYDROXYALKYNES AND 3*H*-PYRROLES

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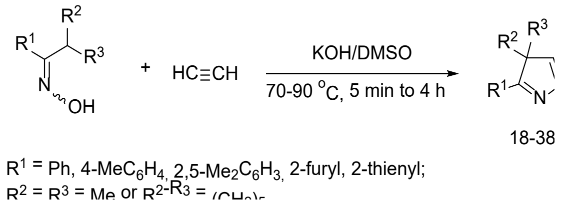
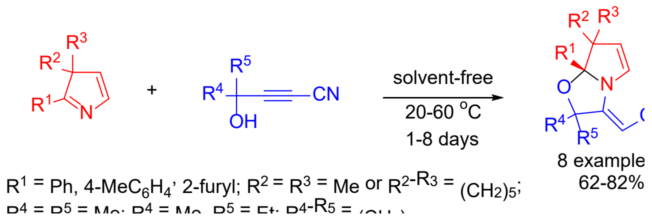
3*H*-Pyrroles, nonaromatic pyrrole isomers, remain understudied due to the instability that stems from their energy excess (12–17 kcal/mol) compared to the 1*H*-isomers [1]. However, these compounds acquire relative stability when two substituents are present at the 3-position. Some representatives of 3,3-disubstituted-3*H*-pyrroles demonstrate, as anticipated, rich reactivity in rearrangement, addition and cycloaddition reactions [2]. Recently, we have deloped a straightforward, one-pot synthesis of 3,3-dialkyl-2-aryl-3*H*-pyrroles from available aryl isoalkyl ketoximes and acetylene using the KOH/DMSO superbasic catalytic system (Scheme 1) [1,3].



Scheme 1

As part of our ongoing study of this intriguing class of pyrroles herein we report on a stereoselective, catalyst- and solvent-free synthesis of (*Z*)-2-(dihydropyrrolo[2,1-*b*]oxazolydine)acetonitriles from 3,3-dialkyl-2-aryl-3*H*-pyrroles and 1-cyano-3-hydroxyalkynes (Scheme 2) [4]. The preference for [2+3]-annulation over the [4+2]-Diels-Alder alternative was rationalized in the terms of the enhanced basicity of the pyrrole nitrogen which directs the cycloaddition onto the C=N bond only.



Scheme 2

The synthesized pyrrolo[2,1-*b*]oxazoles represent promising intermediates in the design of novel pharmaceuticals and building blocks for heterocyclic synthesis. To justify these hopes it can be noted that hydrogenated pyrrolo[2,1-*b*]oxazoles constitute a core structure of natural alkaloids, and are in high demand for the enantioselective synthesis of diverse pyrrolidine derivatives [see ref. 4 and reference therein].

This work was supported by RFBR according to the research project № 17-03-00927.

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SYNTHESIS AND POTENTIAL BIOLOGICAL ACTIVITY OF PYRIDINECARBOXYLIC ACID DERIVATIVES

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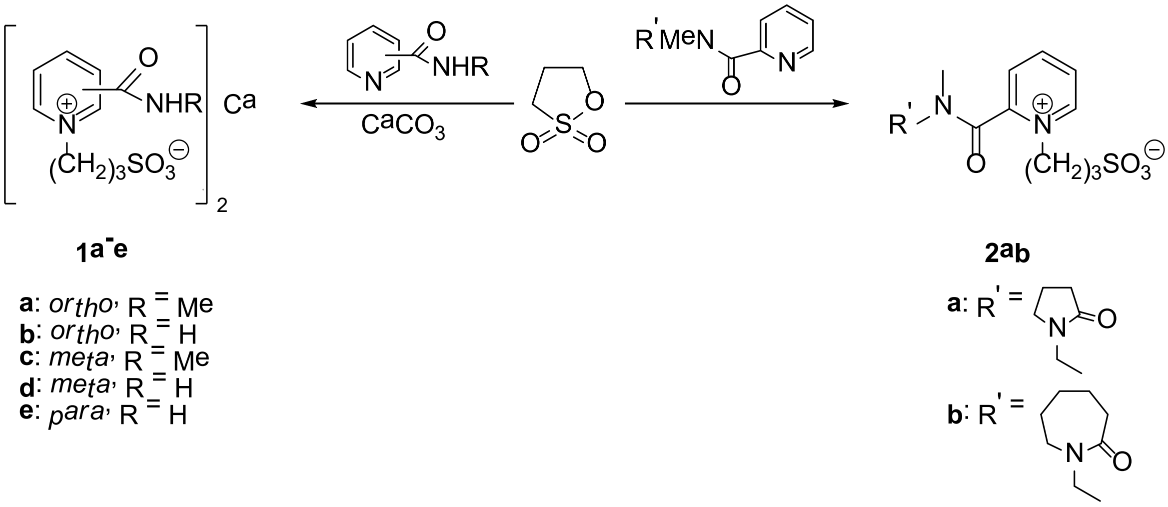
Derivatives of *S*-alkylpyridines have a wide range of biological and pharmacological activities: antimalarial, antiproliferative, antimicrobial, cardiovascular and antiviral [1].

Using computer modeling QSAR, candidate substances were selected, based on the potential biological activity predicted for them, the next substances of the calcium salts of pyridine sulfonates **1a - e** obtained by the reaction of 1,3-propanesultone with pyridine carboxylic acid amides with subsequent processing with CaCO$_3$ (**Scheme 1**). The structure of compounds **1a – e** in solution was confirmed by spectral methods (IR and NMR), and in a solid by X-ray.

Besides that, we carried out the synthesis of compounds **2ab**. In this case substitution product of silylated pyridinecarboxylic acid amides with halogenmethyl lactames was reacted with 1,3-propanesulton (**Scheme 1**).



Scheme 1.

Preliminary biological tests on *in vivo* and *in vitro* models indicate the potential use of the synthesized compounds as anti-ischemic drugs.

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MULTIFERROCENE COMPLEXES BASED ON TRIFERROCENYLTRITHIOPHOSPHITE WITH COPPER(I) BROMIDE: SYNTHESIS AND STRUCTURES.

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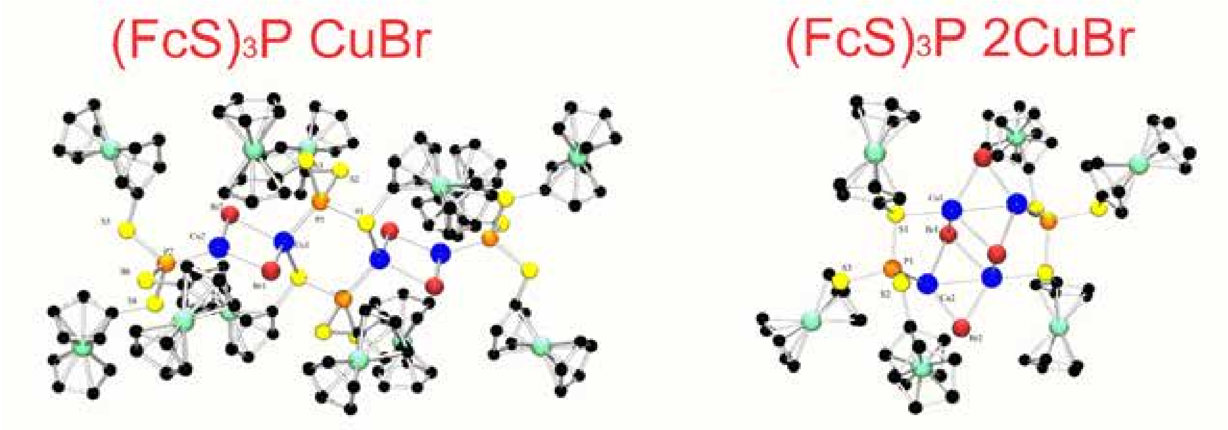
The trithiophosphite has a significant interest as potential ligands. Ability both phosphorus and sulfur atoms to bonding with metal ions lead to realization of different coordination modes that result formation of polynuclear complexes and clusters. The complexation properties of trithiophosphites clearly depend on the metals.

We have found that triferrocenyltrithiophosphite react with copper (I) bromide to form two type complexes depending on stoichiometry of initial reagents with different coordination mode of triferrocenyltrithiophosphite with copper atoms.

Stirring mixture of copper (I) bromide and triferrocenyltrithiophosphite in ratio 1:1 lead to formation of tetrakis((triferrrocenyltrithiophosphite)copper(I)bromide) almost with quantitative yield. Changing the ratio triferrocenyltrithiophosphite/CuBr result the formation of complex another mode type and contain four copper atoms connected by bromide atoms and two molecule of triferrocenyltrithiophosphite as bridged ligands. The all four membered cycles CuBrCuBr are planar that is typical for copper (I) bromide.



The work was financially supported by the grant of President of the Russian Federation (MK-3375.2019.3)

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REGIOCHEMISTRY OF THE REACTION OF PIPERITENONE WITH P–H-PHOSPHONIUM SALTS

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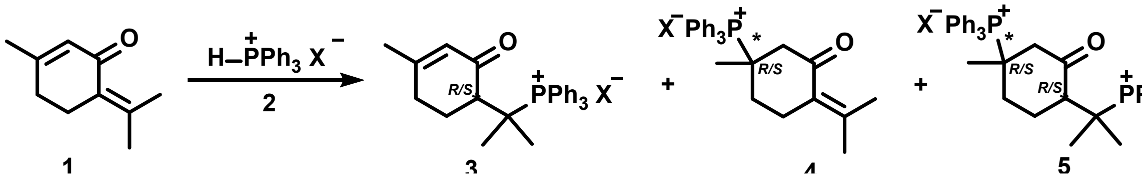
Phosphonium derivatives of polyfunctionalized compounds attract a special attention due to their practically significant properties. Quaternary phosphonium salts exhibit antibacterial, antimicrobial, antimycotic and anticancer activities [1]. It was previously shown that terpenoids bearing unsaturated ketone fragment are easily react with phosphorus-containing nucleophiles to give the cyclic and acyclic derivatives [2, 3]. Herein the peculiarities of the reaction between cyclic monoperpenoid piperitenone (1) and P–H-phosphonium salt (2) are discussed. Piperitenone (1) contains two activated double carbon–carbon bonds and can add one or two molecules of salt (2) to form compounds (3-5) (Scheme 1).



Scheme 1. Reaction of piperitenone with P-H-phosphonium salts.

Regiochemistry of the addition of the P–H-phosphonium salt to piperitenone was found to depend strongly on the reaction conditions. Initially, compound (4) is formed. After removal of the solvent, the content of phosphonium salt (4) decreases and compounds (3) and (5) appear. (Fig. 1)

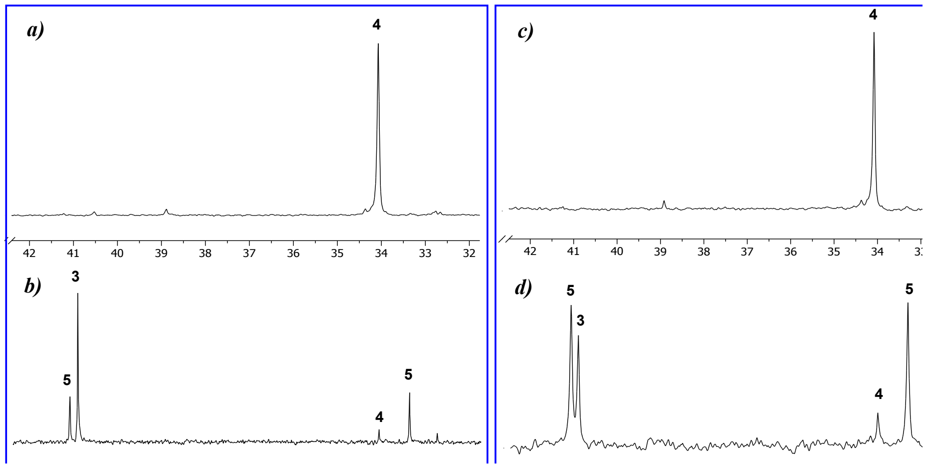


Fig. 1. The ^{31}P-{^{1}H} NMR (243 MHz) spectra of the reaction mixtures of piperitenone (1) and triphenylphosphonium triflate. The ratio of (1) to (2) is 1 : 1 (*a*, *b*) and 1 : 2 (*c*, *d*). a, c – reaction mixture after 16 hours (20 °C), *b*, *d* – reaction mixture after removal of the solvent.

This work was funded by RFBR (grant №18-33-00224) and by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (4.5151.2017/6.7).

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THIENO[3,2-D]PYRIMIDIN-4-ONES: SYNTHESIS AND ALKYLATION

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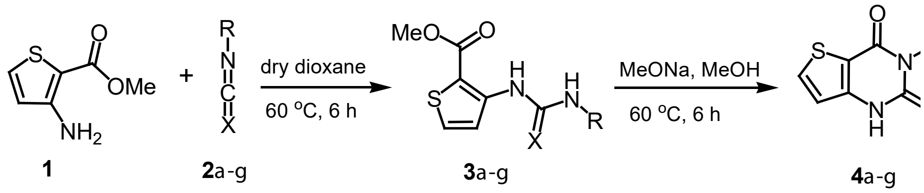
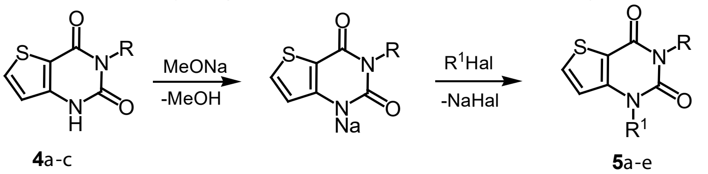
The interest for thieno[2,3-d]pyrimidines is caused by a wide spectrum of biological activity of these compounds. Far less reports about the synthesis of regioisomeric thieno[3,2-d]pyrimidines. Aminogroup in aminoester **1** is a more nucleophilic and carbonyl more electrophilic than methyl 2-aminothiophene-3-carboxylate. The interaction of compound **1** with isocyanates and isothioscyanates **2a-g** initially leads to carbamides or thiocarbamides **3a-g**, alkaline treatment of which leads to pyrimidinediones **4a-c** or 2 -thioxopyrimidin-4-ones **4d-g.**



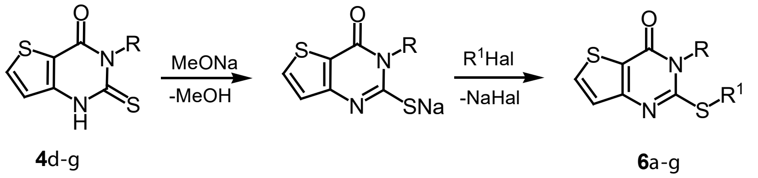
2,3,4: X = O, R = 4-ClC_6H_4 (a), 2,4-FC_6H_3 (b), *i*-Pr (c),
X = S, R = Me (**d**), Ph (**e**), 2-FC_6H_4 (**f**), 4-$MeOC_6H_4$ (**g**)

Pyrimidinediones **4a-c**, due to a movable hydrogen atom at position 1, are able to join the reaction of alkylation.



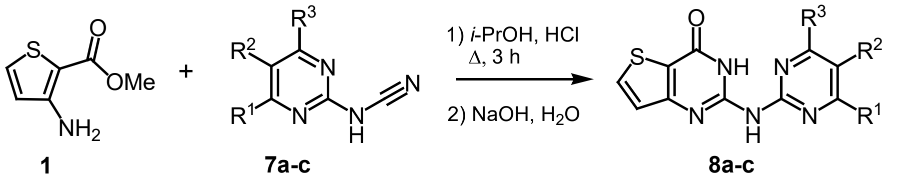
5: R = 4-ClC_6H_4, R^1 = CH_2CN (a),
R = 2,4-FC_6H_3, R^1 = Me (b), CH_2COCH_3 (c
R = *i*-Pr, R^1 = Me (d), $CH_2C_6H_4CN$ (e)

2-Thioxopyrimidin-4-ones **4d-g** alkylated at the sulfur atom. In this case, the compound **4d-g** are also converted into its sodium salt, which under mild conditions with good yields subjected to alkylation.



6: R = R^1= Me (**a**); R = Ph, R^1 = Me (**b**), CH_2CN (c);
R = 2-FC_6H_4, R^1 = Me (d), CH_2CN (e), CH_2COOCH_3 (f);
R = 4-$MeOC_6H_4$, R^1 = CH_2COCH_3 (g)

Structural analog of isocyanates and isothiocyanates are cyanamides. We used the *N*-pyrimidin-2-ylcyanamides **7a-c**. The interaction of мethyl 3-aminothiophene-2-carboxylate with cyanamides is a regioselective process and it leads to *N*-2-substituted 2-aminothieno[3,2-*d*]pyrimidin-4(3*H*)-ones **8a-c**.



7,8: R^1 = R^2 = R^3 = H (**a**); R^1 = R^3 = Me, R^2 = H (**b**); R^1 = Ph, R^2 = R^3 = H (

MARKOVNIKOV CONGRESS ON ORGANIC CHEMISTRY
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BIOLOGICAL ACTIVITY OF PYRROLO-[1,2-A]THIENO[3,2-E]PYRIMIDINES

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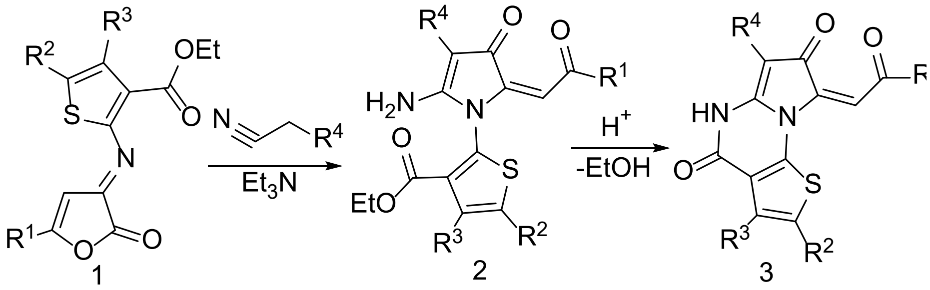
Earlier we proposed a simple method for the production of a series of *N*-substituted 5-aryl-3-imino-3*H*-furan-2-ones by the intramolecular cyclization of *N*-substituted 2-amino-4-aryl-4-oxobuten-2-oic acids in the presence of acetic anhydride [1]. At the same time, the rare type of 2-furanone derivatives seemed extremely promising from the standpoint of high reactivity and the possible presence of biologically active compounds in series of furan derivatives. Moreover, the introduction of a thiophene substituent into the structure at the imine nitrogen atom increases the prospects of these compounds even further. The Gewald reaction products are widely employed in drug discovery as an important biological entity, which were actively employed in synthesis of a variety of target family classes [2].

We synthesized ethyl 2-(2-oxofuran-3(2*H*)-ylideneamino)thiophene-3-carboxylates 1 and investigated their recyclization reactions.



R^1=Ar, Het; R^2,R_3=Alk, Ar; R^4=COOAlk, $CONH_2$

It was found that 2, in the presence of derivatives of cyanoacetic acid, undergo smooth cyclization into tricyclic compounds 3. The mechanism of reactions and biological activity of compounds 2,3 will be discussed.

This work was supported by Russian Science Foundation (№ 18-73-00091).

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NEW 4,5-DISUBSTITUTED HOMOADAMANTANES

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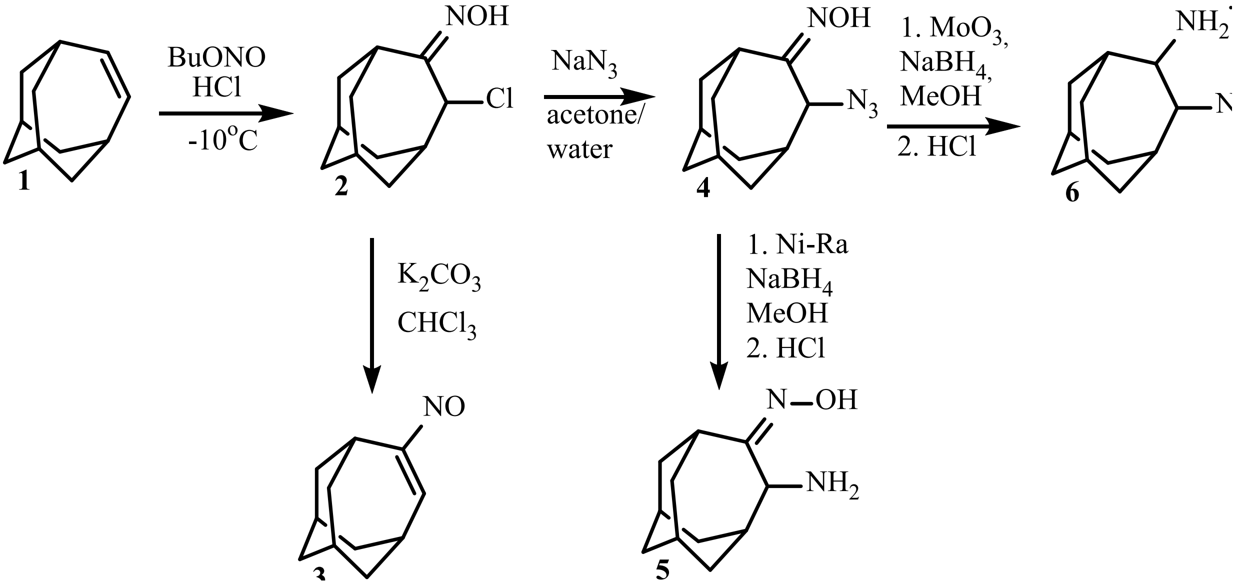
The fragment of homoadamantane can be found in the structure of natural compounds, for example *Hypericum sampsonii*, and synthetic drug candidates and shows a wide spectre of biological activity. The existing methods of preparation of 4,5-disubstituted homoadamantanes are based predominately on cyclization od 3,7-disubstituted bicyclo[3.3.1]nonanes.

We developed a new approach to 4,5-disubstituted homoadamantanes through electrophilic addition to homoadamantene **1**. The addition of nitrosyl chloride, generated *in situ* from butyl nitrite and conc. hydrochloric acid leads to chloroxime **2**, which undergoes elimination yielding nitrosoalkene **3**. The reaction of **2** with sodium azide goes smoothly forming azidoxime **4**, which can be then reduced with sodium borohydride. Noteworthy, that depending on catalyst, rediction can take place either of oxime group leading to aminoxie **5** or azide group leading to aminoazide **6**. The structures of compounds **2-6** were verified by ^{1}H and ^{13}C NMR spectra.



