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RUDN UNIVERSITY

The conference is dedicated to the memory of
Prof. N.S. Prostakov
on the 100th anniversary of his birth

ADVANCES IN SYNTHESIS AND COMPLEXING

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The Fourth International Scientific Conference

In Two Parts

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The present publication was designed to popularize scientific research activity in the field of chemistry and to discuss modern chemical problems on the international level.

The digest is intended for scientists, students, postgraduates and for wide range of readers interested in problems in chemistry.

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Dear Colleagues,

It is our pleasure to extend a very warm welcome to the honorable scientists and young researchers participating in the 4-th International conference "Advances in Synthesis and Complexing" (RUDN University, Moscow, Russia).

This series of conferences has attracted many leading scientists.

The 4-th International conference "Advances in Synthesis and Complexing" is dedicated to the memory of **Prof. N.S. Prostakov** and addresses the following research topics

- *Modern problems of organic chemistry. New methods in organic synthesis, synthesis and properties of heterocyclic compounds, multi-component and domino reactions, stereochemistry of organic compounds, chemistry of macrocyclic compounds, biologically active compounds, chemistry of natural products.*
- *Heterogenic and homogenic catalysis. Physico-chemical methods of investigation, quantum-chemical calculations.*
- *Modern problems of inorganic chemistry. Complexing of metals with polyfunctional N,O,S-containing ligands, physico-chemical investigations of inorganic and coordination compounds and new materials, solidphase synthesis. X-RAY analysis.*

This conference is a platform for promoting cooperation between scientists sharing scientific interests in organic, inorganic and physical chemistry as well as interdisciplinary research in this field.

We are most grateful to all the scientists who have travelled from all corners of the world to Moscow.

We hope that you will find your participation in the 4-th International conference "Advances in Synthesis and Complexing" intellectually stimulating and socially enjoyable.

Chair of the organizing committee

Prof. Dr. Leonid G. Voskressensky

Plenary
and
Key-note Speakers

AeroNanoToxicology project

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In the 21st century - nanotechnology is seen as one of the key technologies. The previous industrial revolution has taught us that rapid technological change impacts on society in a variety of ways. Nanotechnology offers on the one hand various new properties and opportunities and on the other hand - brings new risks and uncertainties.

Sources of nanoparticles can be classified as natural or intentional and unintentional anthropogenic activities. Major natural processes that release nanoparticles in the atmosphere are forest fires, volcanic activities, weathering, formation from clay minerals, soil erosion by wind and water, or dust storms from desert. Man-made nanoparticles are released in the environment during various industrial and mechanical processes. The unfiltered exhaust gases from diesel engines contain large quantities of potentially harmful nanoparticles from the incomplete combustion of fuel. In the fireplace at home, fullerenes like buckyballs or buckytubes are formed when wood is burned. In industrial processes, coal, oil, and gas boilers release tons of nanoparticles unintentionally.

"AeroNanoToxicology" is a project which is intended to develop and introduce new cost-effective physical principles in large-scale production of the control devices and the use of nanoecology in the residential, office, laboratory and production facilities. The cooperation of the Peoples' Friendship University of Russia and the Vyatka State University has led to the elaborating of a new approach for determining the level of potential danger of nanoobjects using "Atmospheric modeling complex".

Fragment-based approach to the optimization of glycosidic inhibitors of blood coagulation proteases: deconstruction, superadditivity, and selectivity

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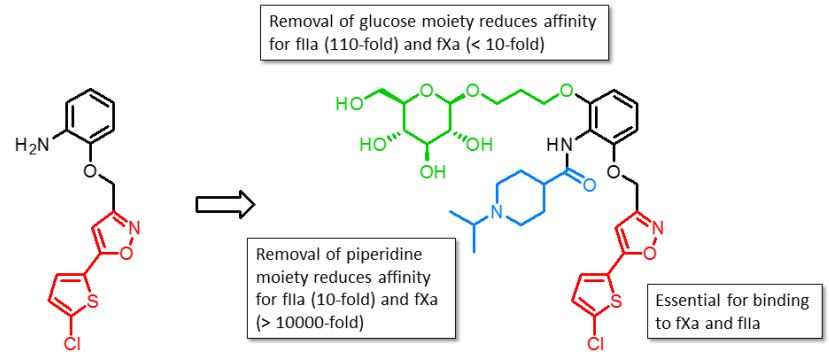
The principle of thermodynamic additivity does not fully apply in complex noncovalent systems, in which the energetics of individual components are not truly independent of each other. Molecular recognition in protein-ligand complexes predominantly occurs through multiple noncovalent interactions, and often ΔG of linked fragments is significantly greater than the sum of ΔG increments from each fragment ('superadditivity' or synergy).

Here we explore ΔG additivity in a fragment-based study of inhibitors of factor Xa (fXa) and thrombin (fIIa), two well-characterized anticoagulant targets. Recently, we reported the β-D-glucose-containing compound **2** as highly potent inhibitor of fXa (K_i = 0.090 nM) and fIIa (K_i = 100 nM), with good anticoagulant and profibrinolytic activities [1,2]. As seen previously for fXa, the chlorothiophene moiety (red) is essential for binding. Removing the glucose moiety (green) reduced affinity for fXa by less than ten-fold and for fIIa by more than two orders of magnitude, whereas removing the piperidine moiety (blue) reduced affinity to fXa by several orders of magnitude. Experimental deconstruction of **2** into smaller fragments revealed a binding cooperativity of the piperidine and propylene-linked β-D-glucose fragments, stronger in fIIa (15.5 kJ·mol^{-1}) than in fXa (2.8 kJ·mol^{-1}).



The crystal structure of **2** bound to fIIa revealed several hydrogen bond interactions between the glucose moiety and basic residues (R221a and K224) implicated in allosteric activation of the protease. In order to extend the exploration of the SARs, the glucose moiety and the piperidine group were modified. A fragment screening through surface plasmon resonance (SPR) and docking calculations provided information useful for designing and optimizing new inhibitors of blood coagulation proteases.

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Dynamic phenomena in catalytic transformations: influence on efficiency and selectivity

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Catalysis is a tremendously developing area of modern chemistry with fascinating recent achievements and conceptual progress (Figure 1) [1].

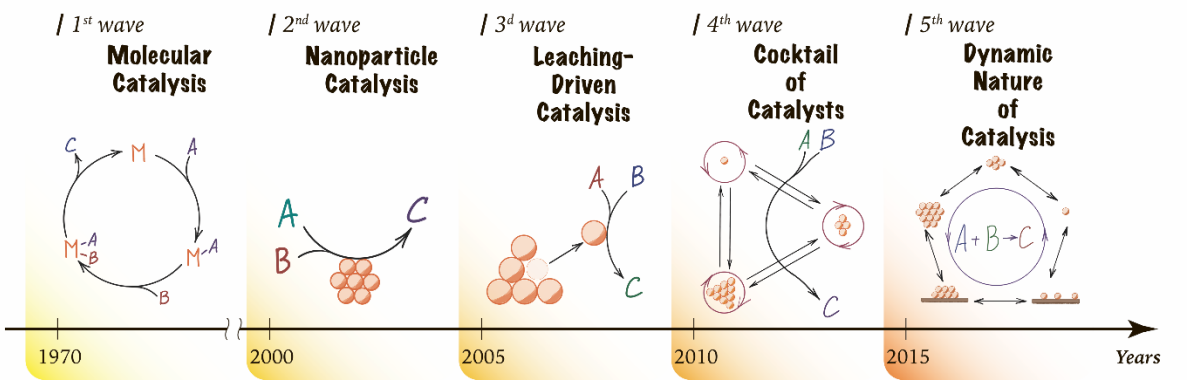

Figure 1. Different "waves" in the development of catalytic reactions [1].

Dynamic behavior of catalytic systems (Figure 2), influence on activity and selectivity, ecological profiles and application in sustainable development will be presented and discussed based on our recent findings [1-4].

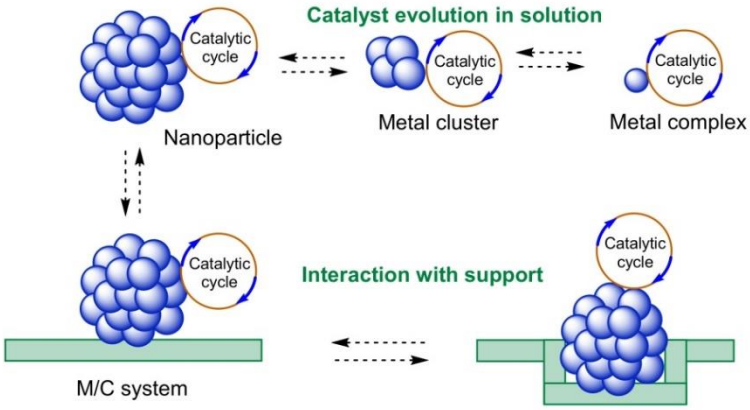

Figure 2. Catalyst dynamics in solution and on the surface of supported systems.

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Advances in heterocycle synthesis

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Heterocyclic compounds constitute the majority of organic compounds. Nitrogen-containing heterocycles are present in many natural compounds, biological probes, chemicals and materials. However, the chemical space which can be occupied by relatively simple bicyclic heteroaromatic compounds has not been fully explored and hundreds of novel molecules still remain to be synthesized. A considerable amount of novel ring systems successfully enter drug space annually. Therefore, the development of novel efficient methods of heterocycle synthesis is highly desired and represents a field of intense investigations.

This lecture is dedicated to recent developments in synthesis and functionalization of heterocycles.[1-9]

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Natural products: an opportunity for discovery

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Our laboratory focuses on the synthesis of complex molecular architectures, including both designed and naturally occurring substances with novel structural features and interesting biological function. To facilitate the execution of efficient and practical syntheses, we also develop novel methodology relevant to medicinal chemistry and complex natural products synthesis. We take advantage of the collaborative, multi-disciplinary research environment at UTSW, and have significantly fortified our chemistry program with molecular pharmacology, biochemistry, and discovery biology.

I will present our rationale for the development of novel methodology relevant to the synthesis of natural products, medicinal chemistry, and ligand design. We developed gold and platinum catalyzed reactions that enable the synthesis of novel oxazole-based dipeptide mimetics, spiroketals, morpholines, dioxanes, and other heterocycles. I will provide examples related to the synthesis of various complex polyketide natural products. Our practical synthetic solutions to natural products have enabled us to access analog collections for meaningful structure-function and mode-of-action studies to investigate their biological effects in vitro and in vivo, and for optimization of potency and pharmacological properties.

Development of novel C–H functionalization methodologies

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We have developed a set of new transition metal-catalyzed C-H functionalization methodologies employing a silicon-tether motif. These methods feature: (a) use of silyl group as a tether between a substrate and a reagent, thus transforming intermolecular reaction into intramolecular reaction; (b) employment of a silicon-tethered directing group, which is traceless or easily convertable into valuable functionalities; (c) use of silyl-tethered hydrosilane reagent; and (d) introduction of new N/Si-chelation concept that allows for a remote activation of aliphatic C-H bonds.

The scope of these transformations will be demonstrated and the mechanisms will be discussed.

Mechanochemistry : a powerful sustainable approach in organic and organometallic synthesis

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A major concern for the development of a sustainable chemical synthesis is the use of organic solvents. These solvents are very often toxic and volatile, the halogenated ones creating major damages to the environment. One of the solutions so far has been to treat and recycle the solvents or to use them as fuel after employing them in a chemical process. A major research effort is now being made to find alternatives to the use of these organic solvents. The challenging approach that we have chosen is to develop organic reactions in the absence of solvent by mechanochemistry.

Mechanochemical activation can be a useful tool for solvent-free organic synthesis. Designed at the beginning for crushing inorganic matter, apparatus such as ball-mills proved their efficacy in some organic chemistry reactions and can be applied on an industrial scale. We have shown that this kind of activation is applicable to the synthesis of important organic molecules, including amino acid derivatives and peptides [1]. In the last years, we have developed this methodology and applied it to peptides such as aspartame or enkephalin or heterocycles such as hydantoins [2]. More recently, in connection with other projects dedicated to green chemistry in our group, we have investigated mechanochemistry in palladium-catalyzed reactions and in the preparation of organometallic complexes [3]. We have shown that mechanochemistry is a sustainable synthetic method avoiding the use of solvents but also a very powerful approach to prepare unprecedented structures.

This work was supported by the CNRS and the University of Montpellier.

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Catalytic stereoselective formation of C-C and C-N bonds in target-oriented synthesis.

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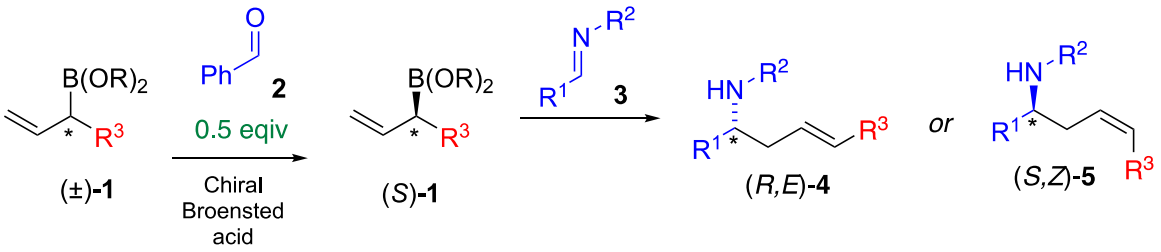
Chiral amines are powerful pharmacophore groups due to their favourable physico-chemical properties that include inherent capability of hydrogen bonding and a wealth of relevant, well-understood structural information. Homochiral amines and their derivatives belong to the class of strategic building blocks for pharmaceutical, agrochemical and fine chemical development.[1]

Scheme



Herein, we present a novel solution to attaining high stereoselectivity in the allylation of imines with secondary allylboronates (Scheme). The method is based on our recently developed kinetic resolution of chiral racemic allylboronates (±)-**1**,[2] which are readily synthesised from simple precursors.[3,4] Conditions of the kinetic resolution catalysed by chiral Brønsted acid TRIP were optimised to afford highly enantioenriched boronates (*S*)-**1**. DFT calculations at TPSSh/cc-pvtz//B3LYP/6-31g(d,p) level of theory were performed on the system to elucidate the origin of the stereodifferentiation.[2] In developing allylation of imines **3** with allylboronates (*S*)-**1**, it was important to ensure that the reaction is stereoselective, i.e. that chirality of the reagent is efficiently transferred into the product and that its selectivity is controlled with respect to the alkene geometry to give either **4** or **5**. In the case of aldehydes, the factors governing stereoselectivity of this process are reasonably well understood. In imines, substitution on the nitrogen brings an additional element of complexity – the steric size of the substituent. Therefore, the method is focused on the allylation of the in situ generated NH imines **3** (R^2 = H),[5] where the steric arrangement of the transition state should resemble that of aldehydes. Details of the development of stereoselective addition of (*S*)-**1** to imines to furnish selectively (*S,Z*)-**5** will be presented.

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Sequentially Pd-catalyzed one-pot syntheses of functional heterocycles

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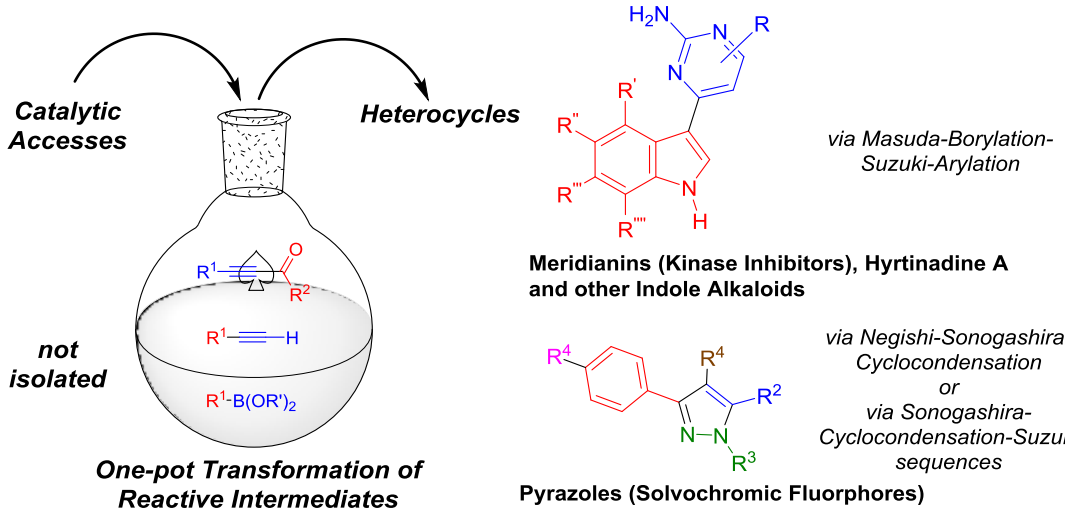
Multi-component and domino reactions are efficient and effective methods in the rapid and diversity-oriented synthesis of heterocycles. In particular, transition metal catalyzed multi-component sequences have recently gained a considerable interest.[1] Most interestingly, in sequentially Pd-catalyzed processes[2] the same catalyst source is operative a second time without further catalyst addition. This one-pot methodological concept is most elegantly applied to the syntheses of highly luminescent pyrazoles[3] and to concise syntheses of marine alkaloids and kinase inhibitors, the latter by applying a Masuda-borylation-Suzuki-arylation sequence.[4]



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C-H versus C-C in activation of propargylic amines under transition-metal catalysis

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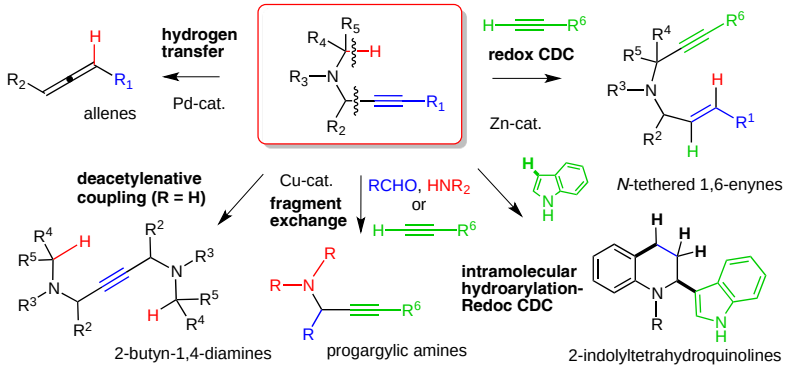
The strategy for the transition metal-catalyzed C-H bond activations has attracted greatest interest in an environmentally friendly process for organic synthesis. In particular, the C(sp^3)-H activation alpha to nitrogen has shown a variety of transformations. We found that propargylic amines undergo the C(sp^3)-C(sp) activation in the presence of Cu(II) catalysts or the C(sp^3)-H activation in the presence of Pd or Zn(II) catalysts (Scheme 1). Propargylic amines underwent the C(sp3)-H activation in the presence of palladium catalysts to form allenes.[1] In contrast, the C(sp3)-C(sp) activation was observed in the presence of copper catalysts to generate the corresponding iminium intermediates and copper acetylides, that reacted with another equivalent of the starting material (R^1 = H) to give the deacetylenative coupling products, 2-butyn-1,4-diamines, in the absence of bases,[2] or reacted with aldehydes, amines and/or 1-alkynes to give the fragment exchanged propargylic amines.[3] Moreover, the propargylic amines underwent the C(sp^3)-H activation by zinc catalysts to afford the hydrogen-migrated vinyl zinc species that reacted with 1-alkynes to give the corresponding N-tethered 1,6-enynes.[4] In this case, a coupling between the C(sp^3)-H of the propargylic amines and the C(sp)-H of 1-alkynes took place and the generated two hydrogen atoms were trapped by the internal alkyne. As a result, redox CDC proceeded during the reaction, and additional oxidants were not necessary for this coupling. Furthermore, intramolecular hydroarylation-redox CDC of N-propargylic anilines with indoles was also catalyzed by zinc(II) to give 2-indolyltetrahydroquinolines.[5] In this transformation, three C–H bonds (two sp^2 and one sp^3) are activated in one shot and these hydrogen atoms are trapped by a propargylic triple bond in the molecule. In this paper, our recent results of propargylic amine-based transformations induced by the transition metal-catalyzed C(sp^3)-H activations[6] will be presented.



Scheme 1. Overview of the C-H and C-C activation-based transformations of propargylic amines

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Converting hay to gold with modern spinning wheels: non-edible, renewable resources as starting materials for the synthesis of fine chemicals utilizing light, flow and mag(net)ic catalysts

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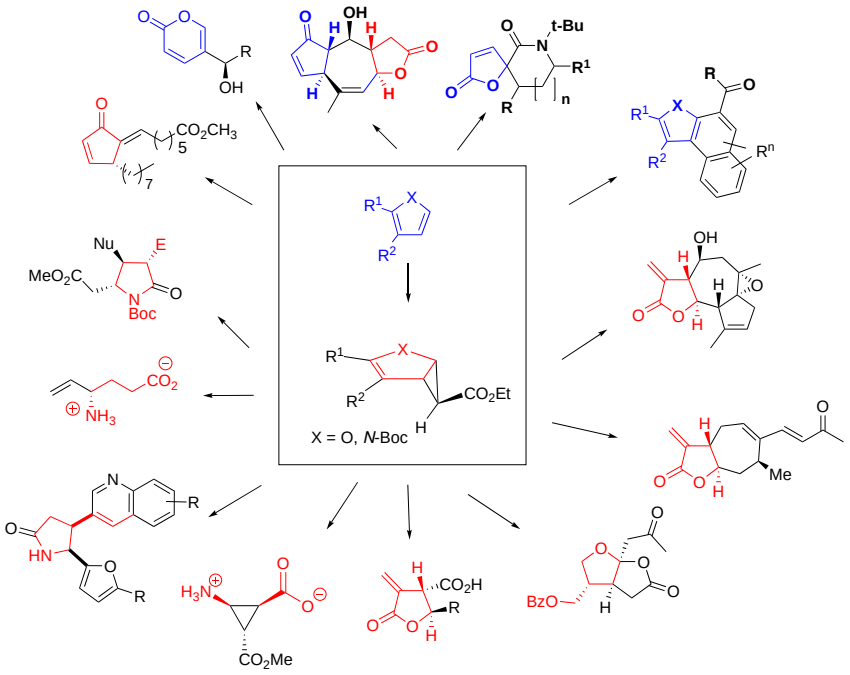
Pyrroles and furans represent readily available bulk chemicals derived from non-edible, renewable resources. Focusing on asymmetric transition metal and visible light photoredox catalysis, we are developing strategies to rapidly convert such starting materials into novel heterocyclic and carbocyclic scaffolds related to natural products or drugs.



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The status of isocyanide based multicomponent reactions in Iran

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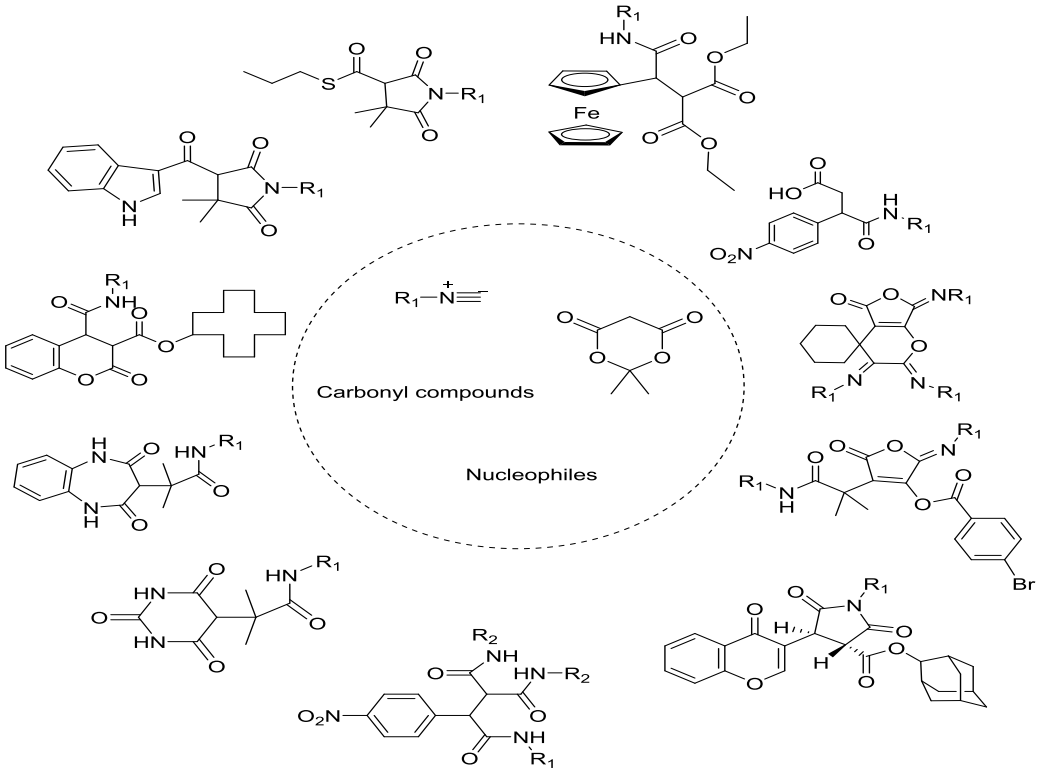

Design and discovery of novel multicomponent reactions which are able to generate useful chemical products may be regarded as a prominent topic in organic chemistry. In this context, isocyanide based multicomponent reactions (IMCRs) are special subclasses of the multicomponent reactions. In this presentation, an overview of the contributions and recent advances made by Iranian scientists in the field of IMCRs between 1999 and 2017 have been reported. With over 400 publications during this period, Iranians are responsible for approximately 8 % of all publications in the world involving IMCRs. Some attractive features of these IMCRs are synthesis of numerous classes of pharmaceutically and industrially valuable heterocyclic and acyclic organic compounds in a one pot manner, carrying out reactions in green reaction mediums like water or ethanol, high atom economies, mild reaction conditions, high yields and catalyst-free processes.

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Domino reactions. The green and economical art of chemical synthesis

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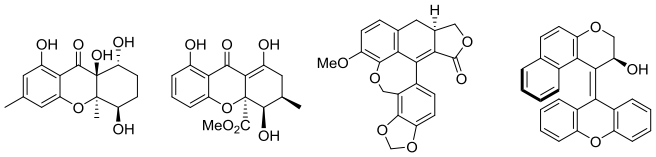
The efficient synthesis of natural products, drugs, agrochemicals and materials is a very important aspect in academia and industry. To allow an ecologically and economically favourable approach in a green fashion the former stepwise procedures must be replaced by domino reactions which allow the preparation of complex molecules starting from simple substrates in a straight forward way. Domino reactions[1] allow the reduction of the amount of waste being formed and the preservation of our resources. Moreover, they are also favourable in an economical way since they consume less time.



The usefulness of the domino concept is demonstrated with the syntheses of the fungal metabolites diversonol[2], blennolide A[3a,] blennolide C[3b] and gonytolide[3b] as well as other natural products of the dimeric tetrahydroxanthenone type[4] using an enantioselective domino-Wacker/carbonylation/methoxylation reaction and of the natural aryldihydronaphthalene lignan linoxepine[4] employing a domino-carbopalladation/Heck reaction. The approach has also been applied for the synthesis of novel materials such as molecular switches[5a-d] and fluorescence dyes[5e,f] using a domino-Sonogashira/carbopalladation/CH-activation reaction.

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Structural tuniong of luminescent and magnetic properties of porous metal organic frameworks

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Two large series of metal organic frameworks (MOFs) were synthesised and structurally characterized. The first series represents anionic frameworks constructed from Zn^{2+} with 1,3,5-benzenetricarboxylate (BTC) anions and amino-cations. An influence of various cations such as NH_4+, $MeNH_3$+, Me_2NH_2+, Et_3NH+, and n-Bu_4N+ was manifested by the structural changes of the anionic Zn-BTC connectivity within the frameworks, and the fluorescence of the corresponding MOFs. The 13 Zn-BTC MOFs with 1, 2 and 3 dimensional structures were obtained and it was clearly demonstrated that cations are acting as structure directing agents. The second series represents MOFs based on the same cationic-anionic structure {Zn-BTC}{ Me_2NH_2+} that was doped with different metals (Co, Cu, Ni, Mn, Ca, Mg and Gd). Obtained materrials have significant differences in their magnetic behavier depending on the nature of the dopant metal atoms. The X-ray diffraction studies did not reveal strutural differences between doped materials, however their luminescent properties were found to be different that might lead to their potential practical applications.

Bridging chemistry and biology through metal catalysis

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We first studied a heavy metal-detoxification protein GolB, a gold-specific binding protein. GolB was recently identified, providing a unique opportunity for the study of the Au-S bond at the molecular level. We measured the rupture force of the Au-S bond to be 165 pN, much lower than Au-S bonds measured on different gold surfaces (~1000 pN). We further solved the structures of apo-GolB and Au(I)-GolB complex using X-ray crystallography.[1] The interaction between silver ions and the CXXC in GolB and copper chaperone Atx1 and GolB revealed that the conserved CXXC metal-binding motif (MBD) coordinated a unique tetrasilver cluster.

Next, inspired by these results from metalloproteins, we designed small-molecule ligands to overcome the copper cytotoxicity of Cu(I) ions, enabling the biocompatible Cu(I)-catalyzed azide-alkyne 1,3-dipolar cycloaddition (CuAAC). The CuAAC reaction could occur on the cell surface, directly visualizing of the dynamics of the biosynthesis of sialylated glycans at the intact heart level.[2a,2b] Application of the biocompatible CuAAC reaction for intracellular modification of proteins realized protein labelling within the cytoplasm of *Escherichia coli*.[2c]

Lastly, by mimicking O_2-enzymes' intermediate M-O-O structure (M=Fe, Cu), we developed new metal-catalyzed C–H activation reaction cascades to access structurally diverse polycyclic phenols in one pot.[3a,3b]

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Oral Reports

(20-40 min)

Applications of "intelligent" reaction media in synthesis of polynuclear heterocyclic compounds

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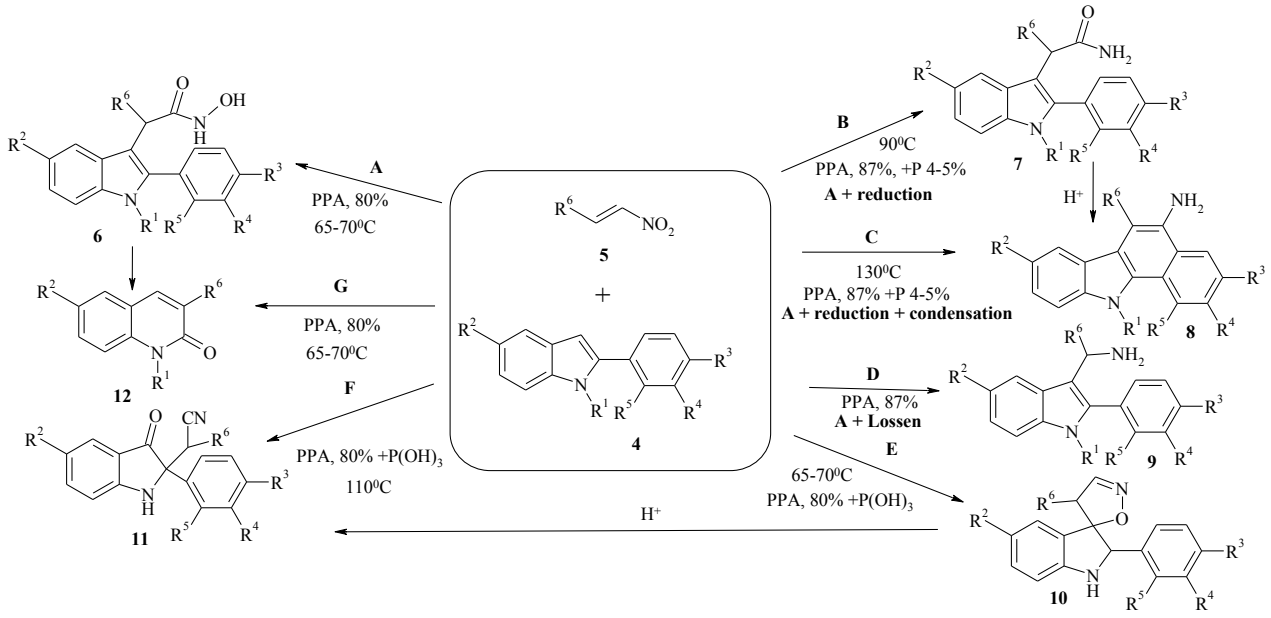
The presentation will describe new methods for direct functionalization of arenes. The emphasis is placed on the recently suggested paradigm of "intelligent reaction media", which currently is being actively developed in our laboratories. The concept of this innovative approach involves increasing of the reaction diversity due to ability to trigger only one of the many possible pathways by incorporating subtle modifications of the reaction media. This approach is illustrated by the following examples [1-4]:



This work was supported by the Russian Science Foundation (grant № 14-13-01108).

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Switchable rearrangements in series of 1,2,3-thiadiazoles and 1,2,3-triazoles

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According classification of L′abbe [1] rearrangements of five membered heterocyclic compounds can be subdivided in five groups based on the number of participating side-chain atoms. These include the rearrangements which operate by a ring contraction-ring expansion mechanism, the Dimroth rearrangement (one atom of the chain), the Cornforth rearrangement (two atoms of the chain), the Boulton-Katritzky scheme (three atoms of the chain). Apart of well known and good studied Dimroth rearrangement these heterocycles can undergo other types of rearrangements with participation of two and three atoms of the chain are studied in less extent [2].

During the study of reactivity of 2-cyanothioacetamides we have discovered reversible rearrangements of 1,2,3-triazole-4-carbothioamides and 5-amino-1,2,3-thiadiazoles. Both rearrangements processes involve two atoms of 4-substituents, opening of the ring to form intermediate diazo compounds and concurrent cyclization of the latter by C=N or C=S bonds to form isomeric heterocyclic compounds and similar in this respect to interconversion of isomeric 4-acetyl substituted oxazoles discovered by Cornforth [3, 4]. There are no reports on the factors govern the direction of the rearrangement of 4-thiocarbonyl-1,2,3-triazoles to 1,2,3-thiadiazoles bearing C=N bond in the chain published in literature.

The reverse rearrangement of 1,2,3-thiadiazole-4-carbamidines and 1,2,3-triazol-4-carbothioamides represent interchange of cyclic thioamide group by carbamidine group of the chain. The reaction in both directions proceeds under very mild conditions, which can be switched by the *change of acidity of the medium. It is first example of this type effect for* Cornforth rearrangement in 1,2,3-triazoles and 1,2,3-thiadiazoles series.

This work was supported by the Russians Scientific Foundation (grant № 15-13-10031).

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Avenues to DNA-encoded small molecule libraries – of a chemoresistant sequence and nanoreactors

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DNA-encoded small molecule libraries (DELs) have found widespread use as screening technology in drug research. [1] They are synthesized through combinatorial iterations of alternated organic preparative chemistry and encoding steps thus yielding large chemical space for screening. [2] Bioactive compounds are identified from these compound mixtures by selection and DNA sequencing. However, only few reactions are available for DEL synthesis, negatively impacting library diversity. Transition metals and acid catalysts grant access to diverse drug-like structures from simple starting materials, but compromise the integrity of the DNA tag mainly by depurination. To make these catalysts available for library synthesis, we utilize a hexathymidine sequence "hexT" in the initial step of DEL synthesis. The tolerance of the hexT sequence to harsh reaction conditions is exemplified by the synthesis of hexT-pyrazole conjugates through a Au(I) mediated annulation reaction in glacial acetic acid (Figure 1A). [3] The hexT conjugates were readily ligated to coding DNA sequences.

A conceptually different strategy to access DELs by transition metal catalysis rests on the steep solubility gradient of DNA-small molecule conjugates. This gradient is mirrored by oil-in-water (o/w) micelles formed by detergents. They separate the water-soluble DNA from the lipophilic core that takes up the conjugated small molecule, catalyst, and reactants. Micellar Suzuki reaction gave DNA-biaryl conjugates from DNA-aryl halide educts and diverse boronates under mild reaction conditions (Figure 1B).

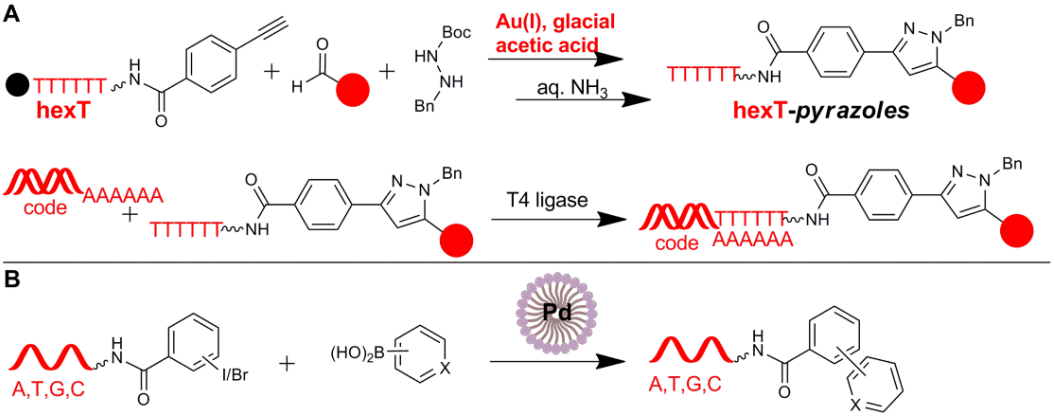

Figure 1: Transition metal-catalyzed approaches to DNA-encoded libraries.

This work was supported by the German Federal Ministry of Education and Research (BMBF) Grant 131605.

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Stevens rearrangement of –(3-phenylpropen-2-yl)(3-arylpropyn-2-yl) ammonium bromides and deamination of obtained amines during vacuum distillation. Intramolecular cyclization of mentioned salts in base catalyzed conditions.