The reported study was funded by RFBR according to the research project № 19-03-00973

A NOVEL GENERAL METHOD FOR THE SYNTHESIS OF FUNCTIONALLY SUBSTITUTED PYRAZOLO[1,5-*A*]PYRIMIDINE

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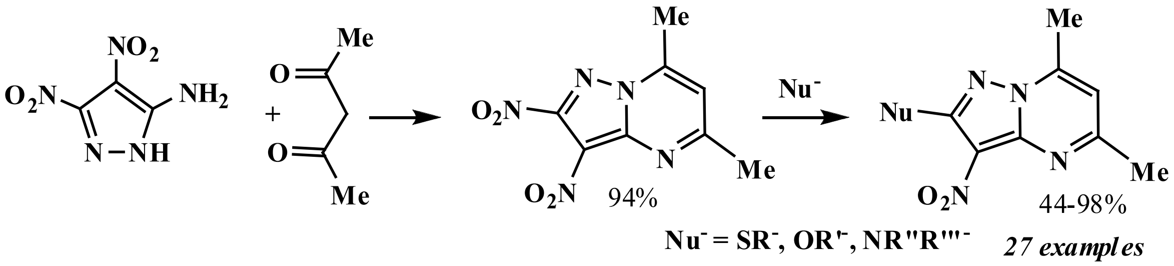
Pyrazolo[1,5-*a*]pyrimidine derivatives have high biological activity and are privileged compounds in medicinal chemistry. This structural fragment is present in a number of compounds that exhibit most diverse physiological activities such as sedative, antidepressant and antiepileptic; antitumor; antibacterial and antiviral.

The overwhelming majority pyrazolo[1,5-*a*]pyrimidines preparation methods are based on condensation of *β*-dicarbonyl compounds or their synthetic analogs with *N*-unsubstituted 3(5)-aminopyrazoles which already have a certain set of functional groups. This significantly limits the structural diversity of the pyrazole moiety in pyrazolo[1,5-*a*]pyrimidines and prevent the understanding of structure-property correlations necessary for further development of directed synthesis of biologically active substances. Therefore, it is highly relevant to design new general synthetic methods for pyrazolo[1,5-*a*]pyrimidines.

We have proposed a method based on nucleophilic substitution of the nitro group in 2,3-dinitropyrazolo[1,5-*a*]pyrimidines that can substantially enhance possibilities of heteroatomic functionalization of the pyrazole moiety in the pyrazolo[1,5-*a*]pyrimidine. Despite a rather facile synthesis of dinitro derivatives of pyrazolo[1,5-*a*]pyrimidines by condensation of 5-amino-3,4-dinitropyrazole with *β*-diketones [1], this approach has not been used so far.



Scheme 1.

An interaction of model 5,7-dimethyl-2,3-dinitropyrazolo[1,5-*a*]pyrimidine with a wide range of heteroatomic *N*-, *S*- and *O*-nucleophiles was studied [2]. It was established that, under mild conditions, regioselective nucleophilic substitution of the nitro group in all cases occurs at position 2, which permitted to synthesize a library of various 2-R-3-nitropyrazolo[1,5-*a*]pyrimidines.

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SUBSTITUTED PYRROLO[3,4-*F*]INDOLE-5,7-DIONE AS EFFECTIVE INHIBITION OF THE MONOAMINE OXIDASE

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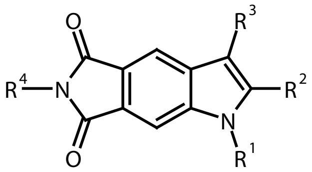
The monoamine oxidase (MAO) enzymes are recognized as pharmacological targets for the treatment of neuropsychiatric illnesses and neurodegenerative disorders. Two MAO isoforms are known, MAO-A and MAO-B. They display different substrate and inhibitor specificities, and based on this, selective inhibitors of the MAOs are employed for the treatment of different disease states. The aim of this study was therefore to discover structures that inhibit the MAOs, with MAO-A selective inhibitors representing potential leads for the development of antidepressants and therapies for heart failure and cancer, while MAO-B selective inhibitors may be used as leads for the development of symptomatic and neuroprotective therapies for Parkinson's disease. Series of pyrrolo[3,4-*f*]indole-5,7-dione derivatives act as good potency in vitro inhibitors of the MAO enzymes [1], [2].

Table 1. The human MAO inhibition potencies of pyrrolo[3,4-*f*]indole-5,7-dione derivatives



N	R^1	R^2	R^3	R^4	IC_{50} (μM)^a		SI^b
					MAO-A	MAO-B	
1	H	Ph	Cl	H	0.250±0.099	>100	>400
2	OCH_3	4-$OCH_3C_6H_4$	CHO	H	0.0496±0.007	0.8706±0.032	18
3	OH	4-$OCH_3C_6H_4$	Br	H	0.0926±0.012	1.196±0.010	13
4	OCH_3	4-$OCH_3C_6H_4$	Br	H	0.04060.008	0.6056±0.079	15
5	OCH_3	4-$C_6H_4CH_3$	Br	CH_3	0.0236±0.008	0.1786±0.026	7.7

[a] All values are expressed as the mean6standard deviation (SD) of triplicate determinations.
[b] The selectivity index is the selectivity for the MAO-A isoform and is given as the ratio of IC_{50}(MAO-B)/IC_{50}(MAO-A).

The results show that the pyrrolo[3,4-f]indole-5,7-diones are potent MAO inhibitors. All compounds exhibit IC_{50} values for the inhibition of the MAO-A isoform in the submicromolar (<1 μM) range.

Among all compounds valuated, **5** is the most potent MAO inhibitor with IC_{50} values for the inhibition of MAO-A and MAO-B of 0.023 and 0.178 μM, respectively. These inhibition potencies may be compared to those of the reference MAO-A inhibitor, toloxatone (IC_{50} 3.92 μM), and the reference MAO-B inhibitors, lazabemide (IC_{50} 0.091 μM), and safinamide (IC_{50} 0.048 mM), which were evaluated under identical experimental conditions [2].

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COMPARISON OF THE KINETICS OF THERMAL DECOMPOSITION OF TYROSINE AND ITS COPPER COMPLEX

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The aim of our work is to compare the kinetics of thermal stability of copper tyrosinate and tyrosine.

We conducted a systematic study of the rate of thermal transformation of copper tyrosinate and tyrosine by static method in a vacuum system[1].

The conversion of tyrosine is not described by the first order reaction equation in the coordinates ln $p\infty - p_0/p_\infty$ - p_t time (t), so the calculation of the constant was made by the half-life at given temperatures:

$$k = \frac{1}{t_{1/2}}$$

Speed constants and activation energy 217±11 kJ/mol, ln k_0 = 38.9 were determined in the temperature range 270-290^{0}C.

In copper tyrosinate observed induction period, as it was in amino acids. The thermal transformation of $CuTyr_2$ in the solid phase was studied at a temperature range of 206-226 °C. This is a typical topochemical reaction occurring in the solid phase at the interface of $CuTyr_2$ and the solid reaction product. The apparent activation energy of the process, which was 228±37 kJ/mol, lnk_0 = 54.1, was determined.

Copper tyrosinate is thermally less stable than individual tyrosine. The ratio of the conversion rate constants of these compounds is illustrated by the graphs of the temperature dependence of the rate constants (ln*k*) presented in Fig.1.

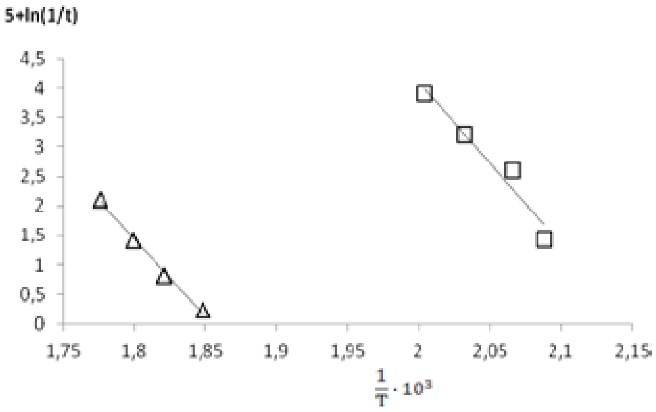

Fig. 1. Temperature dependence of effective reaction rate constants thermal transformation: 1-tyrosine, 2-copper tyrosinate

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NEW METHOD FOR SYNTHESIS OF LINEAR AND CYCLIC UREAS, BASED ON THE ACID-CATALIZED REACTION (3,3-DIETOXIPROPYL)UREA WITH PHENOLS

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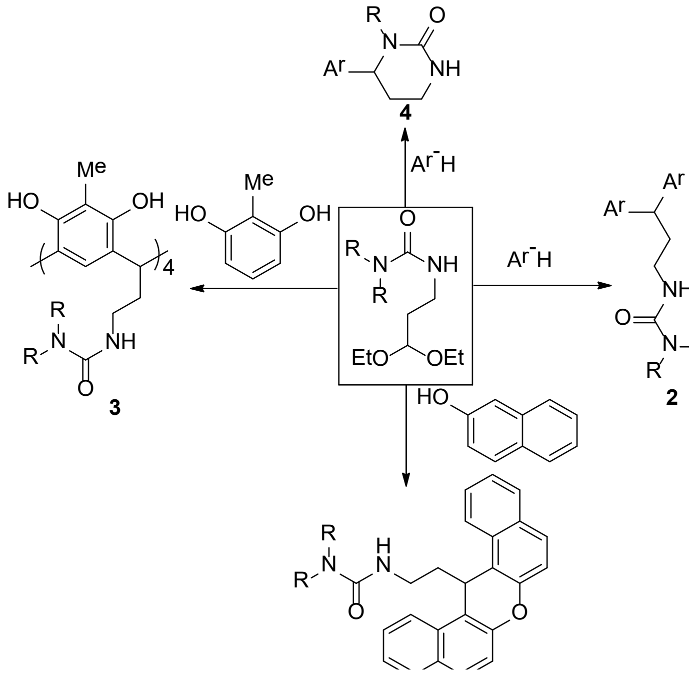
Substituted linear and cyclic ureas are widely used in medicine, agriculture and technology. Ureas containing alkyl aromatic fragments - derivatives of dibenzoxanten **1**, diarylpropane **2**, calixarene **3** and cyclic ureas - tetrahydropyrimidine-2(1*H*)-ones **4** - are an important class of organic compounds due to their high pharmacological activity. However, at the moment there is no common and simple method for the synthesis of these classes of compounds. Therefore, in the present work, a new approach to the synthesis of substituted ureas containing alkylaromatic substituents on the nitrogen atom is proposed. The method is based on the acid-catalyzed reaction of (3,3-diethoxypropyl)urea with various phenols. The advantages of the method include a high yield of the target compounds, mild reaction conditions and the absence of the need to use expensive reagents.



The reported study was funded by RFBR according to the research project № 18-33-00206.

IMPROVING APTAMERS' AFFINITY FOR TARGET PROTEINS BY CHEMICAL MODIFICATION OF NUCLEOBASES

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The use of synthetic oligonucleotides (aptamers) as drugs is a new medical technique that has emerged with the development of nucleic acid chemistry. Aptamers have a complex spatial structure, which determines their unique ability to selectively bind to almost any target. Despite numerous studies of aptamers over several decades, their implementation in clinical practice is hampered by multiple factors: high rates of aptamer degradation, their cross-reactivity, removal of aptamers from the bloodstream as a result of renal filtration, control of action duration, non-specific intracellular interaction, target protein underpurification, and aptamer production automation problems [1].

Creation of effective DNA-aptamer-based drugs requires aptamers to have high stability sufficient for clinical preparation, storage, and use of the drug, as well as pronounced target affinity. Chemical modifications of aptamers can improve these characteristics. This study aims at developing an in silico nucleic acid modification method capable of increasing aptamer affinity. Using thrombin-binding 15-TBA aptamer as an example [2], a virtual screening of all the accessible azides' nitrogenous base modifications by the click reaction of azide-alkyne cycloaddition was carried out (Fig. 1.). A set of compounds capable of increasing anticoagulant properties of the aptamer and prolonging the antithrombotic activity was selected. To test if additional functional groups at nucleotides' position 5 can increase the number of contacts between 15-TBA and thrombin, flexible docking was employed using AutoDock Vina [3], allowing conformational mobility only in the modified part of the specified nucleotide. All the chemical compounds were taken from PubChem library. The selected molecules were modeled in silico using the SMILES notation with a further cycloaddition of azides to the 5-ethynyl-2'-deoxyuridine triple bond. The resulting models were experimentally tested.

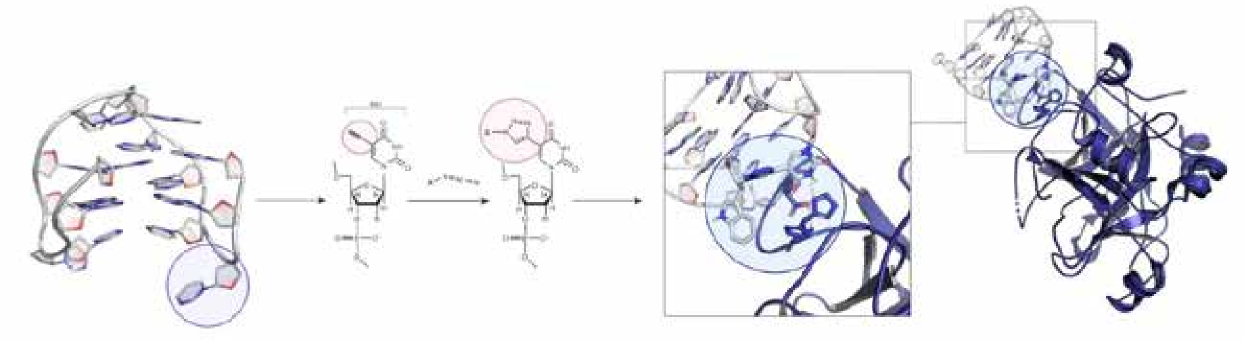

Fig. 1. Chemical modification of nucleobases in 15-TBA

Ministry of Science and Education (RFMEF157617X0095) supported development of docking tools in this study

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CALIX- AND THIACALIX[4]ARENE THIADIAZOLES SYNTHESIS AND SUPRAMOLECULAR PROPERTIES

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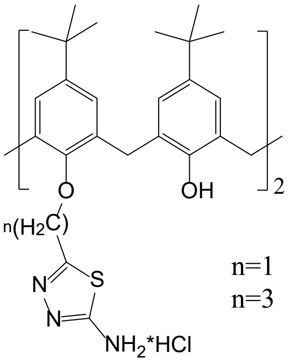
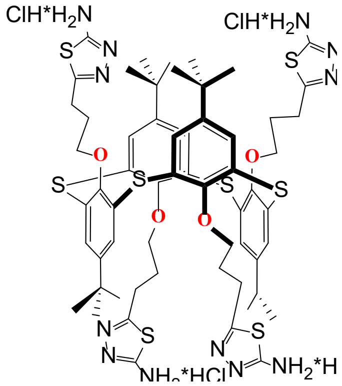
Calixarenes are versatile macrocycles with ability to introduce several appropriate functional fragments to form metal complexes and multivalent binding with target biomolecules. Their easy synthesis, variety of stereoisomeric forms and low toxicity levels make them very promising molecules to use in applications.

Synthesis of calix[4]arene and thiacalix[4]arene derivatives with two or four aminothiadiazole fragments on the lower rim in *cone* (in the case of two fragments) or *1,3-alternate* stereoisomeric form (in the case of four fragments) was carried out.

To evaluate the complexation ability of the calix- and thiacalix 1,3,4-thiadiazoles in base form the method of liquid extraction of their picrates (in a mutually saturated aqueous dichloromethane medium) was used for lanthanide cations silver and some d-metals. A high extraction ability was demonstrated with respect to all metal ions studied.





Obtained macrocycles in the form of hydrochlorides were found to be watersoluble and study of their binding with Calf Thymus DNA (DNA CT) was done using ethidium bromide as fluorescent probe. Size and zeta-potential were measured using dynamic and electrophoretic light scattering.

The obtained thiadiazolyl derivatives of calix- and thiacalix[4]arene are capable of effective interaction with DNA CT. An increase in the number of thiadiazolyl fragments from two to four leads to an increase in the stability constant of the calixarene-DNA complex from 2.1 to 3.6 logarithmic units. It was found that a macrocycle containing four thiadiazolyl fragments in a 1,3-alternate stereoisomeric form is capable of 6-fold compaction of DNA CT, while macrocycle with two thiadiazolyl fragments is capable only of 2-fold compaction.

Conclusion: The obtained thiadiazolyl derivatives of calix- and thiacalix[4]arene are capable of effective bind metal ions and interaction with DNA CT. A macrocycle containing four thiadiazolyl fragments is capable of 6-fold compaction of DNA CT, which is interesting from the point of view of creating non-viral transfection systems for gene delivery.

Funding sources: This work was funded by RFBR (N. 17-03-00389) and partly subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (4.1493.2017/4.6 and 4.5151.2017/6.7).

SYNTHESIS AND MASS-SPECTROMETRY EVALUATION OF THE NOVEL ANTIBACTERIAL CONJUGATES OF GLYCOPEPTIDES WITH KANAMYCIN A

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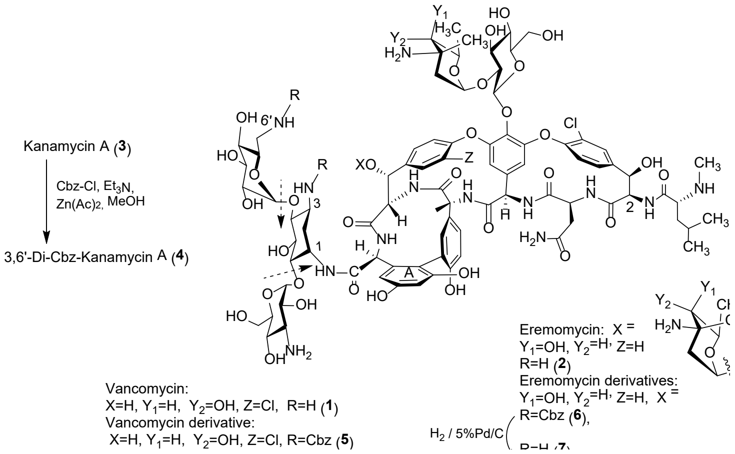
Creating new hybrid analogues based on highly active antibiotics is one of the promising ways for synthesis of new antibacterial agents [1]. Vancomycin (**1**) is a drug of last resort for treatment of severe bacterial infections caused by gram-positive bacteria. Another antibiotic of this class – eremomycin (**2**) was discovered in Gause Institute of New Antibiotics and showed 3-5 times higher efficacy *in vitro* than vancomycin [2]. Kanamycin A (**3**) is widely used in medicine and agriculture. It is known that the amidation of the terminal COOH group of glycopeptides increases their antibacterial activity [3].

The aim of the current work is synthesis and mass spectrometric fragmentation study of new conjugates of antibiotics vancomycin (**1**) and eremomycin (**2**) with kanamycin A (**3**), and investigtion of their antibacterial activity. First, 3,6'-di-Cbz-kanamycin A (**4**) was obtained [4]. Selective amidation of glycopeptides **1** or **2** by the derivative **4** in the presence of PyBOP reagent resulted in 3,6'-di-Cbz-canamycinyl-1-amides of vancomycin (**5**) and eremomycin (**6**). The reduction of the Cbz group in conjugates **5** and **6** was carried out in the H_2 flow over 5% Pd/C (1.5 atm, 2 hours). The removal of the Cbz group in **6** leads to kanamycinyl-1-amide of eremomycin (**7**), and the removal of the chlorine atom in the side chain of amino acid residue of 2 is not observed. The di-Cbz derivative of vancomycin **5** is decomposed under these conditions.

To verify the proper attachment of one antibiotic to another, we conducted tandem mass spectrometry experiments that are effective in studying the structure of hybrid structures of similar structure [5, 6]. Using tandem mass spectrometry, the addition of the terminal COOH group of a glycopeptide to kanamycin A at the position 1 of 2-deoxy-D-streptamine has been proved. For example, compound **7** fragmentation proceeds according to the scheme: (*m/z*) 2022.79 $[M+H^+]$ → 1861.72 $[M - \text{glucosamine} + H^+]$ → 1700.65 $[M - 2\times\text{glucosamine} + H^+]$.

The resulting conjugates are active against gram-positive bacteria, and some are active against vancomycin-resistant strains.



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THE APPLICATION OF **MACRONET MN-200** AS ADSORBENT FOR SOLID-PHASE EXTRACTION OF PROGESTERONE BIOTRANSFORMATION PRODUCTS

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The introduction of a hydroxyl group into a steroid molecule is of great practical importance, since it not only provides a change in the biological activity of the parent molecule towards the desired direction, but also gives possibility for its further modification. Biocatalytic hydroxylation of steroid compounds using enzyme systems of filamentous fungi is an alternative to chemical synthesis. This method allows to reduce the number of stages and is more cost-effective and eco-friendly. Earlier, we showed that the most promising biocatalyst for steroids transformation, in particular, progesterone, is filamentous fungus *Aspergillus nidulans* lac№4 (argB$^-$), producing heterologous laccase A of *Trametes hirsuta* 072. The main products of progesterone transformation were 11α-hydroxyprogesterone, 11α-acetoxyprogesterone and 6β,11α-dihydroxyprogesterone [1].

As a rule, the extraction of transformation products from the culture medium is carried out by the method of liquid-phase extraction using large quantities of organic solvents such as butyl acetate, ethyl acetate, dichloromethane, etc. However, the method of solid-phase extraction on various sorbents has some advantages: it reduces the use of solvents and allows to use the adsorbent repeatedly [2]. Among the known polymeric adsorbents, a special place is occupied by macroporous polystyrenes. The attention towards them is determined by the wide possibilities of their practical use as highly effective sorbents for the isolation and separation of a huge number of organic and inorganic compounds [3].