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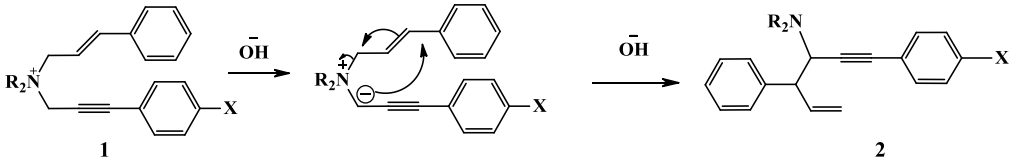
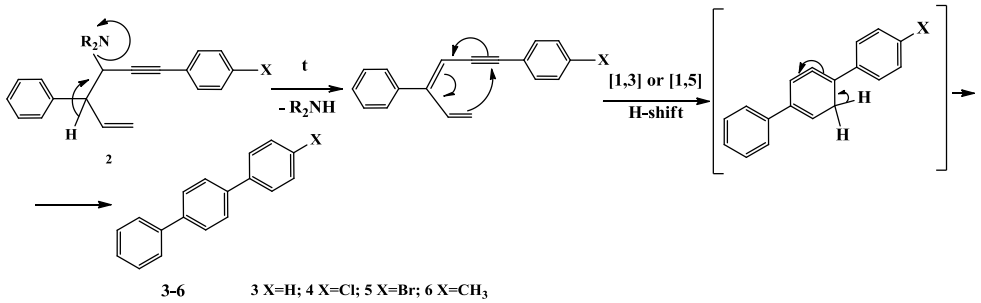
Recently was established that salts **1** under the action of double molar amount of potassium hydroxide in the presence of a few drops of methanol by self-heating undergo Stevens rearrangement, forming amines **2** with 60-65% yields.



Amines **2** in contrast to 1-allyl-1-dialkyl(3-phenylpropyn-2-yl)-, 1-crothyl-1-dimethyl(3-phenylpropyn-2-yl)amines [1] and their methallylic analogs [2] during vacuum distillation undergo deamination and as the final products were obtained *p*-diphenylbenzene (**3**), 4-chloro-1,1':4',1"- (**4**), 4-bromo-1,1':4',1"- (**5**) and 4-methyl-1,1':4',1"-terphenyls (**6**) with high yields. It was discovered the succession of reaction, including formation of compounds **3-6.**



The formation of compounds **3-6** is good chemical evidence that Stevens rearrangement of the salts **1** preferably is realized by conversion of migrating group. These reactions are domino process, have general character and besides of theoretical have also practical significance [3,4].

The cyclization of salts **1** in base catalized conditions in contrast to allyl analogs proceeds with self-heating and -dihydrobenzo[f]isoindolinium bromides are formed in nearly quantitative yields [5]. On the basis of above-mentioned results and IR spectral investigations was established that the phenyl group in third position of allyl group has a positive effect on cyclization. The observed phenomenon is the unique in the field of cyclization of ammonium salts, which contain allyl group alongside with 3-arylpropyn-2-yl fragment.

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Selective C-N, C-C, C-O bond formation with tolerance to functional groups

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Herein we present the concept of using carbon monoxide for atom economical reductive addition without external hydrogen source [1-8]. Following this concept we have shown that N-H and C-H bonds of the reagents could be used as hydrogen source. The process proceeds with high selectivity. Such approach can widely use for synthesis of heterocycles.

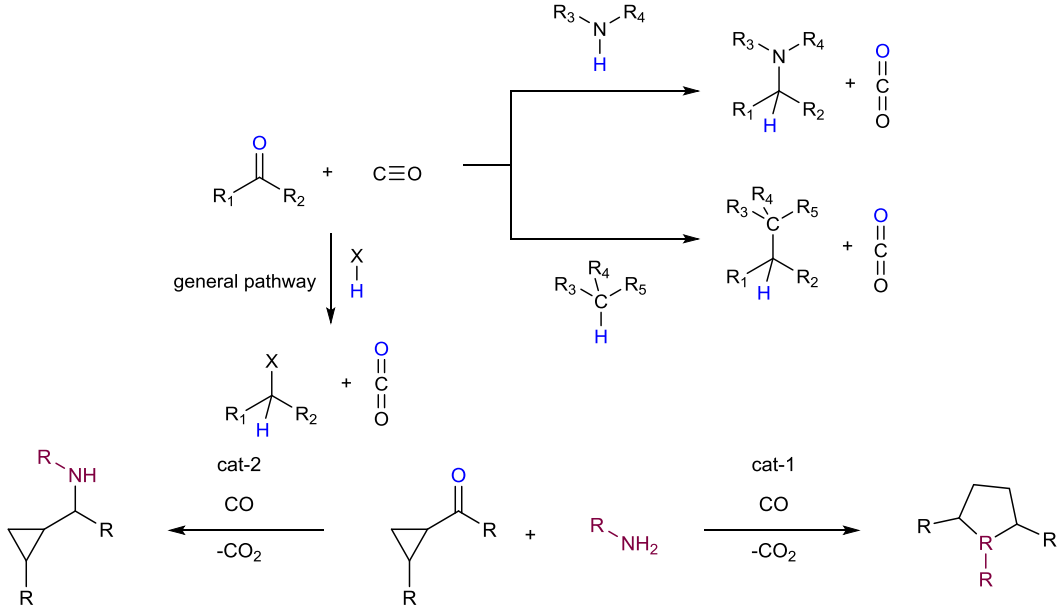

Figure 1

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Transitions of flavylium ion to quinoidal structures with intramolecular co-pigmentation of anthocyanins as the basis for colorful food colors

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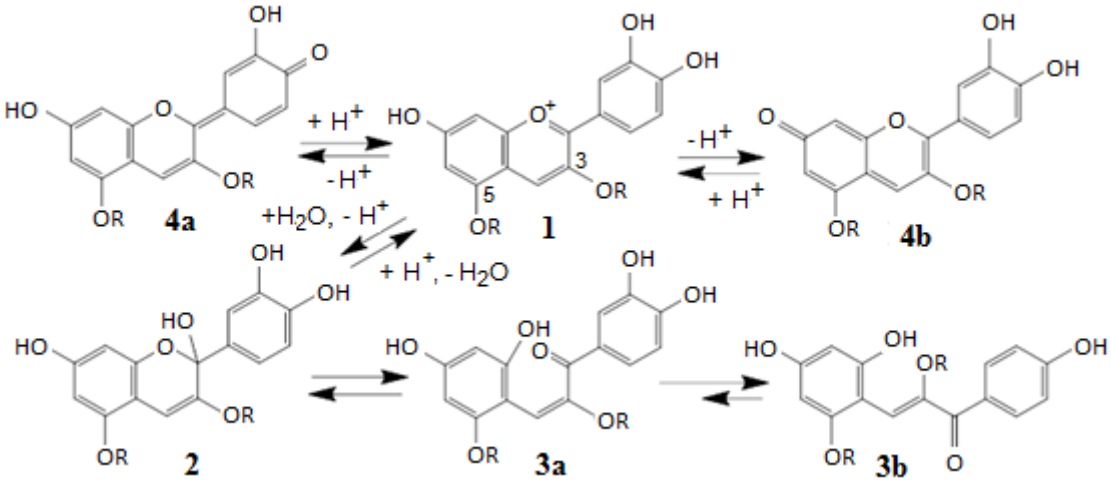
Anthocyanins (**I**) are known to be excellent red food colors with high water solubility as well as high antioxidant power. Meanwhile red color is a property of the only flavylium form (**1**), that exists predominantly in highly acidic (100% at pH < 1) water solutions. The increase of pH leads to formation of some another forms that are colorless (pseudobase, **2**), slightly colored two chalcone forms (**3a** and **3b**) and also colored with bathochromic and hyperchromic shifts quinoidal forms (**4a**, **4b**), the number of the latter is determined by a number of OH-groups in the relevant anthocyanidin structure. The examples of the phenomena are known to be blue Malaysian tea "*pulut tai tai*" *vs* red Egyptian "Karkade" tea, both being colored due to anthocyanins but at different pH.



In the current investigation, it was established that not all anthocyanin extract types are capable to produce blue coloration after increase of pH – the molecules must have aromatic acid acylation and glycosidic radicals in positions 3 and 5 of the anthocyanidin (**1**). The red basil leaves were just the plant source of the anthocyanins. HPLC with mass-spectrometric detection proved them to be cyanidin-3-sophoroside-5-glucosides acylated with caffeic, *p*-coumaric and malonic acids.

Analysis of electronic spectra of different pH water solutions of the anthocyanins revealed the existence of two colored forms (besides of flavylium ion) with different absorption maxima. These structures were unstable in solutions but were markedly stabilized in encapsulated forms with maltodextrin as a polymer matrix. Moreover, at a high concentration (e.g. 1%) of any form of anthocyanins the solutions are almost black because of intensive intermolecular co-pigmentation (stacking). In the case of dried anthocyanin powders the color was bright red, violet, blue or even green just as if all intermolecular interactions were suppressed. So we may conclude that these powders do not contain small drops of anthocyanins encapsulated into maltodextrin matrix but rather have single molecules of anthocyanins divided sterically by the polymer sugar moieties. Thus, a final product may be regarded to as a solid solution.

All the anthocyanin forms were utilized for coloration of decorative cake figures with a stability enough for that type of cooking production.

Planar and sandwich-type porphyrazines with annelated heterocyclic rings: synthesis and physicochemical properties

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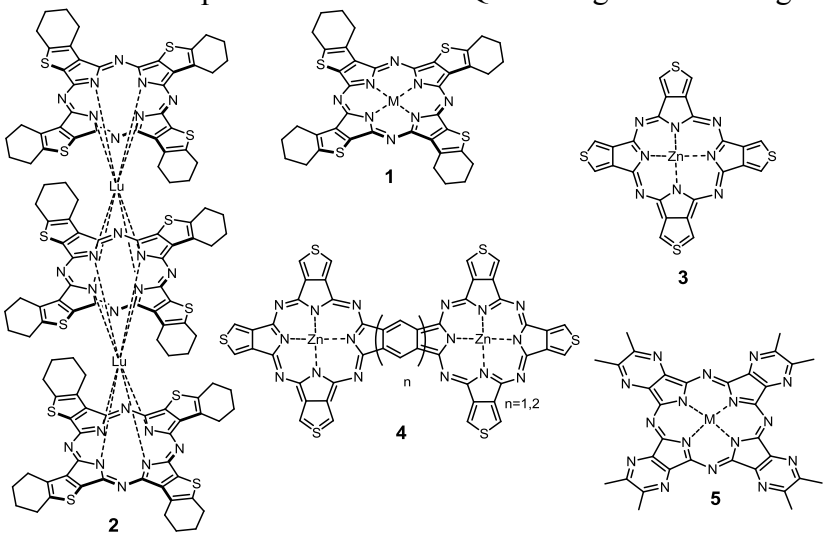
Porphyrazine fused to a heterocyclic ring possesses enhanced conductivity and nonlinear optical properties. Present investigation focuses on porphyrazines, which contain electron rich (thiophene) and electron poor (pyrazine) periphery. The synthetic route to the thieno[2,3-*b*]porphyrazine complexes **1** as a prospective building-blocks for sandwich-type porphyrazines was developed. A heterocyclic ring annelated sandwich-type porphyrazine complex **2** was synthesised for the first time. Spectral properties and aggregation phenomena of target compounds were investigated by UV/Vis and AFM techniques. Electrochromic behaviour of the Zn complex was studied by electrochemistry and spectroelectrochemistry. 3,4-Dicyanothiophene was chosen as initial compound for the synthesis of mono- (**3**) and binuclear (**4**) thienoporphyrazine complexes with a nonclassical thiophene moiety [1]. All units of the porphyrazine periphery are equivalent, and corresponding protons were observed at 8.47 ppm as a doublet. The formation of nanoaggregates in a solid film was shown using AFM technique. On the basis of MCD data the absorption maxima in the Q band region were assigned.



Novel methylsubstituted tetrapyrazinoporphyrazine complexes **5** were obtained in anhydrous medium with high yields. For the first time the cyclization reaction of 5,6-dimethylpyrazine-2,3-dicarbonitrile with $Zn(quinoline)_2Cl_2$ salt was activated by microwave irradiation. Fluorescence and excitation spectra were measured for target complexes. It was demonstrated, that excitation spectra correspond to the shape of nonaggregated complexes.

This work was supported by the Russian Foundation for Basic Research (grants № 16-33-60005, 16-07-00961, 15-03-05890 and 16-33-01089).

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Target diastereoselective synthesis of dispiroheterocyclic structures comprising pyrrolidinyloxindole and imidazothiazolotriazine moieties

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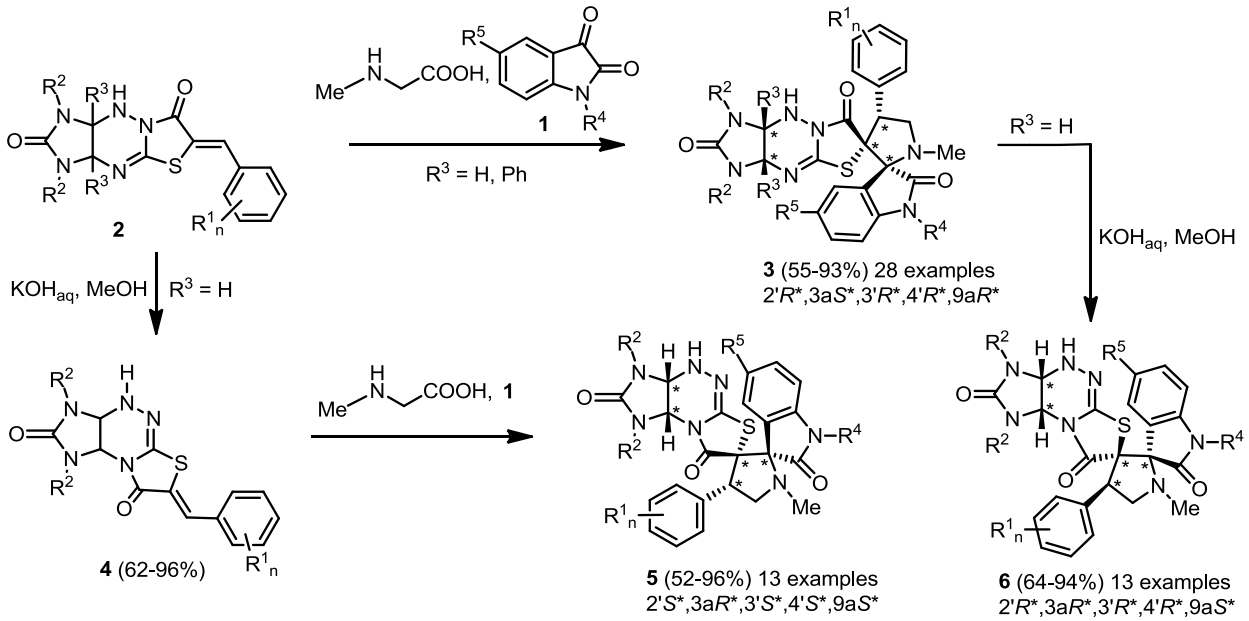
The thiazolo[3,2-*b*]-1,2,4-triazine-*into*-thiazolo[2,3-*c*]-1,2,4-triazine rearrangement has been recently reported as an original method for the synthesis of new heterocyclic system derivatives, i.e. imidazo[4,5-*e*]thiazolo[2,3-*c*]-1,2,4-triazines [1]. The rearrangement occurred in boiling methanol in the presence of aqueous solution of KOH. In the present work we propose to use the rearrangement for the target synthesis of diastereomerically pure dispiroheterocyclic structures comprising pyrrolidinyloxindole and imidazothiazolotriazine moieties.

Earlier we showed that 1,3-dipolar cycloaddition of azomethine ylides generated in situ from isatin derivatives **1** and sarcosine to imidazo[4,5-*e*]thiazolo[3,2-*b*]-1,2,4-triazines **2** led to a single regio- and diastereoisomer **3** (racemate) that was formed via an *anti-exo*-transition state [2]. As expected, the cycloaddition of azomethine ylides to products of rearrangement of compounds **2**, i.e. imidazo[4,5-*e*]thiazolo[2,3-*c*]-1,2,4-triazines **4**, proceeds analogously (*anti-exo*) with formation of diastereoisomers **5**. When dispirocompounds **3** undergo alkali-induced rearrangement other diastereomers **6** (formally *syn-exo*) are formed.



R^1_n = H, 3-NO_2, 4-NO_2, 2-F, 4-F, 4-Br, 2,4-Cl_2; R^2 = Me, Et; R^3 = H, Ph; R^4 = H, Et, Allyl; R^5 = H, Br

The methods for the target synthesis of two different diastereomers of dispiroheterocyclic structures comprising pyrrolidinyloxindole and imidazothiazolotriazine moieties are developed.

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Photoactive supramolecular devices and machines based on unsaturated and macrocyclic compounds

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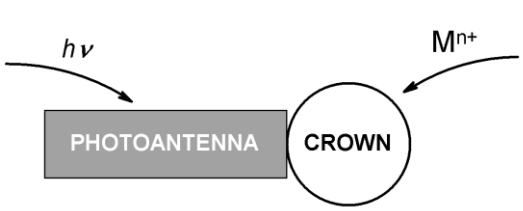
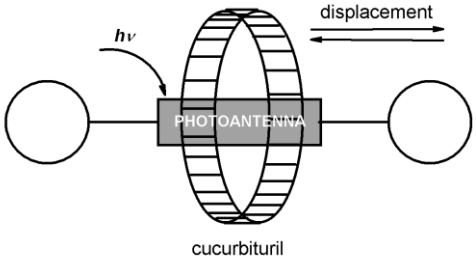
We propose a new unique class of polyfunctional photoactive compounds: unsaturated dyes functioning as photochromes, fluorophores and ionophores [1]. A large body of research has been performed for their synthesis, determination of their spatial structures, study of self-assembly features to give supramolecular systems, and also study of fluorescent, photochemical and complexing properties.

Resulting from the research, we elaborated for the first time universal supramolecular meccano, allowing one to accomplish building-up, with using a limited number of complementary compounds with participation of metal cations and hydrogen bonds, photoactive supramolecular systems of varied architecture with adjusted properties [2]. Within the same class of compounds one can construct in solution, solid and at the air-water interface new types of photoswitchable supramolecular devices, photocontrolled supramolecular machines, photoactive monolayers and monocrystals susceptible to all of the key photoprocesses.



supramolecular devices



supramolecular machines

The high practical value of these studies deserves attention. They provide a new strategy for the design of materials for supramolecular and nanophotonics, which was demonstrated, first of all, by the creation of practically important sensor [3] and photochromic materials [4, 5].

This work was supported by the Russian Science Foundation, the RFBR, the RAS, the Ministry of Science and Education, the Moscow Government, the INTAS, the CRDF, the DFG, the Royal Society, and the ISF.

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Stereoselective construction of piperidines from homoallylamines via new anionic rearrangements. Development of novel potent inhibitors of Influenza A M_2 channel and heat shock protein 90.

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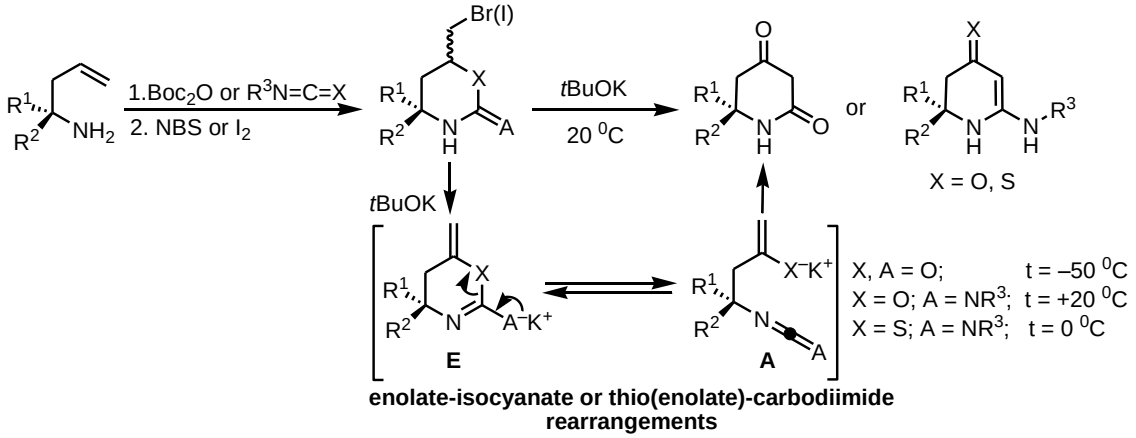
Piperidines occupy privileged place among the variety of the heterocycles, being structural motif of many alkaloids, peptidomimetics, small biologically active molecules etc. as well as key intermediates in syntheses of pharmaceutically relevant compounds. We have elaborated a new concise and efficient method of synthesis of piperidine-2,4-diones and 2-iminopiperidine-4-(thi)ones starting from easily available in enantiomerically pure form homoallylamines [1-4]. The synthetic sequence toward piperidinones consists of three steps: a) acylation of amino group of homoallylamine either with Boc_2O or an (thio)isocyanate; b) cyclobromocarbamation with NBS (I_2); and a key step c) enolate-type rearrangement under the treatment of *t*BuOK. The latter transformation proceeds via the formation of enolate-isocyanate and (thio)enolate-carbodiimide as intermediates.



enolate-isocyanate or thio(enolate)-carbodiimide rearrangements

Combination of adamantane and piperidinone moieties leads to the molecules with potent *in vitro* activity against rimantadine-resistant Influenza A (H1N1) virus strains [5]. Another transformation of 6-substituted piperidine-2,4-diones and 6-amino-2,3-dihydro-4-pyridinones to 2-amino-7,8-dihydropyrido[4,3-d]pyrimidine-5(6H)-ones leads to inhibitors of heat shock protein 90 belonging to the last generation drugs for fighting oncological, viral, fungal and parasitic diseases.

This work was supported by the Russian Science Foundation (grant № 15-13-00109).

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Pharmacologically oriented and high energy furoxan derivatives

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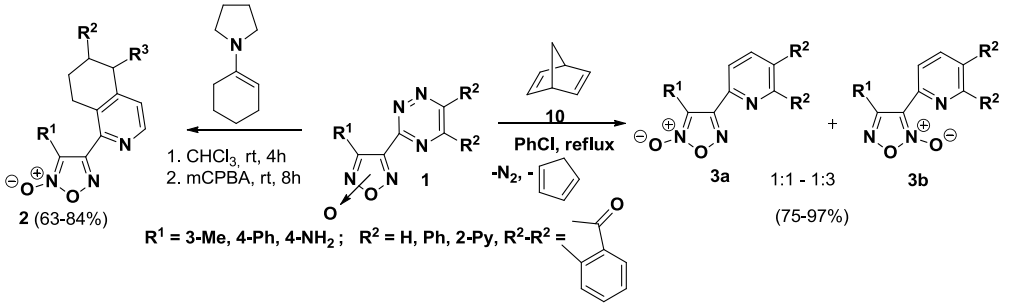
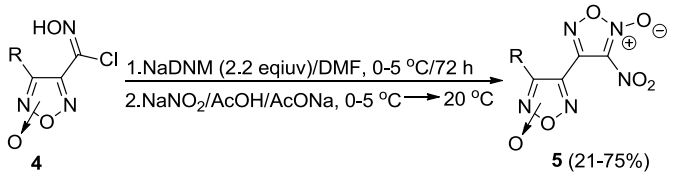
One of the important direction of scientific investigations of our laboratory is the synthesis and reactivity of nitrogen-oxygen containing heterocycles - 1,2,5-oxadiazole 2-oxides (furoxans). Furoxans reveal a wide spectrum of pharmacological activity since their capability to release nitric oxide (NO). On the other hand, the furoxans are of interest as high energy compounds due to a positive enthalpy of formation and the presence of two active oxygen atoms.

This work is devoted to new, effective one-pot approaches for the synthesis of novel pharmacologically oriented hybrid heterocyclic systems incorporating furoxan ring connected with pharmacophoric heterocycles (pyridines, tetrahydroisoquinoline, indenopyridine) or with energy rich 3-nitrofuroxanyl unit. For the synthesis of these structures, we selected an approach, based on the heterocyclization of accessible functional furoxans derivatives – amidrazones and furoxanylhydroxamic acids chlorides.

Two convenient, regioselective and highly effective one-pot methods for the synthesis of new hybrid heterocyclic systems with the furoxanylpyridine core were developed based on the tandem hetero-Diels–Alder/retro-Diels–Alder reactions of (1,2,4-triazin-3-yl)furoxans **1** (products of furoxanylamidrazones and α-dicarbonyl compounds interaction) with 1-(pyrrolidino)cyclohexene and norbornadiene. The methods comprise [4+2]-cycloaddition of enamine or norbornadiene to the 1,2,4-triazine ring of (1,2,4-triazin-3-yl)furoxans followed by one-pot transformation of formed intermediates and afford extensive series of the target structures combining furoxan and pyridine (dihydroisoquinoline, indenopyridine) rings **2** and **3a**,**b** in one molecule in good to excellent yields [1].



A regioselective method for the synthesis of high energy bifuroxanyl systems with the 3-nitrobifuroxanyl core **5**, based on cascade of one-pot reactions (acylation of dinitromethane sodium salt with chlorides **4**, nitrosation of the acylation product, and intramolecular cyclization of the nitrosation product to 3-nitrobifuroxanyl moiety), has been developed [2].



This work was supported by Russian Science Foundation (grant № 14-50-00126)

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Synthesis of 3-amino and 3-alkynylcoumarins from peucedanin

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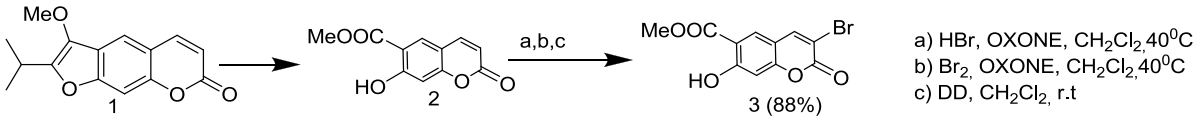
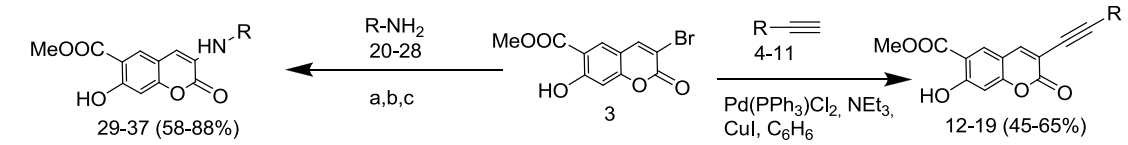
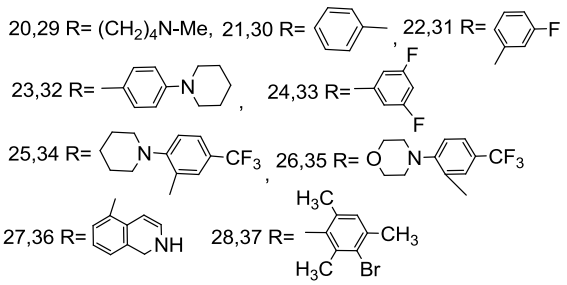
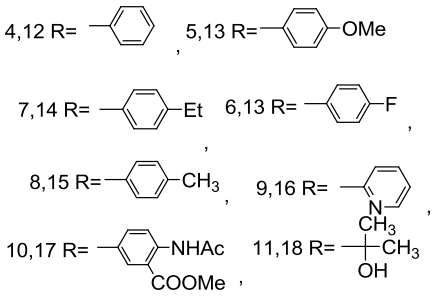
Coumarins are widely present in plants, and both synthetic and plant-derived coumarins are utilized in a wide range of applications in chemical and pharmacology, owing to the optical and promising therapeutic properties [1,2]. Considerable attention was focused on the preparation and application of coumarins with various substituent in the C-3 position. As the starting compound we are using coumarin peuruthenicin **2** obtained from furocoumarin peucedanin **1** according to well-known method [3]. Oxidative bromination of coumarin peuruthenicin **2** yielded the 3-bromo derivatives **3**.



3-Bromopeuruthenicin **3** was involved into the Sonogashira coupling with various alkynes **4-11** and in amination reactions (un-catalyzed and Pd-catalyzed) with amines **20-28**. Starting from 3-bromopeuruthenicin by using of these reactions substituted peuruthenicins of two types: 3-alkynyl- **12-19** and 3-aminoderivatives **29-37** are obtained.







Reagents and conditions: a) $CHCl_3$, boiling, 18 h; b) dioxane, Py, boiling, 12 h;
c) $Pd(OAc)_2$, $CsCO_3$, Xantphos, dioxane, 100^{0}C, 8 h

Structures of compounds were confirmed with spectral methods and elemental analysis data.

This work was supported by the Russian Foundation for Basic Research (grant 16-53-44027) and Russian Science Foundation (grant 14-13-00822).

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Stereospecific [2+2] photocycloaddition of crown-containing styryl dyes with ammonioalkyl substituents

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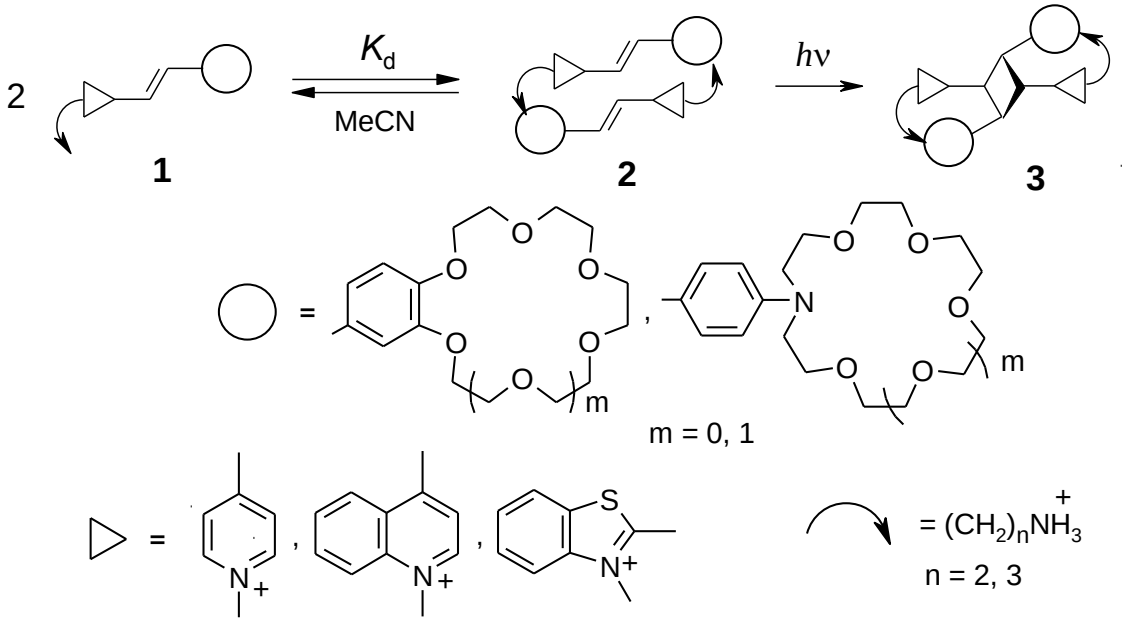
Synthesis of the new styryl dyes **1** containing a crown-ether fragment and a terminal NH_3^+ group in the *N*-substituent of heterocyclic residue was elaborated. It was found that dyes **1** can spontaneously form dimers **2** in both the solid state and in solution (MeCN, CH_2Cl_2) due to the intermolecular binding of NH_3^+ group with crown-ether moiety. The dimers have a head-to-tail pseudocyclic structure. The dimerization equilibrium constants for dyes **1** were estimated by ^{1}H NMR titration in MeCN-d_3 (logK_d up to 8.0).



Visible light irradiation of dimers **2** in solution, thin polycrystalline films and monocrystals induced stereospecific [2+2] photocycloaddition reaction generating cyclobutane derivatives **3** as the single *rctt* isomer. The photocycloaddition quantum yield was varied between 0 and 0.38, depending on the nature of heterocyclic residue, the length of ammonioalkyl substituent and the type and size of crown-ether fragment in dyes **1**. The structures of **1-3** were studied by X-ray diffraction and NMR spectroscopy. Dyes **1** can be utilized in systems of optical registration and storage of information.

This work was financially supported by the Russian Scientific Foundation (14-13-00076) and the Russian Academy of Sciences.

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New method for *in situ* generation of enolateiminium 1,4-dipoles for [4 + 4], [4 + 2] and [4 + 1] dipolar heterocycloaddition reactions

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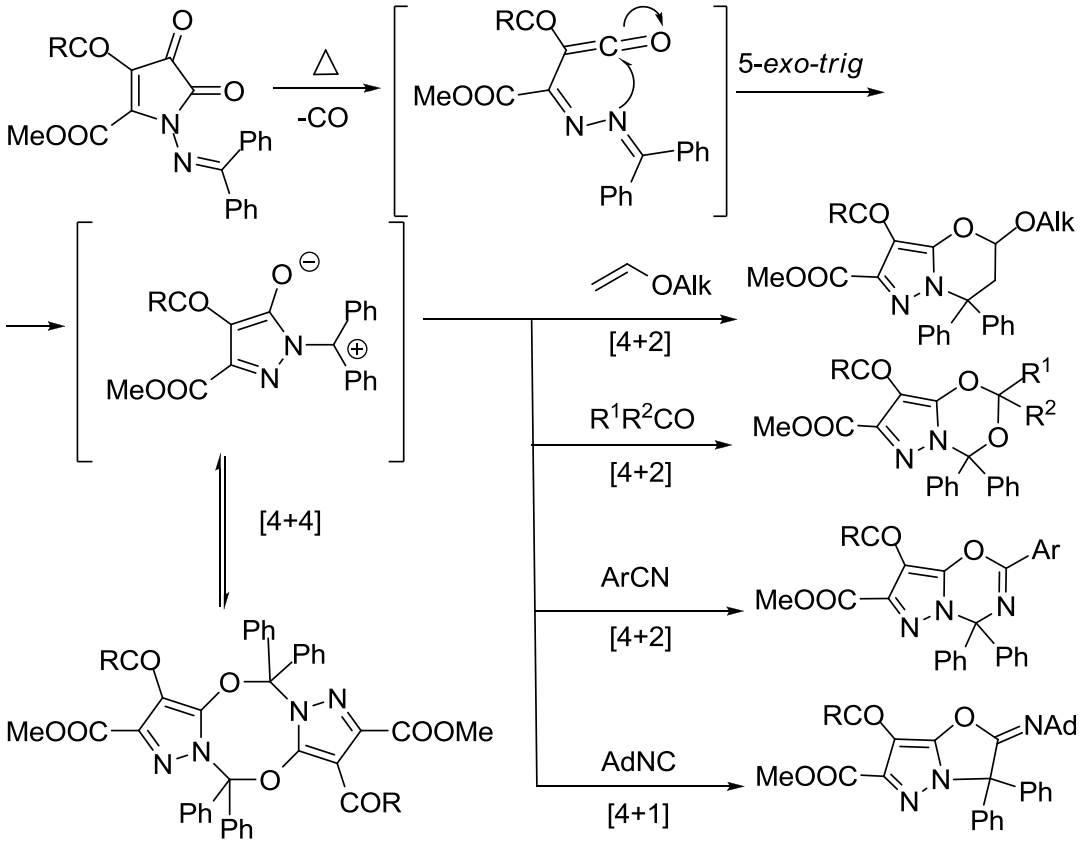
It was previously demonstrated, that thermal decarbonylation of *N*-substituted 2,3-dihydro-2,3-pyrroldiones afforded imidoylketenes, whose chemical behavior largely depends on the nature of substituents at *N*-1. In the frame of our continuous studies of related transformations of imidoylketenes we pondered about possibility of generating hydrazoylketenes in a similar way, and investigating their subsequent transformations.

It was discovered that *N*-(diphenylenamino)pyrrolediones experienced facile CO-extrusion at elevated temperatures and the resulting hydrazonoketenes underwent further 5-*exo*-*trig* ring closures to provide a zwitterionic dihydropyrazolone species, which can be represented by enolate-iminium 1,4-dipole resonance form. In the absence of dipolarophiles, the products of [4+4]-cyclodimerization – bis(pyrazolo)dioxadiazocines – were formed in high yields. We further elaborated on the development of various synthetic schemes involving cycloaddition of these unusual 1,4-dipoles. To this end, we generated the ketenes in the presence of alkyl vinyl ethers, aldehydes, ketenes, nitriles and isocyanides targeting products of [4+2] and [4+1] dipolar cycloadditions.



This work was supported by Ministry of Education and Science of Russian Federation.

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Diversity-oriented synthesis of intensively emissive 3-ethynyl- and 2-triazolylquinoxalines by MCR sequences

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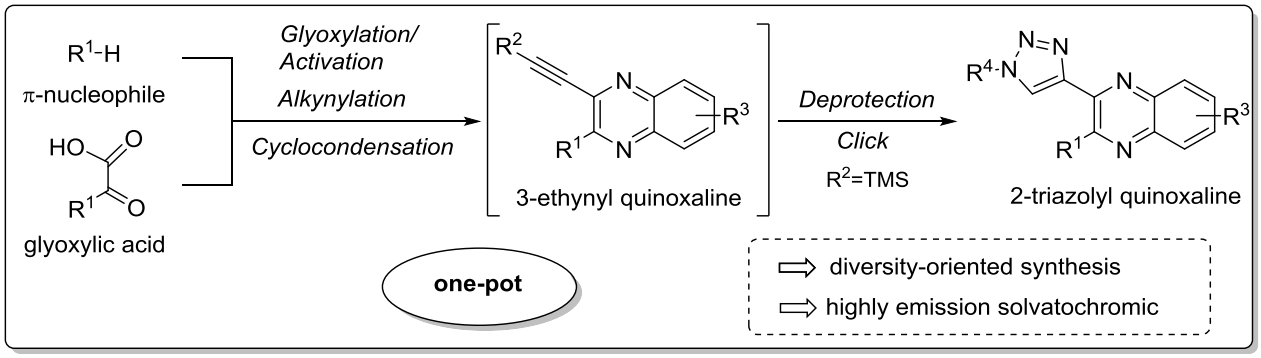
Especially in today's times, the concept of one-pot and multicomponent reactions (MCR) adopts a central position in modern synthetic chemistry. Particularly the formation of fluorophores and chromophores *via* a rapid and elegant MCR approach remains a paramount challenge for organic and materials chemists [1]. Ultimately, with adequate reflection of this issue a crucial aspect of the one-pot fashion is the diversity-oriented nature. With the aid of this methodology substance libraries can be set up. These conceptual approaches has already found its way into the construction of highly luminescent and stable heterocycles. For this purpose, our group has recently developed a set of complementary one-pot syntheses of fluorescent and solvatochromic 3-ethynyl quinoxalines and 2-triazolyl quinoxalines (Scheme 1) [2] based on intermediary ynediones [3].