In this work we studied the possibility of Macronet MN-200 (macroporous polystyrene crosslinked with divinylbenzene) application for solid-phase extraction of progesterone biotransformation products from culture medium without mycelium separation. The progesterone transformation was carried out in complete medium at 37°C, 100 rpm with substrate loading 1 g/l. The adsorbent was loaded into the culture medium after 216 hours of progesterone transformation by fungus. After 12 hours, the products were completely removed. The desorption was performed with acetone at room temperature. A quantitative and qualitative evaluation of the transformation products was performed using TLC and HPLC (in comparison to known standards), ^{1}H NMR, ^{13}C NMR and high-resolution mass spectrometry. The efficiency of solid-phase extraction with repeated use of the adsorbent was shown.

This work was supported by the Grant of Russian Foundation for Basic Research №18-34-00653.

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SYNTHESIS OF BIS(AZACROWN)DIENONES AND SPECTROSCOPIC STUDY OF SUPRAMOLECULAR COMPLEXES BASED ON THEM

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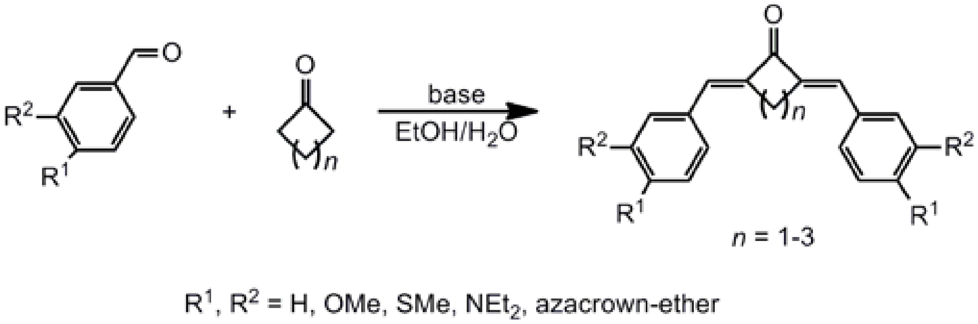
Cross-conjugated dienones of cyclic ketones are widely known for their photochromic and fluorescence properties, which determine their applicability, first of all, as fluorescent probes in biology and agriculture [1], [2]. The purpose of this study was to synthesize a series of dienones with various donor substituents, including azacrown-containing dienones, to study the photophysical properties of the obtained compounds and the possibility to construct photoactive supramolecular systems based on them.



Scheme 1. Synthesis of dienones.

Dienones with various donor substituents and azacrown-containing dienones were obtained by the alkaline aldol-crotonic condensation of aromatic aldehydes with cyclic ketones in the presence of a base (Claisen-Schmidt reaction). The structure of the obtained dienones was determined by NMR-, IR-, UV spectroscopy and elemental analysis.

The formation of supramolecular complexes of azacrown-containing dienones with alkaline and alkaline earth metal cations was studied by electronic spectroscopy methods. The complexation is accompanied by changes in the absorption and fluorescence spectra of dienones. It was found that azacrown-containing dienones forms complexes of different stoichiometry with metal cations. The stability constants of the complexes were determined.

The synthesized dienones and supramolecular systems based on them may be used as components of photoactive supramolecular devices, optical molecular sensors.

This work was supported by the Russian Science Foundation (project № 19-13-00020) and the RAS (Program №38 of the Presidium of RAS).

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FUNCTIONALIZED WATER-SOLUBLE PILLAR[5]ARENES AS THE BASIS FOR BIOCOMPATIBLE SELF-ASSEMBLING NANOSCALE SYSTEMS

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The search for novel substances increasing effectiveness of drug therapy as well as decreasing side effects on the human body is one of the most important goals for modern medicine and biology. The creation of supramolecular systems for targeted delivery of anticancer drug is one of the exciting tasks in medical diagnostics and drug treatment. Nowadays mainly derivatives of biopolymers, cyclodextrins and cucurbit[n]uriles are used for targeted drug delivery. Systems based on these compounds have low toxicity but their functionalization is rather difficult. This fact significantly complicates the possibility to form complex supramolecular receptor structures that can mimic and adapt to different classes of drugs, thereby significantly limiting their application.

We propose to use a multifunctional member of the *para*-cyclophane family - pillar[5]arene in order to satisfy all modern criteria for receptor structures. The relatively young class of macrocyclic compounds, first described in 2008, pillar[n]arenes, attracts the special interest of researchers. Supramolecular systems based on them are especially interesting. Pillararenes like the well-known classes of macrocyclic compounds such as crown-ethers, cyclodextrins, calixarenes, etc. tend to form host-guest complexes. Along with this, the targeted functionalization of pillar[5]arenes by receptor fragments will lead to the formation of self-associates, aggregates of the receptor/agent complex. It will allow to realize different mechanisms of action and the ability for visual detection, which will optimize the therapy strategy. The task of creating a universal mimicking system is far from being resolved despite the considerable efforts which were made in the field of the synthesis of new nanocontainers capable to targeted delivery of drugs. In this regard the use of easily accessible , non-toxic, multifunctional pillar[5]arene platform removes these limitations. Such materials will help to reduce the toxicity of most anticancer drugs, as well as to find their application in personalized medicine and high-tech healthcare.

Thus, we synthesized novel water-soluble decasubstituted derivatives of pillar[5]arene. Then we developed some approaches for non-covalent interaction of synthesized pillar[5]arenes with fluorescent dyes. Self-association of water-soluble pillar[5]arene derivatives was studied. The size and morphology of particles was determined by transmission and scanning electron microscopy. Then, on the basis of the data obtained, we study the aggregation of the resulting nanoparticles (association and aggregation in solution) with therapeutic drugs: ftorafur, 5-fluorouracil.

This work was supported by the RFBR according to the research project № 18-03-00315, № 18-33-01095, № 18-33-20148, № 18-33-00276 mol_a.

ELECTROCATALYTIC PHOSPHORYLATION OF C–H BONDS OF AROMATIC SUBSTRATES WITH THE PARTICIPATION OF TRANSITION METAL COMPLEXES

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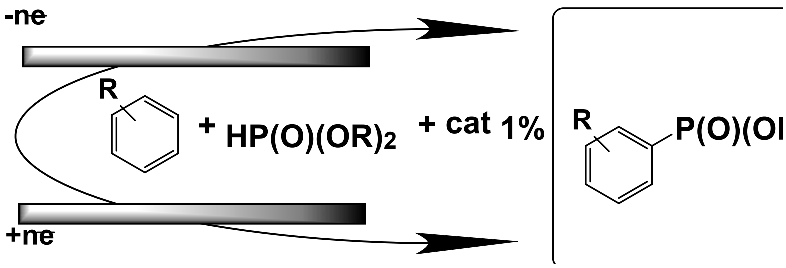
Synthesis of arylphosphonates via direct phosphorylation of aromatic C–H bonds under electrochemical mild conditions is one of the most important approaches, since it meets the generally accepted criteria of green chemistry compared to traditional methods of synthesis. [1-4].

We carried out a series of experiments to obtain various phosphorylated aromatic compounds under electrooxidation and electroreduction conditions using transition metal complexes (Ni^{2+}bpy, Mn^{2+}bpy, Co^{2+}bpy) as catalysts [1-4].



Electrochemical properties of all complexes in the presence of a phosphorylating agent were studied by CVA, and the mechanism of electrocatalytic phosphorylation of aromatic substrates was proposed.

The work was supported by the Russian Science Foundation, grant No. 19-13-00016.

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UNUSUAL AND STEREOSELECTIVE ONE-POT APPROACH TO DIMERIC PYRROLO[2’,3’:4,5]THIENO[2,3-*B*]PYRIDINES

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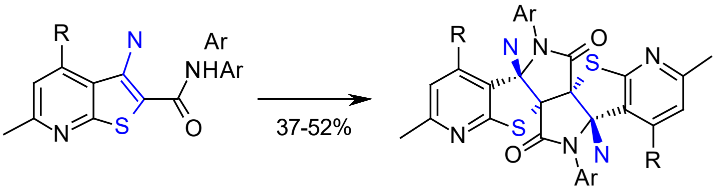
Thieno[2,3-b]pyridines have attracted much attention over the years due to their increasing significance in the field of pharmaceuticals and industrial chemicals. However, there are only a few reports devoted to an oxidation of thieno[2,3-*b*]pyridines. Moreover, the oxidation reactions with functionalized 3-aminothieno[2,3-*b*]pyridines have never been studied before.

Here we report our efforts to prepare new polycyclic thienopyridines through the oxidation of 3-aminothieno[2,3-*b*]pyridine-2-carboxamides with a commercial bleach (10% NaOCl).

The reaction between thienopyridines and 5-fold excess of aq. NaOCl solution was conducted both in 1,4-dioxane at 25-30 °C and CH_2Cl_2 under PTC conditions.



Scheme 1.

The exact structure of the reaction products was proved by detailed analysis of NMR data and X-ray diffraction analysis.

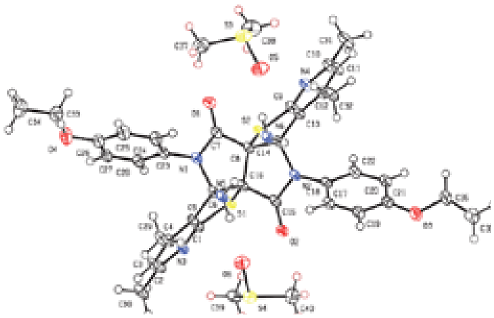


Fig. 1.

We found the unexpected oxidative dimerization of 3-aminothieno[2,3-b]pyridine-2-carboxamides promoted by commercial bleach solution (10% aq. sodium hypochlorite). Several representatives of new heterocyclic system – 7a,14a-diamino-7,14-bis(aryl)-7,7a,14,14a-tetrahydro-6H,13H-pyrido-[3’’’’,2’’’’:4’’’,5’’’]thieno[2’’’,3’’’:4’’,5’’]pyrrolo[3’’,4’’:3’,4’]pyrrolo[2’,3’:4,5]thieno[2,3-b]pyridine-6,13-dione – have been synthesized.

This work was supported by the Ministry of Education and Science of the Russian Federation (grant No. 4.6087.2017/BP).

СИНТЕЗ ДИХЛОРДИАЗАДИЕНОВ НА ОСНОВЕ 4-НИТРОБЕНЗАЛЬДЕГТДА

Сулеймвнова Г.Т., Ахмедова Н.Э.,Аскерова У.Ф.,Гаразаде Х.А.,
Шахмурадова А.А., Гусейнова Л.Р., Бабаева Г.В.,Абдулов М.С., Шыхалиев Н.Г.,

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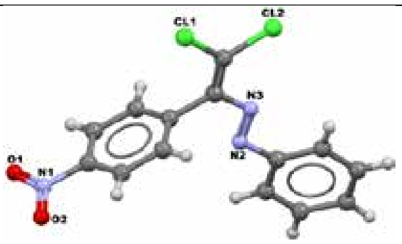
В условиях реакции каталитического олефинирования на основе различных фенилгидразонов бензойного альдегида проведен синтез дихлордиазадиенов [



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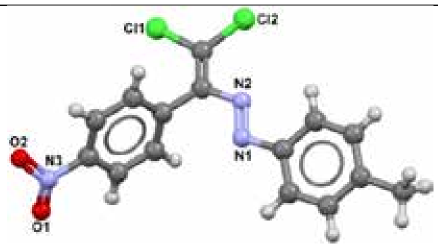

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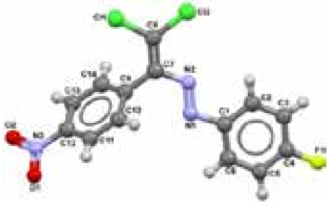

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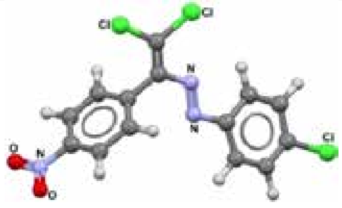

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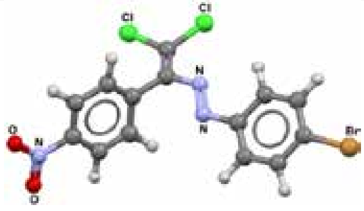

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SYNTHESIS AND PROPERTIES OF POLYMER METAL COMPLEX CATALYSTS OF OXIDATION OF HYDROCARBONS

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One of perspective ways of fixing of complexes of the transitional metals on firm carriers is obtaining complexes with the polymers containing complexing functional groups. At the same time there are additional opportunities of variation of a ligand environment and consequently, and regulations of catalytic properties of complexes by change of the structure and conformations of macromolecules.

Developed earlier principle of prearrangement of complexing polymers is based on use of memory of polymeric composition and consists in exercise of interaction of not noncross-linked polymer with metal ions in solution and the subsequent fixing of optimum for a complexing conformations by cross-linking and removing of metal from the cross-linked system. It was shown that the macromolecules cross-linked thus can remember the conformations preferable to a complexing metal on which prearrangement have been carried out. It leads to the substantial increase of sorption characteristics of polymers that increases their effectiveness at use and expands ranges of application, for example, allows to obtain on its base catalysts with the improved catalytic properties. The polymeric sorbents on the base of polyethylenpolyamin (PEPA) and oligomer of epichlorohydrin and ammonia (EHGA) which are prearranged on a sorption of ions of copper have been synthesised and also their complexes with copper by EPR method have been investigated. It was established that prearrangement provides primary formation in a phase of a complexing polymer evenly of the distributed complexes of identical structure which structure is identical to the structure of complexes of their low-molecular analogs in solutions [1].

Would be of interest to investigate catalytic activity of polymeric complexes of copper in oxidizing reaction. The catalytic activity of prearranged and nonprearranged complexes of copper with PEPA in reaction of liquid-phase oxidation of ethyl benzene have been studied. The ratio of PEPA and EHGA have been 1:1.5. Using of prearranged complexes of copper in oxidizing reaction of ethyl benzene as catalysts leads to increasing in depth of conversion of ethyl benzene in comparison by nonprearranged complexes at identical content of copper. These both catalysts are absolutely identical, have one nature of a polymeric matrix and the same structure, the amount of metal is equal, but distinguish only in a prehistory, and it considerably improves and allows to regulate catalytic properties. The selectivity for hydroperoxide compound is also higher in case of using of prearranged complexes in comparison with nonprearranged, in the presence equal content of copper. It demonstrates in the case of the prearranged complexes that in a phase of the catalyst are formed more uniform active sites, with structure causing higher catalytic activity. Besides, it shows that prearrangment allow to change and regulate the structure of the active sites and consequently, catalytic activity of the metal complexing catalysts. At the same time the greatest activity have been shown by the prearranged complexes containing 2 mg-eqv/g copper.

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CALIXARENE-MODIFIED POLYDIACETYLENE NANOPARTICLES AS PROMISING COLORIMETRIC SENSORS

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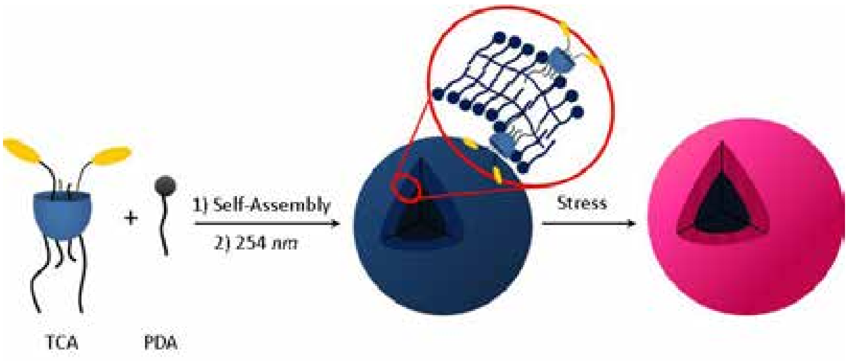
Polydiacetylenes (PDAs) have received increasing attention as smart materials owing to their unique properties. PDAs are used as colorimetric sensors since these conjugated polymers undergo a blue-to-red color change upon various chemical / biochemical and physical stimuli. Calixarenes are macrocycles containing hydrophobic cavities that can hold small molecules or ions. Owing to the ease of their upper and lower rim functionalization, a variety of stereoisomeric configurations, and the preorganization effect, calixarenes are used as supramolecular platforms for molecular recognition, sensing, catalysis and drugs delivery. Thus, combination of calixarene receptors with PDA for the creation of colorimetric sensor devices is a very attractive task that it might lead to more sensitive sensor.

In this study, new modificated PDAs with different thiacalixarenes containing the diacetylene fragments (TCA-PDA) were evaluated for sensing of ions and biomolecules. The structure, hydrodynamic diameter and electrokinetic potential of TCA-PDA were determined with various physical methods such as dynamic light scattering, TEM microscopy. Chromatic properties of the TCA-PDA were shown using both “naked eye” detection and UV-vis spectroscopy.



NEW ANTICANCER CARBOXAMIDES OF HETEROARENE-FUSED ANTHRAQUINONES

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Heteroarene-fused anthraquinones are attracted an interest of medicinal chemists due to a potent inhibition of tumor cells growth via affecting to different cellular targets [1]. For instance, anthra[2,3-*b*]furan LCTA-2034 (**1**) demonstrated a significant and reliable anticancer efficacy on animal tumor models including multi-drug resistant (MDR) variants [2]. Thus, in-depth SAR analysis and further search for more potent and water soluble analogs represents a promising task for the development of new chemotherapeutics.

Bioisostere modification is a useful strategy in molecular modification and drug design aiming to improve activity, pharmacodynamic and pharmacokinetic properties of lead compounds. According this, to obtain new derivatives we firstly developed two original schemes for synthesis of corresponding anthra[2,3-*b*]thiophene- and naphtho[2,3-*f*]indole-3-carboxilic acids **5**,**6** in five and four steps [3,4], respectively, from commercially available quinizarine (**4**). Generation of acyl chlorides of **5**,**6** and next acylation of cyclic diamines gave series **2**, **3** of sulphur- and nitrogen-bearing analogues of anthrafuran **1**.

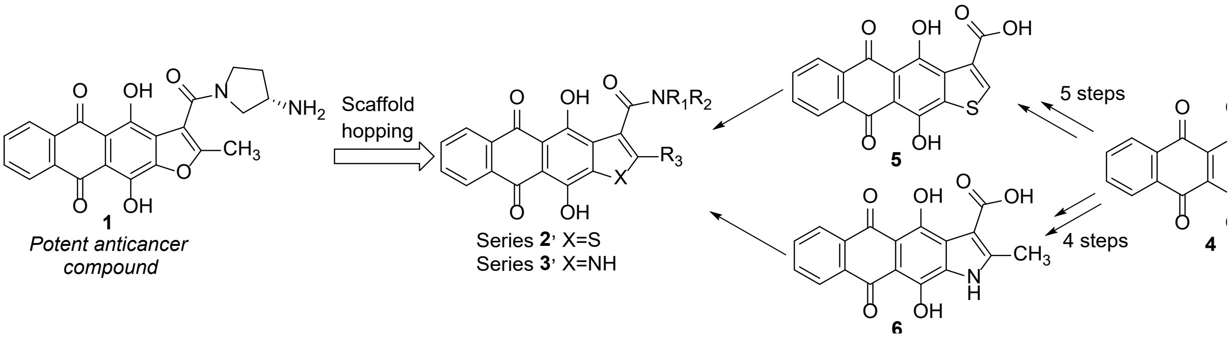

Fig. 1. Anticancer carboxamides of hetarene-fused anthraquinones.

The majority of novel derivatives potently suppressed of proliferation of human cancer cells. Additionally, an inhibition of topoisomerase 1 and Aurora A/B kinases was detected. Gained results indicate the prospectives for further optimization of carboxamides of heteroarene-fused anthraquinones as potential anticancer agents.

This work was jointly supported by RFBR (17-53-45105) and DST (INT/RUS/RFBR/P-291).

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INTERACTION OF 4,8-DIALKOXY-1,3-DIMETHYL-6H-CYCLOHEPTA[C]FURAN-6-YLIUM PERCHLORATE WITH INDOLIZINES.

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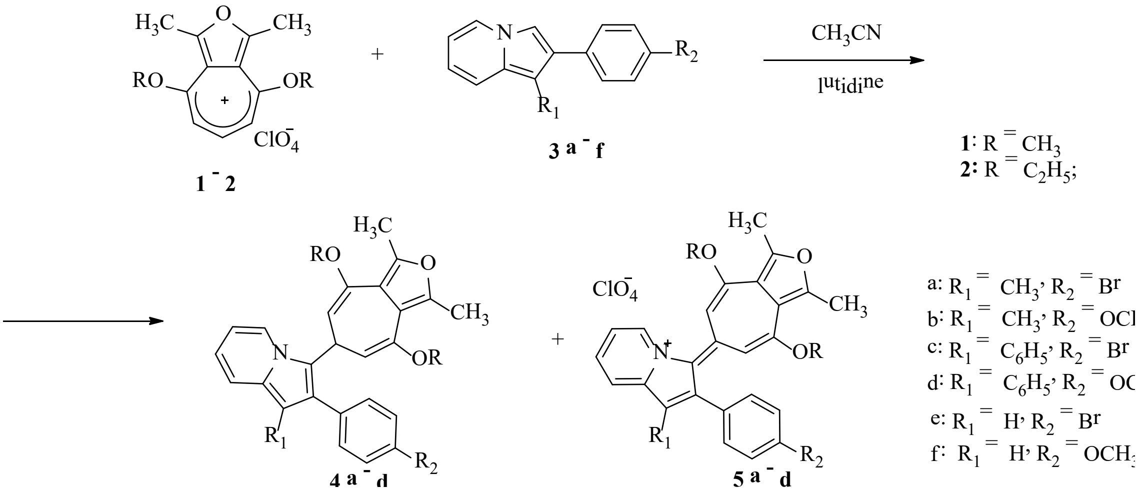
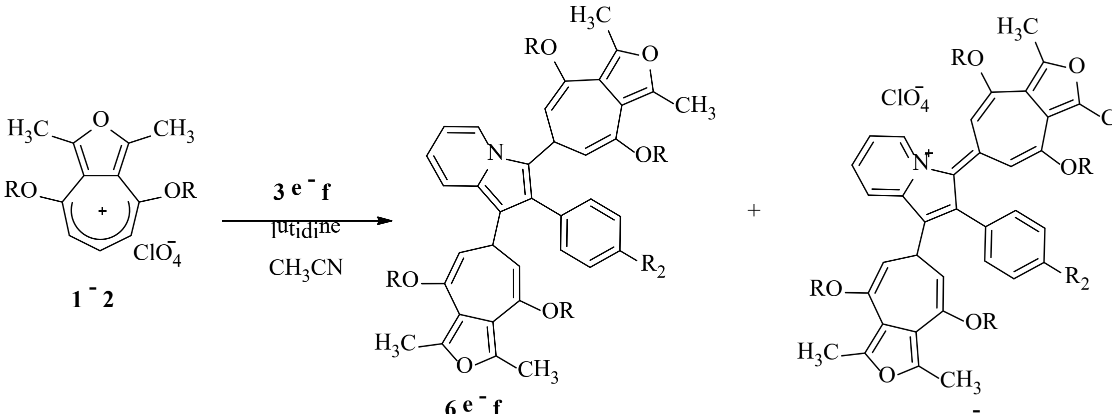
Methods of forming new carbon-carbon bonds are a promising direction for the development of modern organic synthesis. In this regard, of considerable interest is the study of the reactions of the high-electrophilic furotropylium perchlorate with C-nucleophiles. We have developed a method for the synthesis of furutropylic derivatives containing an indolizines fragment at the 6-position of the tropolone cycle. When interacting equimolar amounts of perchlorates **1-2** with indolizines **3a-d** in acetonitrile at room temperature in the presence of lutidine as a base, compounds **4a-d** are formed with good yield. Additionally, with a small yield, it is possible to isolate intensely colored compounds **5a-d** (Scheme 1). The reactions of perchlorates **1-2** with indolizines, unsubstituted at the 1-position **3e-f**, led to the formation of corresponding bis-products **6e-f, 7e-f** (Scheme 2).



Scheme 1.



Scheme 2.

The structure of the compounds obtained was established using NMR spectroscopy, confirmed by mass spectroscopy data.

CONJUGATES OF 4H-THIENO [3.2-B] PIRROL-5-CARBOXYLATE WITH TAURIN AND HIS TETRABUTYLAMMONIUM SALT

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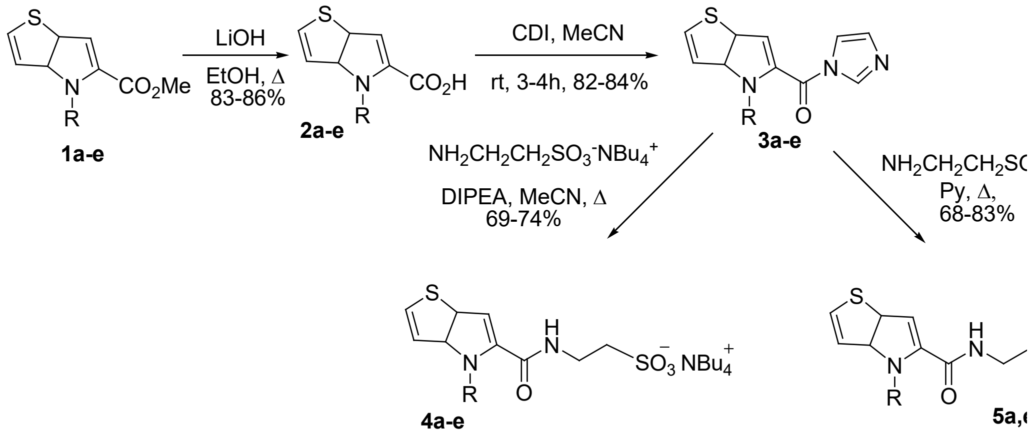
The 4H-thieno [3.2-b]pyrrole-5-carboxylate system is an accepted and actively used platform in the design and improvement of the structures of bioactive compounds. In order to obtain new derivatives in this work we received conjugates **4 a-e** and **5a,e** from the acids **2a-e** described earlier [1-2], which were converted to the more active acyl imidazoles **3a-e** and condensed with the taurine tetrabutylammonium salt or taurine.

It should be noted, that there are a lot of examples of the introduction a natural aminosulfonic acid taurine into the structure of a bioactive compounds [3], but in this case modification of acids **5** structures with taurine in the form of a charged bulky quaternary ammonium salt could give amides **7** new properties including a water solubility.

The reactions of imidazolides **3a-e** obtained from acids **2a-e** with taurine and tetrabutylammonium salt of taurine were carried out in pyridine or acetonitrile in the presence of DIPEA at reflux.



In general, the synthesized taurine-containing carboxamides **4a-e** and **5a,e** are of pharmacological interest, and work in this area will be continued.

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SYNTHESIS OF FLUOROALKYL AND FLUOROALKENYL (HETERO)AROMATIC SYSTEMS BY PREDICTABLE DIRECTED *ORTHO*-C-H ACTIVATION

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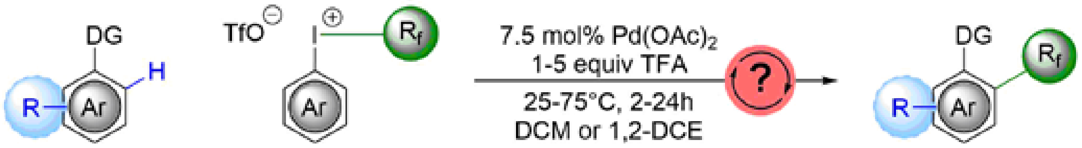
In the last decade, transitional metal catalyzed (Pd, Rh, Co, Ru, Ir, Mn, Cu, Ni) C-H activation has become one of the most extensively studied research topic in synthetic organic chemistry. With this methodology, aromatic C-H bonds can be easily substituted with different functional groups, without any previous functionalization of starting substance. In aromatic compounds, there are many H atom in similar chemical environment, which can raise problems in regioselectivity for first sight. However, the introduction of a directing group (DG) into the aromatic core allows selective metalation in *ortho* position. In our research, we focused on the late-stage introduction of fluorine containing functionalities, in order to their effect on lipophilicity and metabolic stability. Due to the presence of fluorine atoms the electronic properties of the molecules also change and allow further reactions on multifunctionalized aromatic cores.

We present a simple and robust catalytic method for efficient and selective trifluoroethylation[1,2] and fluoroalkenylation reaction of (hetero)aromatic compounds using highly active trifluoroethyl(mesityl)iodonium and related hypervalent iodine salts. The utilization of hypervalent reagents opens new synthetic possibilities and allows mild reaction conditions. Besides the scope and limitations, the mechanism has been investigated.

We aimed to settle a comprehensive theory, which includes numerous diverse experimental results combined with easy and fast geometry optimization. Calculating the required parameters allows to understand complex steric and electronic problems and achieve a predictable system in C-H activation.



DG: Directing Group:
amide, urea, acetyl e.t.c.
R_f : CH_2CF_3, fluoroalkenyl

Why does this work so good?
Is there any rule of thumb to predict?
Mechanism, and theoretical background.

More than
100 examples
up to 97% yield

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DIRECT PHOTOCATALYTIC C-H FUNCTIONALIZATION OF AZINS BY DIPYRRYLMETHANES. SYNTHESIS OF BODIPY DYES

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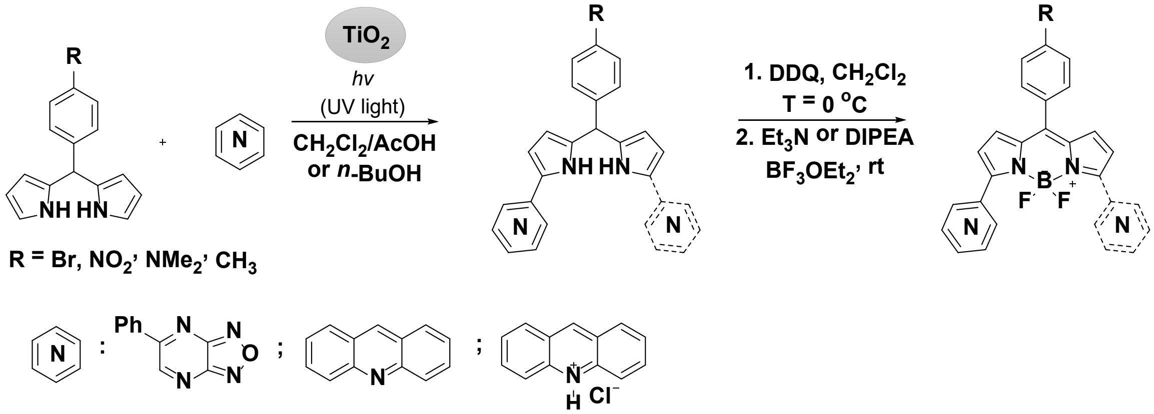
BODIPY dyes are among the widely studied functional chromophores due to their unique properties, such as high photostability, large molar absorption coefficients, bright fluorescence and high quantum yield [1]. BODIPY derivatives are used as chemosensors, laser dyes, emission materials in OLED devices, compounds for photodynamic therapy and organic photovoltaics. A sharp change in the optical properties is observed when heterocyclic fragments are introduced into the BODIPY structure. There are known reactions with BODIPY dyes based on the C-H functionalization strategy, which is gaining popularity as an eco-friendly and atom-economic process.

In the present study, we have investigated the oxidative systems working in heterogeneous phase: air oxygen/nanosized TiO_2/light irradiation [2],[3], which allow to carry out the «azine – dipyrromethane» cross-couplings. It was established that acridine or 5-phenyl-1,2,5-oxadiazolo[3,4-*b*]pyrazine is react with dipyrromethanes in acetic acid-dichloromethane system (1/5). The C-C coupling of activated N-H protonated salt of acridine was found to proceed smoothly at room temperature under neutral conditions. The presented method has the features of a “green” process: the lack of reagents homocoupling, oxidizer - air oxygen, high yields, a by-product – water and easily separate heterogeneous catalyst. The BODIPY derivatives were synthesized by one-pot method in the oxidation of DDQ followed by treatment with $BF_3{\cdot}OEt_2$ from the obtained dipyrromethanes. The product yields were 38–59%.



Scheme 1. Synthesis of BODIPY derivatives

This work was supported by Russian Foundation for Basic Research in the framework of the research project No. 18-33-00927.

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FLUORINATED *ORTHO*-IODOPHENOLS: VERSATILE PRECURSORS FOR THE SYNTHESIS OF POLYFLUORINATED BENZOANNELATED O-HETEROCYCLES

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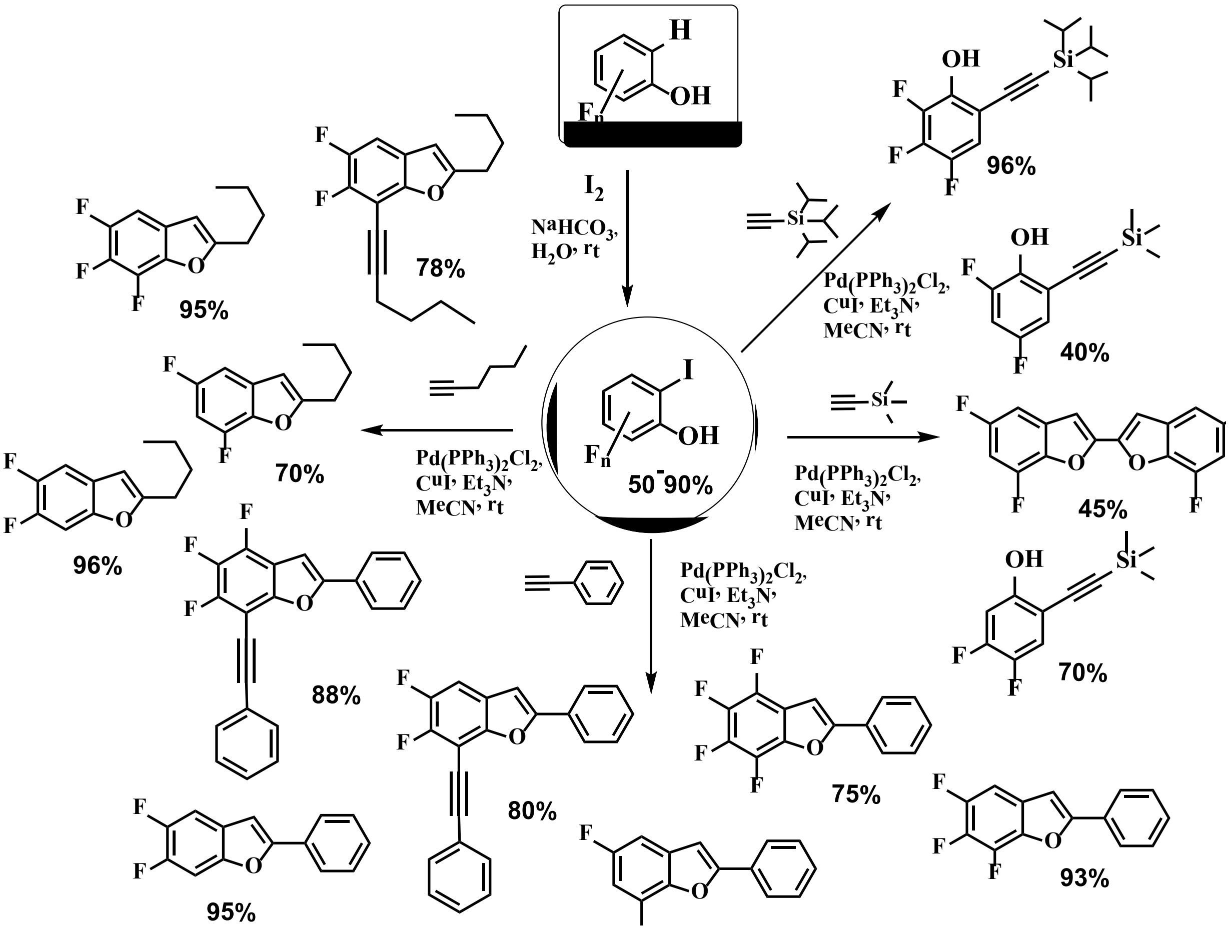
The polyfluorinated benzoannelated heterocycles are structural components in a vast number of biologically active natural and synthesized compounds and pharmaceuticals. We have demonstrated an efficient method for the synthesis of polyfluorinated benzofurans including the Sonogashira cross-coupling of fluorinated *ortho*-iodophenols with terminal acetylene, followed by intramolecular cyclization.



The work was supported by the Russian Foundation for Basic Research (grant No 19-53-53003\19).

SYNTHESIS AND RECEPTOR PROPERTIES OF AZA-CROWN AND HYDRAZIDE FUNCTIONALIZED CALIX[4]ARENES

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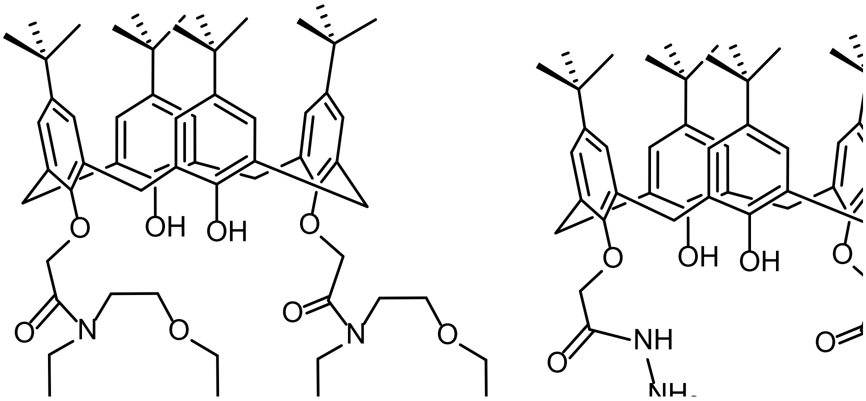
Design of selective and efficient extractants and sensors for metal cations recovery from wastewater is still the problem to be solved. It is noticed that calix[4]arene is very attractive platform for construction of complex molecules with several recognition units and rigid geometry. Introduction of nitrogen-contained fragments in calixarene backbone is very promising in the way to selective metal cation separation.

We synthesized variety of calixarene derivatives with hydrazide or aza-crown moieties. A couple examples are below (Scheme 1).



Scheme 1.

Picrate extraction and membrane transport experiments were carried out. Aza-crown derivatives demonstrated high extraction degree to Pb^{2+} and Ag^{+}. Fully substituted derivative modified by monoaza-12-crown-3 was extremely efficient (E%=48-100%) in a relation to all investigated metal cations from alkaline to heavy metals. Calix[4]arene tetrahydrazide showed extraction degree up to 30% for heavy metals, lanthanides and few d-elements.

Membrane transport results as well as correlation between those two methods for calixarene receptor properties evaluation will be presented as a poster.

The reported study was funded by RFBR according to the research project № 18-33-01131.

MITOCHONDRIA-TARGETED TRIPHENYLPHOSPHONIUM CONJUGATED TRITERPENOID BETULIN DERIVATIVES AS POTENT ANTI-CANCER DRUGS

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Triterpenoids is an important class of natural compounds with over 200 different triterpenoid skeletons. A number of recent publications report the ability of some triterpenoids, such as ursolic, oleanolic and betulinic acids and their derivatives, to inhibit the growth of tumor cells *in vitro* and *in vivo* [1], [2]. There are evidences that triterpenoids and their derivatives cause the death of tumor cells mainly through activation of apoptosis via mitochondrial pathway

Lipophilic cations are promising molecules to improve pharmacokinetic properties of triterpenoids due to high lipid solubility and the ability to readily pass cellular membranes and accumulate into mitochondrion [3].

A series of new triphenylphosphonium derivatives of the triterpenoid betulin (3-lup-20(29)-ene-3β,28-diol) have been synthesized (**1-6**, Fig.1) and evaluated for their cytotoxic effect against human breast cancer (MCF-7), prostate adenocarcinoma (PC-3), and human skin fibroblast (HSF).

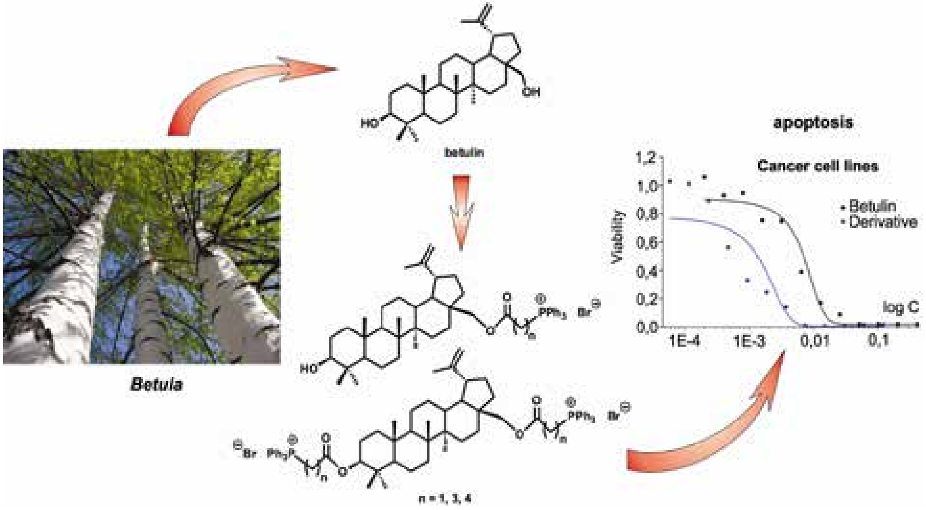

Fig. 1.

The TPP moiety was applied as a carrier to provide selective accumulation of a connected compound into mitochondria. The structure-activity relationship study revealed the essential role of the TPP group for the realization of the betulin effect, while the chemical structure and the length of the linker only slightly influenced the cytotoxicity. Results show that TPP conjugates of betulin exhibit significantly higher cytotoxic effect with lowest IC_{50} value of 0.045 µM (MCF-7/Vinb)

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SYNTHESIS AND INTRAMOLECULAR CYCLIZATION OF PROPARGYLOXY SUBSTITUTED 4-AZIDO-1,2,3-TRIAZOLES

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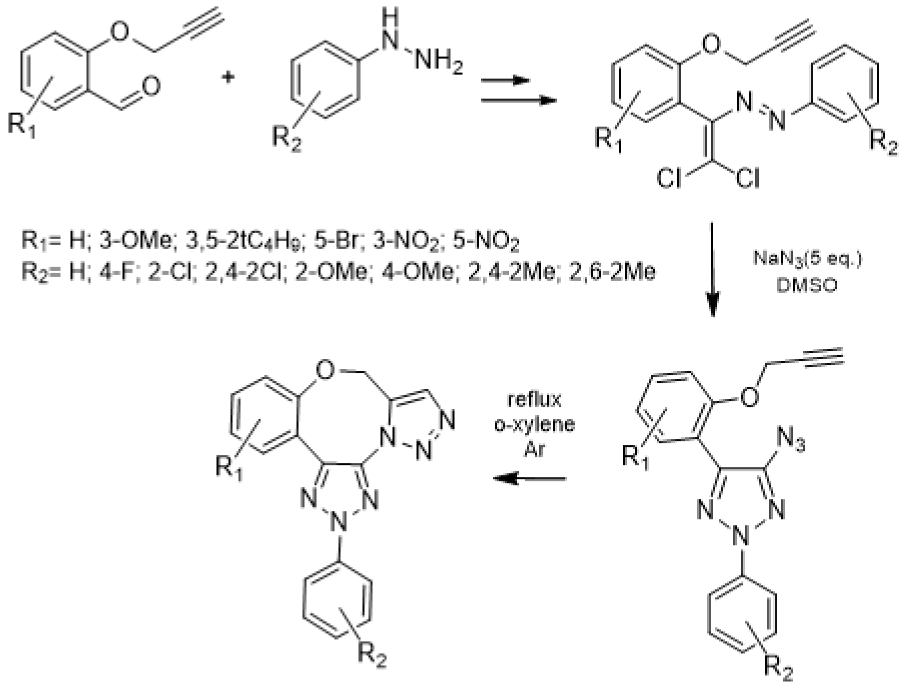
Recently it has been shown that 2-aryl-substituted 1,2,3-triazoles have luminescence in the blue region. This fact made it possible to obtain a family of UV / «blue light-emitting» materials based on them. In this work, we demonstrated the synthesis of 2-substituted 1,2,3-azidotriazoles from variously substituted arylhydrazines and 2-propargyloxybenzaldehydes. The presence of an unprotected triple bond in aldehyde backbone and the azido group in the triazole fragment opens up the possibility of cyclization of these compounds. The initial building blocks are N-monosubstituted hydrazones which served as the basis for development of new 2-aryl-substituted 4-azido-1,2,3-triazoles synthesis method. Subsequent intramolecular cyclization allows to obtain unique condensed heterocycles containing two triazole rings. It should be noted that this heterocyclic system is unknown in the References.