Scheme 1: Diversity-oriented multi-component one-pot procedures for the synthesis of 3-ethynyl- and 2-triazolyl quinoxalines.

Further varied structural changes of the triple bond are conceivable [4]. Consequently, we set out to investigate the reaction scope as well as the photophysical and chemical properties of the synthesized compounds.

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Novel conformationally flexible bromantane analogues: potential urgent synthetic adaptogenes

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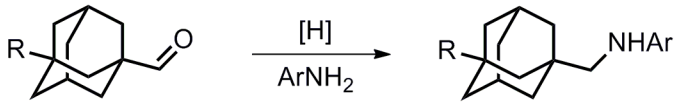
Novel analogues of the domestic drug Bromantane (Ladasten ®), characterized with enhanced conformational flexibility, were prepared by reductive amination of the corresponding adamantane-1-carboxaldehydes with a variety of different aniline derivatives:



R = H, Br, Cl, OH, CN; Ar = Ph, 4-MeC_6H_5, 4-IC_6H_5, 4-BrC_6H_5, 4-HOC_6H_5, 4-$O_2NC_6H_5$, 3-$O_2NC_6H_5$, 4-$H_2NC_6H_4$, 3-$H_2NC_6H_4$, 1-$C_{10}H_7$, 2-$C_{10}H_7$

Synthesis of the starting adamantane-1-carboxaldehydes has been accomplished according to the known method of art [1,2], based upon the Stephen reduction of the corresponding adamantane-1-carbonitriles.

Physical and chemical properties of the novel compounds were extensively studied. Pharmacological activity profile of three of them, most closely related to Bromantane itself, was investigated during in vivo trials.

The work was supported by RSCF (grant № 16-13-00100)

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Antitumor ruthenium compounds with targeting ligands

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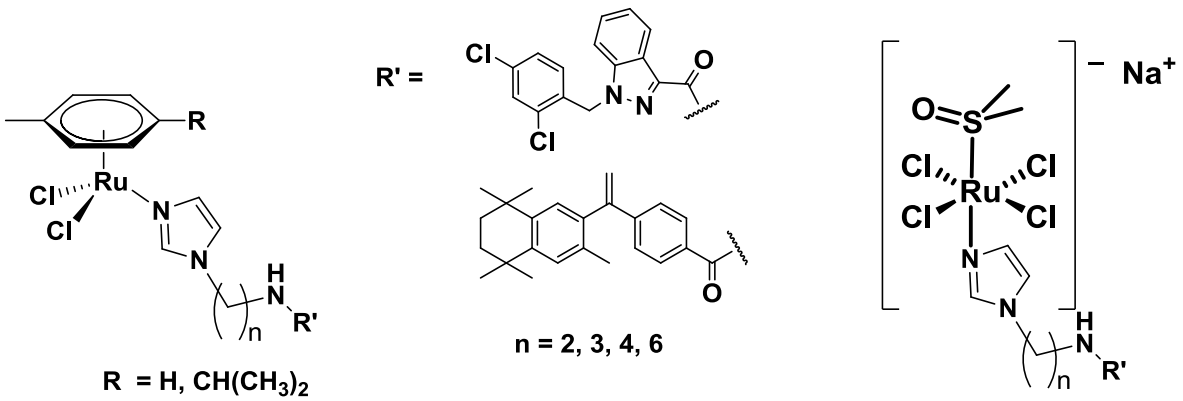
The search for new metal-based anticancer compounds traditionally based on cytotoxic platinum compounds [1]; however, in recent years there has been much of interest in the development of non-platinum anticancer drugs and it was shown that the ruthenium-based compounds could be clinical alternative of platinum drugs.

The tumour specificity of ruthenium compounds can be influence by ligand sphere around metal atom. Linking Ru part to the targeting biologically active organic molecules can strongly increase anticancer properties [2,3]. Lonidamine is known to inhibit the aerobic glycolysis in cancer cells while simultaneously enhancing glycolysis in the normal cells. Bexarotene is agonist of the retinoid X receptor and specific against T-cell lymphoma.

This presentation will focus on the hybrid complexes based on lonidamine and bexarotene tethered to the ruthenium unit via an imidazole group. Ru(II) compounds found to be highly cytotoxic against number of the human cancer cell lines. Importantly, lonidamine-modified complexes were remarkable active against glioblastoma cell lines and the hybrid bexarotene-ruthenium compound, showed highly specific cytotoxicity against cancer cells.



This work was supported by Russian Science Foundation (14-13-00483).

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Electroinduced «Metal-Free» C-H Functionalization of (Hetero)Aromatic Systems

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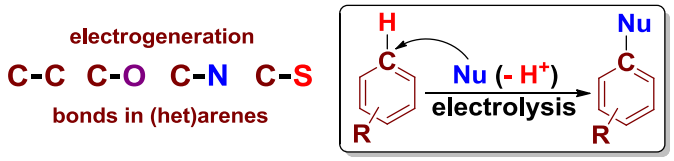
Functionalization of arenes is a key process for their chemical diversity. It provides the applied use of such substances in a wide range of practice areas. Now the functionalization of aromatic C-H bond based on metal complex catalysis [1] or on the basis of the oxidative "metal-free" methodology [2] has become a recognized instrument for arenes modification. Within this ideology, we have developed a number of "metal-free" approaches to C-H modification of arenes using the anode as a "green oxidizing agent" [3 - 5]. They open up the possibility of atom economy and efficient electrosynthesis of substituted (het)arenes, including direct electroinduced nucleophilic substitution of hydrogen in (het)arenes (S_N^H (An) processes) [3 - 5].



The first steps to develop the methodology of the C-H functionalization of the arenes were taken in the 1980s at realization of the original anodic polynitroalkylation of arenes [3 - 5]. Later the effective methods of C-H pyrazolation, triazolation and tetrazolation, as well as acetoxylation of aromatic systems were developed [3 - 5]. In recent years the directions of research were defined by a wide range of expected pharmacological activity of various azolyl-, thiocyanato- and thiolyl- (het)arenes. Thus, a cross-coupling of nitrogen-containing hetarenes was realized leading to azolylpyrroles [6] and azolylanilines as well as electrothiocyanation of a wide range of (het)arenes (including bicyclic pyrazolo[1,5-a]pyrimidines) [7, 8] (the thiocyanato derivatives of latter after transformation into the corresponding mercapto derivatives were used as valuable Nu). In addition, the effective C-H functionalization of dihydroxybenzenes with various thiols (including bicyclic, see above) was carried out leading to pharmacologically active thioethers [9, 10].

In general, the electroinduced "metal-free" C-H functionalization of arenes is a synthetically valuable way of direct C-C, C-O, C-N, C-S and other bonds formation. This approach excludes the use of halogenorganic compounds (as co-reactants) and expensive catalysts, while the electron transfer successfully replaces the use of non-recyclable oxidants.

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The regioisomers of di(benzothieno)thiazines – syntheses and electronic properties

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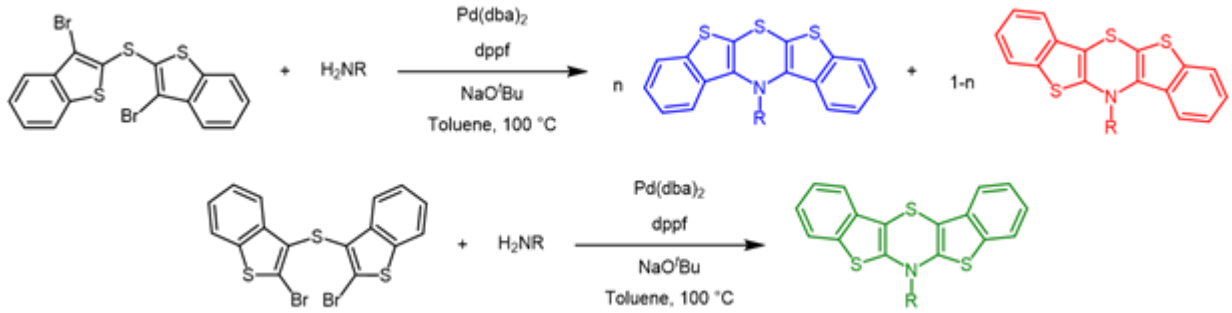
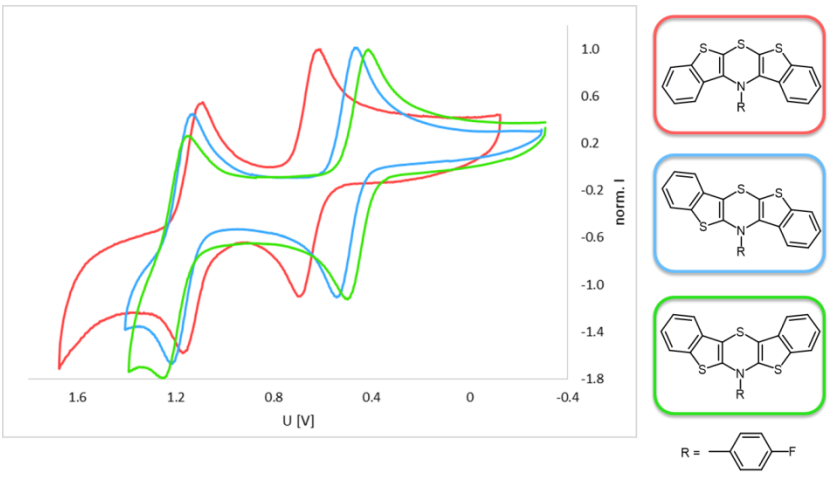
Di(benzothieno)thiazines are annelated derivatives of the parent system dithienothiazine [1]. Dithienothiazines are electron rich organic π-systems, which are reversibly oxidized to stable radical cations and dications. This stabilization results from fully conjugated planarized π-systems of the oxidized specimen. The variation of the substitution pattern should greatly influence the electronic properties of this new polyheterocyclic system. Thus, the first synthesis of the regioisomer of di(benzothieno)thiazine was performed in a similar manner as for dithienothiazines [2]. Surprisingly the ring closing *Buchwald-Hartwig* amination did not specifically lead to the expected *syn-syn* regioisomer but also to the formation of the *syn-anti* regioisomer. This unique isomer formation can be rationalized by a novel palladium catalysis reaction pathway.



Encouraged by the formation of the *syn-anti* regioisomer also the third possible regioisomer of di(benzothieno)thiazine was selectively prepared by using the same method [3]. The three regioisomers show different electronic properties, whereby the varied constitution has a significant influence on the oxidation potentials and the luminescence behavior.



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Tuning the reactivity of the azide anion with metal ions. Nucleophilic addition to *N,N*-bis(oxy)enamines as a case study

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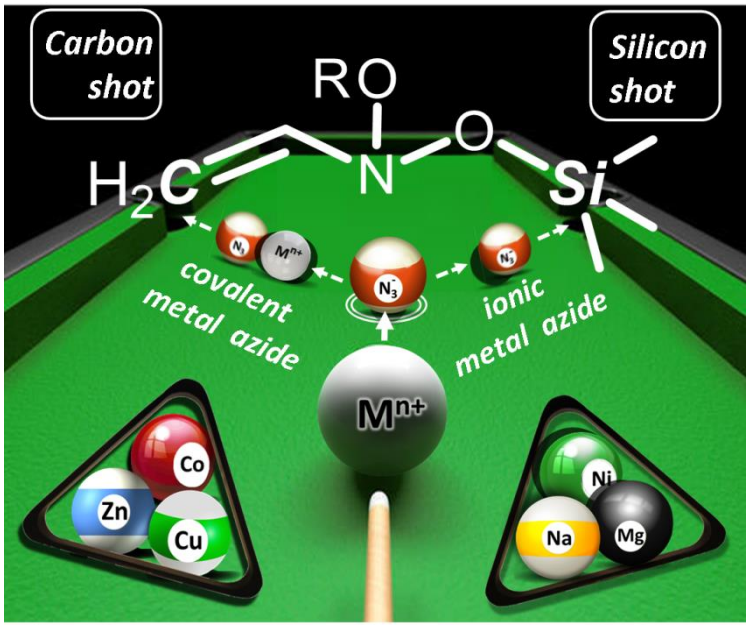
Azide anion is one of the most synthetically useful nucleophiles owing to the key role of organic azides as intermediates in target-oriented synthesis and bioconjugation. In organic synthesis, NaN_3 is commonly used as a source of nucleophilic azide anion. Non-alkali metal azides are explosive compounds, which can hardly be considered as convenient and useful reagents. However, as it is demonstrated in our study the metal ion can modulate the reactivity of the azide anion thus bringing new opportunities for the synthesis of organic azides. A compromise is that the use of a free metal azide is not obligatory, since it can be safely generated in solution by ion exchange from NaN_3 and the corresponding metal salt.



In the presentation, the interaction of *in situ* generated p-, d- and f-metal azides with bielectrophilic substrates such as N,N-bis(oxy)enamines will be discussed (see Figure). A strong correlation between the coordination state of N_3^- in the metal-azide system and its reactivity has been disclosed in these reactions. In particular, ionic metal azides (sodium, magnesium, nickel) react through the initial attack of N_3^- on silicon atom generating conjugated nitrosoalkenes, while strongly bound metal azides (zinc, cobalt and copper) directly transfer N_3^- to the β-carbon atom of bis(oxy)enamines *via* a LA-assisted S_N' substitution of silyloxy-group. α-Azidooxime derivatives prepared using the designed protocols can be stereoselectively reduced to valuable 1,2-diaminoalcohols bearing up to four contiguous stereogenic centers.

This work was supported by the Russian Science Foundation (grant № 14-50-00126).

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Donor-acceptor cyclopropanes ring opening with nitrogen nucleophiles as a key step in the synthesis of azaheterocycles

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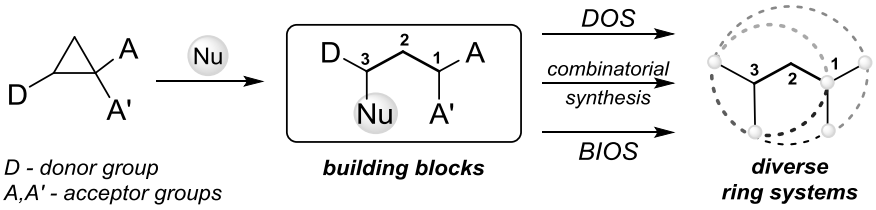
Cyclopropanes bearing donor and acceptor substituents at the vicinal positions demonstrate an excellent reactivity and selectivity in reactions with both nucleophiles and electrophiles as well as in various cycloaddition and annulation processes. Here, we report a synthetic strategy for the synthesis of new azaheterocycles based on stepwise procedures wherein the first step is a three-membered ring opening with nitrogen-containing nucleophiles affording building blocks containing multiple reaction centers tolerant to each other. The next step is a modification of one of functionalities that initiates its reaction(s) with some other functional group of these building blocks producing formation of a new ring *via* cyclization or intramolecular cycloaddition. A broad scope of reactivity of such polyfunctional building blocks as well as multipath of functional groups modifications provide the efficiency of this approach for the diversity-oriented synthesis (DOS) of azaheterocyclic structures. By realization of this general strategy, we have synthesized a variety of mono-, bi- and polycyclic nitrogen heterocycles. As azaheterocycles are abundant in both Nature and medicines, this approach can be also applied in the biology-oriented synthesis (BIOS) of bioactive molecules. In particular, we have applied it for the total synthesis of (-)-nicotine and the formal total synthesis of atorvastatin marketed under the trade name *Lipitor*.



This work was supported by the Russian Science Foundation (grant № 14-13-01178).

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Stereoelectronic chameleons: the donor/acceptor dichotomy of functional groups

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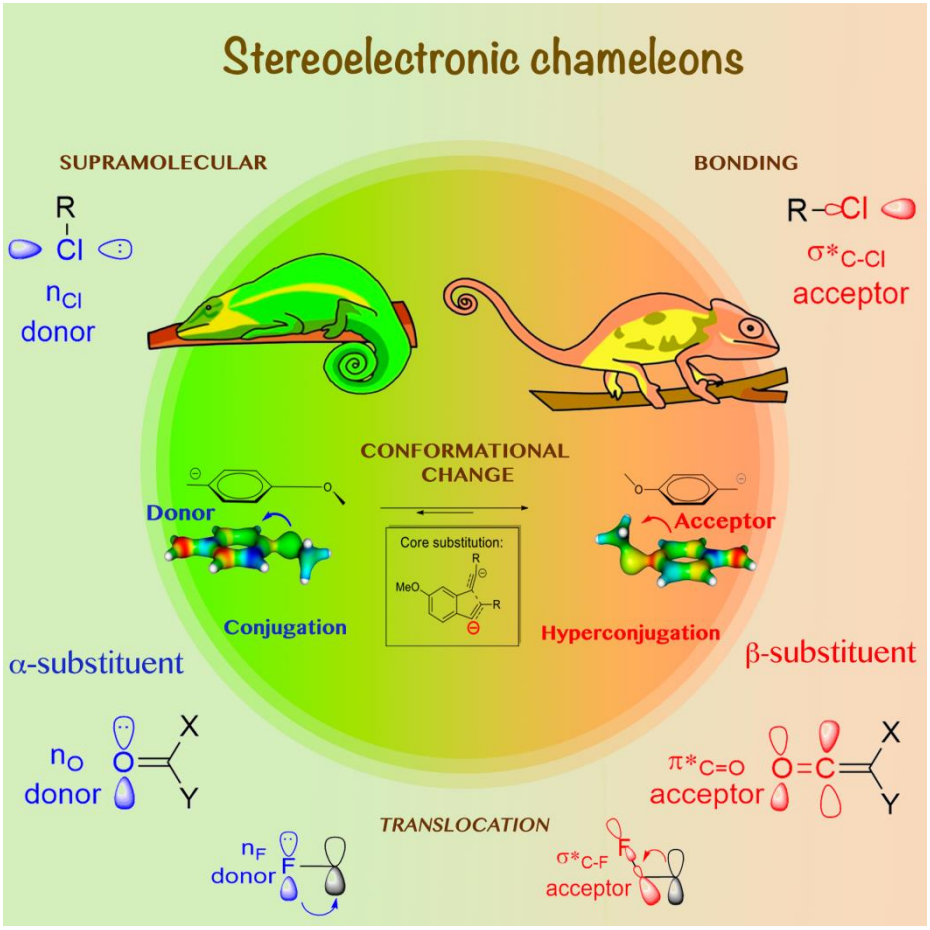
Stereoelectronic factors account for the apparent reversal of donor/acceptor properties of a variety of functional groups by a simple change of their orientation in space. The new reactivity patterns that arise from spatial anisotropy are associated with *chameleonic* behavior of common organic functionalities [1].



Because donor and acceptor properties are often engraved into our thinking about functional groups by the current educational paradigms, such a stereoelectronic "umpolung" can unlock useful ways of thinking about chemical reactivity and open new doors for reaction design. We are looking forward to new examples of stereoelectronic chameleons in control of structure and reactivity.

This work was supported by RSF (grant № 16-13-00114).

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Enantioselective total synthesis of dicerandrol C

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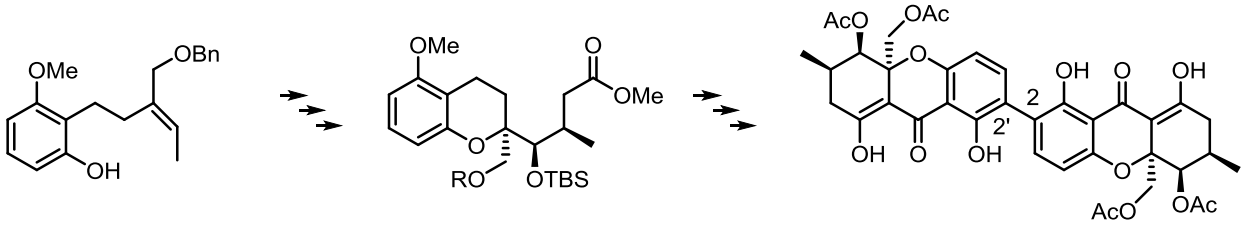
Dicerandrol C belongs to a group of natural mycotoxins containing a dimeric tetrahydroxantenone skeleton [1]. The dicerandrols have been isolated from the fungus *Phomopsis longicolla*, and their relative structure was elucidated by Clardy et al. [2] in 2001 and their absolute configuration has recently been determined by Proksch et al. using calculations [3].

We accomplished the first enantioselective total synthesis of natural dicerandrol C (**1**) as its enantiomer containing a dimeric tetrahydroxanthenone skeleton starting from the enantiopure chromane **3** [4] which was obtained from **2** through a Wacker-type cyclization in the presence of a BOXAX ligand with >99 % ee. This is not only the first synthesis of this type of natural product but it also proves the relative and absolute configuration of the dicerandrols.

After benzylic oxidation of **3** cyclization using $TiCl_4$ and $Ti(OiPr)_4$ led to the tetrahydroxantenone skeleton. Halogenation at the 2 position followed by a Susuki-Miyaura coupling gave the dimeric tetrahydroxantenone which after full deprotection was selectively acetylated to achieve dicerandrol C **1**.



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Oral Reports

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Direct reductive coupling of indoles to nitrostyrenes en route to (indol-3-yl)acetonitriles and (indol-3-yl)acetamides

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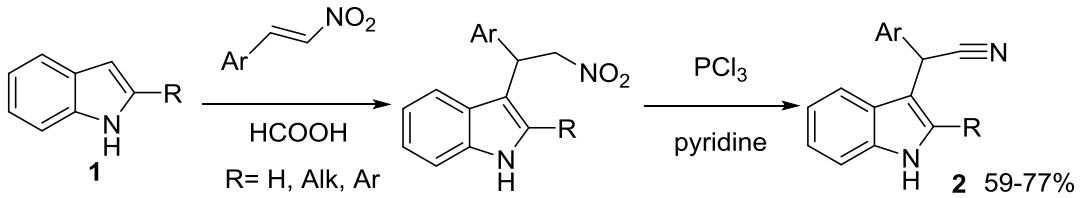
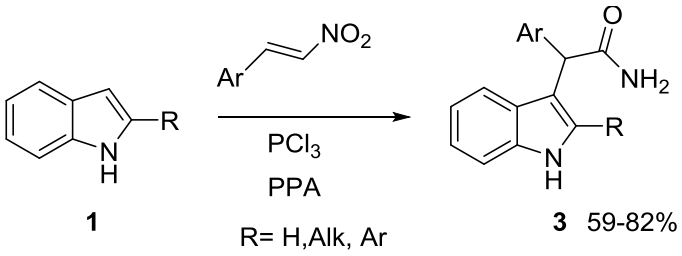
Development of synthetic approaches to alkaloid-mimics embedding the indolyl moiety is one of the central themes of contemporary organic and medicinal chemistry. Such interest caused by various biological activity of species with this fragment. Thousands of synthetic compounds as well as alkaloid were shown. This is a reason why interest in a these compounds and synthetic routes will never go out.

We have recently found the 2-aryl-2-(3-indolyl)-acetohydroxamic acids have significant activity against glioma, melanoma, esophageal, and many other cancer lines intrinsically resistant to apoptosis induction and poorly responsive to treatment with traditional proapoptotic drugs. In our present work, we decided to study indolylacetonitriles related to these compounds. Starting from indoles and β-nitrostyrenes, we needed catalyst for alkylation to be fully compatible with a sensitive indole moiety and reducing agent that used in the second step. We found that formic acid is perfect as catalyst. This allows us to perform transformation as *in-one-pot* process using the addition of PCl_3/pyridine system to reaction mixture. This reduces nitrogroup and decomposes formic acid [1].



The reaction of indoles with nitrostyrene and phosphorous chloride in PPA leads to corresponding (indol-3-yl)acetamides with good yields [2].



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Enathioselective synthesis of indolylacetohydoxamic acids

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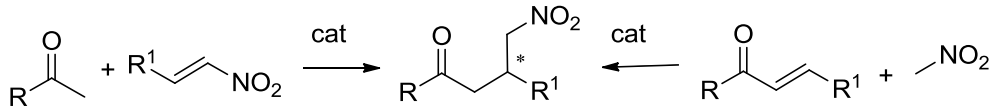
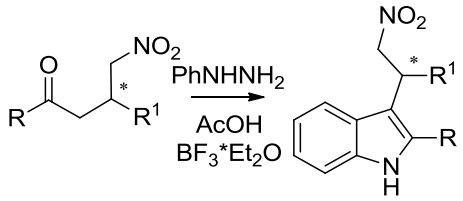
Synthesis of enantiopure organic compounds one of the most important proplems in organic and pharmaceutical chemistry. The most attractive solution to this problem is enantioselective synthesis using chiral catalysts.

In our laboratory we found that some of indolylacetohydroxamic acids show good activities against several cancer cultures. This activity results in search methods for the preparation of individual enatiomers of these compounds .For this reason we developed method of such compounds synthesis using enathiopure precursors in reactions with preservation of configuration.

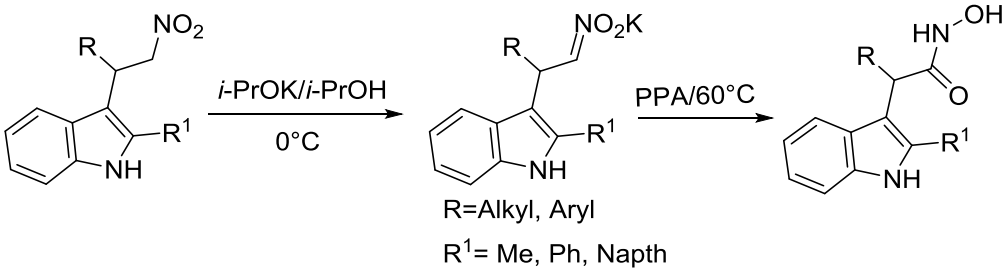
First of all we found that precursors can be obtained with ee>92% by organocatalyzed asymmetric Michael additions.



4-nitro-1-butanones can be converted to 2-indolyl-1-nitroethanes by the mixture of equal amounts of BF_3 etherate and acetic acid. This reaction proceeds under heating for several hours, with no significant resinification and hydroxamic acid formation, the configuration stereocenter was preserved.



In the last part of work 2-(indole-3-yl)nitroethanes were converted to the corresponding hydroxamic acids. We found that action of SeO_2/Et_3N leads to formation of large quantities of by-products. Another method we thied was convertion of corresponding nitronate to hydroxamic acid in polyphosphoric acid medium at 60°C. In fact, the isomerization reaction proceeded instantaneously with preservation of stereocenter configuration.



This work was supported by the Russian Foundation for Basic Research (grant № 16-33-60108 мол_а_дк).

Lightsensitive supramolecular system based on crown-containing unsaturated compounds and cavitands

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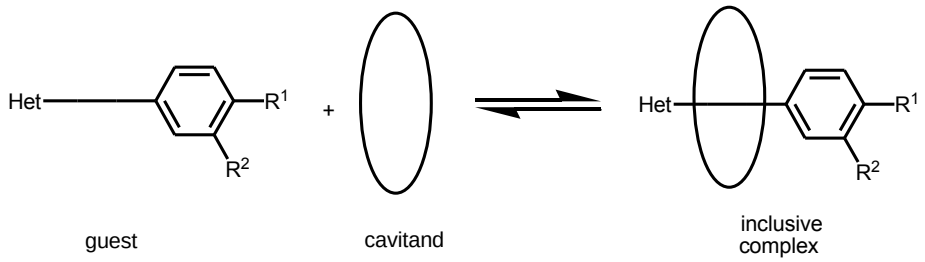
Unsaturated crown-containing and methoxy-substituted styrylheterocycles of the 4-pyridine and 4-quinoline series were synthesized by condensation of methyl-substituted heterocycles with benzaldehydes in the presence of base. Synthesis of 18-crown-6-containing styrylpyridine by condensation of the reagents in Ac_2O was developed. A simple and efficient method for the preparation of crown-containing and methoxy-substituted hetarylphenylacetylenes by the bromination followed by dehydrobromination reactions of the corresponding styrylheterocycles.



Complex formation of styrylheterocycles and hetarylphenylacetylenes with macroheterocyclic compounds (cavitands) – β-cyclodextrins and cucurbit[7]uril – was studied by electronic and ^{1}H NMR spectroscopy methods. It was established pseudorotaxane structure and stability constants of the inclusive complexes of the "host–guest" type.

This work was supported by the RFBR (project № 15-03-001883), the RSF (project № 14-13-00076) and the RAS.

A new method for the synthesis of benzofuran-2-one derivatives

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[b]*Moscow State University, Leninskie Gory 1, 119991, Moscow, Russian Federation*
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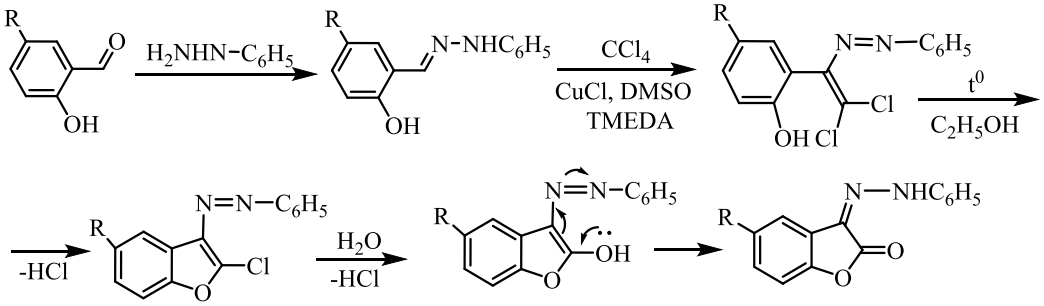
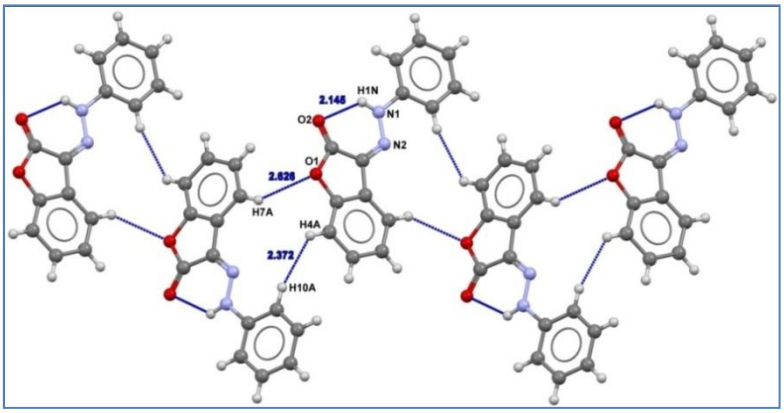
In previously published works we have described in detail methods for the preparation of various derivatives of dichlorodiazobutadienes by the reaction with CCl_4. Also, we have found that the presence of hydroxyl group in the structure of starting aldehyde opened new potential opportunities for this reaction, in particular, a new simple method for producing of benzofuranone-2 [1].

Given the great similarity between the synthesized benzofuranones with already known antibacterial drugs based on furan, we studied the antibacterial activity of the latter. It is found that they affect both on the gram-positive (Staphylococcus aureus), as on gram-negative bacteria (Escherichia coli, Pseudomonas aeruginosa, Rlebsiella pneumonia).



R = H, Br, NO_2, OCH_3



Molecular structure of (z)-3-(2-phenylhydrazono)benzofuran-2(3H)-one

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Macrocycles with dansyl and quinolinyl fluorophore groups as chemosensors

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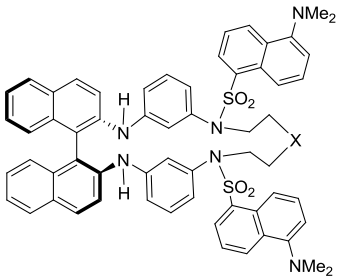
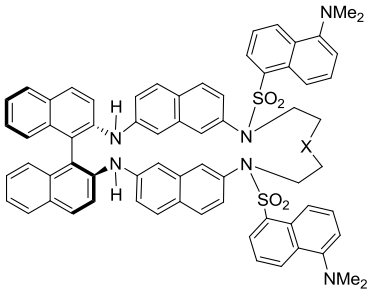
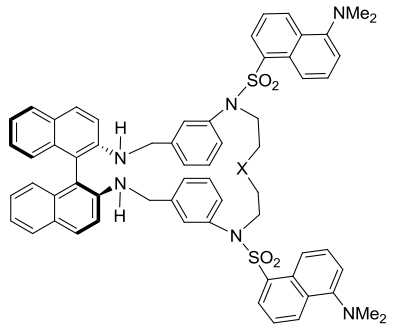
Using methods Pd(0)-catalyzed macrocyclization reactions, macrocycles with *C2*-chiarl fragment of 1,1'-binaphthalene-2,2'-diamine (BINAM) were synthesized in good yields. These compounds differ by the nature of the aryl spacer, the length of the oxadiamine linker and the number of oxygen atoms in it. The macrocycles were modified with two 5-(dimethylamino)-1-sulfonamide (dansyl) fluorophore groups using convenient nucleophilic substitution reactions, and with two 6-aminoquinoline fluorophore groups using the Pd(0)-catalyzed amination reactions. The yields of the fluorophore-decorated ligands were found to be dependent on the nature of the starting macrocycles and reached 99% in the case of dansyl substituents and 73% in the case of quinolinyl substituents.



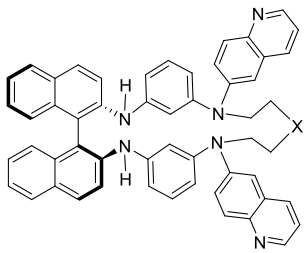
1, X = OCH_2CH_2O, 97%
2: X = $OCH_2CH_2OCH_2CCH_2O$, 16%
3, X = $CH_2OCH_2CH_2OCH_2CH_2OCH_2$, 65%



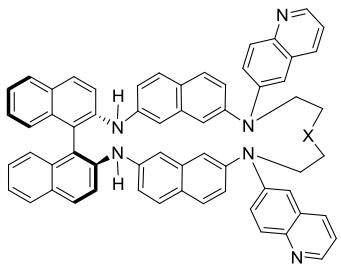
4, X = OCH_2CH_2O, 24%
5, X = $CH_2OCH_2CH_2OCH_2CH_2OCH_2$, 45%
6, X = $(OCH_2CH_2)_3O$, 99%



7, X = OCH_2CH_2O, 61%
8, X = $CH_2OCH_2CH_2OCH_2CH_2OCH_2$, 34%



9, X = OCH_2CH_2O, 36%
10, X = $CH_2OCH_2CH_2OCH_2CH_2OCH_2$, 47%



11, X = OCH_2CH_2O, 72%
12, X = $CH_2OCH_2CH_2OCH_2CH_2OCH_2$, 73%

The coordination of 18 metal cations with these macrocycles and several dansyl and quinolinyl substituted chiral BINAM-containing macrocycles was investigated using UV, fluorescence and NMR spectroscopy, the results were shown to be dependent on the structure of the macrocycle and fluorophore group. UV and fluorescence titration of some dansyl and quinolinyl substituted chiral BINAM-containing macrocycles was carried out using optically pure amino alcohols like (*S*)-(+)-2-phenylglycinol and (*R*)-(-)-2-phenylglycinol (*S*)- and (*R*)-2-amino-3-methyl-1-buthanol (L-and D-valinol), (*S*)-2-amino-1-propanol, (1*S*)-(2*R*)-2-amino-1,2-piphenylethanol, two enough selective molecular sensors for (*S*)-(+)-2-phenylglycinol were developed. The first one containing dansyl fluorophores in the presence of this compound decreased the emission, while the second possessing quinolinyl fluorophores in the presence of (*S*)-(+)-2-phenylglycinol increased the emission with a notable hypsochromic shift of the maximum.

This work was supported by the Russian Foundation for Basic Research (grant № 15-03-04698).

Novel anticancer drugs dispiro-oxindole series based on various types of heterocycles: synthesis and biological testing

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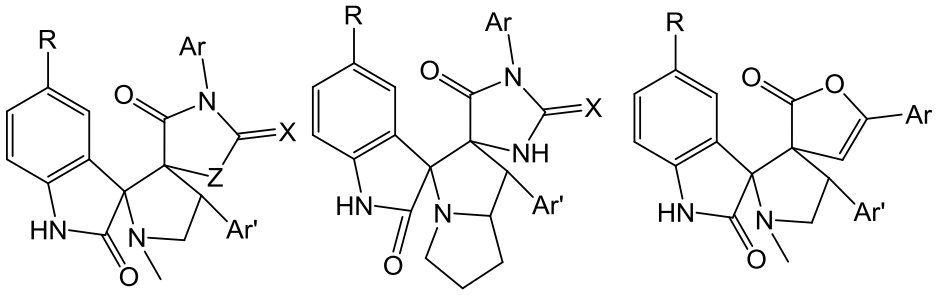
Prostate cancer is one of the leading cancer type in the world: for example, in Russia about 14,000 cases are registered per year. Prostate cancer causes almost 10% of cancer deaths in men and it is one of the main causes of death for older men. In the USA, prostate cancer is the third most common cause of death from cancer [1].

MDM2 inhibitors, containing in its structure spiro-oxindole core are relatively new class of biologically active compounds, it has been reported that these compounds could effectively block the interaction of MDM2 and p53 protein-protein interaction (PPI) [2].

Previously in our group the «hit»-compound with the promising anticancer activity 2,1 μM was found [3]. For this compound the enantioselective separation of two diastereoisomers was made and it was shown, that only one isomer had selectivity and cytotoxic effect for p53. In this work, we describe the synthesis of dispiro-compounds shown below on the base of different types of heterocyclic compounds as substrates for 1,3-cycloaddition:



X=O,S,S(Me) ; Z= NH,S; R=H, Br, Cl

The biological activity of synthesized compounds were studied using MTT assay on HCT $p53^{(+,+)}$, HCT $p53^{(-,-)}$, LNCap and PC3 cell lines.

This work was supported by the Russian Foundation for Basic Research (grant № 16-33-60166).

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Synthesis and biological evaluation of 3-phenyl-quinoxaline-2-carbonitrile 1,4-di-N-oxide derivatives as hypoxia-selective cytotoxic agents

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[3] *Federal State Budgetary Scientific Institution «N.N. Blokhin Cancer Research Center», 24 Kashirskoye Shosse, Moscow 115478, Russia*
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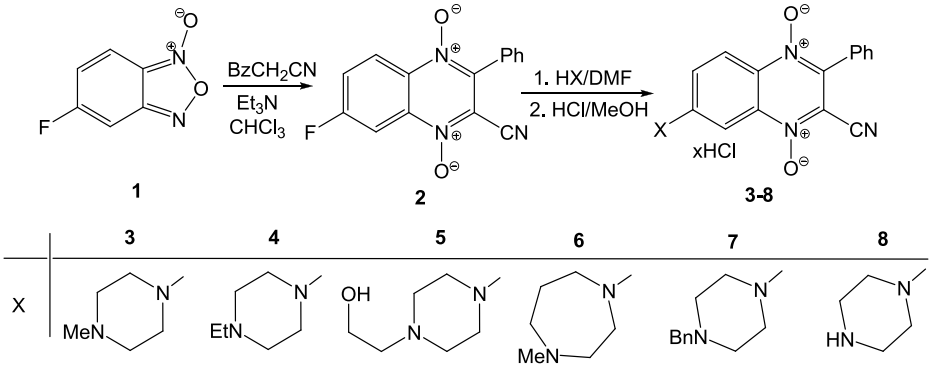
Derivatives of quinoxaline-1,4-dioxide are known as hypoxia-selective anti-tumor agents [1]. Previously described quinoxaline-2-carbonitrile 1,4-dioxide derivatives are water insoluble that complicated their biological evaluation. To overcome this disadvantage, a series of 7-amino-3-phenyl-quinoxaline-2-carbonitrile 1,4-dioxides have been synthesized and evaluated.

The starting compound, 7-fluoro-3-phenyl-quinoxaline-2-carbonitrile 1,4-di-N-oxide (**2**) was obtained by the Beirut reaction based on the condensation of appropriate benzofuroxane **1** and benzoylacetonitrile in chloroform in the presence of triethylamine [2]. The replacement of fluorine atom by piperazines and subsequent treatment with hydrogen chloride in methanol series of novel water-soluble quinoxaline-2-carbonitrile derivatives **3**-**8** was obtained.

All final compounds **3**-**8** were characterized by nuclear magnetic resonance (^{1}H, ^{13}C NMR), ultraviolet (UV) and mass (HRMS) spectra. Cytotoxicity towards cancer cells were assessed by MTT test after 72 h cell growth.



Screening of cytotoxicity of derivatives 7-aminoquinoxaline-2-carbonitrile 1,4-dioxides **3**-**8** showed higher hypoxic cytotoxic activity and selectivity in comparison with cisplatin and tirapazamine against most of tested cell lines, in particular for MDA-MB231 and MCF-7 cells (breast cancer). Thus 7-amino-substituted quinoxaline-2-carbonitrile dioxide **3**-**8** have high hypoxic selectivity against MDA-MB231 and MCF-7 cell lines, with HCR values 3-30 (HCR = $IC_{50(NORMO)}$ / $IC_{50(HYPO)}$), which were significantly higher than for reference drug cisplatin (HCR = 0.7 – 0.8). Moreover, prepared compounds were more active than hypoxia-selective therapeutic agent tirapazamine.

New synthesized compounds **3**-**8** were also showed good antiproliferative activity against chronic myeloid leukemia K562 and its multidrug resistance subline K562/4 mediated by P-gp expression and disfunction of tumor suppressor p53.

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(3+3)-Annulation of donor-acceptor cyclopropanes to 1,2,3-substituted diaziridines. A first example of (3+3)-annulation of two different three-membered rings

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[3] *M.V. Lomonosov Moscow State University, 119991 Moscow, Leninskie Gory 1-3*
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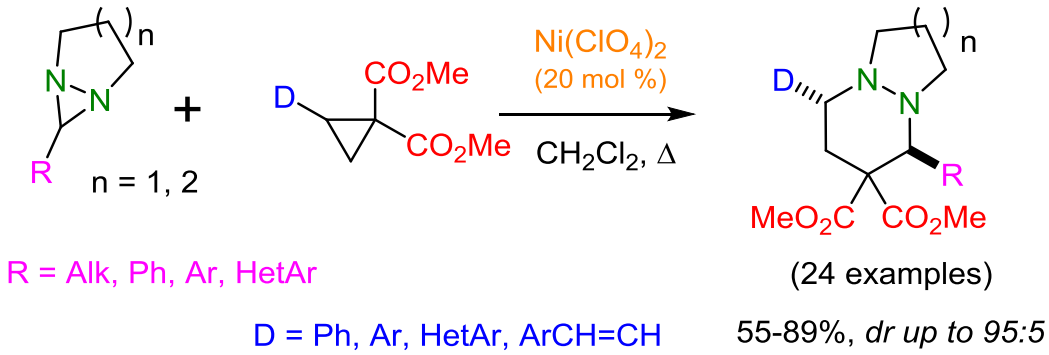
Reactions of the donor-acceptor cyclopropanes (DAC) with diverse amphiphilic agents are in focus of attention of contemporary organic chemists, representing powerful, convenient and stage-economy approaches to construction of a plethora of functionalized carbo- and heterocyclic scaffolds [1].

We report here the $Ni(ClO_4)_2$-catalyzed reaction of DAC with diaziridines which proceeds as an (3+3)-annulation and affords the corresponding pyridazine derivatives with high yield and diastereoselectivity. A broad variety of DAC with aryl-, hetaryl and stryryl donor-substituents was introduced into reaction with a series of 1,2,3-substituted diaziridine derivatives. We propose a stepwise mechanism for the reported transformation involving the nucleophilic attack of the diaziridine nitrogen atom onto Lewis acid-activated cyclopropane followed by the cyclization of the formed 1,6-zwitterionic intermediate. To confirm this hypothesis, we have performed experiments with an optically pure cyclopropane (D = Ph) and isolated the corresponding optically pure pyridazine derivatives (n = 1, 2).



Therefore, a novel reaction of DAC with 1,2,3-substituted diaziridines was disclosed, being the first example of (3+3)-annulation of two molecules with different three-membered rings.

This work was supported by the Russian Science Foundation (grant № 14-13-01178).

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New 2- Thioimidazolinum ligands like copper chelating agents: potential drugs for the treatment of Wilson's disease

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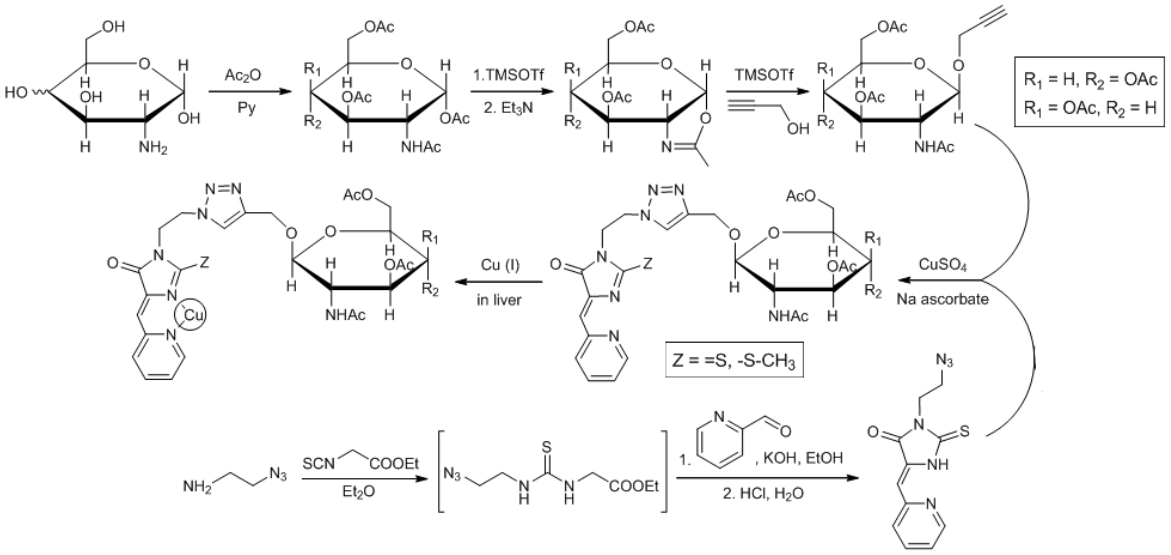
Nowadays Wilson's disease is one of the rare diseases of humanity and it requires new modern methods of treatment. Wilson's disease is a liver pathology characterized by copper dysregulation. This genetic disorder, caused by ATP7B gene mutations, affects the protein which responsible for pumping copper out of hepatocytes and for excreting it from the body. It induces a toxic copper accumulation, especially in hepatocytes. Currently, systemic copper chelation therapies are used to treat this orphan disease. The liver-targeting units are carbohydrates that induce endocytosis in hepatocytes by the membrane asialoglycoprotein receptor (ASGPR), a lectin abundantly and predominantly expressed at the surface of these cells. ASGPR has a high rate of uptake of macromolecules and enables cell-specific drug delivery. This lectin is a hetero-oligomer composed of two homologous transmembrane proteins with a Ca2+-dependent carbohydrate recognition domain that interacts with galactosides, preferring N - acetylgalactosamine (GalNAc). GalNAc is very attractive as a carbohydrate-targeting unit, as it is more selectively recognized with respect to other endogenous lectins that recognize Gal.

In this work we used 2-amino-substituted glucose and galactose as a ligand moiety for comparing the efficiency of inducing endocytosis into hepatocytes of the liver. Preparation of the 2- thioimidazolinum ligands comprising the steps of acylating the monosaccharide, the preparation of 2-tiogidantoin from isothiocyanates and other compounds.



This work was supported by the Russian Foundation for Basic Research (grant № 16-33- 60166).

Synthesis of derivatives of new heterocyclic systems - pyrano[3,4-*c*][1,2,4]-triazolo[4,3-*a*]pyridines

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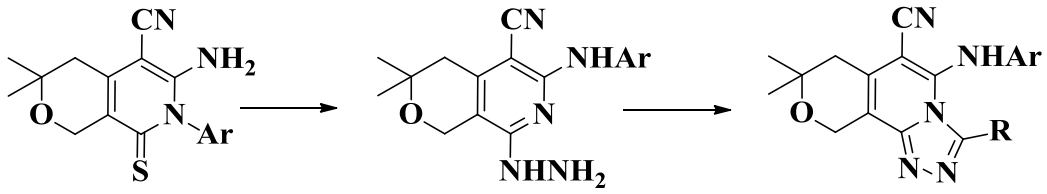
Tricyclic triazolopyranopyridines have been little studied, with only two literature reports found about the synthesis of 1,2,4-triazolo[4,3-*a*]pyrano[3,2-*e*]pyridine [1,2]. The derivatives of pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]pyridines not known in the literature.

This work has been devoted to the synthesis of 8-hydrazinopyrano[3,4-*c*]pyridine derivatives and several further transformations that allowed to prepare new representatives of pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]pyridines. 8-Hydrazinopyrano[3,4-*c*]pyridines were prepared by the rearrangement pyridine ring by the action of hydrazine hydrate.

The rearrangement mechanism was identical to that previously described in the work [3].



The study was perfomed with financial support from the State Scientific Committee of the Ministry of Education and Science of the Republic of Armenia and Russian Foundation for Basic Research within the framework of joint scientific program *(grant №* 15RF-027).

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Design and stereoselective synthesis of novel highly potent phosphodiesterase 4B inhibitors

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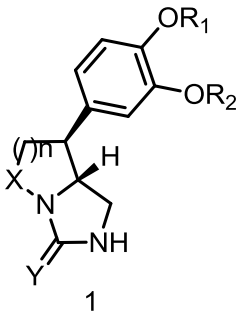
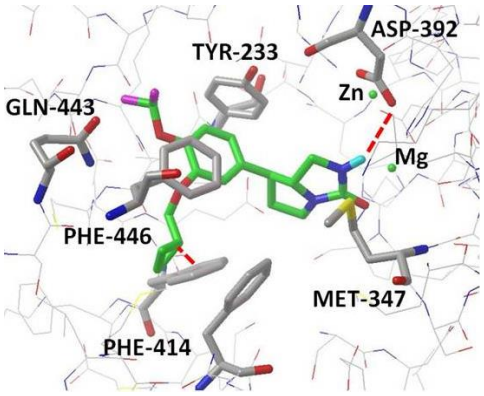
Inhibitors of phosphodiesterase 4B (the enzyme that catalyzes hydrolysis of cyclic adenosine monophosphate and controls its concentration in cells) are used as highly potent pharmaceutical drugs for the therapy of respiratory diseases (e.g. chronic obstructive pulmonary disease and asthma) [1, 2]. The efficiency of PDE 4B inhibitors was proved by *in vitro* and *in vivo* studies [3], but the activity of currently used medicines is still insufficiently high and a lot of them have side effects.

The goal of this project is the development of novel phosphodiesterase 4B inhibitors by means of molecular docking method, followed by their stereoselective chemical synthesis and *in vitro* studies. The molecular structure of target inhibitors is based on a rigid scaffold of bicyclic imidazolidinone **1**. The aromatic (or heteroaromatic) substituent of it can bind effectively with the so-called rolipram site of phosphodiesterase 4B. As a result of our work, several potentially highly active PDE 4B inhibitors were predicted and the approach to their racemic and asymmetric synthesis was developed.



1

R_1 - CH_3, AlkF
R_2 - cycloalkyl, Ar
X - CH_2, $CAlk_2$, O
Y - O, S
n = 1,2



The research was supported by RFBF (grants # 16-33-01063, 17-03-01079 and 17-33-80172).

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Synthesis of fluorinated heterocyclic compounds starting from α,α-difluoro-β-halogenketones

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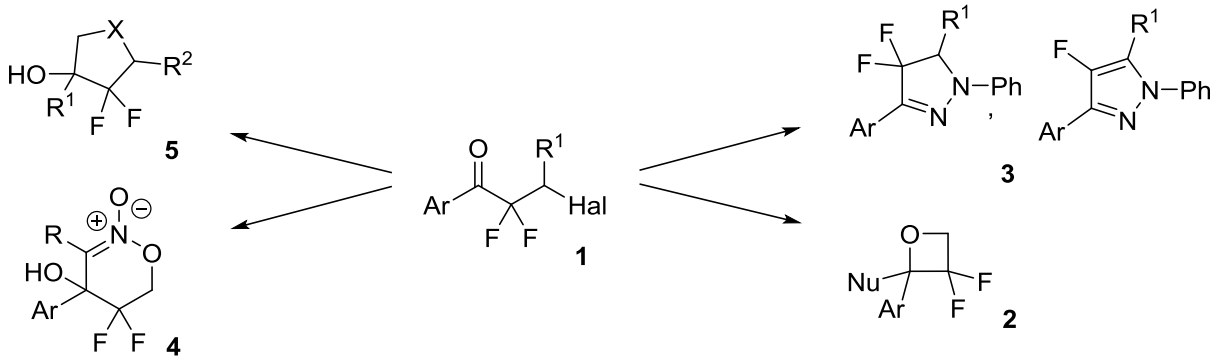
Recently in our group we proposed a convenient method of halogenative difluorohomologation of ketones, which can be performed without isolation of intermediate compounds [1].

α,α-Difluoro-β-halogenketones were proven to be very promising building-blocks for heterocyclic chemistry, granting access to various fluorine- substituted pyrazoles, pyrazolines and oxetanes (**2,3**) [1]. Coupling of **1** with nitroalkanes opens a straightforward approach to 5,5-difluorosubstituted six-membered nitronates **4**, which are difficult to access by other means [2]. Compounds **1** may be easily converted into 3-hydroxy-4,4-difluoropyrrolidines and tetrahydrothiophenes **5** by a two-step sequence, based on methylenation of carbonyl predecessor, followed by coupling with primary amines or sulfides [3].



This work was supported by the Russian Foundation for Basic Research (Project 16-33-00458).

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Reactivity of polyfluoroalkyl-containing lithium 1,3-diketonates: activation by nitrosation

Filyakova V.I.,[a] Boltachova N.S.,[a] Palysaeva N.V.,[b] Slepukhin P.A.,[a] Filyakova T.I.,[a] SheremetevA.B.,[b] Charushin V.N.[a]

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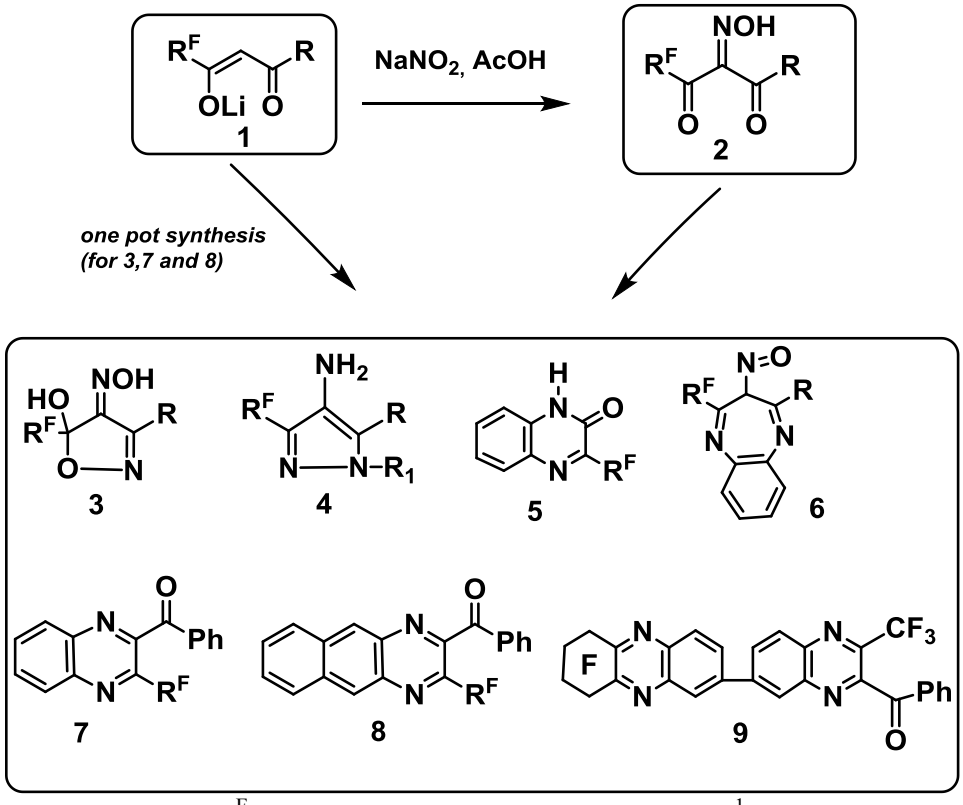
Azoles and azines, bearing a polyfluoroalkyl group are common motifs in biologically active molecules, and their presence in a number of blockbuster drugs and agrochemicals has led to widespread interest in development of new strategies to access these valuable structures.

A reliable method employed to synthesize these compounds is use of cyclocondensation reactions. The recent studies carried out in our laboratories have been focused on exploiting polyfluoroalkyl-containing lithium 1,3-diketonates **1** for the synthesis of acyclic and heterocyclic fluoroalkyl substituted compounds. Herein, we wish to describe the expansion of this approach for cyclocondensations of bi-centered nucleophiles with nitrosated 1,3-diketones, thus leading to isoxazoles, pyrazoles, pyrazines, and diazepines, bearing polyfluoroalkyl groups. From a synthetic standpoint, a diversity of functionalized heterocycles can be obtained, in principle, through this sequence of reactions, involving nitrosation of lithium 1,3-diketonates, followed by condensation of the latter with bifunctional nucleophiles. One-pot process can also be realized to obtain compounds **3**,**7**,**8** in good yields.



R^F = polyfluoroalkyl; R = alkyl, aryl; R^1= H, Ph

This study was performed in the framework of the Federal Program for Support of Leading Scientific Schools (project no. NSh-8922.2016.3.)

Base catalized intramolecular cyclization of – propargyl [3-(4-bromphenyl)prop-2-ynyl]ammonium bromides

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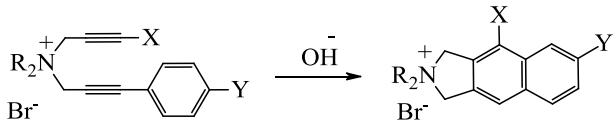
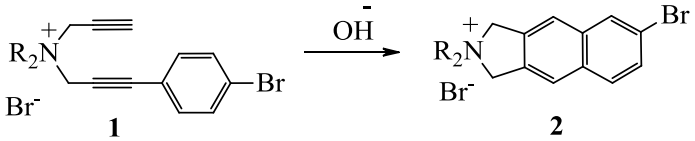
Finding of the ways of synthesis of nitrogen and oxygen-containing heterocyclic compounds is one of the important tasks of organic chemistry. Besides the undoubted theoretical interest they have also practical value: they are included in composition of natural antibiotics, alkaloids, proteins, cardiac glycosides, etc. Among the practically important nitrogen-containing heterocycles there are especially few data relating to a number of isoindolinium compounds and their condensed analogs. This, apparently, can be explained by the deficiency of data relating to the methods of obtaining hard-to-synthesize compounds of this series. In 1969 by A. T. Babayan, E. O. Chukhadjian with co-workers it was shown that ammonium salts containing groups of allylic or propargyl type, along with 3-alkenylpropyn-2-yl, in the presence of 0.2 mol of alkali per mol of initial salt, at room temperature with self-heating undergo intramolecular cyclization. Reaction ends within 5-10 minutes, forming potentially bioactive isoindolinium and dihydroisoindolinium salts with quantitative yields, the synthesis of which by other chemical ways is hard to realize [1]. Later by authors found that in base-catalyzed conditions, with self-heating undergo intramolecular cyclization of ammonium salts containing propargylic type group along with 3-arylpropyn-2-yl, leading to the formation condensed analogs of isoindolinium salts [2,3].



X=H, C_6H_5; Y=H, CH_3, Cl

Among the isoindolinium salts are representatives with pronounced pharmacological activity, which is protected by numerous copyrights of the Soviet Union and patents of RA. Recently it has been established that with self-heating intramolecular cyclization successfully undergo ammonium salts **1**. As a result have been obtained potentially bioactive -6-brombenzo[f]isoindolinium bromides **2** with almost quantitive yields, which by another chemical way is difficult to obtain. It has been established the influence of substituent at the nitrogen atom and aromatic ring.



1 **2**

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Coordination and luminescence properties of novel 1,3-diketone calix[4]arenes

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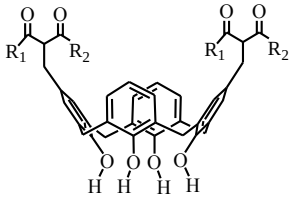
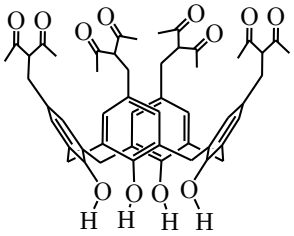
The compounds based on 1,3-diketones are used for solving of many tasks in organic and coordination chemistry and are applied as start reagents for the synthesis of lot of heterocyclic compounds. Moreover, they are known as suitable ligands for the complex formation with metal ions. 1,3-Diketone derivatives and their complexes find application as catalysts and extractants. Luminescent lanthanide complexes attract much attention due to the usage in optical communications, solar energy conversion and bio-medical analysis. It can be explained by the significant antenna effect that 1,3-diketones can exert on the lanthanide-centered luminescence. It is well known also that the calix[4]arene scaffolds are promising for the design of novel ligands as well. In this aspect, we were interested in the introduction of 1,3-diketone substitutes into calix[4]arene platform.



1 $R_1 = R_2 = CH_3$

2 $R_1 = CH_3$, $R_2 = Ph$

3 $R_1 = R_2 = Ph$



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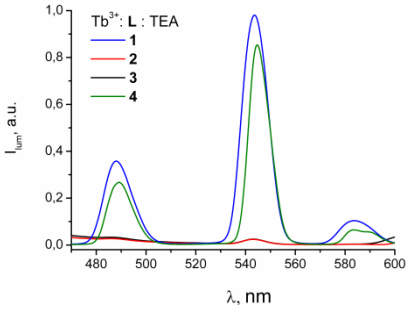
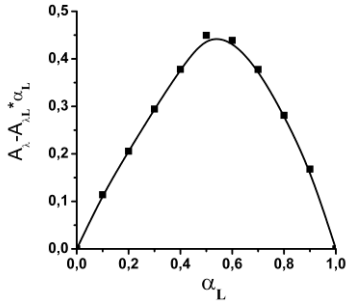
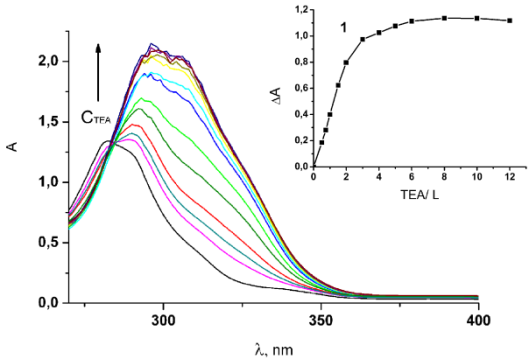


Emission spectra of ligands with Tb^{3+}

L:Ln^{3+} 1:1



The Job plot profile of DMF solution at the varied L:Tb^{3+}



The composition and structure of the synthesized novel ligands as well as their complex formation properties were investigated by using of a variety of physical and chemical methods. The spectral properties of new calix[4]arene derivatives and the luminescent behavior of their Tb^{3+}, Gd^{3+}, Eu^{3+} and Yb^{3+} complexes have been considered with the aim to highlight a structure impact on the complex ability and antenna effect of novel compounds.

This work is supported by the Russian Foundation for basic Research (grant № 16-03-00007 A).

Efficient one-pot synthesis of 6H-pyrrolo[2,3,4-GH]perimidines in polyphosphoric acid

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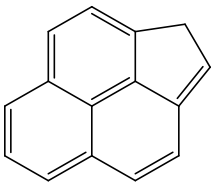
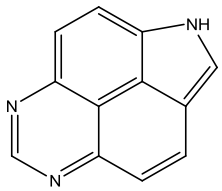
1H-Cyclopenta[cd]phenalenes are interesting polycyclic aromatic architectures that attract the attention due to their physico-chemical properties. Along with pyrene derivatives, such compounds could be used as fluorescent probes, but due to a very low solubility in water and significant carcinogenicity, the potential of these structural fragments for cytological and *in vivo* applications could be limited. We pondered if this issue can be addressed by partial replacement of carbon with nitrogen atoms to afford aromatic polyheterocyclic scaffolds with improved solubility and much lower metabolitic stability.

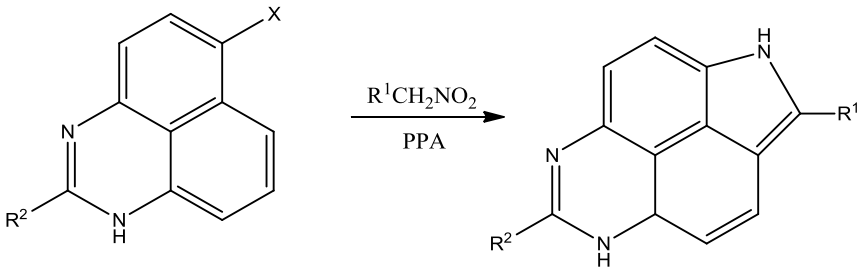


1H-Cyclopenta[cd]phenalene



6H-pyrrolo[2,3,4-gh]perimidine

During the research we have designed a series one-pot and cascade transformations involving an unusual electrophilic behavior of polyphosphoric acid-activated nitroalkanes. These processes involved PPA mediated Schmidt and Beckmann rearrangements, reactions of direct electrophilic amination with azides and acetamidation with nitroalkanes, for the first time arranged in multi-step one-pot processes of increased complexity. The versatility of PPA as an "intelligent" reaction media was showcased.



X = H, NH_2, Ac

Financial support for this work was provided by Russian Foundation for Basic Research (grants № 16-03-00177a and 16-33-00483 mol_a).

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Conformational behaviour of novel 3,7-diazabicyclo[3.3.1]nonane derivatives

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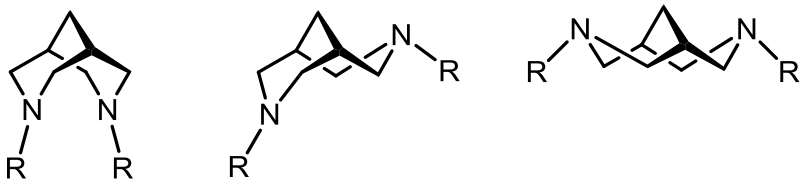
Broad spectrum of biological activity of **3,7-diazabicyclo[3.3.1]nonane** (**bispidine**) derivatives including antiarrhythmic, antiviral, and AMPA receptor modulating, coupled with backbone rigidity and metal complexing abilities made this class of compounds very attractive for medicinal and organic chemists. Moreover, bispidine derivatives show interesting conformational properties. It was shown that these compounds can adopt chair-chair (CC), chair-boat (CB) or boat-boat (BB) conformation depending on the steric and electronic parameters of the substituents (Scheme 1) [1].

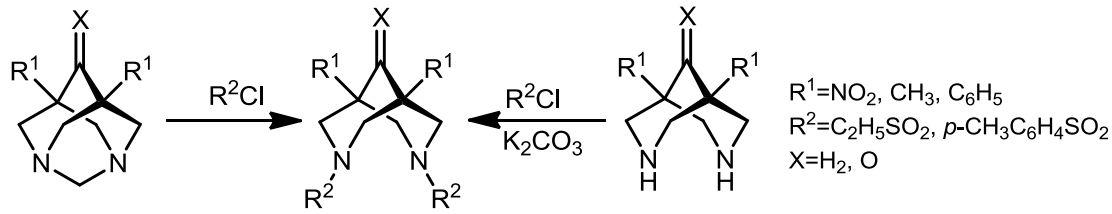


CC **CB** **BB**

Scheme 1. Possible conformations of 3,7-diazabicyclo[3.3.1]nonane derivatives

We have previously employed derivatives capable of conformational switching CB=>CC upon complexation to add stimulus-sensitivity to the liposomal containers and studied the stability and properties of modified bilayers [2-4].

The present study is devoted to the conformational analysis of the novel class of N,N'-disubstituted bispidine derivatives, namely 3,7-disulphonyl-3,7-diazabicyclo[3.3.1]nonanes. The target compounds were synthesized either by direct one-step cleavage of aminal fragment of 5,7-disubstituted-1,3-diazaadamantane or -diazaadamantane-6-one or from corresponding free base of 3,7-diazabicyclo[3.3.1]nonane or 3,7-diazabicyclo[3.3.1]nonan-9-one (Scheme 2).



Scheme 2. Synthesis of target compounds

It was shown that all the synthesized compounds adopted a CC conformation in the crystalline state except for 1,5-diphenyl-3,7-ditosyl-3,7-diazabicyclo[3.3.1]nonan-9-one which was previously shown to exist in a CB conformation [1]. The reasons for such conformational behaviour are now under investigation.

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Binuclear coordination compounds of Cu (II), (I) on the basis of 2-thioxo-tetrahydro-4H-imidazole-4-one: a modification to stabilize Cu 1+ valence state in physiological fluids

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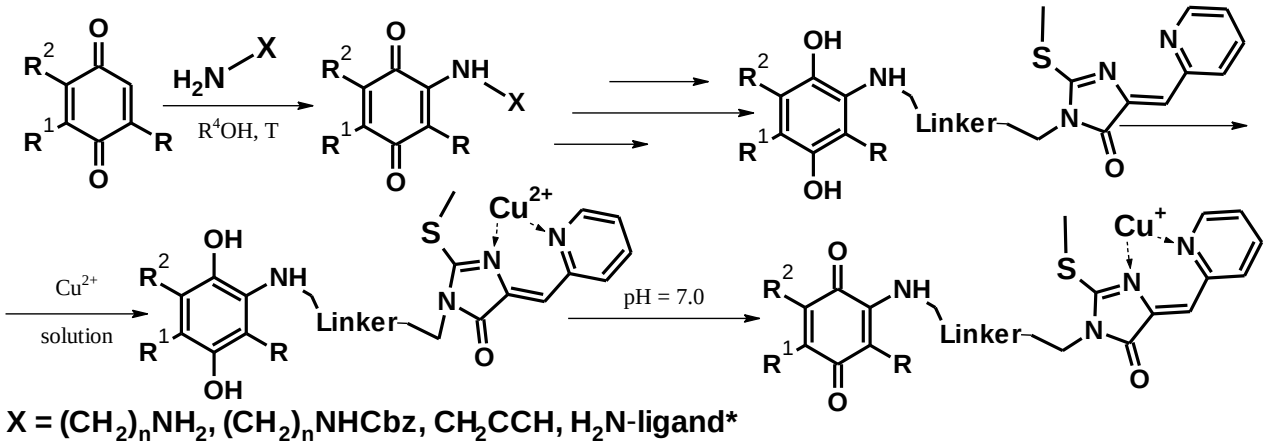
The use of cytotoxic drugs based on platinum has shown that coordination compounds, based on metals, can destroy the cancerous cells, disrupting the structure of DNA, and depriving them of their ability to divide. However, the platinum drugs have a high overall toxicity, and now search is on for anticancer therapeutic agents based on biogenic metals. In particular members of our laboratory have synthesized dinuclear mixed-valence complexes Cu (I, II) containing 2-substituted-5-Alkylthio arylmethylene-4-imidazolin-4-ones, which showed high cytotoxicity against many cell lines [1].

The Cu^{+1} complexes are expected to be more active as antitumor agent and less toxic, compared to mixed valence complexes, due to less metal content in the dosage form, assuming that both complexes are active because of presence of bounded Cu^{+1} atoms in their structure.

But it is necessary to consider that in physiological fluids single valence copper complexes can be oxidized to a valence state of 2+. It has been suggested that the addition of reducing fragment to structure of organic ligand should stabilize the Cu^{+1} valence state. According to calculations using the Nernst's equation the suitable range of electrochemical potentials has hydroquinones (benzoquinone, anthraquinone and menadione in particular).

There are four synthetic routes to the suggested ligands, bearing reducing fragment – hydroquinone and 5-Alkylthio arylmethylene-4-imidazolin-4-one copper binding site: the direct synthesis from quinone and diamine, the synthesis with Cbz-monoprotected diamine, Cu-catalyzed azide alkine cicloaddition click (CuAAC) and amination of quinone with 3-amino-2-thioxo-5-piridylmethilene-tetrahydro-4H-imidazole-4-one* considered.



This work was supported by the Russian Foundation for Basic Research (grant № 16-33- 60166).

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Synthesis of new functionalized 1,2,4-triazoles and their influence on methylation level DNA

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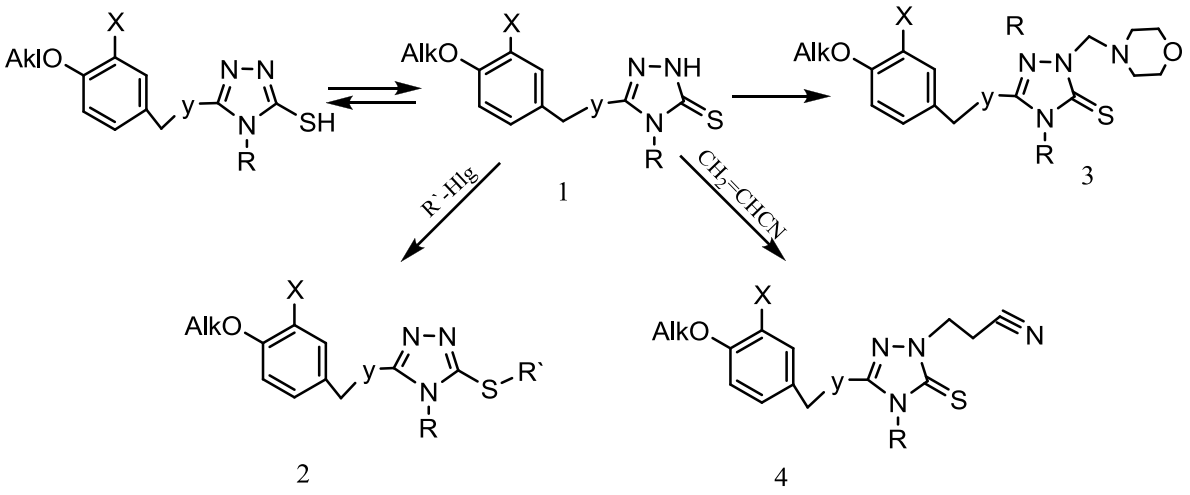
The derivatives of thiol and thionfunctionalized fivemembered ring system 1,2,4-triazole possess a high biological activity, including antibacterial, antiviral, antitumor, antifungal etc [1]. In a continuation of our previous works [2, 3] to search a new active compounds, based on this heterocyclic system and for the study of the relationship between biological activity and chemical structure, herein we report the synthesis and some transformations of new derivatives of substituted 1,2,4-triazoles containing different pharmacophoric groups.



Alk = Me, Et, Bu; X = Cl, Me; Y = 0, $S(CH_2)_2$.
R = Ph, Bn, Allyl; R` = CH_2CO_2H, CH_2CONH_2, CH_2CO_2Et.

As a starting compounds for synthesis was used 3,4,5-threesubstituted triazole 1, which has two reactive sites. The electrophilic substitutions is possible in the position of 3-thiol group (triazoles **2**), as well as in the endocyclic nitrogen atom (triazoles **3,4**).

The investigations showed, that alkylation reactions involved only thiol groups to form the corresponding sulfanylsubstituted 1,2,4-triazoles **2** while the aminomethylation and cyanoethylation reactions takes place exclusively at the N^2 endocyclic nitrogen atoms of **1**.