R_1= H; 3-OMe; 3,5-2tC_4H_9; 5-Br; 3-NO_2; 5-NO_2
R_2= H; 4-F; 2-Cl; 2,4-2Cl; 2-OMe; 4-OMe; 2,4-2Me; 2,6-2Me

This work was supported by the Russian Foundation for Basic Research (Project No.18-53-06006).

AZOLO[1,5-*A*]PYRIMIDIMES AND THEIR DERIVATIVES IN SEARCHING THE AGENTS AGAINST SEPSIS

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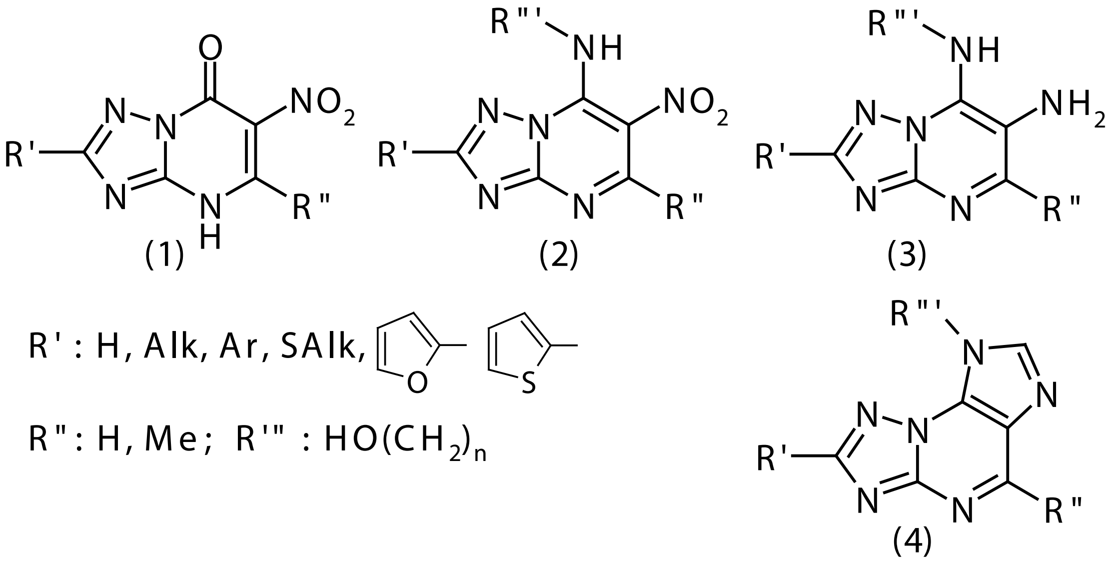
Sepsis which has microbial and viral nature is serious sequela of infectious diseases. The significant funds and intellectual resources of major scientific research collectives are expended to fight the sepsis. The picture of biochemical processes of the sepsis is very diverse, but it has been attracted the attention to the key role of the receptors action in the activation and inhibition of sepsis in recent years. One of the important objects in this direction are adenosine receptors (A_1, A_{2A}, A_{2B}, A_3) and compounds acting on them (agonists and antagonists). The molecular structure of such receptor effectors simulates purines, their azoloannelated analogues and and non-natural nucleosides in most cases.

The objects of the development and creation of agents against sepsis as assumed A_{2A} inhibitors of receptors became triazolopyrimidines (1-3) and triazolopurines (4) which is close in structure to purines.



Scheme 1.

There were analyzed the database, offered the most promising objects, were developed the methods of synthesis and were found the first active compounds in the study. As the most promising members of the group were identified representatives among water-soluble compounds such as (1) which showed an active activity against sepsis. It should be noted that the compounds do not have antimicrobial activity indicating their impact on the regulated processes by receptors.

We thank the Russian Science Foundation grant № 17-13-01096.

PHOTOCHEMICAL AND THEORETICAL STUDIES OF SUPRAMOLECULAR COMPLEXES OF FUNCTIONALIZED STYRYLPYRIDINE DERIVATIVES

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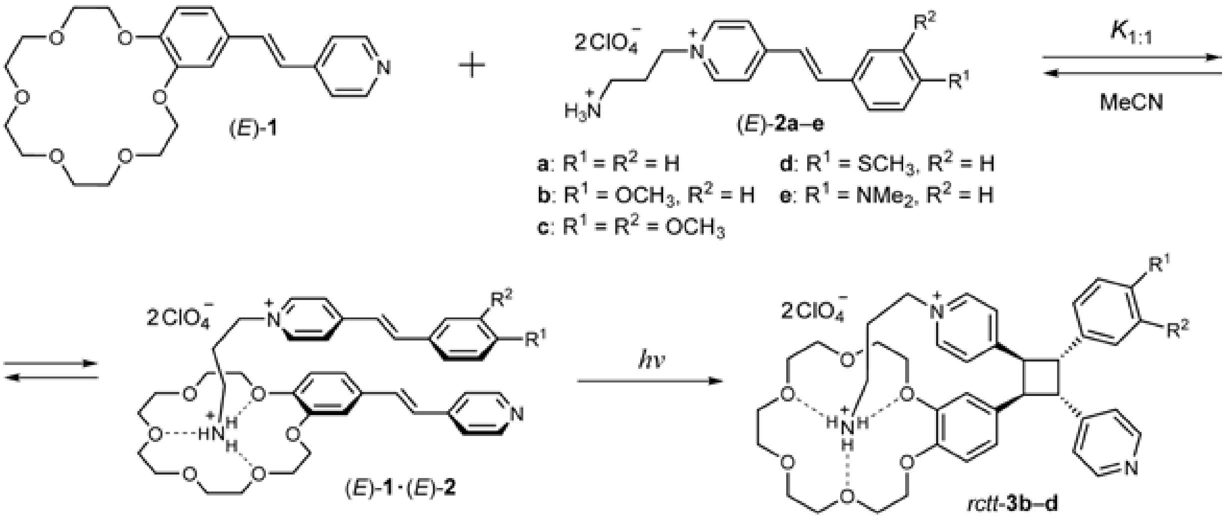
Crown ether-containing styrylpyridine (*E*)-**1** is able to bind styrylpyridinium dyes (*E*)-**2a**–**e** [1,2] *via* hydrogen bonding to form pseudodimeric complexes (*E*)-**1**·(*E*)-**2** in which the styrylpyridine and styrylpyridinium moieties are arranged one over the other owing to stacking interactions. The stability constants ($K_{1:1}$) of complexes (*E*)-**1**·(*E*)-**2** in MeCN were measured using spectrophotometric titration. It was found that the substituents on the benzene ring of (*E*)-**2** have insignificant effect on the complex stability constant.



The photochemical and photophysical properties of styrylpyridinium dyes (*E*)-**2** in free forms and in complexes with styrylpyridine (*E*)-**1** were studied by electronic spectroscopy methods. It was found that the complexation of dyes (*E*)-**2b**–**d** with (*E*)-**1** induces a stereospecific [2 + 2]-cross-photocycloaddition reaction yielding cyclobutanes *rctt*-**3b**–**d**. The quantum yields of this supramolecular photoreaction were measured upon selective excitation of the styrylpyridinium dye. An unexpected result is that with an increase in the S_1 excited state lifetime of the dye (**2b** < **2c** < **2d**, more than 20 times), the photocycloaddition quantum yield decreases (**2b** > **2c** > **2d**, twofold). In order to interpret this effect, the structures of complexes (*E*)-**1**·(*E*)-**2b,d** in MeCN were studied using density functional theory calculations.

This work was supported by the Russian Science Foundation (grant No. 19-13-00020) and the Ministry of Science and Higher Education of the Russian Federation (State Assignment No. 0089-2019-0003).

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SYNTHESIS OF C-3-MODIFIED CARBAPENEMS

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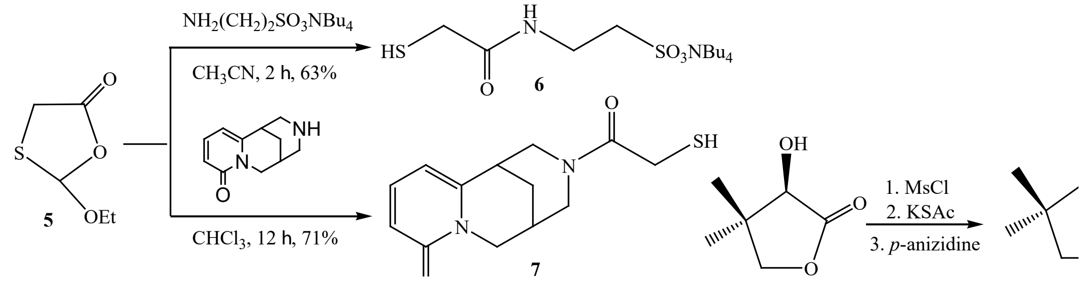
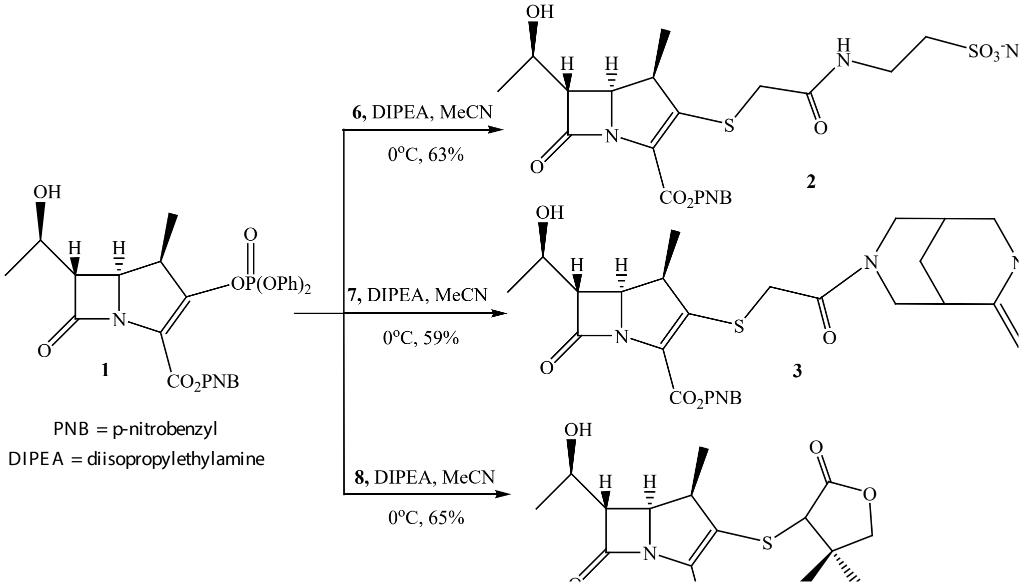
In the synthesis of carbapenem derivatives the most practical approaches are those starting from the key phosphonate **1** [1], in which the diphenylphosphate group under mild conditions is replaced by the RS-substitute of the RSH thiols with the formation of the corresponding carbapenems. In order to obtain the new carbapenems **2-4** in the reactions of Ad_NE-substitution of the phosphate group **1**, we used thiols **6**,**7**, obtained by condensation of 2-ethoxythiolanone **5** [2] with taurine tetrabutylammonium salt and cytisine, and thiol **8**, synthesized from pantolactone by substitution of the OH group in 3 stages with SH (Scheme 1).



Scheme 1.

Reactions of carbapenemenol phosphate **1** with thiols **6–8** in acetonitrile at 0°C in the presence of DIPEA led to new target compounds **2–4** (Scheme 2).



PNB = p-nitrobenzyl
DIPEA = diisopropylethylamine

Scheme 2.

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This work was supported by Russian Science Foundation (project no. 15-13-00039П).

NI-IR DUAL PHOTOREDOX CATALYSED SYNTHESIS OF 2-BENZYLPYRROLIDINES UTILIZING SULFONIUM-SALTS

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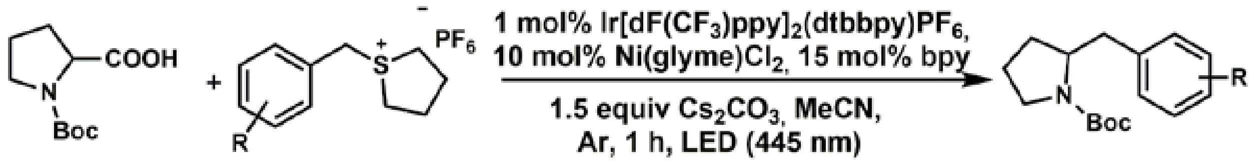
2-Benzylpyrrolidines has a variety of medicinal applictaions and their sythesis got considerable attention in the past [1].Our research group wished to build this moety from sulfonium salts as stable products capable of transition metal catalysed cross couplings [2]. With the rise of photochemical transformations new paths became available for the construction of complex molecuels. Theese systems are well established for a variety of substrates. In our work we were able to expand the existing methodologies [3] and combine the radical generation by photoexcited iridium and cross coupling of benzyl sulfonium-salts enabled by nickel.

We showed that sulfonium-salt are compatible with the conditions of a photochemical reaction and demonstrated the process on a variety of substrates. The reaction provided the appropriate 2-benzylpyrrolidine up to 74% isolated yield in a simple one step procedure using cheap and readily avaiable *N*-boc-proline as a starting material.



18 examples
14-74% isolated yields

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8-YLIDENEBENZAZECINDIENES-4,6

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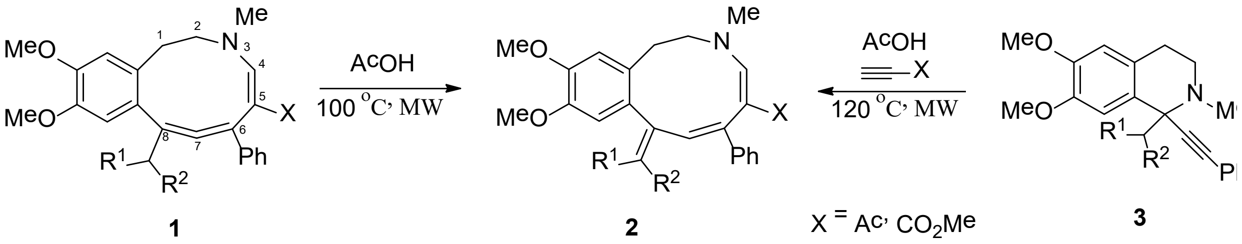
Being structural fragments of a number of alkaloids, nitrogen-containing heterocycles and macrocycles are quite common in nature [1]. Many of them, as a rule, possess biological activity [2]. Recently, we have developed a synthesis of a new class of benzazecines with an allene`s fragment from 1-*R*-1-phenylethynyl-substituted isoquinolines and activated alkynes [3]. In this report, we describe methods for producing 8-ylidenebenzazecindienes-4,6



We found that allenes **1** with an alkyl or benzyl group in position 8 turn into benzazecinediens-4,6 **2** under the action of acetic acid at 100 °C under microwave activation, since the formation of a conjugate system turned out to be more profitable than allenes. The isoquinolines **3** in acetic acid also are transformed into 8-yliden substituted **2** under the action of terminal alkynes at 120 ° C under microwave activation. Ylidenebenzazecines **2** are formed as geometric isomers on the double bond of position 8.

The publication was prepared with the support of the Russian Science Foundation (project № 18-73-10057).

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SYTHESIS OF BISTRIAZOLES BASED ON THE BISPIDINETETRAONE SCAFFOLD

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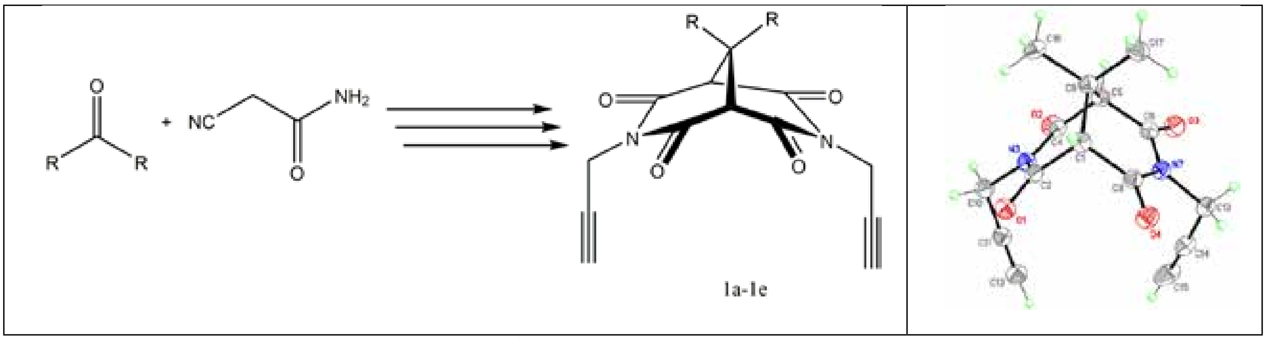
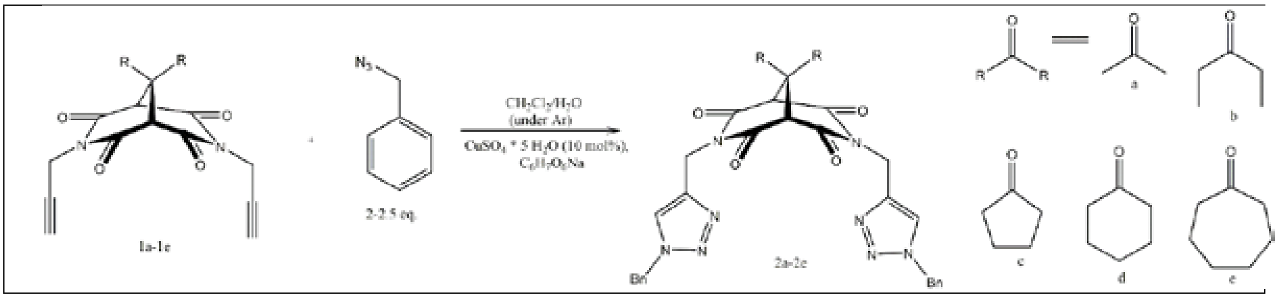
3,7-Diazabicyclo[3.3.1]nonanes (bispidines) have proven to be valuable in multiple areas - they have been studied in computer modellling as serine protease inhibitors [1] and can be used as building blocks in the design of biologically active compounds [2] or in the synthesis of copper-based imaging agents for positron emission tomography [3]. On the other hand, 2,4,6,8-tetraoxobispidines (bispidinetetraones) can be considered as conformationally rigid analogue of bispidines[4], and thus are useful as copper chelating reagents for potential use as ligands for positron emission tomography.



Scheme 1. General scheme of synthesis of N,N'-dipropargybispidineltetraones and crystal structure of **1a**

The aim of this work was to synthesize a series of 2,4,6,8-tetraoxobispidines functionalized with 1,2,3-triazoles at both nitrogens. Target compounds were obtained by sequential synthetic transformations - condensation of cyanoacetic ester with ketones, intramolecular acidic heterocyclization, alkylation with propargylbromide (Scheme 1) and finally [3+2] cycloaddition with benzylazide (Scheme 2).



Scheme 2. Synthetic scheme of [3+2] cycloaddition

A series of experiments was performed aiming to find the best reaction conditions for the cycloaddition step. These results together with structural studies of the target bis-triazoles will be described in the report.

This work was supported by Russian Science Foundation 19-73-20090

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CATIONIC LIPOSOMES MODIFIED WITH ALKYLTRIPHENYLPHOSPHONIUM BROMIDES

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Among nanocontainers for various substrates, including medicines, the following carriers can be distinguished: liposomes, polymers, solid lipid nanoparticles, microemulsions, etc. Liposomes consist of a hydrophilic water core and a hydrophobic lipid bilayer, thus they are universal carriers of both hydrophilic and hydrophobic substances. Recently, there has been a tendency to make targeted carriers to achieve better results. As a vector, the triphenylphosphonium cation is of particular interest because of the delocalized positive charge and affinity for mitochondria.

The purpose of this work was to obtain cationic liposomes based on 1,2-dipalmitoyl-sn-glycero-3-phosphocholine, noncovalently modified by alkyltriphenylphosphonium bromides (TPPB-n) with different lengths of hydrocarbon radical.

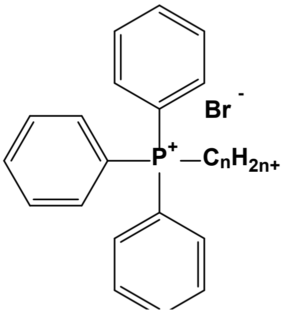

Fig. 1. Chemical structure of alkyltriphenylphosphonium bromides (TPPB-n)

We have monitored the hydrodynamic diameter and electrokinetic potential of hybrid liposomes depending on the lipid/surfactant ratio in time with the aim to determine the optimal composition having a sufficient positive charge for targeted delivery. It was found that increasing the length of surfactant's alkyl radical (up to TPPB-14) leads to an increase in the positive charge of the liposomes. Probably, amphiphiles with a longer hydrocarbon radical are able to more effectively integrate into the lipid bilayer and retain in it. The most optimal results of stability were obtained for hybrid liposomes based on 1,2-dipalmitoyl-sn-glycero-3-phosphocholine and TPPB-12.

This work was supported by Russian Science Foundation (project № 19-73-30012)

TAUTOMERIC TRANSFORMATIONS OF BENZO[2]THIENO[2,3,4-IJ]-2,7-NAPHTHYRIDINES

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In course of our investigation of the reactions of intramolecular cyclization involving nitrene generated from the azido group of 3-azidothieno [2,3-b] pyridine-2-carboxilates, we synthesized representatives of the new condensed heterocyclic system – 6*H*-benzo[c]thieno[2,3,4-ij]-2,7-naphthyridine.

Studying an alkylation of naphthyridine **1**, we encountered a curious fact: using a bulk alkylating agent, instead of desired alkylation product, we obtained a compound **2** that was identified as 3-*H* isomer — ethyl 2-phenyl-3*H*-benzo[c]thieno[2,3,4-ij]-2,7-naphthyridine-5-carboxylate according to mass spectrometry and NMR spectroscopy data.