The structures of the synthesized compounds were confirmed by IR, ^{1}H NMR spectroscopy dates.

The preliminary screening of synthesized compounds showed a significant influcnce on the methylation level of tumor DNA.

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Synthesis of tissue-specific ligands conjugates for the targeted drug delivery to hepatic cells

Hapko V.V., Maklakova S.Yu., Beloglazkina E.K., Zyk N.V., Majouga A.G., Koteliansky V.E.

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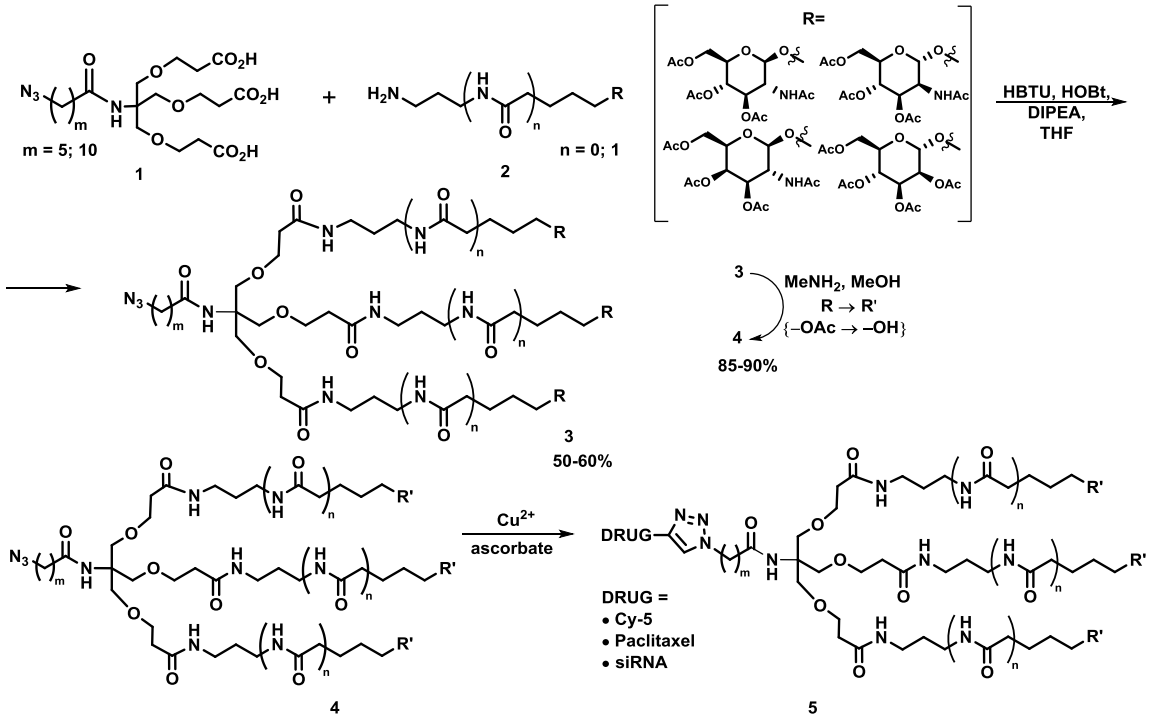
Targeted delivery is a promising approach for various drugs, since it allows both to essentially reduce active concentration of the drug and its toxicity. For the delivery into hepatic cells, asialoglycoprotein receptor (ASGPr) appears to be an appropriate target. This is connected with its predominant and abundant presence on hepatocytes, selective binding with sugar moieties and ability to transport macromolecules through a cell membrane. It is known that the best binding with the receptor is obtained in the case of using branched ligands containing several *N*-acetylgalactosamine residues (*vide infra*) [1].

Liver macrophages (Kupffer cells) are known to be involved in the liver's response to various stresses [2]. To facilitate drug delivery into this type of hepatic cells, mannose receptor abundantly expressed by Kupffer cells might be considered as a suitable target for the synthesis of specific ligands.

This work is devoted to the development and optimization of synthetic approaches to aforementioned ligands.



Scope of applications of synthesized ligands was demonstrated by conjugation with various therapeutic agents. For the conjugates obtained biological studies were carried out.

The work is supported by Russian Scientific Foundation, grant №14-34-00017.

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A three-component one-pot synthesis of multifunctionalized 5,8-dihydropyrido[2,3-d]pyrimidin-4(3*H*)-one and 5,6,7,8,9, 10-hexahydropyrido[4,5-*b*]quinolines.

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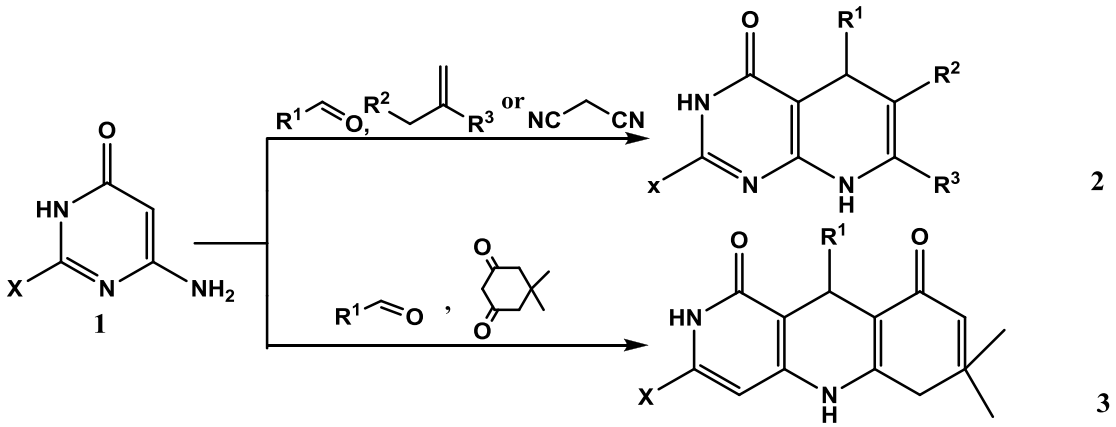
Multicomponent one-pot reactions are of increasing importance in organic and medicinal chemistry. They are leading to interesting heterocyclic scaffolds are particularly useful for the creation of diverse of potentially bioactive molecules for biological screening. Pyrido[2,3-*d*] pyrimidines and pyrimido[4,5-*b*]quinolines represents a heterocyclic ring system of considerable interest because of several biological activities associated with this scaffolds. Some analogues have been found to act as antitumor agents, while others are known antiviral, antibacterial [1,2], antifungal agents [3].

Herein we report a three-component synthesis of novel multifunctionalized pyrido[2,3-*d*] pyrimidine **2** and pyrimido[4,5-*b*]quinolone **3** scaffolds, employing one-pot condensation reactions of 2-substituted 6-aminopyrimidin-4-ons **1**, aromatic or heterocyclic carbaldehydes, dimedon and dicarbonyl compounds, using standard thermal conditions.



2,3 X=NH_2 , OH, SH ; R^1=Ar, Het ; R^2=Ac, CO_2Et, CN ; R^3=Me, NH_2

According to obtained dates some of the studied compounds causes a marked inhibition of methylation level of tumor DNA. Some correlation between in vitro and in vivo dates were determined.

References

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1,3-Dipolar Cycloaddition of Nitrones to Gold(III)-Bound Isocyanides

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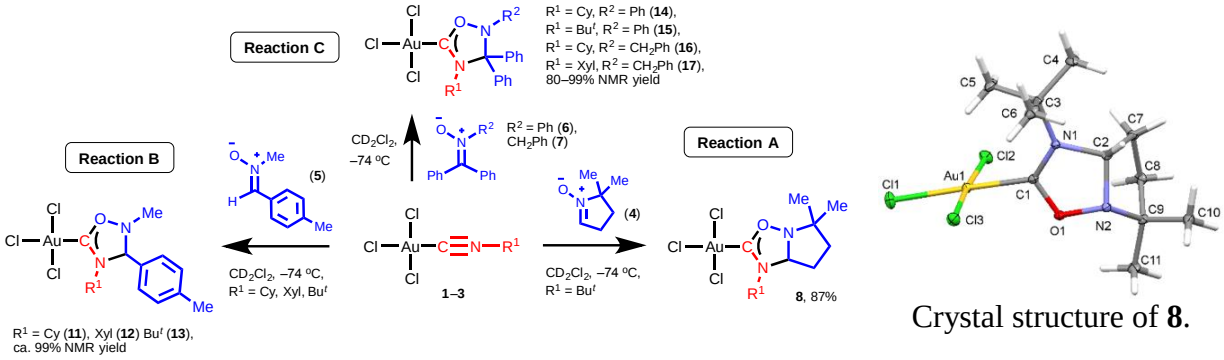
Complexes with *N*-heterocyclic carbenes (NHCs) have become one of the most important classes of catalysts for contemporary organometallic catalysis [1]. Whereas complexes of nearly all transition metals with NHC ligands have been prepared, including gold(I)-NHCs, generation of gold(III)-NHCs is rarely described [2].

In pursuit of our studies, we have recently discovered the first example of 1,3-dipolar cycloaddition of nitrones to gold(III)-bound isocyanides leading to corresponding gold(III)-bound NHCs. Thus, treatment of gold(III)-isocyanides [$AuCl_3(CNR^1)$] (R^1 = Xyl **1**, Cy **2**, Bu^t **3**) with an equimolar amount of 5,5-dimethyl-1-pyrroline-*N*-oxide (**4**) in CH_2Cl_2 at −74 °C leads to the generation of the heterocyclic aminocarbene species **8** (**Route A**) in 87% isolated yield. The reaction of equimolar amounts of the *aldonitrone* *p*-TolCH=N^+(Me)O^- (**5**) or the *ketonitrones* $Ph_2C=N^+(R^2)O^-$ (**6**, **7**) with **1**–**3** in CD_2Cl_2 at −70 ºC revealed the formation of the carbene complexes **11**–**13** or **14**–**17**, as studied by ^{1}H NMR (**Routes B** and **C**). Compound **8** was characterized by elemental analyses (C, H, N), ESI-MS, IR, and 1D (^{1}H, ^{13}C{H}) and 2D (^{1}H,^{1}H-COSY, ^{1}H,^{13}C-HSQC, ^{1}H,^{13}C-HMBC) NMR spectroscopic techniques, while compounds **11**–**17** were characterized by 1D (^{1}H, ^{13}C{H}) and 2D (^{1}H,^{13}C-HSQC) NMR. Structure of compounds **8** and **13** were additionally established by single-crystal X-ray diffraction [3].



Crystal structure of **8**.

This work was supported by the Russian Science Foundation (grant 14-43-00017), Russian Foundation for Basic Research (grant 16-33-60123) and the Grant Program of the President of Russian Federation (grant MK-7425.2016.3). Physicochemical studies were performed at the Center for Magnetic Resonance, Center for X-ray Diffraction Studies, Center for Chemical Analysis and Materials Research (all belong to Saint Petersburg State University).

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New Pd(II) and Ni(II) complexes with 5-aryisoxazole ligands: synthesis and catalytic activity in cross-coupling reactions

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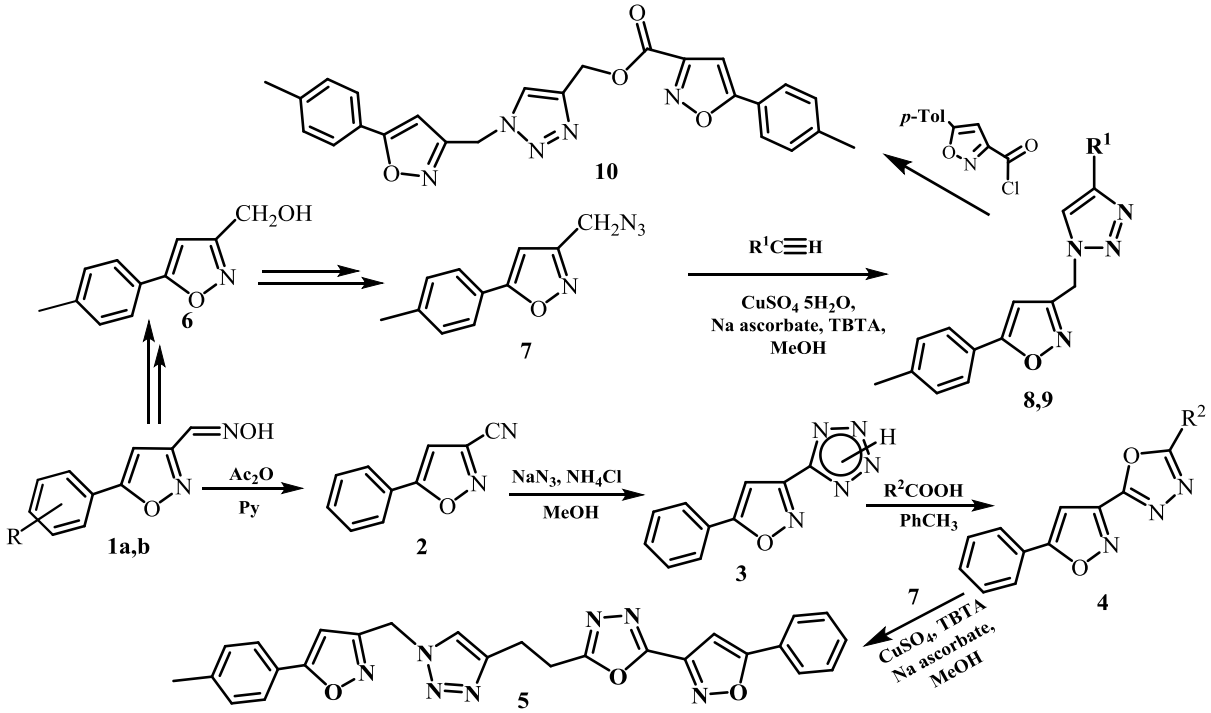
Cross-coupling reactions are widely used in the synthesis of practically valuable products for medicine, agriculture, electronics and other industries. For example, they account for 17% of the total number of different types of reactions used in the synthesis of drug substances [1]. The best-known catalysts for these reactions are palladium complexes [2]. Some complexes of other transition metals have been proposed but they are usually less effective. The ligand nature in the metal complex has a great influence on the activity of the catalyst.

We synthesized a series of isoxazole derivatives with several azole heterocycles in one molecule (**1-10**) which are promising as ligands for transition metal complexes.



R = H (**a**), 4-Me (**b**) ; R^1 = CH_2OH (**8**), Me_2C-OH (**9**); R^2 = $CH_2CH_2C{\equiv}H$

Using these ligands (L) the new Pd(II) and Ni(II) complexes were obtained which have the composition $LPdCl_2$ and $LNiCl_2$ respectively. The synthesized palladium complexes exhibit the highest catalytic activities in Suzuki, Heck and Sonogashira reactions.

This work was supported by the Belorussian Foundation for Basic Research (grant № X16P-006) and Russian Foundation for Basic Research (grant № 16-58-00059-Bel_a).

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Synthesis of phosphoryl-substituted azaheterocycles using hydrazides of phosphorylthioformic acid

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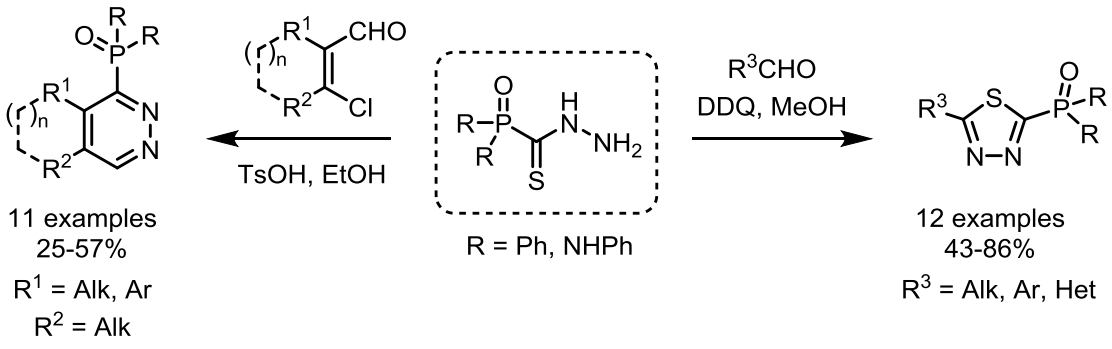
Phosphoryl-substituted azaheterocycles belong to an important class of organophosphorus compounds due to their applications in medicinal chemistry, material sciences, and organic synthesis. [1] Therefore, the development of new efficient synthesis of these molecular targets remains an active area of research.

Herein, we report a previously unknown, convenient and highly reactive hydrazides of phosphorylthioformic acid reagent for the concise synthesis of medium–ring P,N-heterocyclic systems. Based on our previous results [2] and the chemistry of hydrozones, we have elaborated flexible synthetic approaches towards unknown POR_2 functionalysed 1,3,4-thiadiazoles and pyridazines with chemoselective control of heterocyclization patterns.



Phosphamide and phosphine oxide derivatives of pyridazines were exclusively synthesized *via* condensation of β-chlorovinilaldehydes with hydrazides of phosphorylthioformic acid. The method was found quite general since both aliphatic and aromatic aldehydes and steroid derivatives reacted smoothly providing diverse pyridazines. Using non-functionalized aldehydes as a substrate in one-pot oxidation protocol, 2-phosphoryl substituted 1,3,4-thiodiazolines were obtained in high yields and minimum synthetic steps. This transformation was performed with different aryl, hetaryl or aliphatic aldehydes.

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Photochemical behaviour of styryl dyes with sulfonatopropyl substituents in solutions and in the presence of cucurbit[8]uril

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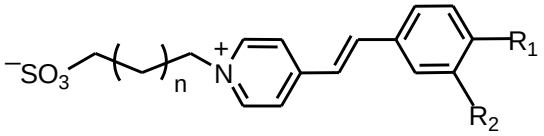
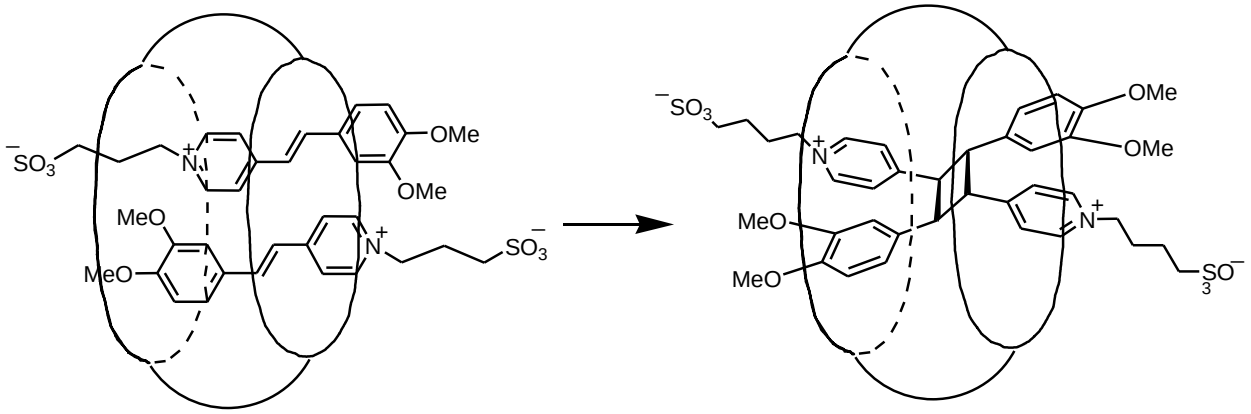
It is known that styryl dyes are capable of forming inclusion complexes of cucurbiturils in aqueous solutions.

The subject of particular interest as a 'guest' molecule for the complexation properties studies of cucurbiturils are sulfonatoalkyl derivatives of styryl dyes. Owing to their betaine structure, these compounds show higher solubility compared to their cation analogues and are able to form stable complexes with cavitands.



1: n=1, R_1=R_2 = OMe
2: n=2, R_1=R_2 = OMe
3: n=1, R_1+R_2 = $(OCH_2CH_2)_6$

It was found that in crystals of the complex the vinylpyridine fragments of each dye are located directly in the cavity. Nevertheless, the arrangement of components is unfavorable for the proceeding of [2+2]-photocycloaddition reaction. However, such a reaction takes place upon visible-light irradiation giving the only isomer of possible cyclobutane derivatives.



In this study, the length of N-substituent in heterocyclic moiety and the steric volume of aromatic fragment of styryl dye were varied to determine their impact on stability of the complexes and ability of the dye to undergo [2+2]-photocycloaddition reaction.

This work was supported by the Russian Science Foundation (grant № 15-13-00163).

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Synthesis of PSMA targeted pH-dependent prodrugs

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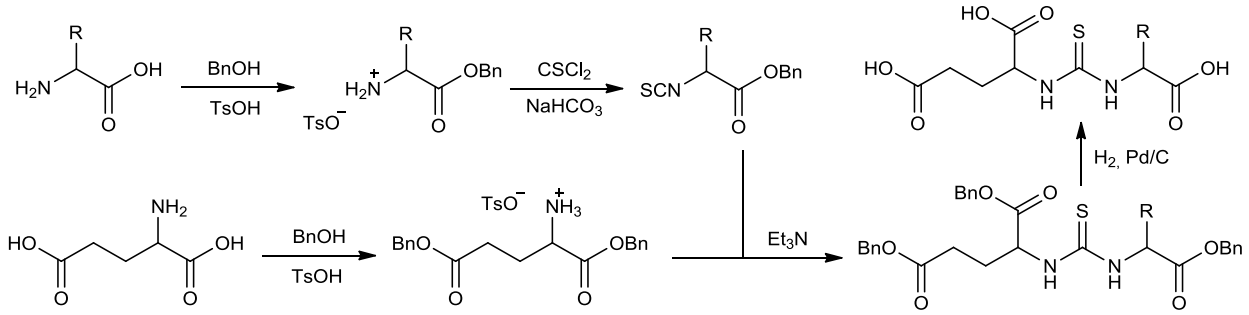
Nowadays the photodynamic therapy (PDT) with using photosensitizers is among the most progressive cancer treatments and is actively investigated for light-accessible cancers such as prostate. For improving the tumor-specific delivery of photosensitizers the last can be targeted to prostate-specific membrane antigen (PSMA) that overexpressed on the surface of prostate tumors and in the neovascular endothelium of most solid tumors such as lung, colon, pancreas, renal cell and melanoma. Majority of small-molecules PSMA ligands/inhibitors involves glutamate ureas moieties and demonstrates improved pharmacokinetic features and principally blood clearance in comparison with traditionally applied for PDT antibodies. Many studies on early diagnostics and treatment of tumor diseases based on the lower pH of tumor cells in contrast with healthy cells, but there is no article's observing the intramolecular interactions of urea moieties within tumor cells.

In this work the intramolecular cyclization processes of PSMA-targeted thioureas on low pH conditions (pH~6) are studied. Thioureas are easily enabled for acidic cyclization with producing the cytotoxic 2-thyohydantoines. Synthesis of thioureas from glutamic acid and different α-aminoacids involves preliminary protection of carboxyl groups of amino acids, obtaining isothiocyanate from α-aminoacid by reaction with thiophosgene, condensation of thiourea and deprotection of benzyl groups:



A number of synthesized PSMA targeted thioureas was evaluated for cytotoxicity and PSMA binding affinity and studied for its metabolism in tumor cells.

This work was supported by the Russian Foundation for Basic Research (grant № 16-33- 60166).

Synthesis and biological evaluation of doxorubicin-albutoin and paclitaxel-albutoin twin drugs

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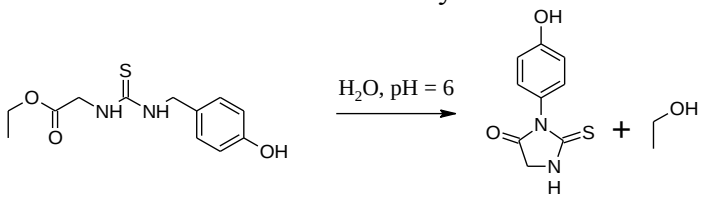
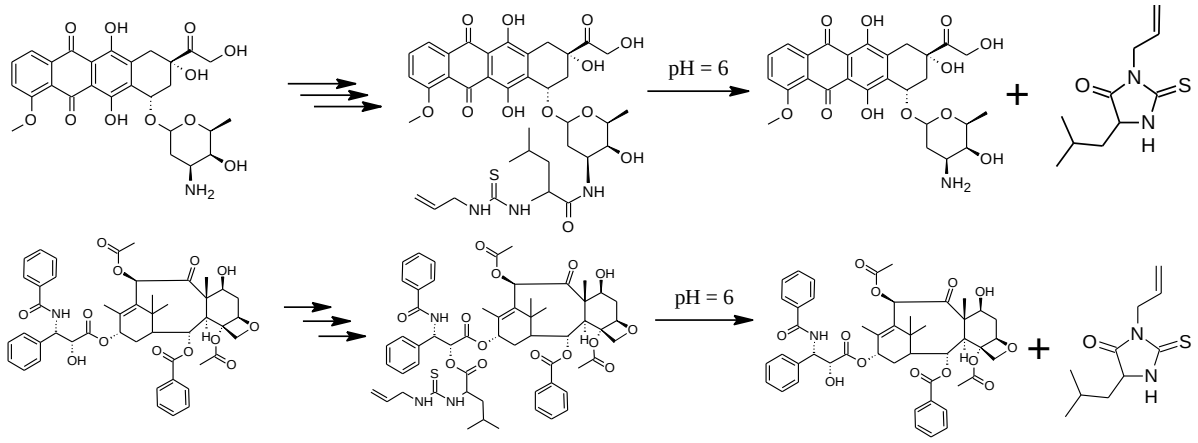
Almost all of the drugs currently used for chemotherapy have a lot of side effects due to their general toxicity. Therefore, synthesis of selective antineoplastic agents possessing low general toxicity is now subject of numerous studies.

Twin drugs are defined as compounds containing two pharmacophore components, which are expected to produce pharmacological effects of individual pharmacophores. In particular, we anticipated that doxorubicin-albutoin and paclitaxel-albutoin twin drugs should act as antineoplastic and anticonvulsant agents. They are also expected to exhibit low general toxicity, whereas their structure dramatically differs from the structure of doxorubicin and paclitaxel respectively.

It is known that the extracellular fluid of tumors is significantly more acidic than the extracellular fluid of normal tissues with pH values 5.6-6.9 and 6.9-7.3 respectively [1]. Also, we have shown that some thiourea derivatives are able to cyclize under acidic conditions (pH=6):



Given the above, we synthesize thiourea-based compounds bearing antineoplastic and anticonvulsant pharmacophores:



In the near future, it is being planned to study the cytotoxicity of the obtained compounds towards HEK-293, SiHa, A-549 cell lines using MTT assay and to compare the results with the data obtained for normal cells.

This work was supported by the Russian Foundation for Basic Research (grant № 16-33- 60166).)

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Solvent-free synthesis method of 1,3-bis(benzo-1,2,3-triazolyl)propane

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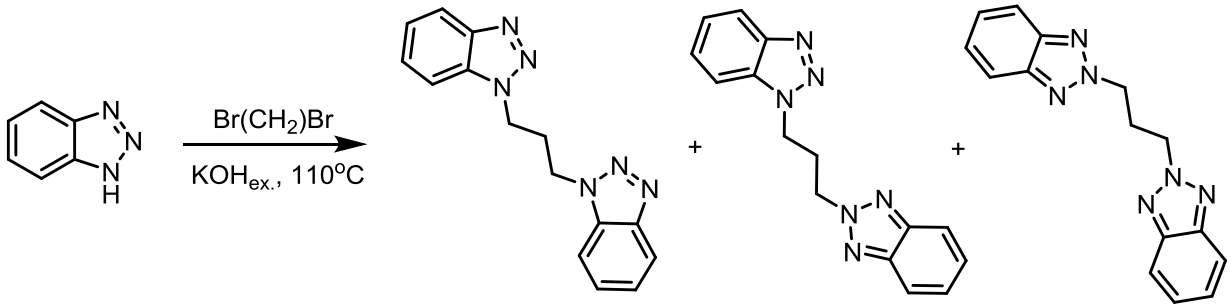
Metal-organic frameworks (MOFs) are extremely perspective structures. They consist of regulated organic ligands and complexing metal ions. MOFs can have a gas storage ability; they can be applied in catalytic or drug delivery systems. To produce original MOFs new organic ligands are needed.

1,2,3-Benzotriazole derivatives are synthesized with superbasic medium in an aprotonic solvent commonly [1,2]. The series of bis(benzo-1,2,3-triazole)alkanes was obtained with KOH excess in anhydrous DMSO at 80°C. Yields were about 80% [3].

The possibility of solvent-free synthesis was demonstrated by the obtaining of 1,3-bis(benzo-1,2,3-triazolyl)propane. KOH powder, 1,2,3-benzotriazole and 1,3-dibromopropane were loaded in a screw-cap vial, fused at 110°C during an hour. The reaction mixture was dissolved in water and extracted with dichloromethane. The extract was washed with water. The solvent was distilled under vacuum, product was dried.



Overall yield of 1,3-bis(benzo-1,2,3-triazolyl)propane isomers was 67%. Product composition was proved by gas chromatography mass-spectrometry method. The solvent-free synthesis of ligands significantly simplifies preparation and purification processes.

This work was supported by Russian Science Foundation, project № 15-13-10023.

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Donor–acceptor complexes of bis(18-crown-6)azobenzene with bisammonium derivatives of heterocyclic compounds

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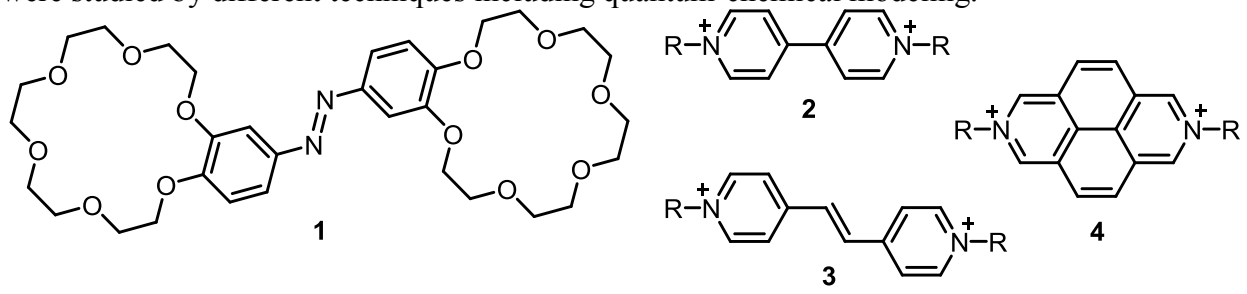
Previously we described the synthesis of supramolecular donor–acceptor complexes of bis(18-crown-6)stilbene with bisammonium derivatives of heterocyclic compounds [1,2]. The complexes were shown to possess a high stability in solution due to the double macrocycle–ammonium ion interaction. They can be used as "off–on" fluorescent indicators for metal cations [2] and as convenient model systems to study ultrafast electron transfer reactions [3].

In order to evaluate the effect of the nature of the donor component on the properties of the supramolecular complexes, we synthesized bis(18-crown-6)azobenzene **1**, a weaker electron donor in comparison with the analogous stilbene. The structure, thermodynamic stability and photochemical properties of complexes of azobenzene **1** with bisammonium compounds **2–4** were studied by different techniques including quantum-chemical modeling.



It was found that the stability constants of complexes **1**·(**2–4**) are lower (up to tenfold) in comparison with the corresponding complexes of bis(18-crown-6)stilbene. The quantum yield of *E–Z* photoisomerization of azobenzene **1** decreases by an order of magnitude upon complexation with viologen **2** (excitation in the region of the $\pi\rightarrow\pi^*$ absorption of **1**). This fact is attributable to relatively fast excited-state electron transfer reaction between the complex components. The charge-transfer absorption band of complex **1**·**2** is unobservable because it lies between the more intense bands associated with the local $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ electronic transitions of **1**.

This work was supported by the Russian Science Foundation (project № 14-13-00076) and the Russian Academy of Sciences (Branch of Chemistry and Material Sciences).

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Oxidative coupling of sulfonyl hydrazides under the action of electric current

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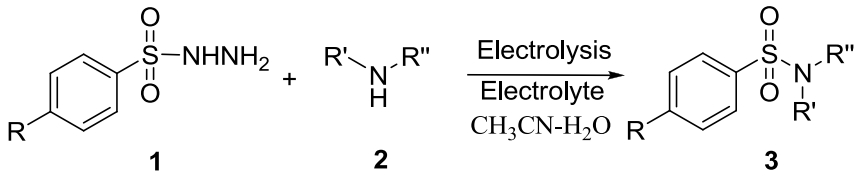
Over the past decades the methods of oxidative coupling are finding ever-widening application for the construction of structures containing N-S bonds, which are frequently used as antibacterial, antiinflammatory and antitumor agents. It is caused by the great diversity of employed starting reagents and mild reaction conditions. Sulfonyl hydrazides are often applied as S-reagents: sulfonyl radicals are generated from them in the presence of various oxidants **[1]**. These radicals can enter into a number of oxidative coupling processes.

Electric current is widely used for the conducting of redox processes with organic compounds. This is due to its low price and availability, a great variety of electrochemical reactions mechanisms and no need for waste utilization, which is formed when chemical oxidants are employed **[2]**.

We for the first time carried out oxidative N-S coupling reaction with the use of sulfonyl hydrazides **1** by the action of electric current. Amines **2** were used as N-components. As a result, sulfonamides **3** were obtained in 56-98% yield (Scheme 1).



Scheme 1

The process is conducted in undivided electrochemical cell with cheap and available graphite anode and iron cathode employing halides as redox mediators and supporting electrolytes. This system allows to achieve high current densities and consequently to carry out gram-scale syntheses in short time **[3]**.

This work was supported by the Russian Science Foundation (grant №14-23-00150).

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Transformation of *β*-carbolinium quaternary salt with salicylaldehyde derivatives

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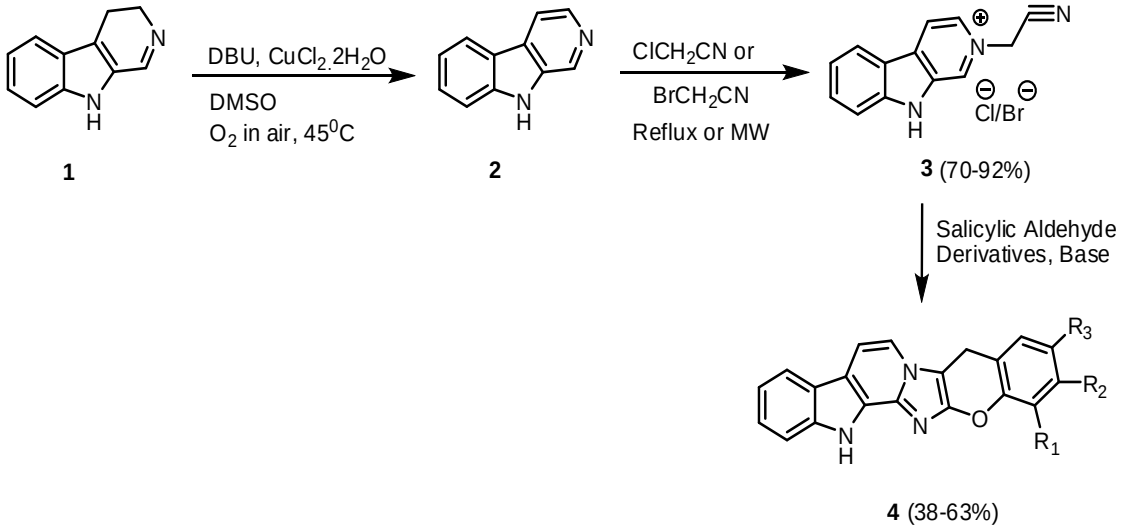
β-Carboline compounds from natural and synthetic sources are a class of indole alkaloids with the remarkable biological and pharmacological properties [1–2]. Several studies on structure-activity relationship of β-carbolines [3-4] shown that anticancer activity is one of outstanding properties of these compounds.

Inspired by that, we study on this kind of compound including synthetic method and their bioactivities. We wished to design a simply synthetic way affording the *β*-carboline scaffold. One-pot cascade reactions have many advantages over multistep sequences such as a reduction of the time reaction, a removal of the step of isolating unstable intermediates, a reduction of the purification step [5-6]. In the present work, we report the synthetic result of hexacyclic substances **4** containing *β*-carboline moiety as key subunit based on the reaction of *β*-carbolinium salt with salicylaldehyde derivatives.



1 **2** **3** (70-92%) **4** (38-63%)

Three components including a salt (**3**), a salicylic aldehyde derivative and a base in an appropriate solvent were refluxed for 4h affording the desired compounds **4** (38-46%). Their bioactivities of these new substances will be presented in another report.

This work was supported by the Vietnam NAFOSTED program and Russian Foundation

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New quinazoline derivatives as perspective components for optical materials

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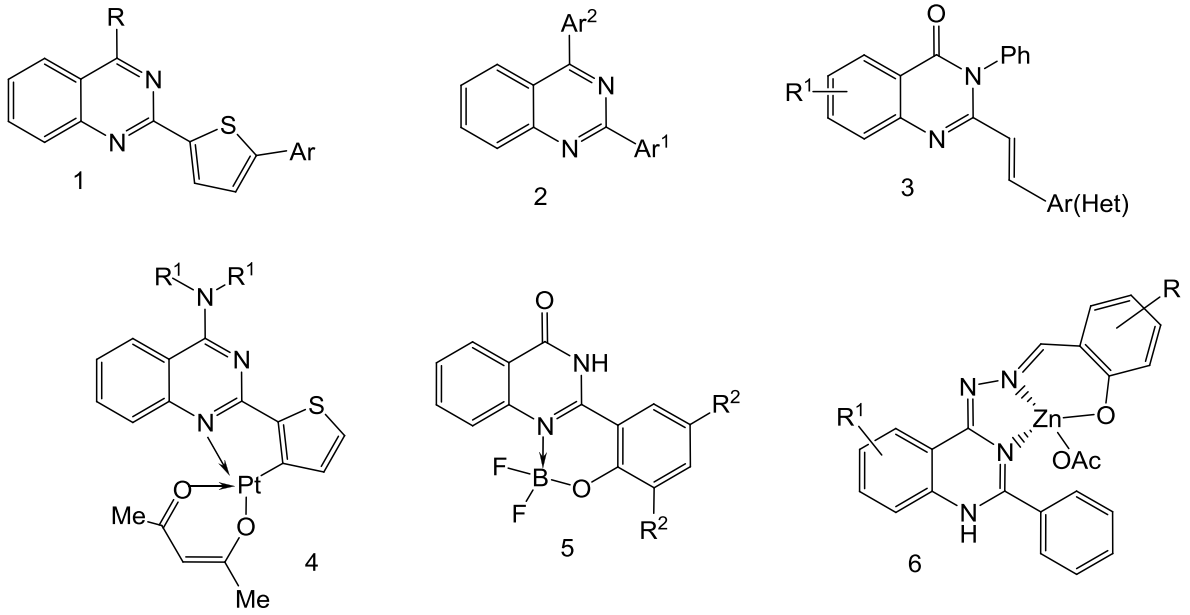
Benzodiazine derivatives have found technical applications as dyes, electroluminescent materials, organic semi-conductors, materials for solar cell devices and as suitable ligands in coordination chemistry [1, 2].

The synthesis of the series of push-pull aryl 2-(thiophen-2-yl)quinazoline derivatives **1** has been achieved, and the ability of some of these molecules to function as colorimetric and luminescent pH sensors has been demonstrated with significant color changes and luminescence switching upon the introduction of acid [3]. Novel 2,4-diarylquinazolines **2** as well as 3-phenyl-*trans*-2-(aryl/heteryl)vinyl-3*H*-quinazolin-4-ones **3** have been obtained and their photophysical properties have been studied. Synthetic approaches to chelate compounds with quinazoline ligands **4-6** have been developed [4, 5].



This work was supported by the Russian Foundation for Basic Research (grant № 17-03-00306) and Russian Scientific Foundation (grant 16-43-02020).

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Acylation of resorcinarene with *N,N*-dimethylcarbamoyl and *N,N*-dimethylthiocarbamoyl chlorides. Factors determining the reaction performance

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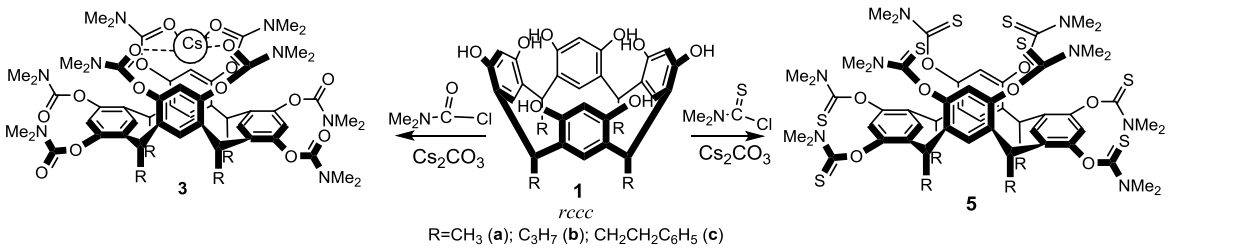
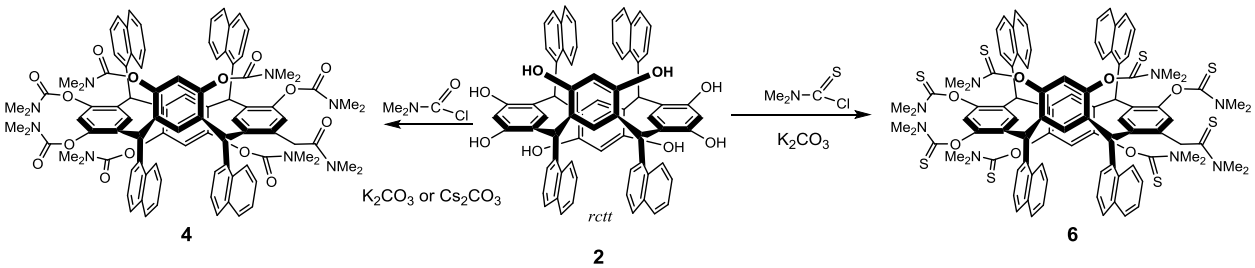
Carbamoylation and thiocarbamoylation of resorcinarenes in the presence of alkali metal carbonates were studied. The effects of the pre-organization of the resorcinarene molecule, the base used, and the nature of the acylating reagent on the reaction outcome were demonstrated.

In the interaction *rccc* resorcinarenes **1** with the carbamoyl chloride reaction proceeded more effectively in the presence of Cs_2CO_3, due to the a high capacity of octacarbamoylated resorcinarenes **3** in conformation *boat* for recognition, binding, and recovery of cesium cations. Choice of bases (Cs_2CO_3, K_2CO_3) had no substantial effect on the results of carbamoilation of *rctt* tetranaphthylresorcinarene **2.** In both cases, the reaction ended in the formation of an individual compound: octacarbamoylated derivative **4.**





Thiocarbamoylation of *rccc* resorcinarenes **1** in the presence of Cs_2CO_3 proceeded selectively and led to the fully acylated resorcinarenes **5**. Under the same conditions, acylation of tetranaphthylresorcinarene **2** with *N,N*-dimethylthiocarbamoyl chloride afforded a mixture of compounds with different degrees of functionalization. Octa(thiocarbamate) **6** could be obtained in good yield only in presence of K_2CO_3.

The work was supported by the Russian Foundation for Basic Research (grant № 15-03-03345a).

Synthesis of dichlorodiazobutadienes from nitrobenzaldehydes

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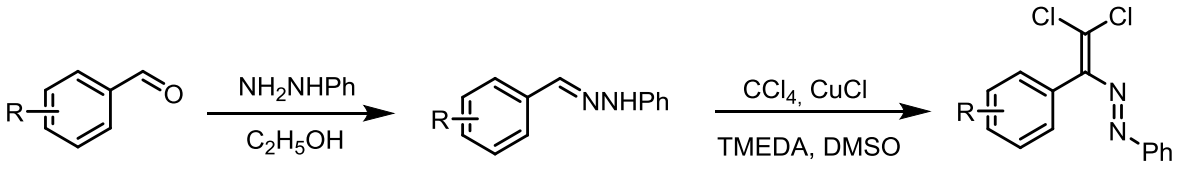
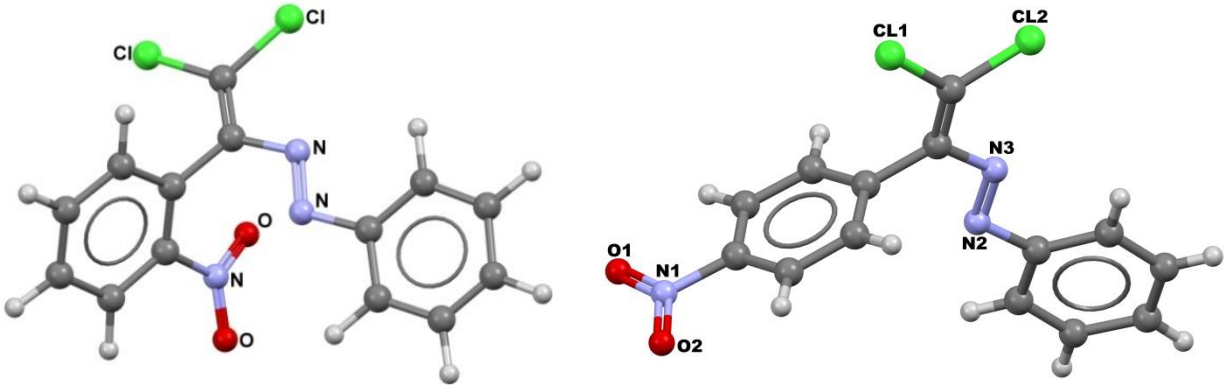
We studied the reactions of N-substituted hydrazones of nitrobenzaldehydes. The presence of conjugated π-electron system of dichloro-substituted carbon with acceptor azo group in obtained compounds, opens up new ways for the synthesis of various structures. At the same time, considering the fact that the synthesized products have chlorine atoms in the structure, they are of interest for the study of non-covalent halogen-halogen interactions[1]. The study of nature of non-covalent as the heteroatomic, and homoatomic halogen-halogen interactions and the ability to manipulate them, will allow to obtain the crystalline structures, which can be used for the construction of supramolecular structures. It is also known that a nitro group can be considered the main source of NO, which is one of the necessary and universal regulator of metabolic functions and unique signaling molecule, whereby the cells can exchange information. So research of these compounds as biologically active systems is of particular interest.



R= 2-NO_2, 3-NO_2, 4-NO_2



Molecular structures of ***(a)*** *(E)-1-(2,2-dichloro-1-(2-nitrophenyl)vinyl)-2-phenyldiazene,* ***(b)*** *(E)-1-(2,2-dichloro-1-(4-nitrophenyl)vinyl)-2-phenyldiazene*

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Studies in the field of new rearrangement in the series of 7-benzyl-2,7-naphthyridine derivatives

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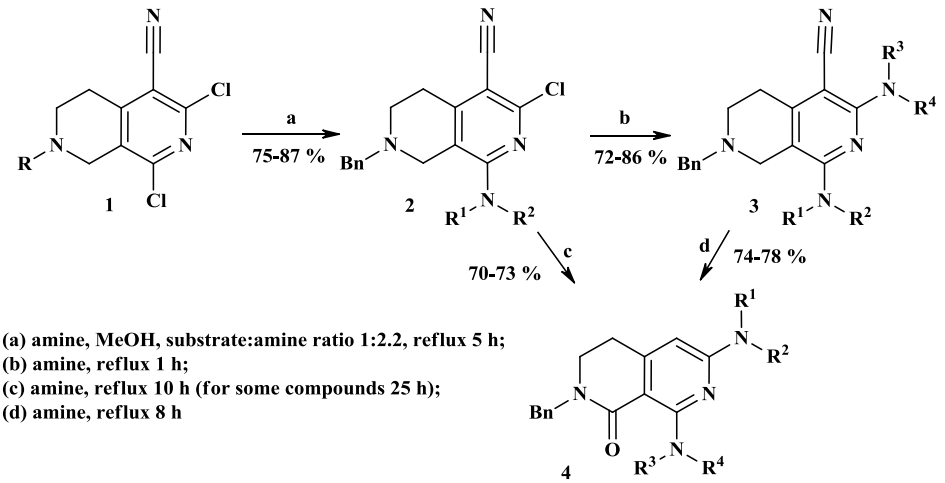
In our previous paper [1] the reactivity of 7-methyl-2,7-naphthyridine **1a** with several primary and secondary cyclic amines was examined. The accurate investigation of the course of this nucleophilic process has shown that during this reaction an unexpected rearrangement could occur: the structure of the rearrangement products was confirmed by different spectroscopic methods (IR, ^{1}H and ^{13}C NMR, MS) and as well as by X-ray analysis. Continuing our research in this field, herein we describe the synthesis and the rearrangement of 7-benzyl-2,7-naphthyridine derivatives **2**. Thus, by refluxing compounds **2** with some primary amines for 10 h, the relevant rearrangement products, 2-benzyl-6,8-diamino-3,4-dihydro-2,7-naphthyridin-1(2*H*)ones **4** were obtained. Compounds **4** were also obtained starting from the relevant intermediate products: 1,3-diamino derivatives **3**. During these investigations we have found some new results. Thus, by comparing the data obtained with 7-benzyl-3-chloro-2,7-naphthyridines **2** with those observed in the instance of 3-chloro-7-methyl-2,7-naphthyridines [1] it has been ascertained that the replacement of the methyl group on the piperidine ring of the 2,7-naphthyridine system with the benzyl one led to the following new situation:

a) the rearrangement took place significantly slowly and in some cases it did not occur at all;
b) the temperature at which the rearrangement occurred was significantly higher.



1. a: R = Me; **b**: R = Bn; **2**–**4**. R^1, R^2, R^3, R^4 = H, alkyl; R^1+R^2 = cycloalkyl.

Moreover, we have found that in the case of some secondary amines the rearrangement (whose mechanism has been elucidated by us [1]) could occur with some difficulty.

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Chalcone-based synthesis of 1,3-diaryl-3-isothiocyanatopropan-1-ones

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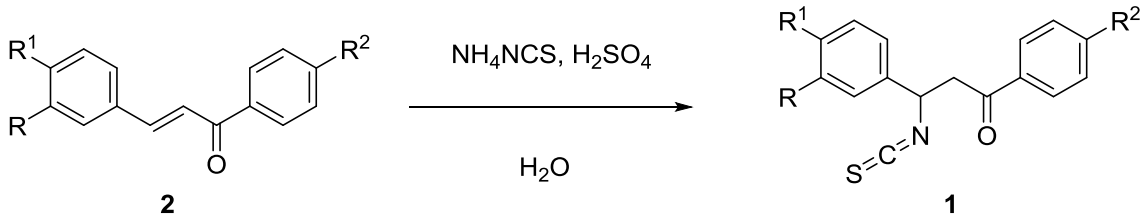
β-Isothiocyanato aldehydes and ketones with two highly reactive functional groups are valuable starting materials for the synthesis of a large number of nitrogen-containing heterocyclic compounds [1]. Commonly, they are prepared by the addition of thiocyanic acid to α,β-unsaturated aldehydes and ketones in water. Success of this reaction is highly dependent on the substrate structure, particularly on the nature of substituents. Therefore, although a number of isothiocyanates starting from alkyl-substituted unsaturated carbonyl compounds was described in the literature, there are only few reports on preparation of aryl substituted isothiocyanates [2]. Here, we present a simple and general procedure for the preparation of 1,3-diaryl-3-isothiocyanatopropan-1-ones **1** from chalcones **2** [3].



2 **1**

R, R^1, R^2 = H, Me, OMe, *t*-Bu.

We found that isothiocyanates **1** could be prepared in good to moderate yields by reaction of chalcones **2** with thiocyanic acid generated *in situ* by treatment of thiocyanate ammonium with dilute sulfuric acid. This reaction proceeded under heterogeneous conditions, and its result (yield and purity of **1**) depended on a number of factors, including molar ratio of reagents, concentration, temperature, and reaction time. Principal condition for successful proceeding of the reaction is the formation of emulsion in the reaction mixture. It should be stressed that its formation does not depend on the melting point of the starting chalcone as evidenced by our data. The optimal overall volume of water was found to be 0.38 mL per 1 mmol of chalcone, and the chalcone/NH_4NCS/H_2SO_4 molar ratio was found to be 1:6:3. If emulsion did not form at room temperature under these conditions, first, slight heating at 50 °C for 1.5 h should be applied, second, 3 equivalents of H_2SO_4 should be added.

The prepared isothiocyanates **1** were used in the synthesis of 7-aryl substituted 2,4,5,6-tetrahydro-3*H*-1,2,4-triazepine-3-thiones [4].

This work was supported by the Ministry of Education and Science of the Russian Federation (basic part of government order, 4.9596.2017/BCh) and the Russian Foundation for Basic Research (grant No. 15-03-07564).

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Role of conformations of substituted 1,4-diazepine heterocycle in synthesis of diazepinoporphyrazine complexes

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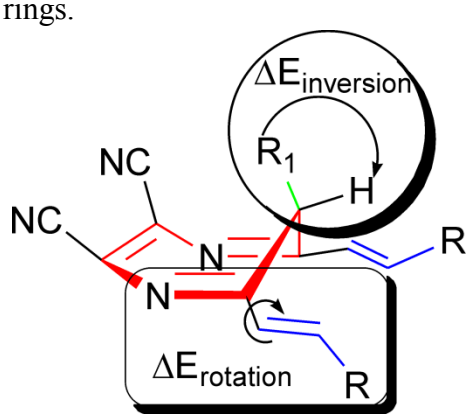
The synthesis of tetrapyrrolic macrocycles containing 1,4-diazepine moieties is a promising direction for creation of new photosensitizers [1] The physicochemical properties of these compounds can be easily changed by introducing various substituents into the 1,4-diazepine heterocycle [2–4]. Thus, the development of synthetic approaches to form various substituted 1,4-diazepine-2,3-dicarbonitriles should greatly improve the accessibility of precursors for the synthesis of macroheterocyclic photosensitizers with annulated 1,4- diazepine rings.



A series of 5,7-bis(2'-arylethenyl)-6*H*-1,4-diazepine-2,3-dicarbonitriles, including derivatives substituted with propyl group at the C6 position, has been prepared [5]. 2D NOESY NMR spectroscopy combined with quantum-chemical calculations at the B3LYP/6-31G(d,p) level of theory demonstrated that steric effects play a key role in the conformational behavior of n-alkyl-substituted 1,4-diazepinodicarbonitriles in solution.

Analysis of the experimental and theoretical data on the intramolecular, steric, and electronic interactions in 5,7-bis(2'-arylethenyl)-6*H*-1,4-diazepine-2,3-dicarbonitriles reveals effective ways to control the physicochemical properties of both 1,4-diazepinodicarbonitriles, and the macrocycles based on them, by changing the nature of the substituents introduced into the 1,4-diazepine heterocycle. In summary, we have demonstrated the possibility of controlling the selective synthesis of low symmetry diazepinoporphyrazines by changing the conformation of substituted 1,4-diazepine heterocycle for the first time.

This work was supported by RFBR (Grant Nos. 17-03-01371, 16-33-00097, 15-03-05890) and the Council under the President of the Russian Federation for State Support of Young Scientists and Leading Scientific Schools (Grant MD-2991.2017.3).

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Imidazo[2,1-*b*]benzothiazoles: A novel class of $GABA_A$ receptors modulators

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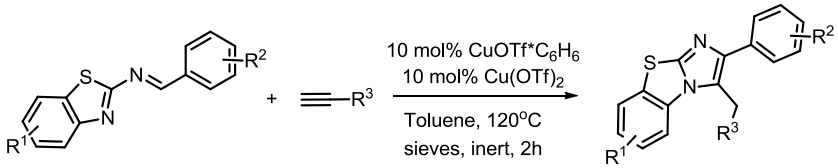
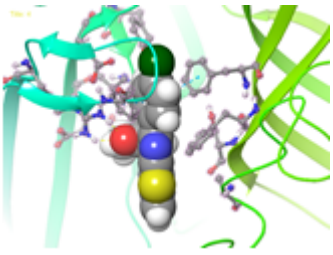
The γ-aminobutyric acid type A receptor ($GABA_AR$), a heteropentameric chloride ion channel, is the principle target for the major inhibitory neurotransmitter, γ-aminobutyric acid (GABA), within the central nervous system (CNS).[1] The clinical use of drugs that alter $GABA_AR$ function as anxiolytics, hypnotics and anticonvulsants provides ample proof of concept that the $GABA_A$ receptor represents a validated target for medicinal chemistry. $GABA_AR$ are modulated by a variety of drugs such as benzodiazepines (BDZ), barbiturates, neurosteroids and imidazo[1,2-*a*]pyridines. The pharmacological properties of $GABA_AR$ modulators are largely determined by their binding sites. Thus the use of BDZ binding site modulators is associated with undesirable effects including reduced coordination, cognitive impairment, increased accident proneness, physical dependence, and withdrawal symptoms.

In the present study, we disclose the results of our studies on a new series of $GABA_AR$ BDZ binding site modulators. With the aim of obtaining active compounds we have focused our efforts on the imidazo[2,1-*b*]benzothiazoles – structural analogs of imidazo[1,2-*a*]pyridine drugs. Imidazo[2,1-*b*]benzothiazoles ligands have been optimized with respect to affinity for the $GABA_AR$ BDZ binding site by using a molecular docking optimization approach. A number of predicted high affinity ligands have been obtained *via* tandem copper-catalyzed *5-exo dig* condensation of acetylenes with Schiff bases derived from 2-aminobenzothiazoles and aromatic aldehydes [2,3]. Screening of their affinity for BDZ binding site of $GABA_AR$ using competitive radioligand binding studies reviled high-affinity interactions (IC_{50} 10-2000 nM). Anxiolytic activity and low toxic effects *in vivo* were estimated using zebrafish model. Two ligands (R^1 = H, R^2 = *o*-Cl, *o,p*-Cl, R^3 = $CONMe_2$) were selected as hit-compounds displaying subnanomolar affinities (IC_{50} 6-10nM), comparable with zolpidem comparison drug (IC_{50} 32nM).



R^1, R^2= EDG, EWG; R^3= CO_2X, $CONX_2$

33-76%



R^1= H; R^2= Cl; R^3= $CONMe_2$
IC_{50}= 10 nM

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Synthesis and spectral properties of linear and cyclic polyamino functionalized BODIPY

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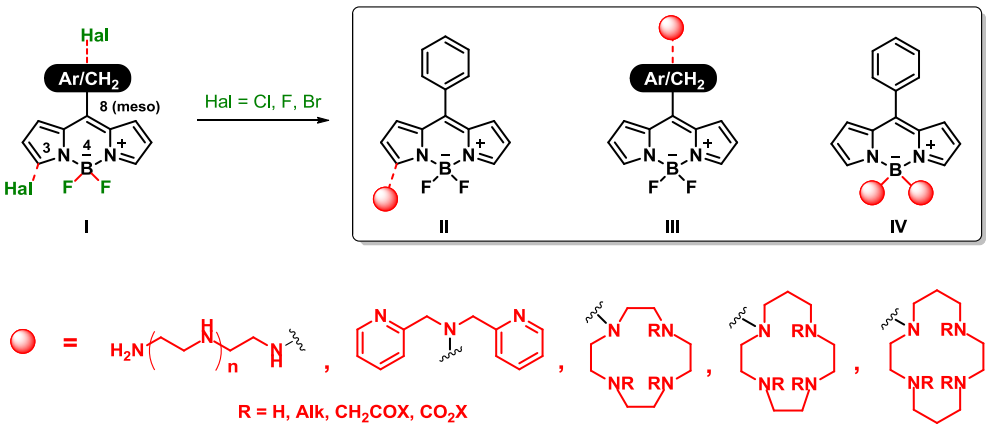
The development of sensitive 'multitechnique' heavy metal ion sensors allowing simultaneous detection with UV-vis, fluorescence spectroscopy and "naked eye" have gained much research interest due to the great demand for their application in many fields such as biochemistry, environmental chemistry, food chemistry and life science. [1] Such sensors represent the modular structure consisting of chelator linked directly or through short spacer with fluorescent moiety or a structure wherein receptor is a part of fluorophore π-electron system.

Herein we report on the synthesis of new series of linear and cyclic polyamine functionalized 4,4-difluoro-4-bora-3a,4a-diaza-s-indacenes (Bodipy) derivatives **II-IV** from **I** and their UV-vis and fluorescence spectroscopy studies [2]. In addition complexation abilities of dipicolylamine, cyclen, triacetamide-cyclen and aminomethylhomocyclen Bodipy dyes towards various metal ions (Ag^{+}, Cd^{+}, Co^{2+}, Cu^{2+}, Hg^{2+}, Ni^{2+}, Pb^{2+}, Zn^{2+}) were disclosed. To establish the application borders of "polyamine-Bodipy" sensor principle and to find the perfect fit between the dye structure and its spectroscopic characteristics we modified Bodipy-core in 3-, 4- and 8-positions different in their influence mechanisms on fluorescence.



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Synthesis and structure of lactam-containing phenolic derivatives

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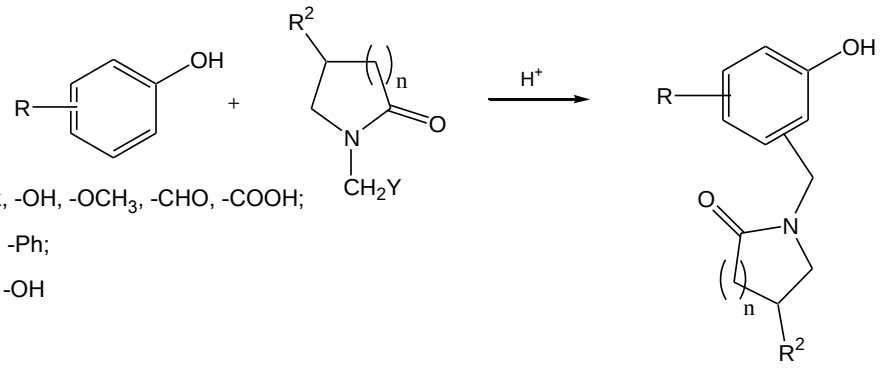
Phenols are wide-spread compounds possessing various biological activities, such as antioxidant, bacteriostatic, anti-inflammatory and antiseptic. Lactams are also bioactive substances with nootropic, antihypoxic and analeptic effects. We have not enough literature about lactam-containing phenolic derivatives, thus their synthesis and studying of their properties are useful for the development of new drugs.

Target compounds were prepared in the Tscherniac-Einhorn reaction [1, 2]. Generally, the scheme of the reaction is the following:



R = -Alk, -OH, -OCH_3, -CHO, -COOH;

R^2 = -H, -Ph;

Y = -Cl, -OH

n = 1,3.

26-80%

Several systems were used: “chloroform – trifluoroacetic acid” [3], “acetonitrile – trifluoroacetic acid” and “water – acetic acid”. In some cases (salicylic and gallic acids) the catalyst was not necessary. We obtained derivatives of catechol, resorcinol, hydroquinone, thymol, vanillin, phloroglucinol, salicylic and gallic acids with fragments of pyrrolidone, 4-phenylpyrrolidone or caprolactam.

The structures of synthesized compounds were confirmed using IR and NMR spectroscopy, X-ray crystal and elemental analyses.

Target compounds may be used as perspective drugs for oncology treatment due to their low toxicity. Some of them (especially with pyrrolidone fragment) can also possess nootropic activity.

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An efficient and stereoselective approach to 14-membered hexaaza macrocycles using novel semicarbazone-based amidoalkylation reagents

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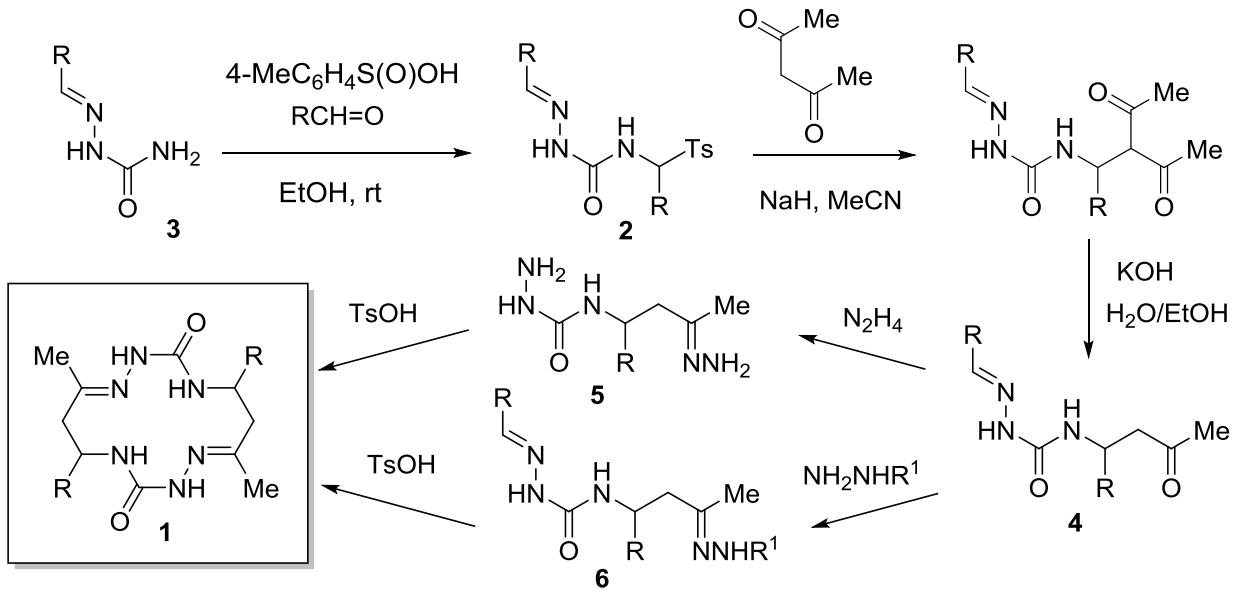
Polyaza macrocycles are of considerable importance in various fields of chemistry, biochemistry, medicine, and material science. The unique features of these heterocycles arise from their ability to bind to different inorganic and organic cations, anions, and neutral molecules. Although a large variety of polyaza macrocycles have been synthesized, the design of new members, particularly tetradentate 14-membered hexaazacycles, is a topic of great interest. Among them, 14-membered 1,2,4,8,9,11-hexaaza macrocycles, particularly bis-semicarbazones **1**, remain underexploited. Herein, we describe a new stereoselective strategy for multi-gram synthesis of these compounds starting from previously unknown α-amidoalkylation reagents, 1-arylidene-4-(tosylmethyl)semicarbazides **2**.

Sulfones **2** were prepared by the three-component condensation of semicarbazones **3** with the corresponding aromatic aldehydes and *p*-toluenesulfinic acid. Reaction of compounds **2** with the Na-enolate of acetylacetone, followed by base-promoted retro-Claisen reaction and treatment of the obtained 4-(3-oxobutyl)semicarbazones **4** with hydrazine or methylhydrazine gave hydrazones of 4-(3-oxobutyl)semicarbazides **5** or 4-(3-oxobutyl)semicarbazones **6**.



R = Ph, 4-MeC_6H_4, 4-*t*-BuC_6H_4, 4-$MeOC_6H_4$; R^1 = H, Me

The prepared hydrazones **5** and **6** were converted stereoselectively into 14-membered cyclic bis-semicarbazones **1** under acidic conditions. Especially high selectivity (*trans*/*cis* ≥ 97:3) was observed upon the macrocyclization of 4-(3-oxobutyl)semicarbazone hydrazones **6**. Plausible reaction pathways and stereochemistry of the above cyclizations will be discussed.

This research was financially supported by the Russian Foundation for Basic Research (Grant No. 15-03-07564)

Poster Session

Synthesis of dichlorodiazobutadiene derivatives based on tetrafluoroterephthalic aldehyde

Maharramov A.M.[a], Ahmedova N.E.[a], Asgerova U.F.[a], GurbanovA.V.[a], Gajar A.M.[a], Shikhaliyev N.Q.[a], Shastin A.V.[b], Nenajdenko V.G.[b]

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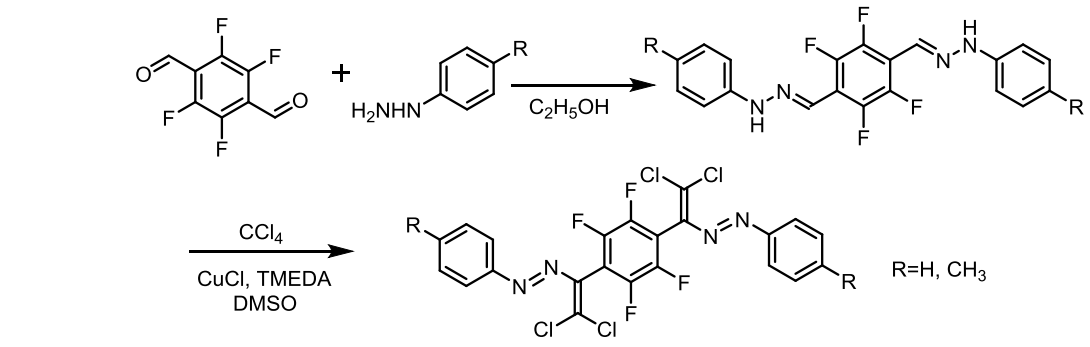
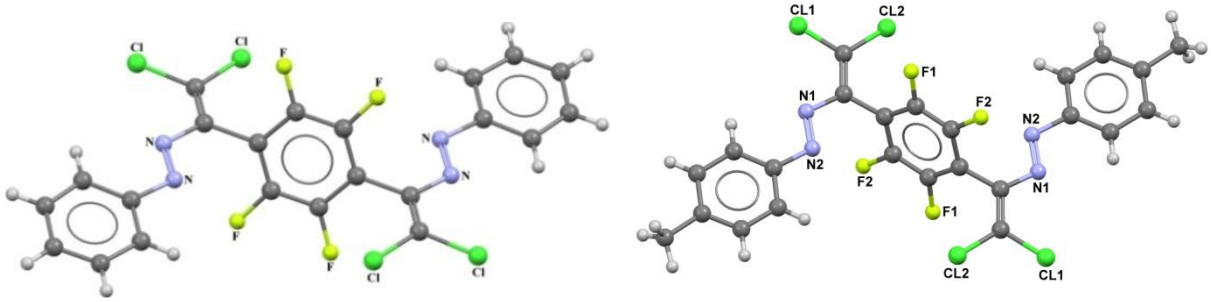
Previously we have synthesized halogenated derivatives of divinylbenzenes using the catalytic olefination reaction with bis-hydrazones of terephthalic, isophthalic and 2,3,5,6-tetrafluoroterephthalic aldehydes [1]. These compounds are prone to form multiple noncovalent intermolecular halogen-halogen bonds in crystal packing. Synthesized bis-halogenalkenes can be used as a model for studying of noncovalent "halogen-halogen" bonds in compounds having carbon-halogen bond.

On the basis of reaction of N-substituted phenylhydrazones of tetrafluoroterephthalic aldehyde with carbon tetrachloride the corresponding diazadienes were prepared. It was observed the presence of non-covalent intermolecular CI···F halogen-halogen bonds in the crystal packing. Also the presence of F···H intermolecular hydrogen bonds and CI → π interactions in the crystal structure was found.





Molecular structure of bis-dichlorodiazobutadienes with tetrafluorophenylene bridge

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The synthesis and biological activity of new 2H-benzimidazole 1,3-dioxides

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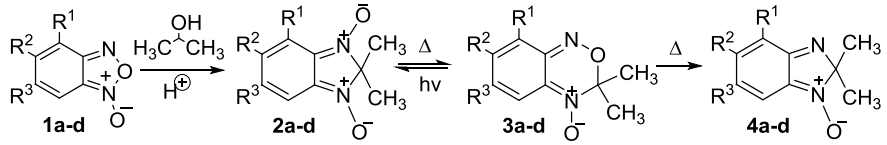
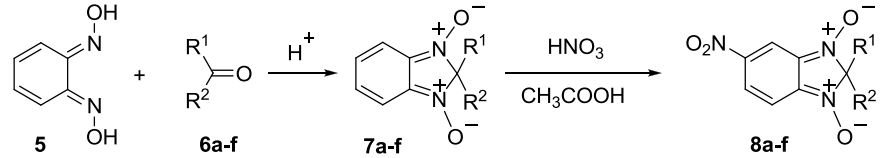
2*H*-benzimidazole 1,3-dioxides exhibit high biological activity and can be used as drugs against parasites *Tripanosoma cruzi* and *Leishmania spp*. About 30 millions of people are infected by these parasites and more than 400 millions are constantly under threat of infection according to the World Health Organization. As a result of our work, we have synthesized new 2*H*-benzimidazole 1,3-dioxides (**2a-d**), which according to the literature show high biological activity against the parasites *Trypanosoma cruzi* and *Leishmania spp.* as a result of the interaction of benzo[1,2-*c*][1,2,5]oxadiazole *N*-oxides derivatives (**1a-d**) with isopropyl alcohol in sulfuric acid.

An interesting property of 2*H*-benzimidazole 1,3-dioxides (**2a-d**) is the ability to be isomerized to benzoxadiazine *N*-oxides (**3a-d**) when heated, and with prolonged heating, one oxygen atom is split off to give mono-*N*-oxides of 2*H*-benzimidazole (**4a-d**) as the end products of thermal reaction. In the light, the obtained benzoxadiazines are very unstable and can be easily isomerized to the parent 2*H*-benzimidazole-1,3-dioxides (**2a-d**).



a) $R^1 = R^3 = Cl$; $R^2 =$ H; b) $R^1 = OCH_3$; $R^2 =$ H; $R^3 = Cl$;
c) $R^1 = NO_2$; $R^2 = R^3 =$ H; d) $R^1 = R^3 = Cl$; $R^2 = NO_2$;

Furthermore, we also proposed a new method for the preparation of 2*H*-benzimidazole 1,3-dioxides (**7a-f**) by the reaction of *o*-benzoquinondioxime (**5**) with ketones (**6a-f**). Further nitration of obtained compounds makes it possible obtainment of a wide range of Sepin-1 analogues with various substituents in the 2-position (**8a-f**).



a) $R^1=R^2=CH_3$; b) $R^1=CH_3$; $R^2=CH_2Cl$; c) $R^1+R^2=-(CH_2)_4-$;
d) $R^1+R^2=-(CH_2)_5-$; e) $R^1=CH_3$; $R^2=CH_2COOCH_3$; f) $R^1=CH_3$; $R^2=CH_2CH_2COOCH_2CH_3$

The resulting compounds (**2a-d, 3a-d, 4a-d**) were studied for antimicrobial and hemolytic activities *in vitro*. As a result of the biological tests, it was shown that 2*H*-benzimidazole 1,3-dioxides (**2a-d**) and 3*H*-benzo[1,2,5]oxadiazine-4-oxides (**3a-d**) show good biological activity among the classes of compounds, and removal of oxygen atom from the benzimidazole cycle (compounds (**4a-d**)) worsens the biological activity by several times.

This work was supported by the President of the Russian Federation, grant MK-4838.2016.3.