Ethyl 2-phenyl-6*H*-benzo[*c*]thieno[2,3,4-*ij*]-2,7-naphthyridine-5-carboxylate 1

Ethyl 2-phenyl-3*H*-benzo[*c*]thieno[2,3,4-*ij*]-2,7-naphthyridine-5-carboxylate 2

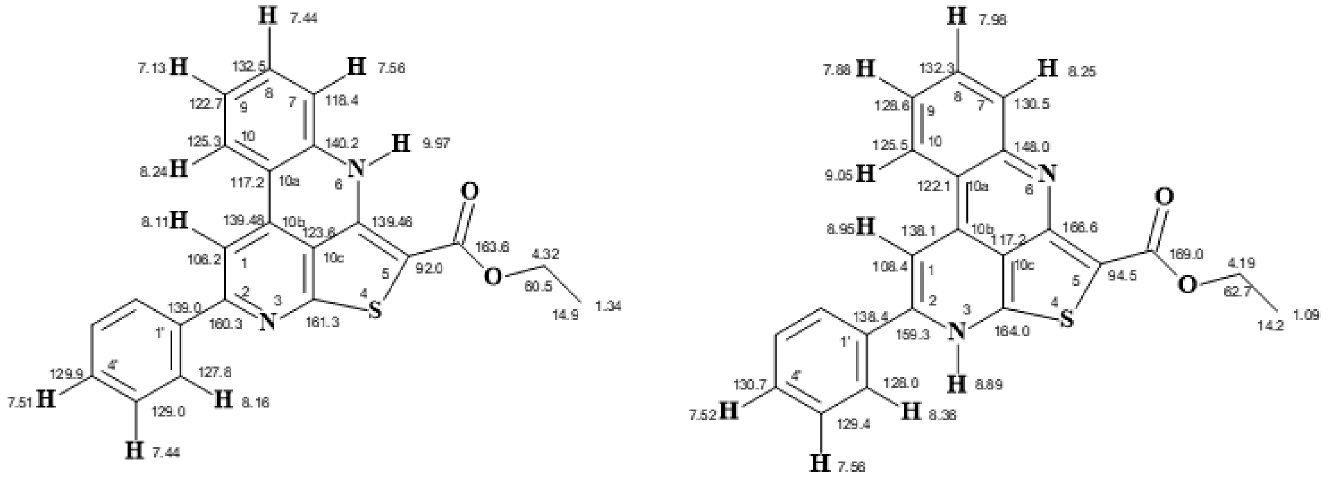

Fig. 1.

It is found that 6*H*- → 3*H*- isomerization occurs when the 6H-isomer is treated with sodium hydride in absolute dioxane. Probably, the proton removal from the nitrogen atom leads to the formation of a delocalized anion which, in turns, transforms into more stable tautomeric form – ethyl 2-phenyl-3H-benzo[c]thieno[2,3,4-ij]-2,7-naphthyridine-5-carboxylate.

Several examples of the tautomeric transformation will be presented.

This work was supported by the Russian Foundation of Basic Research (RFBR) (grant No. 18-33-00184/18).

SUBSTITUTED 4,5-DIAZAFLUORENES IN KNOEVENAGEL REACTION

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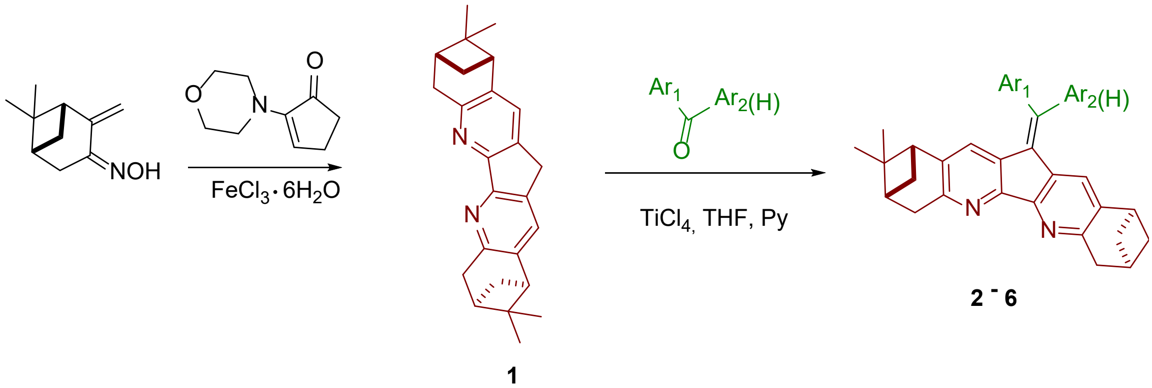
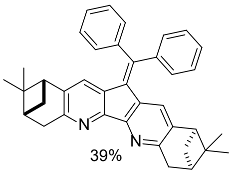
Substituted bipyridines get significant interest in coordination chemistry [1]. Recently we prepared 4,5-diazafluorene **1** from (+)-oxime pinocarvone [2]. Now we report reaction of Knoevenagel condensation of 4,5-diazafluorene 1 and series of aromatic ketones. Alkenes **2** – **6** were prepared in moderate yields.





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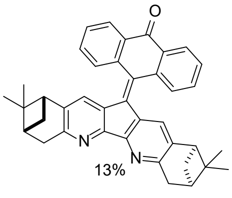

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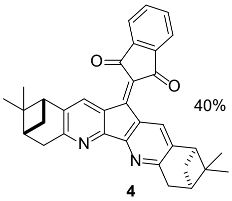

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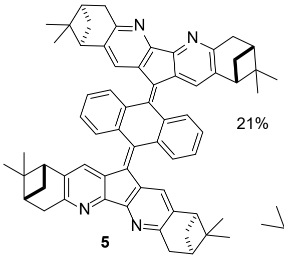

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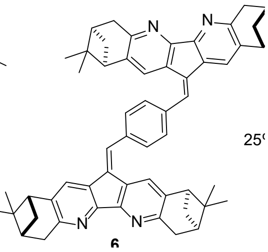

6

We used system of 2 eq. $TiCl_4$, excess of pyridine and THF as a solvent. Much excess of $TiCl_4$ gave insufficient results. We tried other condensation conditions (NaH, then $SOCl_2$, Py). It gave desired products but in lower yieds probably due high reactivity 4,5-diazafluorene anion. Compounds **5** and **6** can be used as ditopic ligands.

This work was supported in part by the Russian Foundation for Basic Research, Grant 18-33-00243 (mol_a).

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BIODIESEL FROM LIGNOCELLULOSIC MATERIALS

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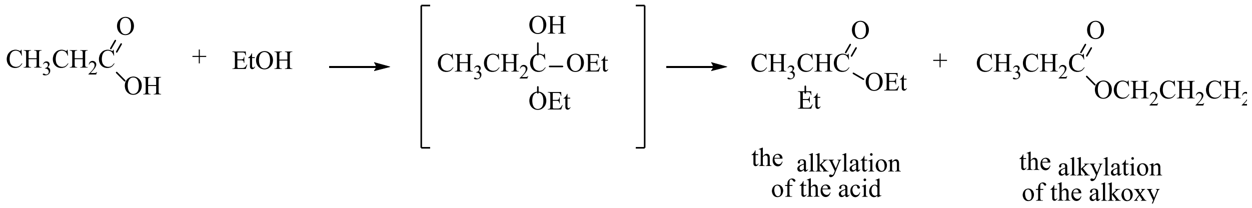
New methods for the processing of lignocellulosic materials expand the range of products and intermediates for the synthesis of oxygenate additives, obligatory components of high-octane fuel compositions. Light fatty acids (acetic, propionic, butyric acids, LFA), the products of the biocatalytic conversion of carbohydrate raw materials with the specialized acidogenic microbial associations [1], can be transformed into a fuel form by esterification under conditions of formation of supercritical fluids (SCF) of ethanol. This eliminates the use of catalysts, reduces the process time to minutes, and reduces the total energy consumption. It was shown that the SCF-process is not limited to the formation of the expected ethyl carboxylates. A multicomponent mixture of esters of higher ethylated LFA homologs is formed. Alkoxy fragments of carboxylates are also ethylated. Possible intermediates of ethylation can be diethyl-ortho-carboxylates of a previously unknown structure corresponding to the addition of an ethanol molecule to the carbonyl group of the ester. Such an ester was detected in case of the esterification of butyric acid under SCF conditions. Diethyl ortho-butyrate was identified by gas chromatography-mass spectrometry [2].



Scheme 1.

The mixtures of esters formed under SCF conditions taking into account the origin of the initial LFA can be considered as an easy analog of biodiesel and used without separation into components.

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SYNTHESYS AND ANTIPROLIFERATIVE ACTIVITY OF SERIES OF SALICYLIDENE INDOLE-2-CARBOHYDRAZIDES

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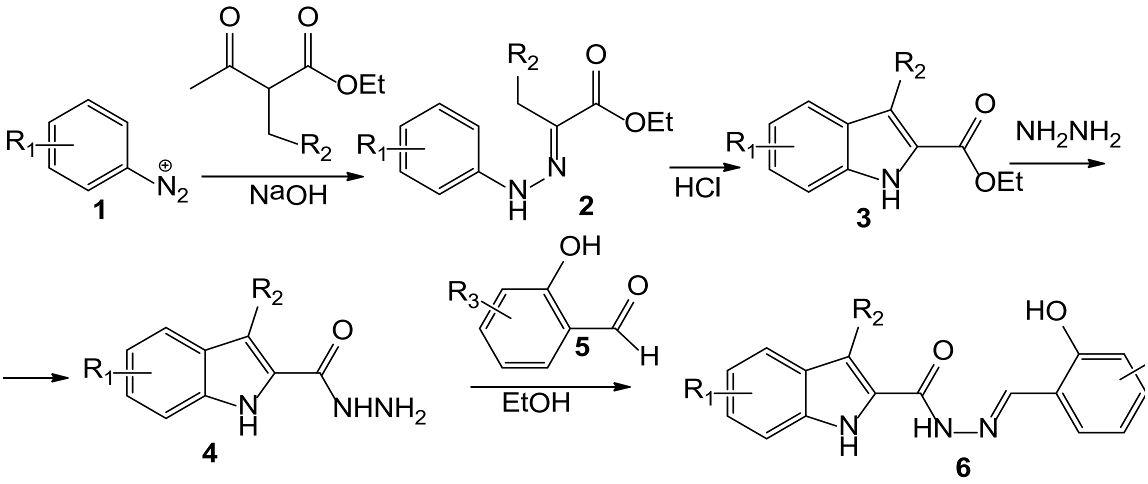
Various heterocyclic acylhydrazones are attracted an interest of medicinal chemists due to their interesting biological properties such as high antimicrobial and anticancer activity [1, 2]. It is known, that presence of hydroxy group at *ortho*-position to the aldehyde component of acylhydrazones potentiated their bioactivity. Thus, some acylhydrazones obtained from salicylaldehyde and its derivatives, potently blocked the proliferation of tumor cells [2, 3] via the inhibition of oncogenic protein and lipid kinases or by chelation of metal ions from regulatory proteins [3, 4].

For structure – activity relationship studies, we have prepared a series of salicylidene indole-2-carbohydrazones **6** by condensation of various salicylaldehydes **5** with substituted indole-2-carbohydrazides **4** (Scheme 1). Starting ethyl indole-2-carboxylates **3** were prepared from diazonium salts **1** and 2-substituted acetylacetic esters via Japp – Klingemann reaction and subsequent cyclization of hydrazones **2** by the Fisher procedure. Further, ethyl indole-2-carboxylates **3** were converted to hydrazides **4** by the treatment with hydrazine hydrate in ethanol.

Some of synthesized salicylidene indole-2-carbohydrazides **6** potently inhibited the proliferation of adenocarcinoma cell (HCT-116) in micromolar and submicromolar concentration. Thereby, founded chemotype **6** is prospective for in-depth biological evaluation and further anticancer drug development.



Scheme 1. Synthesis of a series of salicylidene indole-2-carbohydrazides **6**.

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THERMAL TRANSFORMATION OF HETEROCYCLIC AMINO ACIDS

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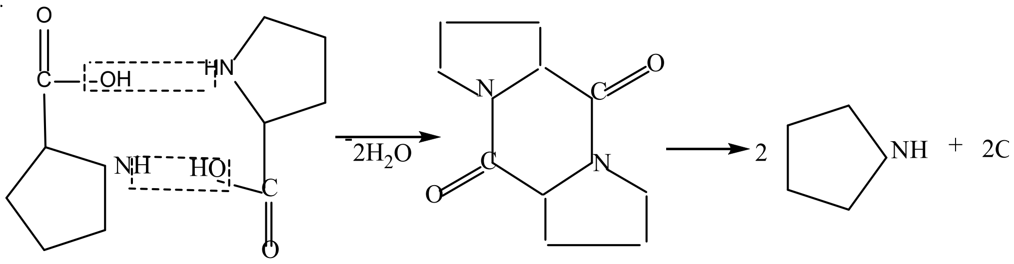
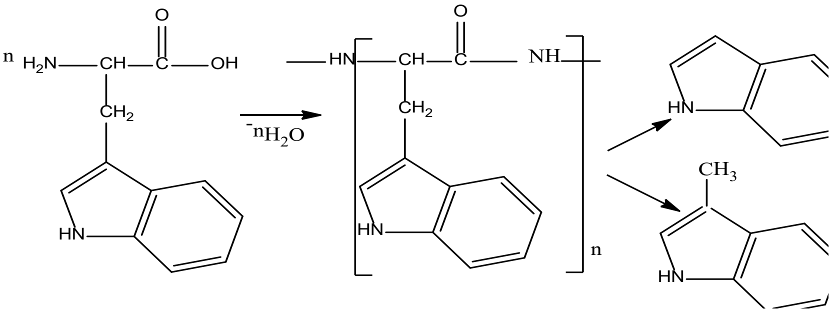
Heterocyclic amino acids are used to produce biological active substances, as well as polymeric materials[1]. Solid phase thermal transformations of tryptophan (Trp), histidine (His) and proline (Pro) were carried out in a vacuumed static system in glass vials of constant volume with glass membranes[2]. The kinetic parameters of thermal conversion are given in the table.

	Trp	His	Pro
T, ◦C	240-270	230-280	205-230
k230103,c-1	4.2	8.7	770
E, kJ/mol	179±10	190±6	212±11

It can be seen that the effective activation energy of thermal transformation grows on going from Trp to Pro, the rate constants of the process of turning Pro are almost two orders of magnitude higher than the corresponding Trp constants. The rates of His and Trp transformations differ 1.5 - 2 times. The heterocyclic fragment of Pro is in close contact with its acidic group. As a result, there are opportunities to implement the processes of cyclization and splitting of closely located active groups. Thus, in the case of Pro, the entropy factor works, and this provides Pro with higher rates of thermal transformation in a number of studied amino acids. Chromato-mass spectrometry, IR spectroscopic and MALDI-TOF MS analysis determined the composition of the reaction products. The probable mechanism of solid phase thermal transformation is presented for Pro (I) and Trp (II).



(I)



(II)

The process of thermal transformation of His is similar to the transformation of Trp, since the structure of His repeats the structure of Trp, but imidazole is present instead of the indole heterocycle in His.

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SELF-ASSEMBLY OF CUCURBITURILS AND CYCLODEXTRINS TO SUPRAMOLECULAR MILLSTONES WITH NAPHTHALENE DERIVATIVES

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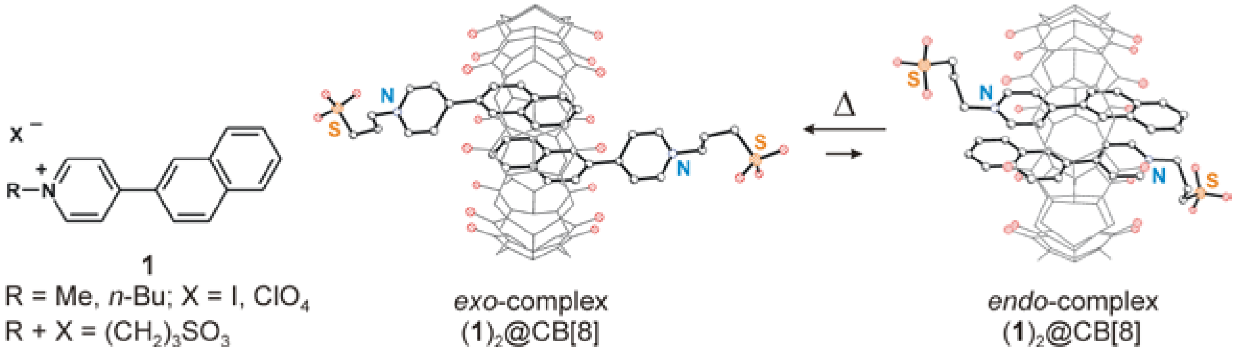
Quaternary 4-(2-naphthyl)pyridinium salts **1** with various *N*-substituents were synthesized. The structure of these salts was determined by X-ray crystallography. The self-assembly of the salts with cavitand molecules – β- and γ-cyclodextrins (CD) and cucurbit[7,8]urils (CB[*n*]) – in aqueous solutions was studied by electronic spectroscopy and ^{1}H NMR spectroscopy, including spectrophotometric, fluorescence, and ^{1}H NMR titrations.



Scheme 1. Structure of compounds **1** and structure of complexes $(\mathbf{1})_2$@CB[8] in solution and crystals.

The formation of inclusion complexes of different stoichiometry and stability, was observed, depending on the structure of *N*-substituent in the quaternary salt and the cavitand nature and cavity size. It was found that the stability of 1:1 inclusion complexes for all of the guests tends to increase in the series γ-CD < β-CD << CB[7] ≈ CB[8]. The complex formation with CB[*n*] results in considerable changes in the absorption and fluorescence spectra of compounds **1**. Physical motion of the long guest molecules in the CB[*n*] cavities was detected. For the 2:1 complex formed by compound **1** (R = $(CH_2)_3SO_3^-$) with CB[8], this translocation, resembling the millstone operation, is not only observed for the first time by ^{1}H NMR spectroscopy, but is also confirmed by X-ray crystallography. In crystals, the cavitand was located either above the naphthalene residues of a dimeric pair of guest molecules (*exo*-complex) or above the centers of their conjugated moieties (*endo*-complex) [1].

The detected trends of the translocations in the inclusion complexes of the cavitands can be used to design supramolecular devices and machines, in particular, supramolecular assemblers, and to develop information recording and storage devices at the molecular level.

This work was supported by the Russian Foundation for Basic Research (project 18-03-00214).

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MECHANISM OF REACTIONS OF ATRANES AND THEIR QUASI- AND HYPOANALOGUES WITH NUCLEOPHILIC REAGENTS

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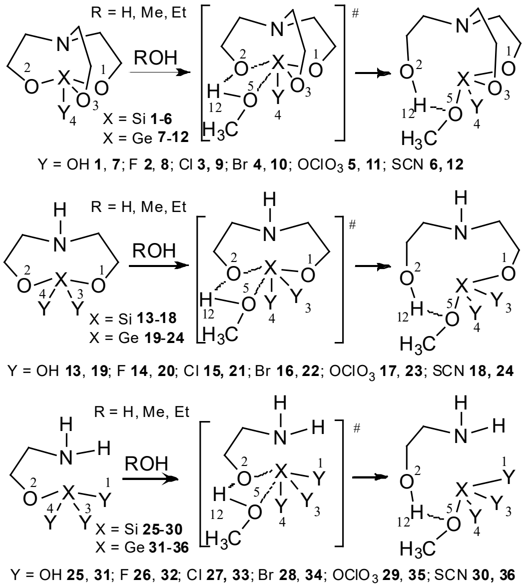
Metallatranes (primarily silatranes and germatranes), their bicyclic analogues – ocanes, and monocyclic – hypoatranes have a high and specific bioactivity, which can be explained by their unusual trigonal-pyramidal structure containing the transannular bond N→X (X = Si, Ge) and the presence of various exocyclic substituents. We performed a theoretical study of the reactions of substituted atranes **1**-**12**, ocanes **13**-**24**, and hypoatranes **25**-**36** with water, methanol, and ethanol by the method DFT B3PW91/6-311++G(d-f,p) (Scheme 1).



The calculations of all reactants were carried out, and all elementary steps were found. In all cases, the descents from transition state in the direction of the initial molecule or the reaction product were performed for the confirmation of conformity of the found structure of TS. The calculations were performed without taking into account the solvent.

According to DFT calculations, the molecules of **1**-**36** initially form pre-reaction complexes with the methanol molecules, transforming into the transition states, which as a result of the breaking of Si–O2 or Ge–O2 bond are converted into the products. The reactions of **1**-**36** with ROH (R = Me, Et) are controlled by the thermodynamic factors. The annular *endo*-configurations of the products are stabilized by the dative interaction N→X (X = Si, Ge) and various intramolecular hydrogen bonding.

Scheme 1.

The results obtained were compared with the data on interaction of **1**-**36** with H_2O: hydrolysis of hypoatranes is characterized by lower energies of activation and slightly lower positive Gibbs energies than the hydrolysis of the corresponding ocanes and atranes [1], [2]. Special attention was paid to changes in the strength of the N→X bond (X = Si, Ge) in the reaction products. Features of the structure of reagents and products, details of the mechanism of nucleophilic reactions established will be discussed.

This work was supported by Russian Foundation for Basic Research (grant 16-03-00100).

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SPECTRAL PROPERTIES AND SOLVATOCHROMIC BEHAVIOR OF NEW FLUORESCENT HETEROAROMATIC BIS-*PERI*-FUSED AZOXONIUM CATIONS

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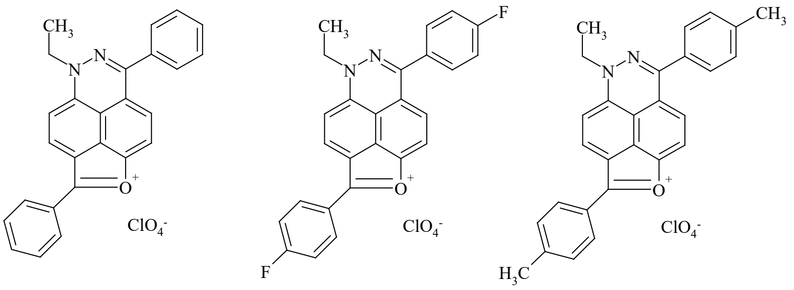
Spectral and photophysical properties of novel fluorescent heteroaromatic bis-*peri*-fused azoxonium cations isolated as salt with perchlorate anion as the counter-ion have been thoroughly investigated by means of UV/vis and photoluminescence (PL) spectroscopy in aprotic solvents [1].