Actions of melamine salt of bis (oximethyl) phosphinic acid – melafen, to biological experimental objects

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Melafen - heterocyclic organic phosphor compound, synthesized at the A.E. Arbuzov Institute of organic and physical chemistry of RAS for the plant growth regulation. Melafen was used as aqua solutions, at wide concentration's region (10^{-2}, 10^{-3}, 10^{-4}, 10^{-5} M). The main our task was the clearing of Melafen influence on the structural properties of experimental objects of animal's origin, because there are the relationships with plants and animals and chemical compounds. The primary targets for biological active substances (BAS) at animal's cells are the cellular membranes and their components. When BAS introduced to the blood-vascular system the first targets become the blood cells - erythrocytes that were isolated. And then erythrocytes were emancipated from hemoglobin by of hypo osmotic hemolysis under cooling ($4C^0$) for preparing of ghosts. The erythrocyte ghosts are the outer erythrocyte membranes with all elements of cytoskeleton that are typical for the most of animal cells**.** The Melafen interactions with membrane bounded proteins at ghost were tested by the differential scanning microcalorymetry (DSC) method that allowed us to receive the protein microdomains organization at membranes. It is known that there are five identified endothermic phase transitions of protein's microdomains (*A, B_1, B_2, C, D*) at erythrocyte's ghosts when registered by the DSC. The *A*- transition is determined by the microdomains denaturation of cytoskeleton, set up of complex α - and β- spectrin and actin. The denaturation of spectrin-actin complex microdomain results in disappearance of *A*-transition. That is followed by the total loss of erythrocytes and ghost membranes deformability. B_1-the transition is linked to denaturation of membranous microdomain, set up of ancyrin and proteins of bands 4.1, 4.2 and demantin. B_2-transition is linked with denaturation of cytoplasm fragment of protein band-3 microdomains. *C*-transition is linked with denaturation of membrane fragment 55 κDa of proteins band-3, which are ion-channels microdomains. *D*-transition is linked with unidentified proteins denaturation and membrane bubbling microdomains. Melafen aqueous solutions caused some restructuring of protein's microdomains, which consist of several proteins as a rule, on freshly-isolated preparations (3-9%), and in the process of ageing of the erythrocytes ghost (table. 1). The small structural changes are representative for biological responses.

Table 1. Melafen influence on temperature dependence of relative enthalpy (at thermograms - peak *A*) of membranes suspensions of erythrocyte ghosts at the first day after receiving of erythrocyte ghosts.

Erythrocyte ghosts	ΔC_p*	Δ (%)**
Without of Melafen	17,1+_0,01	
10^{-5} M Melafen	17,6+_0,01	+3%
10^{-3} M Melafen	18,6+_0,01	+9%

*Δ Cp - change of relative heat capacity (J/K),

**Δ (%) - the different quantity, where 100% - the quantity of control answer.

Melafen didn't exert the great destructive actions to the isolated membranes (with cytoskeleton) under the concentrations that regulate the plant and seeds growth. But the small Melafen influencing was essential to the functioning of animal's membrane-bounded proteins, when the bigger Melafen concentrations. Small effects of organic compounds to the structural properties of biological objects are multiplied when proteins functions are registered.

An approach to polycyclic cyclopropylketones and polycarbonyl compounds *via* direct oxidation of spirocyclopropane derivatives

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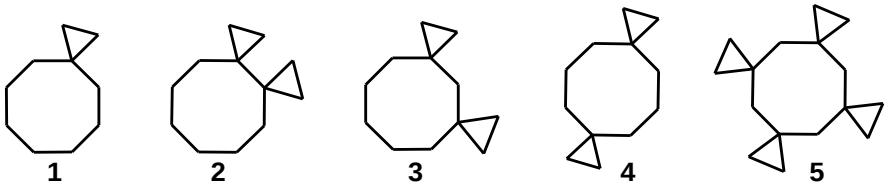
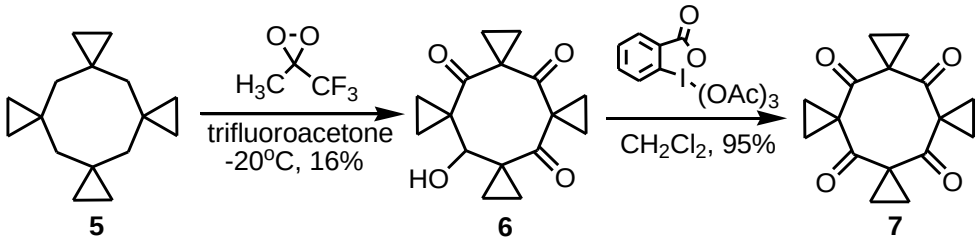
Functionalization of saturated hydrocarbons via direct oxidation of C-H bonds is the subject of a growing interest during the past decades as a base for development of novel synthetic strategies and a model of fermentative processes in nature.

Cyclopropane moiety is known to activate the adjacent methylene groups towards oxidizing reagents. Searching for synthetic pathways to polycarbonyl compounds via direct oxidation of activated C-H bonds we elaborated the preparative approaches to hydrocarbons **1-5**, containing spirocyclopropane moieties, and investigated them under the treatment with various oxidants (ozone, CrO_3, trifluoroacetone peroxide).



The difference of reactivity of methylene groups in dependence from chemical environment was studied, and the compound **1**, containing single spirocyclopropane substituent, was shown to undergo one-fold oxidation, while in the case of polyspirocyclopropanes the one-stage formation of polycarbonyl compounds was observed. The oxidation via "dry" ozonolysis was found to be the most selective, while trifluoroacetone peroxide appeared to be the most efficient of the oxidants.



The treatment of the hydrocarbon **5** with trifluoroacetone peroxide followed by Dess-Martin periodinane allowed the exhaustive four-fold oxidation and offered ready access to the unique non-enolizable tetraketone **7** – a compound attractive from both theoretical and preparative point of view.

This work was supported by the Russian Foundation for Basic Research (grant 16-03-00467-a).

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PASE synthesis of new 5-C substituted 2,4-diamino-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitriles

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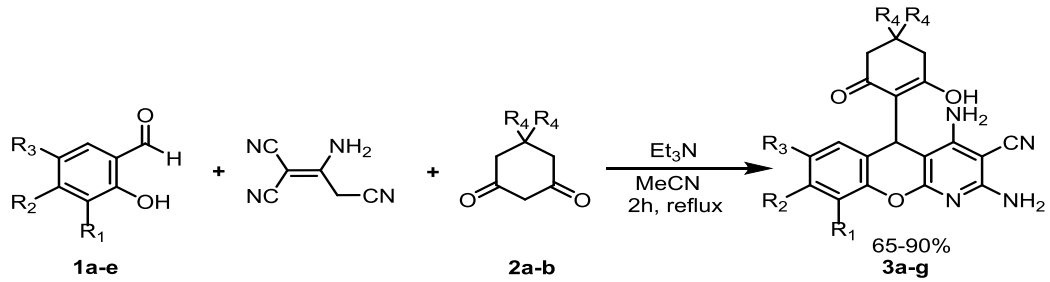
Cyano-functionalized chromeno[2,3-*b*]pyridines inhibit mitogen-activated protein kinase-activated protein kinase 2 (MK-2) and suppress the expression of TNFα in U937 cells [1], and also increase the level of phosphorylated cofilin in HCA2 cells, making chromeno[2,3-b]pyridines possible therapeutic option in the treatment of Werner syndrome [2].

The combination of pot, atom and step economy (PASE) in the synthesis provides a new line of approach towards developing environmentally friendly synthetic technologies [3].

In the present study we found multicomponent synthesis of 5-C substituted chromeno[2,3-*b*]pyridines from salicylaldehydes **1a-e**, 2-aminoprop-1-ene-1,1,3-tricarbonitrile and cyclohexane-1,3-diones **2a-b**. In the presence of 10 mol % of Et_3N as catalyst and acetonitrile as solvent chromeno[2,3-*b*]pyridines **3a-g** was obtained in 65-90% yields (2h, reflux):



1a-e

1a: $R_1 = R_2 = R_3 = H$,
1b: $R_1 = R_3 = H$, $R_2 = OMe$,
1c: $R_1 = OMe$, $R_2 = H$, $R_3 = Br$
1d: $R_1 = R_2 = H$, $R_3 = Cl$,
1e: $R_1 = R_2 = H$, $R_3 = Br$

2a-b

2a: $R_4 = H$
2b: $R_4 = Me$

3a-g

3a: $R_1 = R_2 = R_3 = R_4 = H$,
2b: $R_1 = R_3 = R_4 = H$, $R_2 = OMe$,
2c: $R_1 = R_2 = R_3 = H$, $R_4 = Me$
2d: $R_1 = R_3 = H$, $R_2 = OMe$, $R_4 = Me$
2e: $R_1 = OMe$, $R_2 = H$, $R_3 = Br$, $R_4 = Me$
2f: $R_1 = R_2 = H$, $R_3 = Cl$, $R_4 = Me$
2g: $R_1 = R_2 = H$, $R_3 = Br$, $R_4 = Me$

The procedure found by us utilizes simple equipment; it is easily carried out, final compounds do not require further purification and isolated by simple filtration followed by washing with a small amount of methanol.

This work was supported by the Council at President of the Russian Federation (grant MD-380.2017.3).

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Synthesis of nitro-substituted pyrrolo[2,1-*a*]isoquinolines

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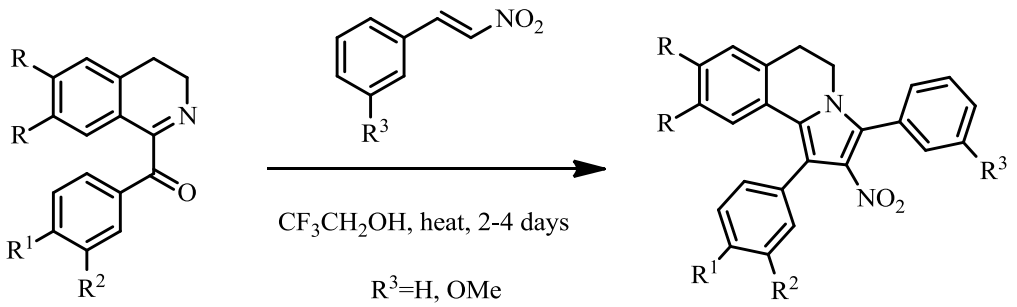
The pyrrolo[2,1-*a*]isoquinoline core is a common motif in numerous bioactive alkaloids and pharmaceuticals. Compounds based on this structure are potential fungicide and bactericide agents [1]. Skeleton of pyrrolo[2,1-a]isoquinoline has a TRI antidepressant JNJ-7925476, which is currently under development by *Johnson & Johnson* © [2]. Also was predicted *in silico* anti-inflammatory and MCF-7 breast cancer cell line growth inhibition effects of *trolline* [3]. This alkaloid relates to the pyrrolo[2,1-*a*]isoquinoline series. Thus, due to their biological relevance, the development of efficient methodologies to rapidly construct the pyrroloisoquinoline scaffold remains highly desirable.

Earlier it was shown that the pyrroloisoquinoline structure can be synthesized from alkynes with electro-withdrawing groups and 1-aroyl substituted isoquinolines [4]. Such approach allowed us to hypothesize that 2-nitro substituted compounds **2** could be obtained in the reactions with activated alkenes such as nitroalkenes in the same conditions. Reaction of 1-aroyl substituted isoquinolines (**1a, 1b, 1c**) with nitroalkenes was carried out in 2-4 days with heating in 2,2,2-trifluoroethanol to produce corresponding pyrroloisoquinolines in middle yields.



1a: R=OMe,R^1=Cl,R^2=H
1b: R=R^1=R^2=OMe
1c: R=R^1=R^2=OEt

2 (42-56%)

This work was supported by the Russian Foundation for Basic Research (grant № 17-03-00605).

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Synthesis amides 3-oxo-2-piperazinecarboxylic acid in continuous flow

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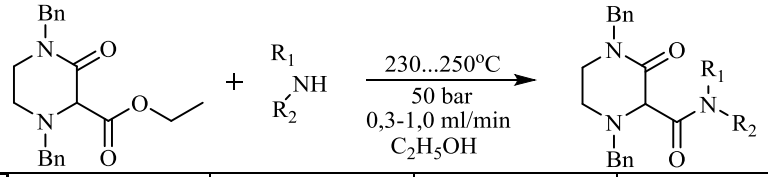
Amides of 3-oxo-2-piperazine carboxylic acid are key synthons for the synthesis of a variety of biological activity compounds [1]. However, the proposed synthetic approach to such amides *via* the sequence: hydrolysis to the carboxylic acid; formation of the corresponding acyl chloride, followed by treatment with an excess of secondary amine or ammonolysis under base catalysis, did not result in the formation of the desired amide and afforded only products of decarboxylation [2].

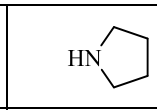
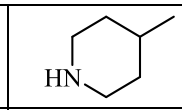
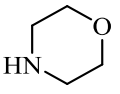
Previously [2], we have demonstrated the possibility of ammonolysis of ethyl 3-oxo-2-piperazinecarboxylate with secondary amides by heating the initial ester in an autoclave with the secondary amine (pyrrolidine) at 230°C for 90 minutes.

However, the scaling of the reaction presents severe difficulties as the process requires a uniform heating of the reaction mixture and a strict compliance to the proper heating time. At that, the increase of the reaction loadings often results in an increase of the amount of decarboxylation product and significant tarring of the reaction mixture while the yield of the desired products drastically falls.

Therefore, we investigated the possibility of a continuous flow ammonolysis of ethyl 3-oxo-2-piperazine carboxylate.

A steel capillary tube with a diameter of 1/16" and a total volume of 8 ml was used as a reactor for the synthesis of amides in a continuous flow. Heating and temperature monitoring was performed with a Phoenix flow reactor (*Thales Nano*). Ethanol was chosen as a solvent and the concentration of ester and a secondary amine was 13 mM. The optimal reaction conditions resulting in a full conversion of starting materials were determined for each of the obtained amides by careful screening of the reaction temperature and the amount of the reaction mixture passing through the heated reactor.



R_1 / NH / R_2					
Flow rate, ml/min	1	0,5	0,3	0,3	0,3
T, °C	240	230	240	250	240
Yield, %	64	62	80	79	66

The reaction conditions were optimized by varying the temperature and flow rate to afford the desired amides in 62-80% yields and avoid the tarring of the reaction mixture. It is noteworthy that, although the reactor's volume is only 8 ml, the application of ammonolysis in a continuous flow is not limited by the amount of reactants.

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Michael addition of organocopper reagents to non-protected 3-(2-nitrovinyl)indoles

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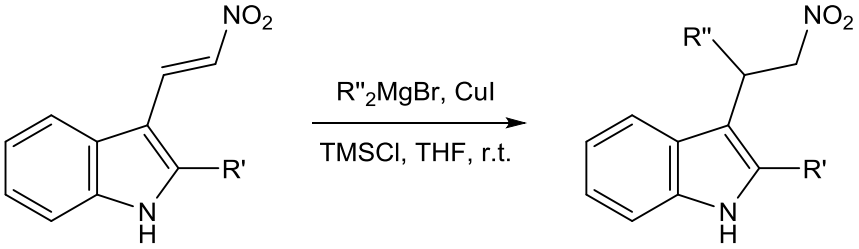
Conjugate addition reactions of organocopper reagents to *α,β*-unsaturated carbonyl compounds represent important methods for carbon-carbon bond construction. Less "popular" but still quite important reaction is copper-catalyzed Michael addition to various nitrovinyl-derivatives. Initial investigations by our group of such reactions with *α,β*-unsaturated enoates showed their high stereoselectivity in chiral environment [1], what led to an additional research in the field of organocuprates conjugate addition mechanism establishment [2].

To our knowledge, Michael addition on nonprotected 3-(2-nitrovinyl)indoles is rather a rear occurrence. Considering important role of indoles for the synthesis of biologically active instances, availability of substrates and selectivity of such reactions, it can be considered as an important omission. Recent examples include solvent-free Michael addition of various nucleophiles to these substrates by ultrasound activation [3].

3-(2-Nitrovinyl)-1*H*-indoles are easily available through Vilsmeier reaction directly from parent indoles. Corresponding 2-substituted indoles were made by Fisher indole synthesis. Organocopper reagents were obtained by classical procedures with a major improvement like all the reactions were carried out under room temperatures.



R' = H, Ph; R'' = Ph, *p*-Tol, 1-Naph

TMSCl, a widely used promoter for the reactions with organocuprates, probably served as a temporary protection for 1*H*-indole position. Reactions of the utilized substrates with organocopper reagents without addition of TMSCl did not yield products at all or required extended time of reaction. Obvious coloration of the reaction mixture observed in such case led us to a conclusion that *N*-anion was generated.

In conclusion, the Michael addition of organocuprates on nonprotected indole derivatives provided straightforward access, avoiding the steps of protection/deprotection. The methodology was extended to different examples with good to excellent yields, which should open the way to non-natural tryptamine derivatives and other related compounds. Our future work will study the enantioselective control of the reaction on sugar-derived substrates aiming the synthesis of natural compounds with useful properties.

This work was supported by the Russian Science Fund (grant № 14-13-01108).

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The synthesis of isoindolocarbolines based on substituted tryptamines

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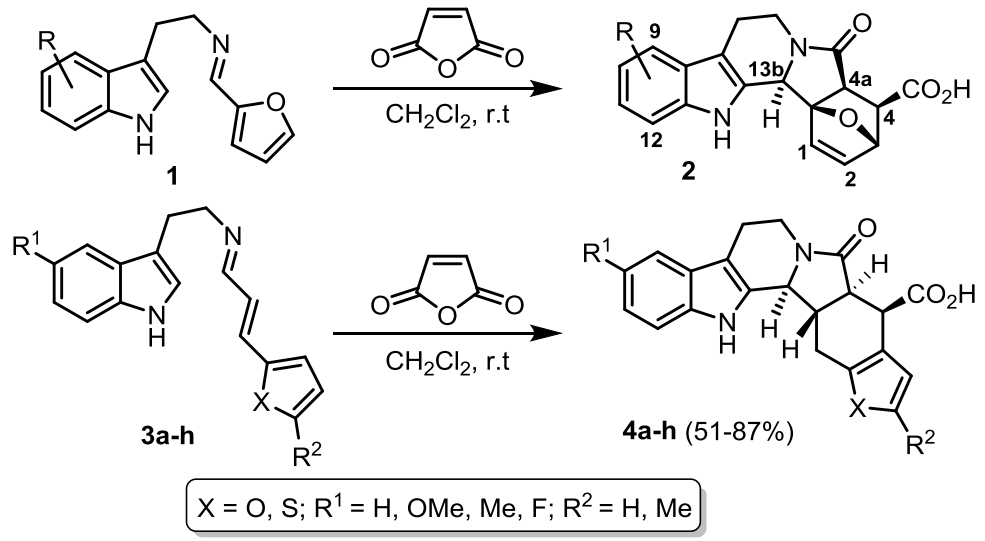
Previously, an efficient one-pot synthesis of 3,6a-epoxyisoindoles annelated with oxazine, oxazole, thiazine, thiazole, pyrimidine and other heterocyclic fragments was introduced by our group [1, 2]. The method was based on the tandem N-acylation/intramolecular cycloaddition (the intramolecular Diels-Alder reaction of furan, IMDAF) reaction between α,β-unsaturated acid anhydrides and α-furyl substituted azaheterocycles. The typical example of its application is demonstrated here by the example of conversion of azomethines **1** into isoindolocarbolines **2**.

The aim of this study was to investigate the behavior of vinyloges of azomethines **1** – indoles (**3**) under the same reaction conditions. Compounds **3** undergo the previously undescribed cascade of transformations, which includes the N-acylation and the Pictet–Spengler stages, followed by the IMDA reaction of the intermediate maleic amides, and spontaneous prototropic tautomerism, leading to carbolines (**4**) annulated with the furoisoindole fragment. Both these cycles, carbolines and furoisoindole, are related to the so-called pharmacophore fragments.



The reaction proceeds under very mild conditions and with a relatively high yield.

This work was supported by the Russian Foundation for Basic Research (№ 16-03-00125).

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Synthesis and structure of 1-alky-6-aryl-3*a*,6*a*-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-diones (glycolurils)

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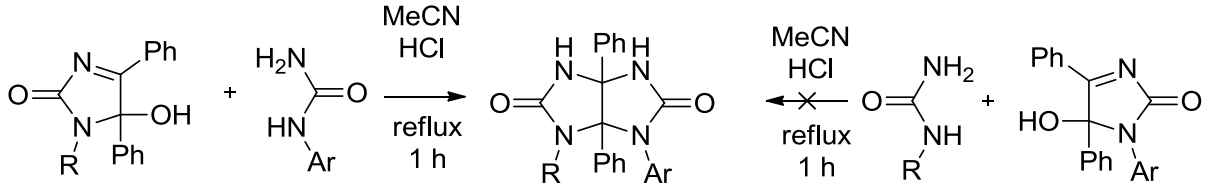
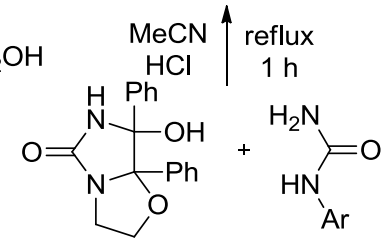
Glycolurils are used as psychotropic agents, anion-binding receptors and molecular capsules. In recent years, great attention has been paid to 1,6-substituted glycolurils, which are used as an efficient molecular template for intramolecular Claisen-type condensation and in combinatorial and supramolecular chemistry.

A general method for the synthesis of symmetrically 1,6-disubstituted 1,5-diphenylglycolurils is condensation of benzyl and 1-substituted ureas. However, general method for the preparation of 1,5-diphenylglycolurils with different substituents at N(1) and N(6) is absent (only several examples were synthesized).

In this work we discovered a new general approach for the synthesis of asymmetrically 1,6-disubstituted glycolurils **1** (1-alkyl-6-aryl-3a,6a-diphenyltetrahydroimidazo[4,5-d]imidazole-2,5(1H,3H)-diones). Compounds **1a-j** (68-90%) were prepared by the reaction of 1-alkylimidazolones **2a-d** or imidazooxazole **3** with 1-aryl ureas **4a,b** in the presence of hydrochloric acid, but 1-aryl imidazolones **5a,b** with 1-alkyl ureas **6a-e** under the similar conditions did not react.



R = Me, Et, Pr, Bu, $(CH_2)_2OH$
Ar = Ph, p-ClC_6H_4



1 Ar = Ph, R = Me (**a**), Et (**b**), Pr (**c**), Bu (**d**), $(CH_2)_2OH$ (**e**),
Ar = p-ClC_6H_4, R = Me (**f**), Et (**g**), Pr (**h**), Bu (**i**), $(CH_2)_2OH$ (**j**).

The structures of the obtained compounds **1a-j** were proved by a set of methods including ^1H and ^{13}C NMR spectroscopy and high-resolution mass spectrometry. The structures of **1a,b,e,f** have been additionally confirmed by X-ray diffraction analysis. We have found that in the solid state compounds **1a,b,e,f** formed H-bonded tapes by the homorochiral recognition process. Moreover, glicolurils **1a,b,f** are racemic conglomerates.

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The authors would like to thank Dr. Yu.V. Nelyubina (INEOS RAS) for technical assistance.

Dispiro-indolinones as potential small molecular inhibitors p53-MDM2 protein-protein interaction: synthesis and biological testing

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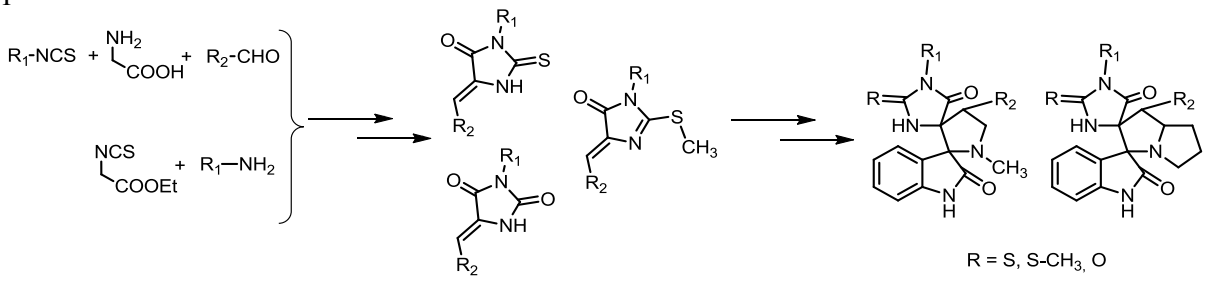
The protein p53 is the genetic factor, which binds with DNA chain in case of its damage. Protein MDM2 could interact with p53, which can lead to the formation of cancer cells. [1,2]

In this paper a new method for synthesis MDM2 inhibitors on the base on dispiro-indolinones [3] is discussed. The synthesis of dispiro-compounds produced from commercially available reagents is described. These compounds could be obtained with high yield from commercially available reagents and don't need special purification techniques. [4]

A study of citotoxicity of synthesized substances on PC3, LNCap, HCT $p53^{(+,+)}$ and HCT $p53^{(-,-)}$ cell lines is discussed.



This work was supported by the Russian Foundation for Basic Research, project № 16-33-60166.

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1-Phenylethynyl substituted chromeno[3,2-c]pyridines: synthesis and properties

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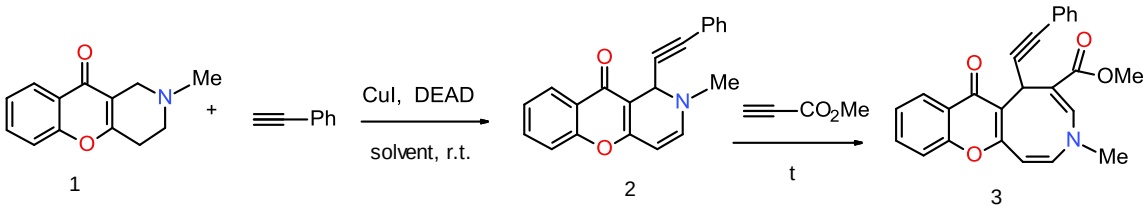
Earlier, we have investigated reactions of chromeno[3,2-c]pyridines with activated alkynes in different conditions. We supposed, that introduction of phenylethynyl substituent in this heterocyclic system would increase diversity of possible products of its conversion due to reactions of such substituents with alkynes yielding allenes [1]. Keeping this in mind, we have preformed a reaction of chromeno[3,2-c]pyridine **1** with phenylacetylene in presence of CuI and DEAD in THF, as it was described for isoquinolines [2]. However, the process was accompanied with dehydration of tetragydropyridine ring yielding **2**. Compound **2** reacts with methylpropiolate in trifluoromethanol forming azocine **3** with low yield.



The structures of all synthesized compounds have been proved by complex of spectral methods. The structure of 2-methyl-1-phenylethynyl-1,2-dihydro-10*H*-chromeno[3,2-c]pyridin-10-one **2** was confirmed by a single crystal X-ray analysis.

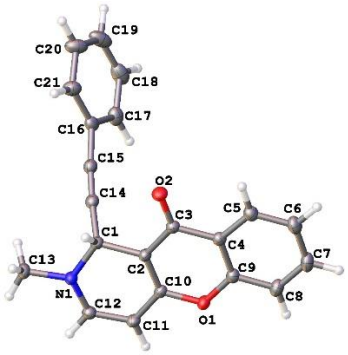


Figure 1. Molecular structure of **2**

Mass and IR spectra were registered using instruments of of the Shared Research and Educational Center of Physic-Chemical Studies of New Materials, Substances and Catalytic of RUDN.

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The synthesis and antibacterial evaluation of the new 1,2,4-oxadiazoles containing 2-imidazoline moiety

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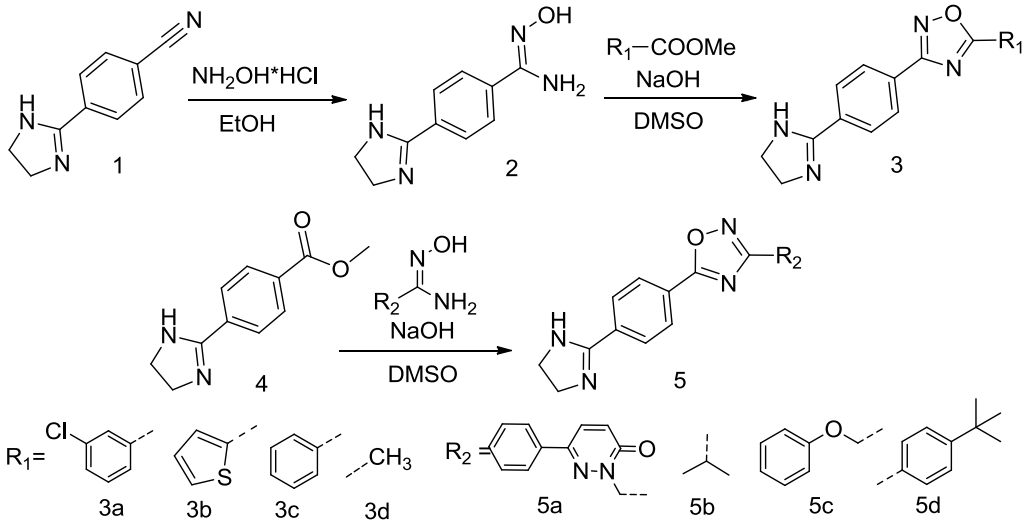
In last year's, there has been a sustained interest in researching and developing new antimicrobial agents to overcome the emergence of the microbial resistance. The recent publications in high-impact medicinal chemistry journals [1] demonstrate that highly active DNA – dependent RNA polymerase inhibitors were founded among 2-imidazolines. Such inhibitors can be used in the cure of contagions. At this work a set of novel structurally diverse 1,2,4-oxadiazole decorated with the 2-imidazoline moiety (**3** and **5**) was synthesized via the condensation between amidoximes and carboxylic acid esters in superbase medium NaOH/DMSO. The use of superbasic medium methodology [2] for synthesis of target compound (**3** and **5**) offers the possibility to obtain the high yields of 1,2,4-oxadiazole derivatives using amidoximes precursors with the presence of other nucleophilic centers in soft conditions (r.t, 2 - 8 h).



The two series of 1,2,4-oxadiazole **3** and **5** were evaluated for their antibacterial activities using express pH-dependent micro-dilution tests in liquid media [3] against *lactobacillus acidophilus* (Ep 317/402) and *bifidobacterium animalis* (BB-12). The best compounds from this set showed potent antibacterial activity, which is comparable with the drug pefloxacin.

The publication was financially supported by the Ministry of education and Science of the Russian federation (the Agreement number 02.a03.21.0008)

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Synthesis of the ionic compounds based on N-ethoxyethylpiperidine, trimecaine and piromecaine and their potential biological activity prediction *via* PASS

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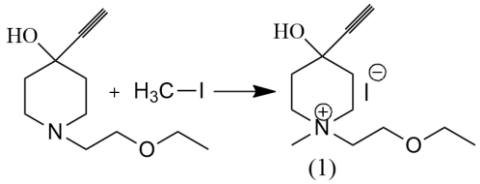
One of the main strategies of the search for new biologically active compounds is a combination of two or more pharmacophore groups in one compound [1]. The presence of piperidine ring and/or secondary amide group appears to be very interesting for exploring new biologically active compounds [2]. To define the range of biological activity of new synthesized compounds we used PASS online service (Prediction of Activity Spectra for Substances) [3], which helps to predict biological and pharmacological effects, action mechanisms and also toxicity and adverse impact of a compound.

At first, the ionic compound based on 1-(2-ethoxyethyl)-4-acetyl-4-hydroxypiperidine and methyl iodide - 1-(2-ethoxyethyl)-4-ethynyl-4-hydroxy-1-methylpiperidine iodide was synthesized (1). Synthesis was carried out in acetonitrile under the reflux with further product recrystallization from acetone. Based on the foregoing method, 1-(2-ethoxyethyl)-4-ethynyl-4-hydroxy-1-ethylpiperidinium iodide (2), N, N-diethyl-2-(mesitylamino)-N-methyl-oxoethanaminium iodide (3), N,N-diethyl-2-mesytil-amino-N-(-2-(2-methoxyethoxy)ethyl)-2-oxo-ethaneammonium bromide (4), 1-butyl-2-(mesytilcarbomoil)-1-methyl-pyrrolidinium-1 iodide (5) and 1-butyl-2-(mesytilcarbamoyl)-1-ethyl-pyrrolidinium-1 iodide (6) were synthesized.



(1)

The results of PASS prediction of potential biological activity and potential toxic effects illustrate that N-ethoxyethylpiperidine derivatives (compounds (1) and (2)) showed spasmolytic, ovulation inhibition and progestin antagonist potential activity, from the other hand these two compounds showed possible teratogen and embryotoxic effects; trimecaine derevatives (3) and (4) showed cardiotonic, spasmolytic and calcium channel activator effects with twitching, apnea and euphoria possible toxic effects; piromecaine derivatives (5) and (6) showed gastrin inhibitor, membrane integrity antagonist and general pump inhibitor potential activity, as well as twitching, euphoria and sneezing possible toxic effects.

The results will be used in the field of synthesis of new ionic compounds and new drug candidates.

This work supported by Ministry of Education and Science of Republic of Kazakhstan under Grants 1318/GF4, 1752/GF4, 0650/GF4 and 0251/PTF.

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Reaction of C,C- and O,C-cycloaminomethylation of phenol by *N,N-bis*(methoxymethyl)amines

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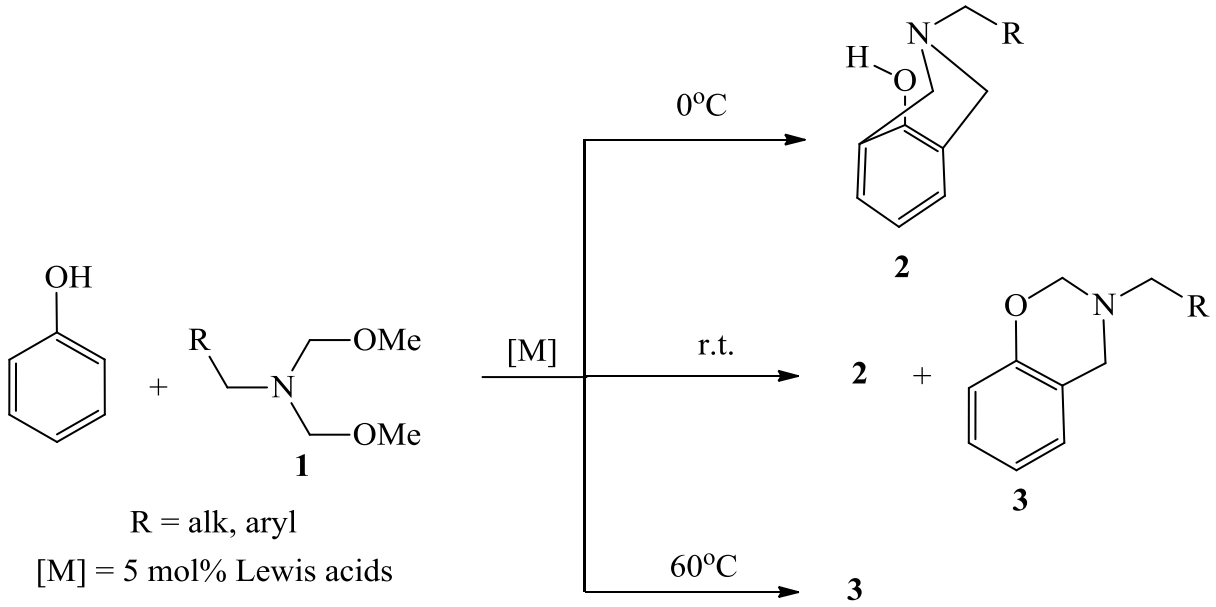
C-aminomethylation reaction of phenol was used for the synthesis of substituted *ortho*-amino derivatives which were applied as corrosion inhibitors and antioxidants [1,2].

The first time, we carried out C,C-cycloaminomethylation at *ortho*-, *ortho*-positions of phenol by the action of *N,N-bis*(methoxymethyl)amines **1** [3] at 0°C in the presence 5 mol% of the Lewis acid [M] with formation of 2-hydroxybenzoxazines **2**, which contains the distorted benzene ring in the structure [4].



It has been shown that cycloaminomethylation of phenol by reagent **1** at 60°C proceeds on the pathway of O-,C-cyclocondensation to form mainly benzoxazines **3** with yield more than 70%. It should be added that conducting the reaction at r.t. gives a mixture of fused phenols **2** and **3**.

Thus, the report discusses a new method for the synthesis of 3-azabicyclo[3.3.1]nona-1 (9),5,7-trien-9-ols **2** with angular distortion of the benzene ring at the *ortho*-, *ortho*-positions.

This work was supported by the Russian Foundation for Basic Research (grant № 14-03-00240_A, 14-03-97023 r_ Povolzhie_a).

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The Diels–Alder reaction between *bis*-furyl dienes and hexafluorobutyne

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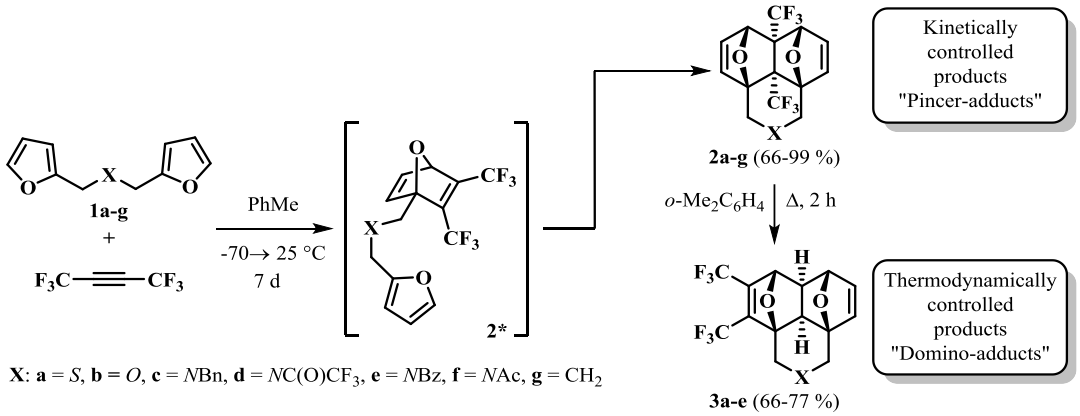
This work is a continuation of our group researches in the field of the tandem intramolecular [4+2] cycloaddition of alkenes and alkynes, bearing *electron withdrawing* groups, to furyl dienes [1-3].

It was shown previously [4], that *bis*-furyl dienes **1** react with dimethyl acetylenedicarboxylate (DMAD) at room temperature forming adducts of the kinetic control (**2**).

The present work describes peculiarities of the interaction between *bis*-dienes **1** and DMAD. Hexafluorobutyne was chosen because of its unique dienophile properties, and because the cycloaddition with its participation is practically not described in literature.