1 **2** **3**

Fig. 1. Chemical structures of 1-ethyl-3,7-diarylbenzofurocinnolinium perchlorates **1**-**3**.

Solvatochromic fluorescence properties of the compounds obtained are determined by intermolecular electrophilic-nucleophilic interactions of the cations with solvent molecules. Gutmann's donor numbers correctly assess the solvent effect on the cation spectral characteristics. Compounds **1-3** are effective fluorescent dyes characterized by the quantum yields reaching 0.67 and fluorescence lifetime up to 4.18 ns. Single-exponential fluorescence decay of the azoxonium cations is disturbed in the DMSO solvent possessing strong Electron-Pair-Donor properties and is accompanied by a sharp decrease (up to 0.03) of the fluorescence quantum yields. Coordinating interaction of the DMSO molecules with Electron-Pair-Acceptor center of the cations leads to the appearance of an additional efficient non-radiative channel of the energy deactivation of the electronic excitation.

Solvatochromic behavior and photostability of new fluorescent cations open perspectives for practical application as fluorescent probes for estimation of the nucleophilic properties of the aprotic solvents and their mixtures.

This work was supported by the Ministry of Education and Science of Russian Federation within the framework of the State Assignment for Research, project № 4.6759.2017/8.9.

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DIVERSITY ORIENTED TARGET FOCUSED SYNTHESIS (DOTS) APPROACH FOR OPTIMIZATION OF BET-INHIBITORS

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BET-proteins, acting as epigenetic readers, play an essential role in cancer development. A medium throughput screening of previously designed chemical library [1] allowed identification of two new BET-inhibitors with unique profiles of BET-selectivity [2].

Here, we report a time and cost-efficient integrated strategy named DOTS (Diversity Oriented Target Focused Synthesis) for optimization of identified molecules. This strategy contains a focused-chemical-library design and virtual screening coupled with robotic diversity-oriented *de novo* synthesis and automated *in vitro* evaluation. The virtual library is generated by combining an activated fragment, corresponding to the substructure binding to the target, with a collection of functionalized building blocks using *in silico* encoded chemical reactions carefully chosen from a list of one-step organic transformations relevant in medicinal chemistry (Fig. 1).

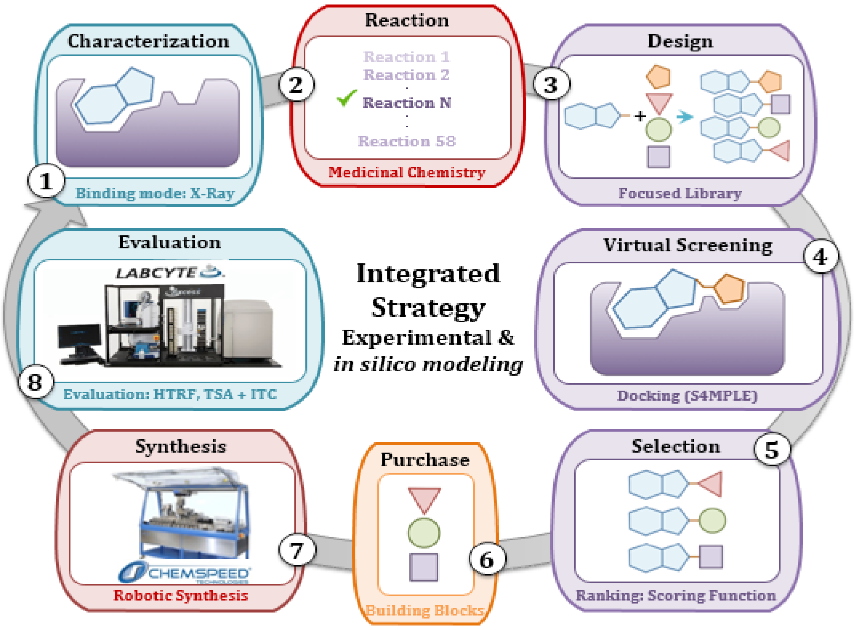

Fig. 1. Schematic workflow of the DOTS pipeline

This optimization led to the validation of several compounds with improved affinity by several orders of magnitude [3]. One molecule demonstrated up to 100-fold improvement of affinity to the target and pronounced selectivity toward BD1. Dose-response downregulation of *c-Myc* levels in low micromolar range in cell assays allowed the validation of the identified molecule as a chemical probe.

This work was supported by a Metchnikov Ph.D. fellowship from the French government and a fellowship from the Fondation ARC pour la Recherche sur le Cancer

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UNUSUAL RESULT OF THE INTERACTION OF 3-PHENYLPYRAZOLIN-2 WITH ISATIN

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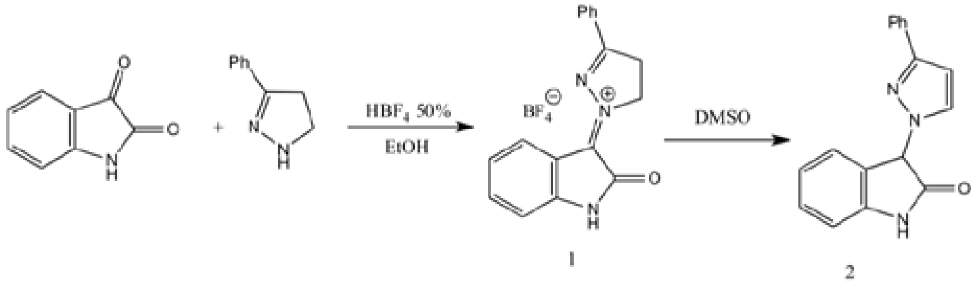
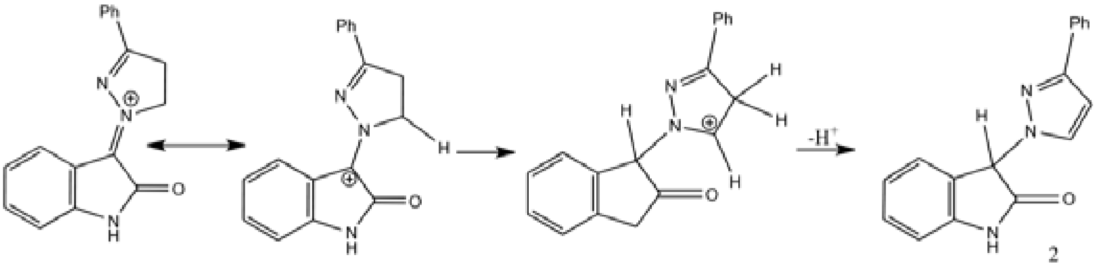
Moscow State University Chemycal Department

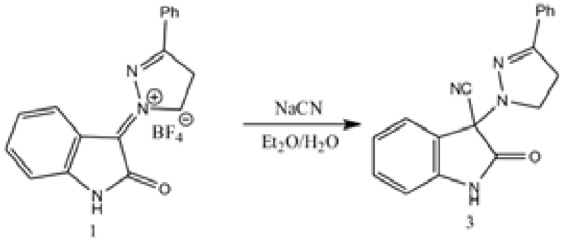
Recently, we have studied the interaction of pyrazolines-2 with carbonyl compounds leading to the formation of alkylidene and arylidene salts [1]. An interesting result was obtained by the reaction of 3-phenylpyrazolin-2 with isatin, carbonyl groups in which have different reactivity. Reaction under standard conditions (C_2H_5OH, 50% HBF_4) [1] leads to the formation of an isatin pyrazoline 1 derivative (Scheme 1), which transformed into pyrazole 2 in a DMSO solution.

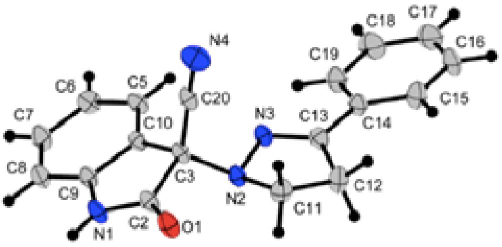


We suppose that when the salt is dissolved, the 1-3 hydride shift and proton elimination is realized, which leads to aromatization of the compound 1



The isatin derivative 1 enters into nucleophilic addition reactions characteristic of alkylidene and arylidene salts.





This work was supported by RFBR (grant # 18-03-00680)

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NEW METHOD OF SYNTHESIS DERIVATIVES OF DIARYLMETHANE CONTAINING AMINOETHANOSULPHONATE FRAGMENTS, BASED ON THE REACTION OF FUNCTIONALIZED ACETALS WITH REZORCINOLS

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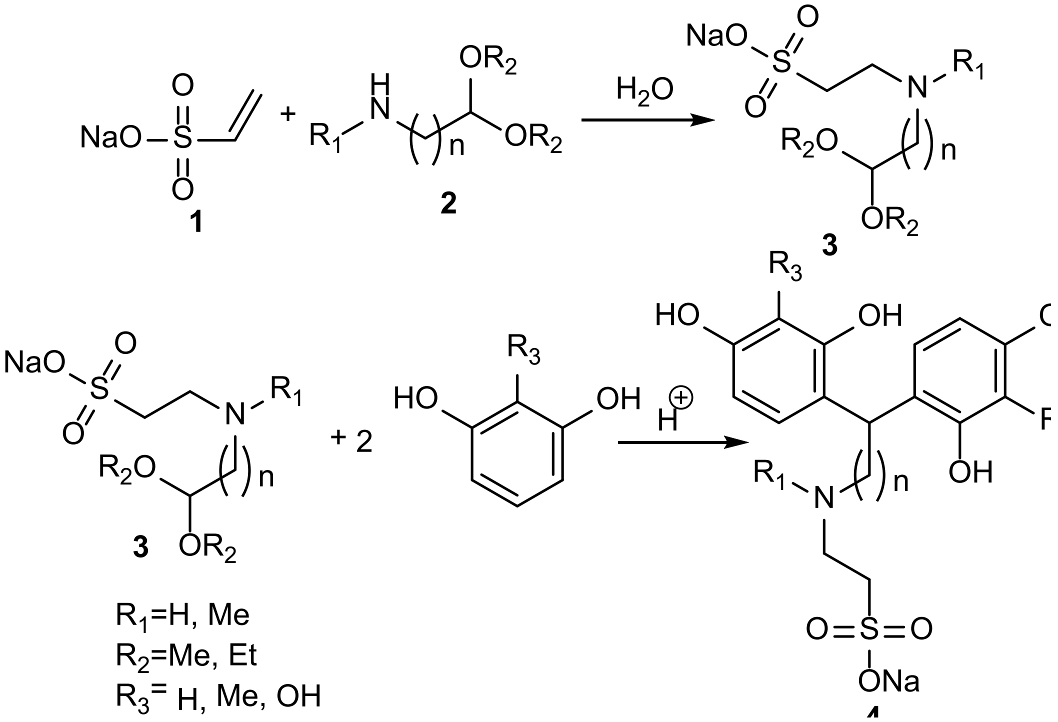
Aminoethanesulfonic acid derivatives are biologically active substances exhibiting anti-myotic, cytostatic, bactericidal and insecticidal properties. However, the number of simple and convenient methods for the synthesis of this class of compounds is currently limited. Therefore, in the present work, a new approach to the synthesis of aminoethanesulfonic acid derivatives containing aryl fragments has been proposed. At the first stage, aminoethanesulfonates **3** were synthesized, as a result of the interaction of amino acetals **2** with sodium vinyl sulfonate **1**. As a result of the acid - catalyzed reaction of acetals **3** with resorcinol, new diarylmethane derivatives **4** were obtained.



The reported study was funded by RFBR and Government of the Republic of Tatarstan according to the research project № 18-43-160004.

THIACALIX[4]THIACROWN-ETHER IONOPHORES AT THE AIR–WATER INTERFACE

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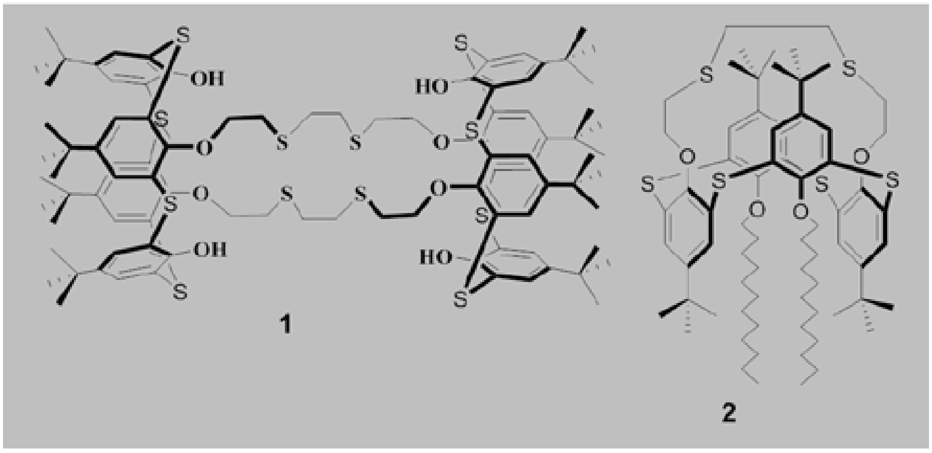
Design of new materials based on nanosized supramolecular systems is one of the important directions in fundamental research. Calixarene macrocycles are of particular interest for the design of these systems due to their facile modification and a variety of stereoisomeric forms. Combination of two macrocyclic scaffolds, such as crown-ethers and calixarenes would provide synergetic effect in molecular recognition phenomena, in particular, towards alkali metal ions and lanthanides. Even greater potential of these conjugates can be implemented in ultrathin Langmuir films [1], where necessary packing density and orientation of molecules are achieved.

The aim of this work is to evaluate the potential of thiacalix[4]thiacrown-ethers as film-forming molecules using Langmuir method.



Scheme 1.

Two structural types of (thia)calix[4]thiacrown-ether in *cone* and *1,3-alternate* configurations (Scheme 1) have been synthesized through the Mitsunobu reaction of thiacalix[4]arenes with 3,6-dithia-1,8-octanediol. The structure of the compounds was characterized using 1D/2D NMR spectroscopy. Thiacrown ligands on a thiacalix[4]arene scaffold 1 and 2 showed the ability to form thin films at the air-water interface, with the horizontal orientation of biscalixarene molecules 1 in bilayer and vertical orientation of *1,3-alternate* thiacrowns 2 in monolayer.

This work was supported by the Program of Fundamental Studies of the Presidium of the Russian Academy of Sciences 14P "Physical Chemistry of Adsorption Phenomena and Actinide Nanoparticles".

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SYNTHESIS OF 1,3,4-OXADIAZOLES WITH BISELENOPHENYL MOIETY

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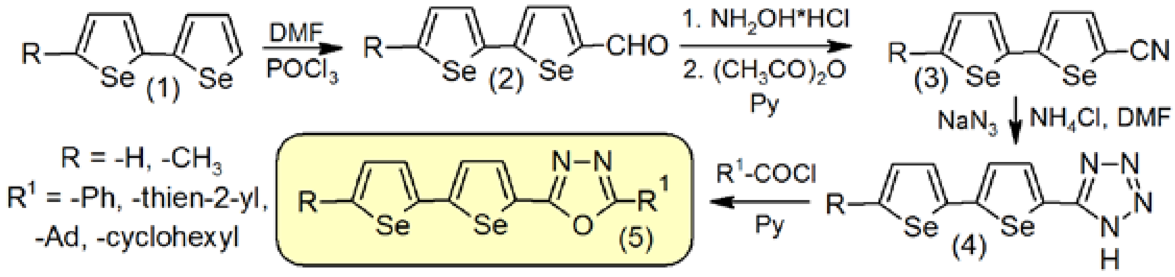
Materials with optical properties based on aromatic and heteroaromatic structure represent a wide perspective for single electron transistors, solar cells, organic photovoltaics and field effect transistors [1]. Oligo- and polythiophenes with «heavy» atom of sulfur have interest as perspective building blocks at NLO properties design [2]. Derivatives of 2,2'-bithiophene have properties of highly effective and photostable fluorophores, active laser media for optical quantum generators [3].

Special interest is to find changes in optical properties of the biselenophene derivatives with «superheavy» selenium atom, which are the closest heteroanalogs of bithiophene. Synthesis of the main 5'-(tetrazol-5-yl)-2,2'-biselenophene (**4**) represented on Scheme 1.



Scheme 1.

Formylation of initial 2,2'-biselenophenes (**1**) via Vilsmeier-Haack reaction gives formylderivatives (**2**), which converted in the one-pot synthesis into corresponcing carbonitriles (**3**). C-tetrazolylbiselenophenes (**4**) were synthesized via 1,3-bipolar cycloaddition of ammonium azide in DMF media. Electrondonating nature of biselenophenyl moiety has no influence on yield of compounds, however, it increases the reaction time in comparison with 2,2'-bithiophene analogs. Thermal acylation of compound (**4**) with chloroanhydrides of various carboxilic acids leads to biselenophenyl-1,3,4-oxadiazoles (**5**). Targeted selection of chloroanhydrides allowed to get chained linear heteroanalogs of PPO, PVD and POPOP.

It should be noted that presence of couple «superheavy» atoms of selenium in the structure leads to efficient fluorophores from violet to orange region of visible spectrum, but with fast photo- and chemical degradation.

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SYNTHESIS AND BIOLOGICAL ACTIVITY OF N-(INDOLYL) TRIFLUOROACETAMIDES BASED ON SUBSTITUTED 6-AMINOINDOLES

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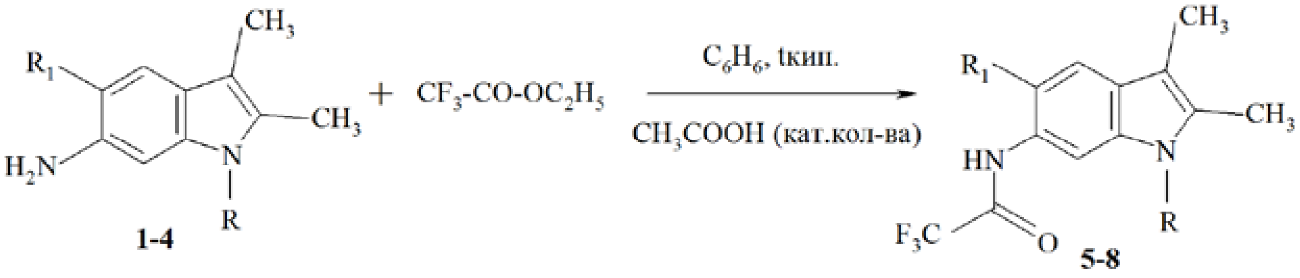
We have previously found that all trifluoromethyl derivatives of benzaminoindoles possess some or another by antimicrobial activity [1].

Moreover, the activity of these compounds against microbial strains depends on the nature of the substituent and the structure of the compound of the indole. It was established that the derivatives of 4-, 6-, 7-aminoindoles exhibit the greatest inhibitory activity. So the compounds obtained on the basis of 7-amino-2,3-dimethyl-, 7-amino-1,2,3-trimethylindoles and ethyl trifluoroacetate show antimicrobial activity, comparable to dioxidine widely used in clinical practice [2].

Continuing research in this direction, we studied the behavior of substituted 6-aminoindoles **1-4** in reaction with trifluoroacetic acid ethyl ester. It was found that when boiling in benzene with an excess of ethyl trifluoroacetate in the presence of a catalytic amount of glacial acetic acid, the aminoindoles under investigation are converted into the corresponding *N*-(indol-6-yl)trifluoroacetamides **5-8**, which according to the spectra of NMR ^{1}H, ^{19}F, UV, of the mass-spectra, irrespective of the nature of the substitution in the benzene and pyrrole fragments of the indole system, have an amide tautomeric form only.



1,5 R=H, $R_1=CH_3$; **2,6** $R=R_1=CH_3$; **3,7** R=H, $R_1=OCH_3$; **4,8** $R=CH_3$, $R_1=OCH_3$

Compounds **5-8**, was screened for antimicrobial activity against the standard strains of *Staphylococcus aureus* 29213, *Escherichia coli* 25922, *Pseudomonas aeruginosa* 27853, *Streptococcus pyogenes* 1238, *Klebsiella pneumoniae* 9172. Like the analogous *N*-(indol-7-yl)trifluoroacetamides, compounds **5-8** show high antimicrobial activity.

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SYNTHESIS OF THE HIGH-TEMPERATURE SELF-HEALING POLYMERS

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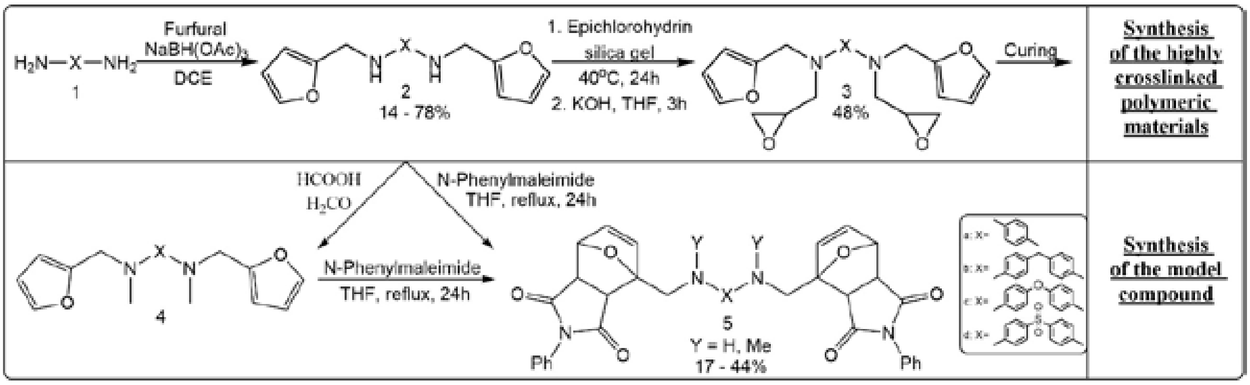
Composites due to their high durability and a variety of thermomechanical properties in combination with small weight are excellent alternative to metals in many industries. However, one of the problems in widespread use of the fiber-reinforced plastic is the complexity of prediction of defect formation and propagation in epoxy binder layer. Defects in polymer structure, even microcracks, can significantly reduce the strength of a composite material. In this regard the self-healing materials are an object of the increased scientific interest for several decades. The reversible Diels-Alder reaction is often used for achievement of polymer self-healing ability. [1] Nevertheless, the serious restriction of this method is the low temperature of the reverse Diels-Alder reaction (T(rDA)) which is usually not exceeding 110-120°C that narrows the operating range of the received polymeric materials. [2]

In this work, we investigate the possibility of extending the operating range of the polymeric materials by increasing T(rDA). We have suggested that the increasing of the T(rDA) can be achieved by the formation of the intramolecular hydrogen bonds between the protons of the NH groups and the oxygen atoms of the maleimide fragments. To study this hypothesis, the synthesis of model compounds (5, Scheme 1) was proposed.

We propose a synthetic strategy for getting new epoxy-containing monomers to create self-healing binders with improved thermomechanical properties. The scheme for the synthesis of the epoxy resin type (3) consists of two stages: reductive amination and epoxidation. It is worth notice that one of the initial reagents of the synthetic scheme is furfural - a compound obtained from bio-renewable raw materials, in particular, from various agricultural wastes. This reduces the cost of the target compound and makes the process of its production more environmentally friendly.



Scheme 1.

This work was supported by Russian Foundation of Basic Research (RFBR) grants 18-29-18036 and 18-29-18037.

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NOVEL N,O(S)-DONOR LIGANDS FOR SEPARATION OF F-ELEMENTS: SYNTHESIS AND STUDY OF PROPERTIES

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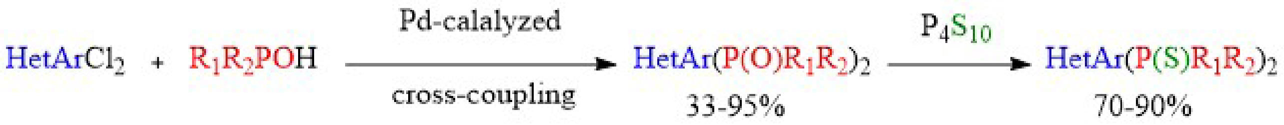
Recycling of spent nuclear fuel (SNF) is a very important scientific and applied problem. One of its aspects is the isolation of radioactive minor actinides and their separation from lanthanides. The actinides is the main source of radiation hazard of SNF due to their significant lifetimes and heat release. One of the ways to separate highly radioactive wastes (HRW) from SNF is the liquid-liquid extraction using suitable organic ligands. To the best of our knowledge there is no acceptable process for isolation of minor actinides from SNF and HRW, though ongoing studies are conducted in many laboratories. Nevertheless, the search for new extractants with high efficiency, selectivity and resistance to severe conditions is of current interest in modern radiochemistry. The purpose of our work is the design of new extractants for isolation of minor actinides, their synthesis and the establishment of structure-complexation properties relationships.

As pre-organized frameworks nitrogen heterocycles were used. Oxygen and sulfur atoms in phosphine oxide and phosphine sulfide groups, respectively, were used as donor atoms. Phosphorylation was successfully conducted for a number of compounds by means of Pd-catalyzed cross-coupling. Sulfur-containing compounds were obtained from corresponding oxide substances by the use of phosphorus (V) sulfide. Yields of all reactions are in range from good to excellent.



All target compounds as well as intermediate compounds were characterized by ^{1}H, ^{13}C and ^{31}P NMR, IR, and mass-spectrometry. Several compounds were structurally characterized by X-ray diffraction.

The compounds obtained were used in extraction experiments on model pair Am/Eu. The values of distribution (D) and selectivity (SF) coefficients were measured for all ligands; several oxide compounds showed SF as high as 35, which was excellent result. Sulfur-containing reagents showed inverse extraction behavior (predominant bonding with lanthanide instead of actinide) under certain experimental conditions.

Financial support for this work comes from RFBR № 18-33-00626.

THE FIRST REPRESENTATIVES OF ASYMMETRICAL CAGE PHOSPHONATES

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Phosphorus-containing cage compounds possess unusual reactivity and physical properties. They are promising structures from fundamental and practical viewpoints. Practical interest is determined by the possibility to employ these compounds as complexing agents, ligands in metal-complex catalysis, organocatalysts, multifunctional drugs and other types of activities [1], [2].

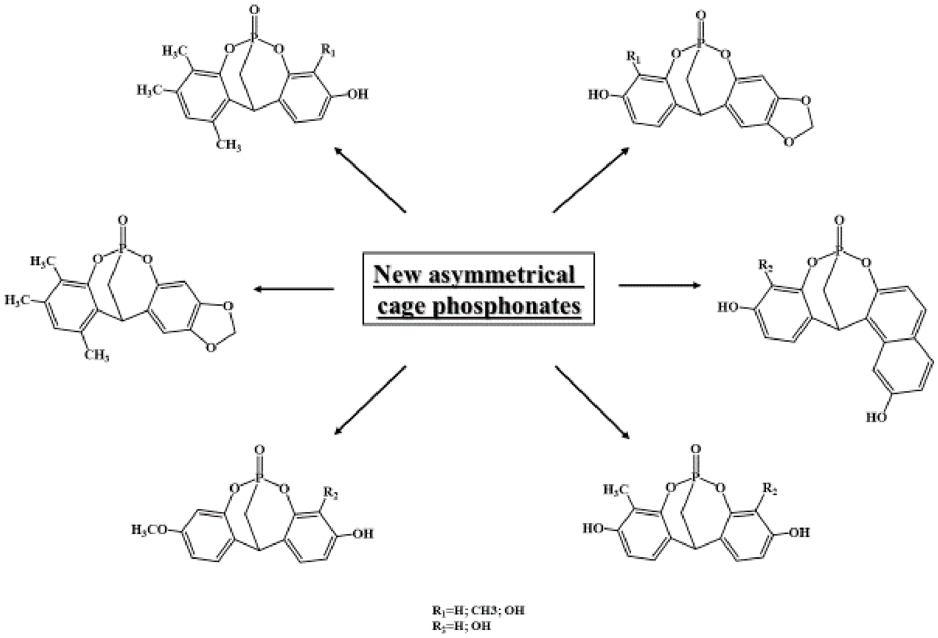

Fig. 1. New asymmetrical phosphorus-containing cage compounds

The structure and composition of the compounds have been elucidated from ^{1}H, ^{31}P, and ^{13}C NMR spectroscopy, mass-spectrometry (MALDI-TOF) and elemental analysis.

This work was supported by the Russian Foundation for the Basic research (grant no 17-03-00254).

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EQUATION-CONSTRAINED LEARNING IN THE CASE OF THE ARRHENIUS EQUATION

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A new approach to modeling functionally related reaction properties is proposed. For example, Arrhenius equation gives the dependence of the rate constant lgk of a chemical reaction on the absolute temperature T, a pre-exponential factor lgA and activation energy of the reaction. It is possible to build model that predicts the rate constant of the reactions as the difference of the values of the Arrhenius equation parameters predicted by two linear models:

$$lgA = Xw_A$$

$$E_a = Xw_E$$

$$lgk = w_A X - (RT)^{-1} w_E X$$

Model learns by minimizing the error of the rate constant prediction. Regression coefficients can be estimated using the ordinary least-squares method. At the same time, experimental data on the activation energy and per-exponential factor of the reactions are not used during training the model. It should be noted, that if there is enough data on the experimental values of the activation energy of the reactions, the error functional can be expressed in the form:

$$E(w_A, w_E) = a(y_K^{exp} - (X_K w_A - TX_K w_E))^T (y_K^{exp} - (X_K w_A - TX_K w_E)) + (1 - a)(y_E^{exp} - w_E X_E)^T (y_K^{exp} - w_E X_E)$$

The dataset of 1849 cycloaddition reactions [1] were used to build model. Three types of the models were developed. When a is 0, the common error functional E is reduced to the classic individual model built on the experimental data of the activation energy of the reactions. When a is 1, the error functional E is reduced to the model $E_K(w_A, w_E)$ that is built on the data on the experimental values of the rate constant. This type of model learns to predict rate constant of the reactions following the functional relationship between the rate constant, activation energy and pre-exponential factor given by the Arrhenius equation. When **a** takes values between 0 and 1, experimental data on the rate constants and the activation energies of the reactions are simultaneously used to train the model. Such an approach makes it possible to increase the accuracy of prediction of the activation energy of reactions compared to individual models in the case of a small amount of experimental data on the activation energy.

We have shown that the model that learns to predict activation energy without using any prior information on the experimental values of the parameters of the Arrhenius equation agrees well with the experimental data.

The work was funded from the Russian Government Program of Competitive Growth of Kazan Federal University, the program of State Assignments for science (Projects No. 4.1493.2017/4.6 and No 4.5151.2017/6.7).

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COBALT CATALYZED AQUEOUS DEHYDROGENATION OF FORMIC ACID

Zhou Wei, Zhihong Wei, Anke Spannenberg, Haijun Jiao, Kathrin Junge, Henrik Junge and Matthias Beller*

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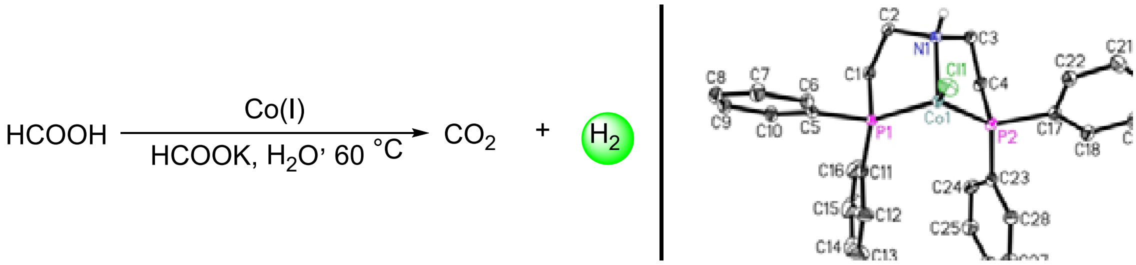
Formic acid (FA) is a promising liquid organic hydrogen carrier in the context of safe and reversible storage of hydrogen. Here, the first molecularly-defined cobalt pincer complex is disclosed for the dehydrogenation of formic acid in aqueous medium under mild conditions. Key to success is the usage of a Co(I) PNP pincer complex. Under optimal conditions, a maximum TON of 7166 was obtained after 70 h. Mechanistic studies showed carbon monoxide coordination to Co results in catalyst deactivation and DFT computations support an innocent non-classical bifunctional outer-sphere mechanism.



FACILE SYNTHESIS OF 2,2′-BIBENZIMIDAZOLES VIA ACID-CATALYSED REARRANGEMENT OF 3-CYANOQUINOXALIN-2(1*H*)-ONES WHEN EXPOSED TO *O*-PHENYLENEDIAMINES

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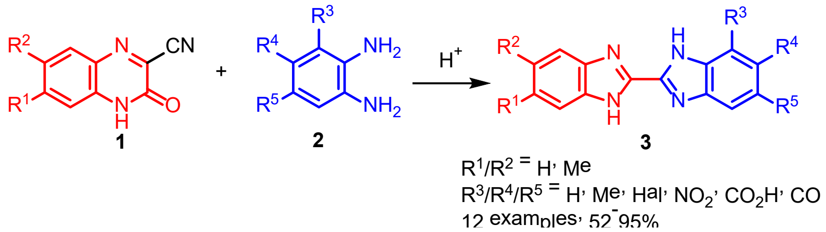
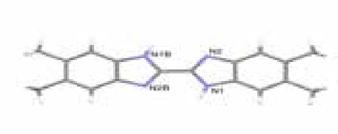
2,2′-Bibenzimidazoles are very interesting starting compounds for the synthesis of a variety of systems with useful properties such as tunable luminescence or light harvesting. The most popular synthetic procedure for the synthesis of 2,2′-bibenzimidazoles involves condensation reaction of *o*-phenylenediamines with oxalic acid or oxamide. These employ use of strong acids (hydrochloric acid, polyphosphoric acid) as catalyst and toxic solvents (ethylene glycol, diethylene glycol), sometimes combined with high temperatures. In the present report, we describe a new convenient method for the synthesis of a series of substituted 2,2′-bibenzimidazoles **3** using the Mamedov Heterocyclic Rearrangement [1]. 2,2′-Bibenzimidazole system is formed as a result of acid-catalyzed rearrangement of 3-cyanoquinoxalin-2(1*H*)-ones when exposed to *o*-phenylenediamines.

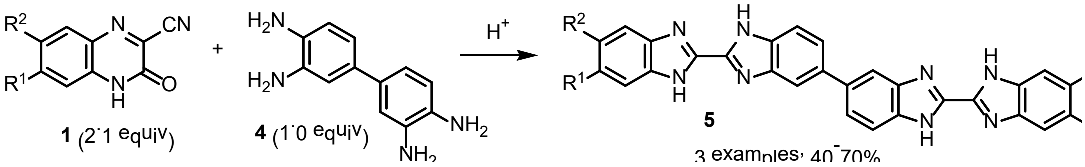


R^1/R^2 = H, Me
$R^3/R^4/R^5$ = H, Me, Hal, NO_2, CO_2H, CO
12 examples, 52–95%



It should be pointed out that CN group in quinoxalin-2(1*H*)-ones **1** is a highly specific substituent for the rearrangement, because, almost uniquely, it performs two functions: (1) its electron-withdrawing ability permits attach of the nucleophile on position 3; (2) having done this, it then acts as a leaving group.

We have also found that when 3,3′-diaminobenzidine was employed as a bis-*o*-bifunctional nucleophile in the reaction with quinoxalin-2(1*H*)-ones **1** under similar reaction conditions, the bibenzimidazole dimers **5** were obtained.



The experimental details including spectral peculiarities of the structures will be discussed.

This work was supported by the Russian Science Foundation (grant No. 18-13-00315).

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STIMULI-RESPONSIVE POLYMER NANOCARRIERS BASED ON RESORCINARENE DERIVATIVES

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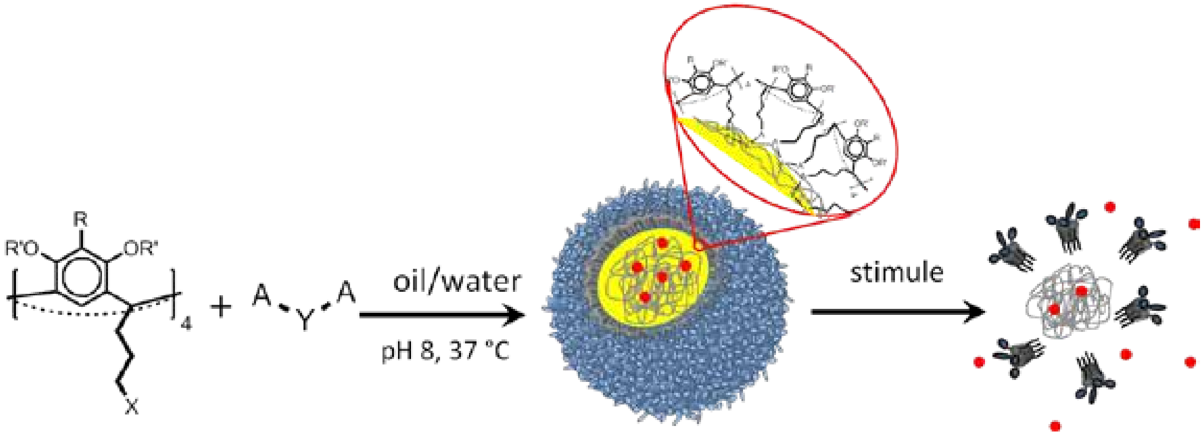
Polymeric containers are promising targets for a large number of applications in medicine and technique. For their creation, liposomes, polymersomes, mesoporous materials or organometallic scaffolds are used. The disadvantage of these systems is low stability and poor retention of encapsulated substrates, which complicates their widespread use. We offer a simple method for creation of polymeric containers. The method is based on the self-assembly of amphiphilic resorcinarene to form microemulsion in oil-water media with the next polymerization with sensitive bridges. The synthesis and physic-chemical properties of the polymeric containers based on resorcinarenes will be present. The containers were investigated in the controlled binding/release of substrates for biological application, as well as in creation catalytically active nanocomposites. The results showed that the containers exhibit good inclusive characteristics. It can also be used as a matrix for stabilizing metal nanoparticles and creation of nanocomposites for catalysis.



Work supported by Program of Competitive Growth of KFU and by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (4.1493.2017/4.6 and 4.5151.2017/6.7). The work was partly founded by RFFI N. 19-03-00429.

USNIC ACID AS AN ANTITUMOR AGENT

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Today, the treatment of cancer is one of the most important tasks for world health. Cancer mortality is second only to cardiovascular diseases. Despite all this, today there is no universal therapy, and therefore the search for new approaches and methods is needed to solve this problem.

An important area of medicinal chemistry, which allows you to get new, effective anticancer drugs, is the use of synthetic transformations of plant metabolites [1]. Usnic acid (UA) is a lichen metabolite, it has the broadest spectrum of biological activity and attracts the attention of researchers as a potential low molecular weight bioregulator for a number of areas in the pharmaceutical industry [2]. Usnic acid is a product from the secondary metabolism of the fungal partner and it is widely distributed in species of Cladonia, Usnea, Lecanora, Ramalina, Evernia and Parmelia [3].

It was demonstrated that UA strongly inhibited in vivo angiogenesis in a chick embryo chorioallantoic membrane assay and vascular endothelial growth factor-induced mouse corneal angiogenesis model. In a mouse xenograft tumor model, UA suppressed Bcap-37 breast tumor growth and angiogenesis without affecting mice body weight. In an in vitro assay, UA not only significantly inhibited endothelial cell proliferation, migration and tube formation, but also induced morphological changes and apoptosis in endothelial cells [4].

UA is a good component for creams, gels, dressings that are used after cancer-related surgery.

Thus, UA is considered as promising anticancer agent of new generation.

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SYNTHESIS OF NEW 2,2-DIARYL 1,3-INDANDIONES WITH CARBAMATE FUNCTION

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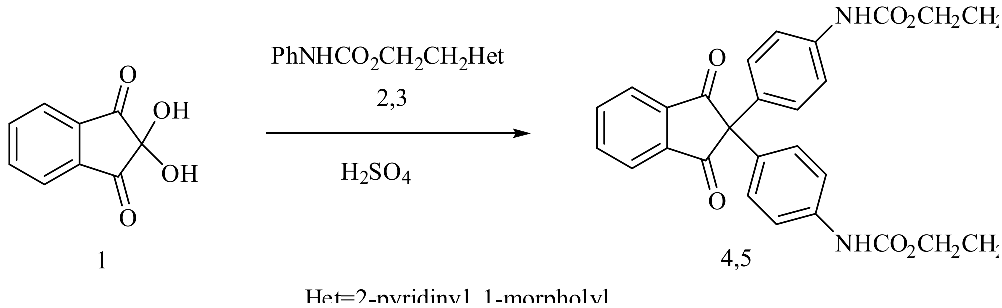
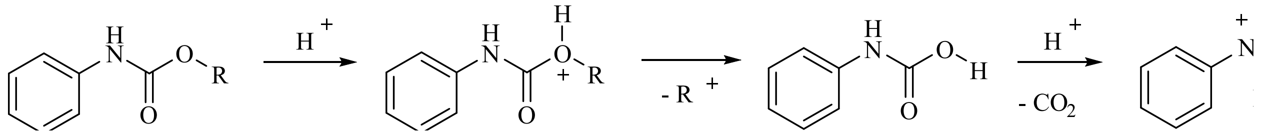
Ninhydrin and its derivatives are widely used in the synthesis of various poly(hetero)cyclic structures [1]. In the development of research [2] on the synthesis of new polycyclic compounds with carbamate groups, we studied ninhydrin condensation (**1**) with some N-substituted aromatic carbamates in conc. sulfuric acid at room temperature and with stirring for 8 h.

It has been established that condensation of ninhydrin (**1**) with 2-(2-pyridinyl)ethyl- and 2-morpholinoethyl N-phenylcarbamate (**2,3**) results in 2-(2-pyridinyl)ethyl N-(4-{1,3-dioxo-2-[4 - ({[2-(2-pyridinyl)ethoxy]carbonyl}amino)phenyl]-2,3-dihydro-1H-inden-2-yl}phenyl)carbamate (**4**) and 2- morpholinoethyl N-{4-[2-(4-{[(2-morpholinoethoxy)carbonyl]amino}phenyl)-1,3-dioxo-2,3-dihydro-1H-inden-2-yl]phenyl}carbamate (**5**) with yields of 90-93%.



In the case of methyl N-2-pyridylcarbamate, the original carbamate was isolated from the reaction mixture, and the reaction with benzyl N-phenylcarbamate was accompanied by the cleavage of the benzyloxycarbonylamino group in conc. sulfuric acid with intensive evolution of carbon dioxide. A similar result was observed when using allyl N-phenylcarbamate.

Probably in these cases, protonation of the alkoxide oxygen atom occurs with the formation of an oxonium structure, which is stabilized by the elimination of a stable cation, resulting in an unstable phenylcarbamic acid, which is decarboxylated.



The composition and structure of compounds (**4,5**) are confirmed by elemental analysis, IR, ^{1}H NMR spectroscopy. The synthesis of compounds (**4,5**) opens up the possibility of obtaining salts.

This work was supported by Foundation of the Ministry of Education and Science of the Russian Federation (project no. 4.9288.2017BCh).

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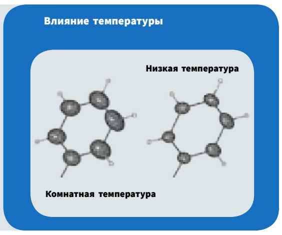

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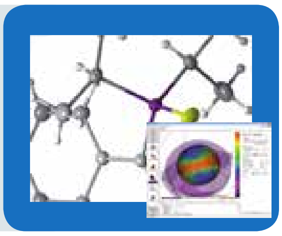

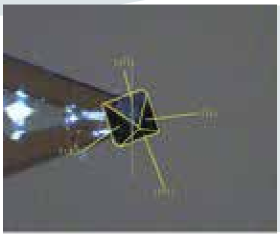

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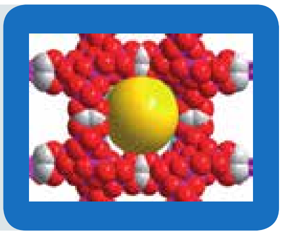


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