The reaction between furans **1a-g** and hexafluorobutyne was performed at -70 °C in sealed ampoule (after that, the reaction mixture was left at rt). In the most cases, the pincer-cycloadducts **2a-g** were obtained in almost quantitative yields. Then, the products of kinetic control (**2a-e**) were transformed into the products of thermodynamic control (**3a-e**) by short boiling in *o*-xylene.

This type of reaction is unique, because it is an exceptionally rare example of a complete kinetic / thermodynamic control in the Diels-Alder reaction. According to the obtained results, the intramolecular [4+2] cycloaddition reaction is reversible and proceeds *via* the formation of the intermediate **2***.

This work was supported by the Russian Foundation for Basic Research (№ 16-03-00125).

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Synthesis of series of 3-aryl-6,7-difluoroquinoxaline-2-carbonitrile--1,4-dioxides

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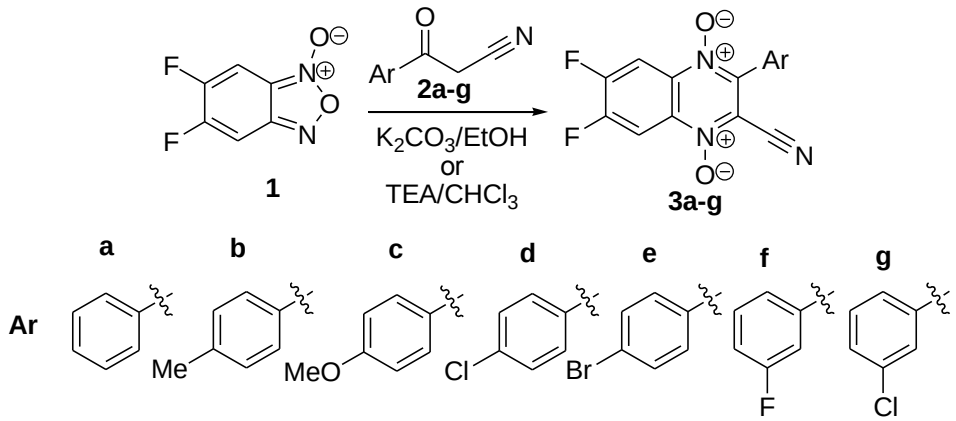
Derivatives of quinoxaline 1,4-dioxides is well known class of bioactive compounds potent against bacteria, fungus and tumor cells [1]. Antitumor potential of 6,7-difluoroquinoxaline-2-carbonitrile 1,4-di-*N*-oxide were investigated recently [2]. In this way it was important to investigate an influence of substituent in position 3 of quinoxaline 1,4-dioxide core on antiproliferative properties of these compounds. So, the aim of our research was preparation of series of 3-aryl-6,7-difluoroquinoxaline-2-carbonitrile-1,4-dioxides.

For the preparation of target compounds **3a-g** the Beirut reaction of 5,6-difluorobenzofuroxan (**1**) [3] and corresponding arylacetonitrile **2a-g** [4] in the presence of base was used. Firstly, potassium carbonate as a base in ethanole was tested. Unfortunately good yield of the product at this conditions was observed only for unsubstituted phenyl in position 3 of quinoxaline-1,4-dioxide (e.g. Ar = Ph: yield 65%; Ar = *p*-Cl-C_6H_4: yield 31%; Ar = *m*-Cl-C_6H_4: yield 27%). So, another bases and solvents were tried for the Beirut reaction and finaly triethylamine in chloroforme were chosen. At this condition yields of target compounds are found to be higher than in the presence of potassium carbonate (e.g. Ar = *p*-Cl-C_6H_4: yield 65%; Ar = *m*-Cl-C_6H_4: yield 63%).



All synthesized quinoxaline-1,4-dioxide were characterized by spectral methods (^{1}H and ^{13}C NMR, HRMS ESI).

Thus, our synthetic studies led to preparation of series of potential bioactive compounds, antiproliferative properties of which will be test soon.

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Synthesis of indolyl(thienyl)maleimides containing phenanthroline receptor

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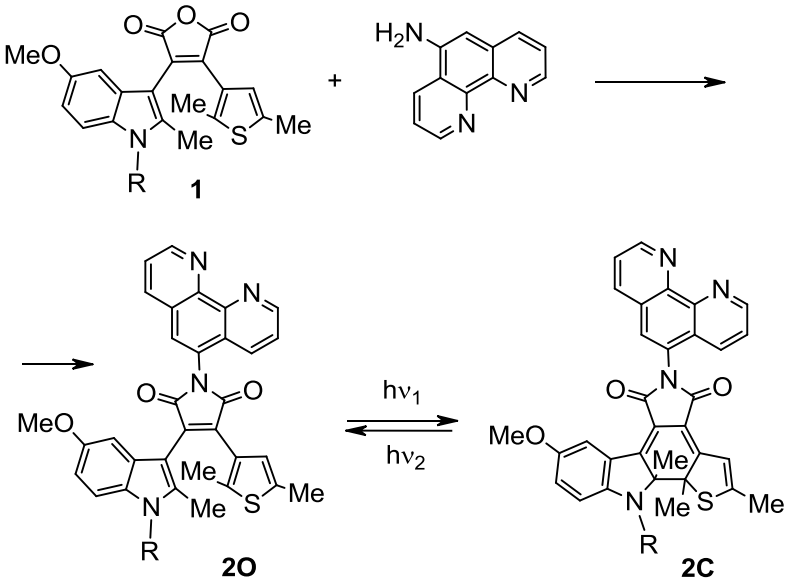
Bistable photochromic compounds are of considerable interest to create new polyfunctional materials for molecular electronics, optical molecular memory, photodynamic chemosensors, and biosensors [1-3]. An important role belongs to dihetarylethenes, which possess isomeric forms with high fatigue resistance, thermal and photostability and are capable to display fluorescent, magnetic, chemosensor and complexing properties. The introduction of receptor phenanthroline fragment into furandione bridge of **1a-c** leads to photoswitchable chemosensor systems **2a-c** existing in ring-opened form **O**.



R = Me (**a**), Et (**b**), CH_2Ph (**c**)

The irradiation of indolyl(thienyl)maleimides **2O** in solutions results in formation of colored ring-closed isomers **2C.** These compounds also reveal chemosensor activity towards metal cations.

This work was supported by the Russian Foundation for Basic Research (grant № 16-03-00102).

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Metal catalysed electrochemical functionalisation of aromatic C-H bonds

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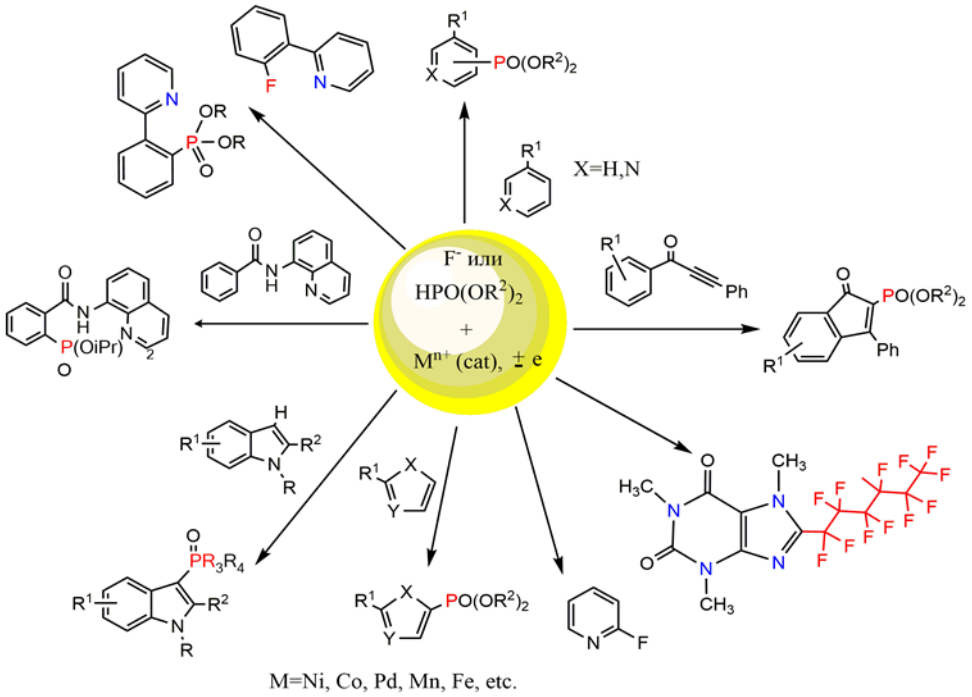
New methods that allow for the incorporation of fluorous or phosphorous synthons into a molecule at late synthesis stage are desperately needed. Metal-catalyzed coupling procedures would greatly facilitate the construction of fluoro- or phosphorous organic molecules; however they have been slow to develop. Achieving site selectivity in C–H functionalization reactions is a significant challenge. We propose a one-step catalytic method for introduction of fluorine- and phosphorus-containing functional groups to different compounds with C(sp^2)-H bonds assisted by electrochemical reduction or oxidation of metal complexes under mild conditions. The catalytically active form of metal complexes (Ni^{III} or Pd^{III}, Fe^{II}, etc.) is generated and regenerated on the electrode without specially added reducing agents (or oxidants). We aimed to develop a mild method for the functionalization of simple arenes and more complicated substrates (for example, caffeine) and to utilize relatively inexpensive perfluoroalkyl iodides as RF precursors and dialkylphosphites as P-precursors and rarely used accessible, reasonable and nontoxic iron and silver compounds as catalysts. Key organometallic intermediates are isolated and characterized. Possibilities and advantages of directed metal-induced aromatic C-H-fluoroalkylation, phosphorylations etc. are demonstrated.



This work was supported by Russian Science Foundation (grant № 14-23-00016).

Iron or nickel complexes bearing diphosphine and BIAN ligands as electrocatalysts for the H_2 evolution

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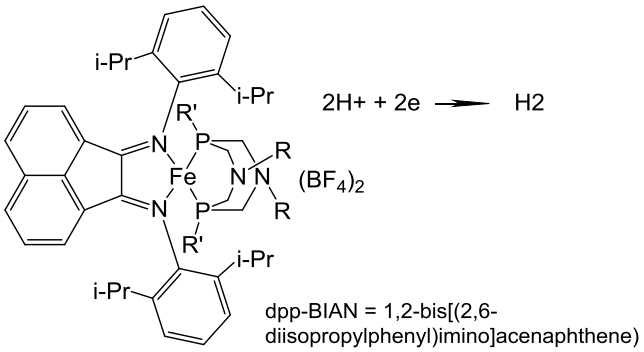
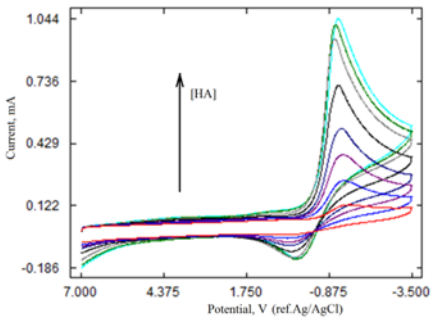
Over the past several years, much effort has been undertaken to construct artificial systems, and to understand the mechanism of proton reduction by [FeFe]-H2ase mimics. Nevertheless, the activity of the artificial systems for H_2 evolution is still low. The classical Fe^IFe^I organometallic complexes $[(\mu\text{-xdt})Fe_2(CO)_6]$ (xdt = dithiolate linkers) highly resemble the active site of [FeFe] hydrogenases so they have been used as biomimetic model complexes for mechanistic studies of H_2 evolution. Among hundreds Fe_2 complexes, the most common derivatives contain phosphine ligands, which substitute one or more COs. Upon phosphine substitution, the reduction of the Fe_2 complexes shifts toward more negative potentials. Unfortunately, most of the phosphine-substituted derivatives are unstable after redox events. It was reported that $[Ni(P^R{}_2N^{R'}{}_2)_2]^{2+}$ complexes are highly active catalysts for H_2 production and oxidation, and bidirectional catalysts active for both H_2 production and oxidation, where $P^R{}_2N^{R'}{}_2$ is a cyclic 1,5-diaza-3,7-diphosphacyclooctane ligand. Unfortunately, similar iron complexes do not exhibit catalytic activity under the conditions studied. We assumed it would be possible to involve the iron complexes with diazadiphosphocyclooctane ligands in hydrogen catalysis by entering the additional redox active ligand into the iron coordination sphere. Iron complexes bearing diphosphine ligands with positioned pendant amines along with non-innocent dpp-BIAN ligand have been investigated by cyclic voltammetry, which is the usual way to demonstrate electrocatalytic ability for hydrogen evolution. Cyclic voltammograms (CVs) in CH_3CN have been recorded in the presence of increasing amounts of acids (Figure 1). The catalytic reactivity of these new mixed ligands iron complexes at low overpotential was demonstrated. Catalysis potential for all complexes is around -0.5V ref Fc^+/Fc in THF, so it is very low overpotential of hydrogen evolution.





This work was supported by RFBR (grant № 16-03-00195)

Quaternary *N*-(2-pyridyl)-DABCO salts: one-pot *in situ* formation from pyridine-*N*-oxides and reactions with nucleophiles – a mild and selective route to substituted *N*-(2-pyridyl)-*N'*-ethylpiperazines

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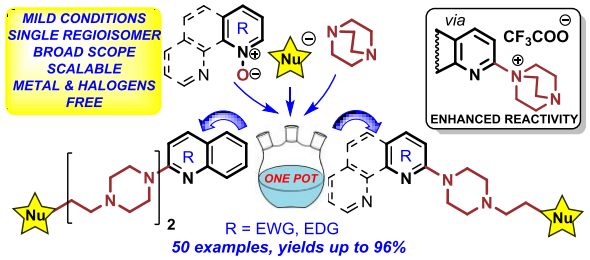
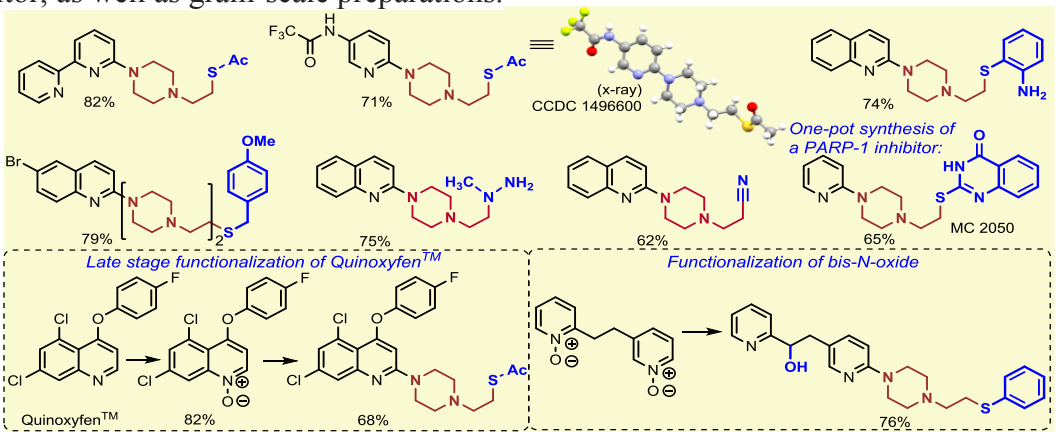


The *N*-heteroarylpiperazine and ethylpiperazine motifs are common for several known active pharmaceuticals and remain privileged subunits frequently used in drug discovery programs, agrochemicals, ligands and functional materials. Known synthetic methods toward these structures are based on laborious multistep sequences and using of uncommon preassembled starting materials. Moreover this methodology generally based on the S_NAr-chemistry which significantly limited to substrates containing electron-withdrawing groups.

We have developed a new methodology for a rapid and modular access to this privileged scaffold. Importantly, the developed protocol proved to be very general and efficient for the substrates containing substituents of different electronic nature. azine rings. This new method employs readily available heterocyclic *N*-oxides as starting materials, DABCO (1,4-diazabicyclo[2.2.2]octane) as a source of ethylpiperazine moiety and various nucleophilic reagents. The sequence involves an amination of C–H-bonds in activated heterocyclic *N*-oxides with DABCO followed by a C–N-bond cleavage in the quaternary ammonium intermediates with external nucleophiles. Our method allows for the rapid and simple preparation of N-heteroarylpiperazines under very mild reaction conditions with high yield and regioselectivity. In all cases, a >99:1 C2/C4 selectivity was observed; for 3-substituted pyridines and quinolones, C2/C6 selectivity as well as reactivity were seemingly dominated by steric factors. The method features a mild reaction conditions, high positional selectivity, and excellent functional-group tolerance. The utility of our approach is demonstrated by the late-stage site-selective functionalizations of complex molecules; a rapid modular assembly of MC2050, a potent PARP-1 inhibitor; as well as gram-scale preparations.



This research was supported by the RFBR.

The study of the correlation of the binding energy of peptide ligand complexes with hybrid antibiotics vancomycin-azithromycin and eremomycin-azithromycin with antibacterial activity

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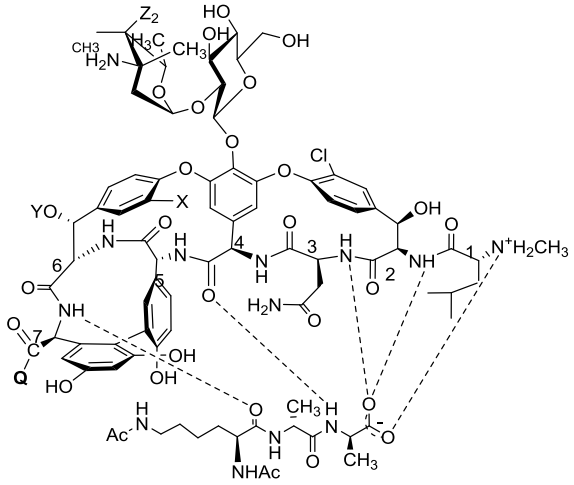
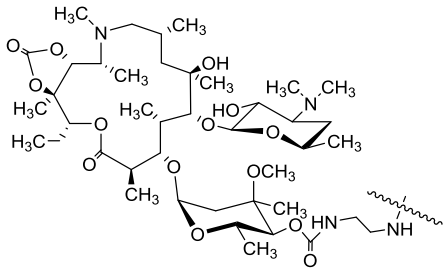
One of modern strategies that can solve the problem of antibacterial resistance is the development of dual-acting hybrid antibiotics – structures that contain two covalently linked antimicrobial drugs that interact with different targets in a bacterial cell [1].

Antibacterial activity of hybrid antibiotics vancomycin-azithromycin (C11, C12-carbonate) and eremomycin-azithromycin (C11, C12-carbonate) was evaluated. Quantum chemical calculations of energy these hybrid antibiotics with a model tripeptide ligand α,ε-di-Ac-*L*-Lys-*D* -Ala-*D*-Ala by the semiempirical PM6 method using a software package Spartan-10 [2] provided data on geometrical parameters of these complexes along with the energy of their formation and the influence of protonation of the $NHCH_3$ group. A correlation between the energy of formation of antibiotics-ligand complexes and antibacterial activity of hybrid antibiotics against Gram-positive bacterial strains was found.



A) α, ε - di-Ac-L-Lys-D -Ala-D-Ala (**LAA-**)



Vancomicin$^+$ + LAA- (1a)

R=OH; X=Cl; Y=H;
Y=эремозаминил–α
Z_1=OH; Z_2=H; **Q**=OH

Eremomycin$^+$ + LAA- (2a)

R=OH; X=H;

Z_1=H; Z_2=OH; **Q**=OH

Vanco-azithro$^+$ + LAA- (5a) Q =

Eremo-azithro$^+$ + LAA- (6a) Q=

This work was supported by the Russian Foundation for Basic Research (grant № 16-34-60110*).*

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Detection of metal cations using aza- and diazacrown ethers modified with fluorophore groups

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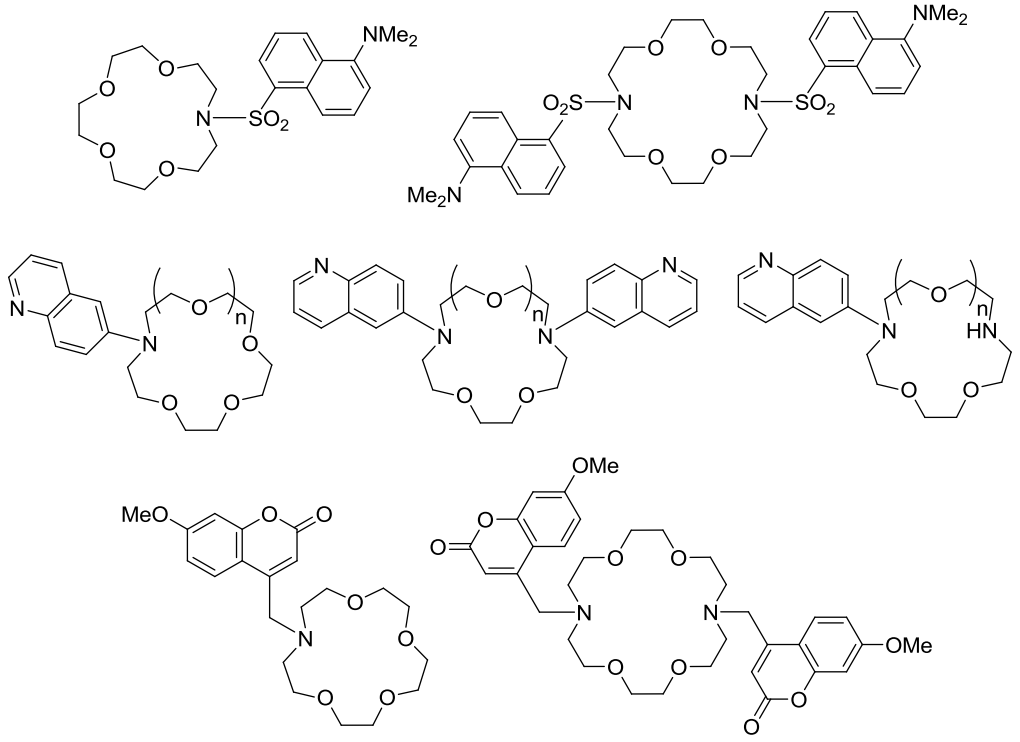
Using simple nucleophilic substitution reactions, aza- and diazacrown ethers were modified with dansyl and 7-methoxycoumarine fluorophores while the introduction of the quinolinyl fluorophores was achieved using Pd(0)-catalyzed heteroarylation of aza- and diazacrown ethers with 6-bromoquinoline.



The synthesized ligands were tested in the coordination of 22 metals cations taken as corresponding perchlorates or nitrates: Li(I), Na(I), K(I), Mg(II), Ca(II), Ba(II), Al(III), Mn(II), Cr(III), Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Pb(II), Hg(II), Ag(I), Ga(III), In(III), Y(III), Sr(III) using fluorescence spectroscopy. The emission of the dansyl derivative of 1-aza-15-crown-5 ether was quenched by Cu(II), Cd(II), Co(II), Cr(III), Ba(II), Pb(II), Al(III), Ga(III), while with In(III) a new emission band emerged with hypsochromic shift of the maximum. Didansyl derivative of the diaza-18-crown-6 ether was more selective as only excess of Co(II) slightly quenched the emission and Cu(II) (5 equiv.) diminished it 3 times.

With the quinolinyl derivatives of aza- and diazacrown ethers no good selectivity was observed in all cases, but the dependence of the emission quenching on the structure of the ligand was unique in each case.

The emission at 525 nm of 7-methoxycoumarine derivative of 1-aza-15-crown-5 ether diminished in the presence of Ag(I), Cr(III), Co(II) while in the presence of Li(I) it increased substantially. Some metals like Pb(II), Cu(II), Cd(II), Zn(II), Mn(II), Y(III), Mg(II), Ca(II), Ba(II) led to a new strong emission with maximum at 410 nm.

This work was supported by the Russian Foundation for Basic Research (grant № 15-03-04698).

Cu(I) catalyzed N-arylation of triazolopyrimidinones by diaryliodonium salts under MW-iradiation conditions

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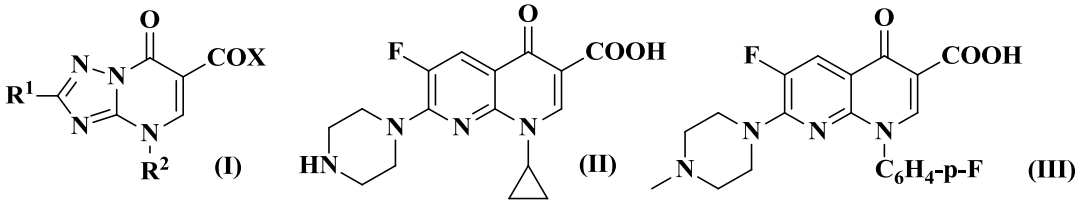
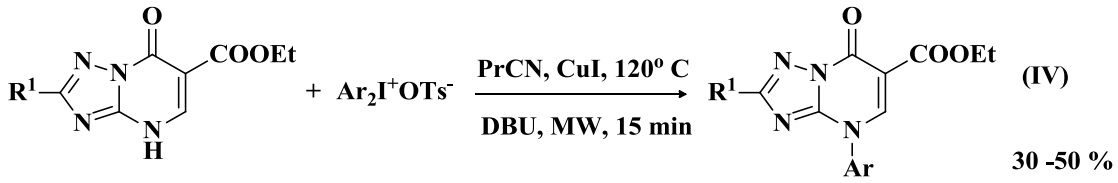
Easy available triazolopyrimidinones **I** (R^1 = H, Alk, Ar, $NAlk_2$; R^2 = H, X = OEt, NHAlk) are famous precursors of CB_2 cannabinoid receptor inverse agonists (R^1 = MeNBz; $R^2 = C_5H_{11}$; X = AdNH) **[1]**, perspective antiviral drugs (R^1 = H, Alk; R^2 = H, Alk; X = OEt, NHAlk) **[2]** and antibiotics ($R^1 = CF_3$, R^2 = H, X = OH) **[3]** - nearest analogues of fluoroquinolone carboxylic acids such as cyprofloxacine **II**. Modern antibiotics of the same structure contain N-Ar fragments instead of N-Alk groups, for example difloxacine **III:**



N-alkylation of triazolopyrimidinones **I** (R^2= H) proceeds without complications, though our attempts to realize direct N-arylation of **I** failed both using the classic method of Buchwald-Hartwig amination with aryl halides in the presence of Pd-complexes **[4,5**] and with boronic acids in the presence of $Cu(OAc)_2$ according to Chen-Evans-Ley protocol **[6]**. In our opinion, both approaches faild because of strong chelated binding of the catalyst metals by the substrates, which leads to withdrawal of catalyst from reaction mixtures.

Earlier, we have proposed methods for the N-arylation of nitroazoles by diaryliodonium salts in the presence of copper salts **[7]**. This method can be applied for arylation of triazolopyrymidinones **I** with further transformation of esters **IV** to the corresponding acids or amides:



R^1= H, CH_3, CF_3 **Ar = Ph, p-$CH_3C_6H_4$, p-ClC_6H_4**

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Asymmetric Friedel-Crafts reaction indoles with coumarin-3-carbonylates

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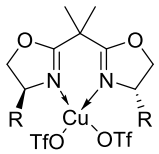
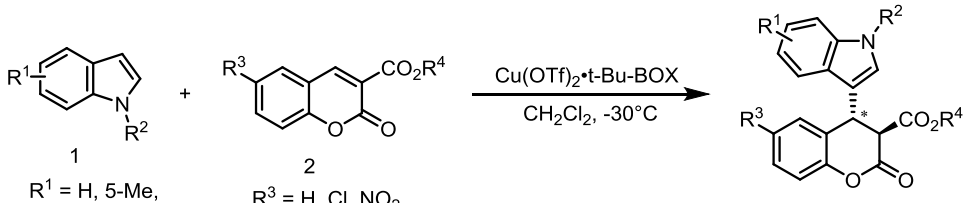
Substrates contains a fragment of indole or 3,4-dihydrocumarin are very interesting to medicine because they are present in many natural products and biological active compounds. It is use surprising that there have been attempts to unit both fragments in one molecules. These relations are known in both catalytic and noncatalytic versions. Along with indole another electron-rich aromatic compounds and nucleophiles were also tried in reactions with coumarin derivatives.



R-BOX, R = Bn, Ph, i-Pr, t-Bu

In this work we for the first time described the results of asymmetric version of Friedel-Crafts reaction between indoles and coumarin-3-carbonylats under catalytic condition using chiral complex $Cu(OTf)_2$·R-BOX (R = Bn, Ph, i-Pr, t-Bu) as a catalyst. It is known that bis(oxazoline) ligands belong to so-called privileged ligands and used often in asymmetric Friedel-Crafts alkylation.



1
R^1 = H, 5-Me, 5-OMe, 4-OMe
R^2 = H, Me

2
R^3 = H, Cl, NO_2
R^4 = Me, Et

3
yield: 40-81%
ee: 60-88%

We found the best condition of this reaction. We observed only trans-diastereomers for all reaction conditions The chiral complex $Cu(OTf)_2$·t-Bu-BOX was showed the most enantioselectivity for this asymmetric Friedel-Crafts reaction. Products of reactions were obtained with high yields (up to 81%) and high enantiomeric excess (up to 88%).

Synthesis, structure, and complexing of *N*-methylazacrown-ether styryl dyes

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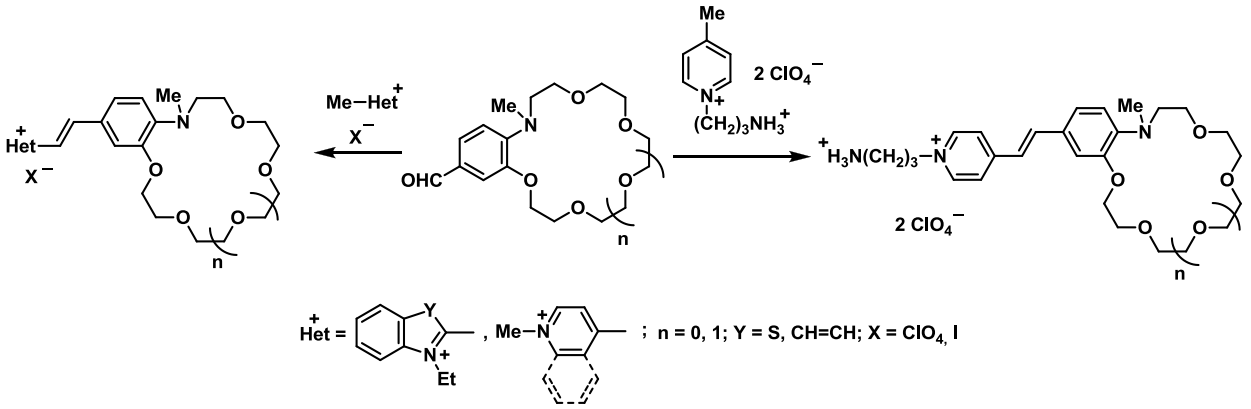
Benzannulated azacrown-ether derivatives are of significant interest for the preparation of photoactive crown compounds [1].

The 2-benzothiazole-, 4-pyridine-, and 2- and 4-quinoline-based styryl dyes containing an *N*-methylbenzoaza-15(18)-crown-5(6)-ether moiety were synthesized. The dyes were prepared in high yields (up to 89%) by condensation of *N*-methyl(formylbenzo)azacrown ethers with quaternary salts of heterocyclic bases in the presence of an organic base [2, 3].



A detailed electronic spectroscopy study revealed high performance of the dyes having an alkyl *N*-substituent in the heterocyclic moiety as optical molecular sensors for alkali and alkaline-earth metal cations [2]. They demonstrate strong cation-induced hypsochromic shifts in the absorption spectra (up to 136 nm) and cation-triggered emission with the enhancement factor reaching 61. The structural features of dyes and their metal complexes were studied by NMR spectroscopy and X-ray diffraction.

Spontaneous "head-to-tail" dimerization of the dyes having ammoniopropyl *N*-substituent in the heterocyclic moiety via the formation of numerous hydrogen bonds between the terminal NH_3^+ groups and crown-ether fragments was detected in solutions using ^{1}H NMR and electronic spectroscopy methods [3, 4].

This work was supported by the Russian Foundation for Basic Research (grant № 16-03-00267).

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Synthesis of alternating donor-acceptor copolymers based on (dithieno)dicyanovinyl and (cyclopentadithiophene)dicyanovinyl

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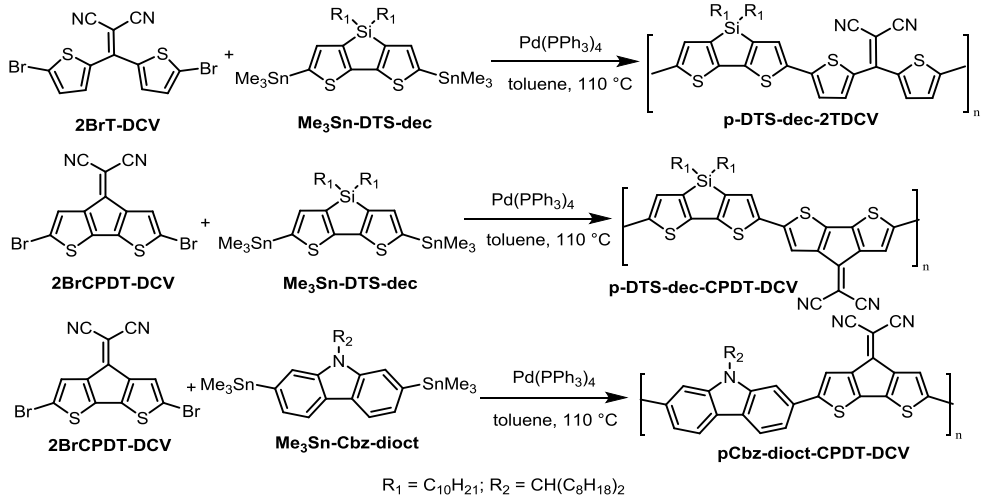
Nowadays, the development of the new efficient polymeric materials is the one of the prior branch of modern photovoltaics. Over the past years, new donor copolymers have been synthesized, which leading to increase the power conversion efficiency (PCE) of the organic solar cells (OSCs) based on them up to 10% [1]. Despite on huge number of the publications in this area, it is not always possible to obtain efficient donor copolymer because of the number of demands: definite positions of lowest unoccupied and highest occupied molecular orbitals (LUMO and HOMO) for the best conformity to the using fullerene acceptor's LUMO and HOMO levels, narrow band gap, wide absorption spectra, high solubility in the organic solvents.

One of the most popular approach, which allow to obtain efficient donor copolymer, is alternating in the polymer's chain both donor and acceptor fragments. By changing the number and electronegativity of such fragments, it is possible to adjust LUMO and HOMO levels and bandgap thoroughly.

The aim of this work was to synthesize alternating donor-acceptor copolymers with strong acceptor fragments: (dithieno)dicyanovinyl (**2T-DCV**) and (cyclopentadithiophene)dicyanovinyl (**CPDT-DCV**) and donor fragments: dithienosilol (**DTS**) and carbazole (**CBz**).



$R_1 = C_{10}H_{21}$; $R_2 = CH(C_8H_{18})_2$

At the first step, three new copolymers : **pDTS-dec-2T-DCV**, **pDTS-dec-CPDT-DCV** and **pCbz-dioct-CPDT-DCV** were synthesized using Stille reaction and characterized with NMR, element analysis, IR, GPC. At the next step, these copolymers were examined as donor materials in fabricating OSCs with convinient achitecture: ITO/PEDOT:PSS/copolymer : $PC_{71}BM$/Ca/Al. It was shown, that after OSCs optimization the best PCE was in the case of using **pCbz-dioct-CPDT-DCV**, which was up to 4%.

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Domino-reaction of 1-aroyl-3,4-dihydroisoquinolines with symmetric alkynes

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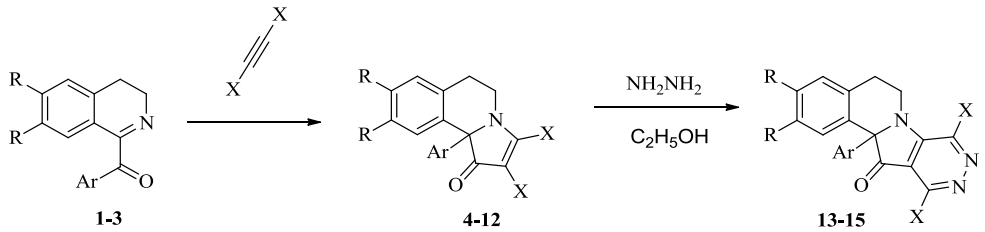
Pirrolo[2,1-*a*]isoquinolines exhibit a broad spectrum of biological activity which leads to increased interest in the development of new approaches to the synthesis of these heterocyclic compounds. Previously, we described a three-component reaction of 3,4-dihydro-1-aroylisoquinolines with terminally activated alkynes in alcohols for the formation of 3,4-dihydropyrrolo[2,1-*a*]isoquinolines [1].

Now we present a related transformation that proceeds in an alternative direction; the reaction with symmetric alkynes in aprotic solvents to produce 3,4-dihydropyrrolo[2,1-*a*]isoquinolines with with ester and ketone groups on the pyrrole ring. Reaction optimization was performed using the reaction of drotaveraldine with dimethylacetylenedicarboxylate. Initially, pyrroloisoquinoline **4** was obtained in 23% yield from the reaction conducted in Et_2O. Replacing Et_2O with benzene or toluene, increased the yield 35% and 73%, respectively. The optimal conditions were used in the reactions of various 1-benzoylisoquinolines **1-3** with dimethylacetylenedicarboxylate, diethylacetylenedicarboxylate and dibenzoylacetylene.

Scheme 1



1 R=OEt, Ar=3,4-$(EtO)_2$Ph
2 R=OMe, Ar=3,4-$(MeO)_2$Ph
3 R=OMe, Ar=p-Cl-Ph

After we have researched the condensation of corresponding pyrrolo[2,1-*a*]isoquinolines **6**, **9**, **12** with hydrazine in ethanol. Formation of pyridazine cycle was confirmed using ^1H and ^{13}C NMR, IR spectroscopy, and mass spectrometry. Attempt of ammonolysis of pyrroloisoquinolines containing ester groups with hydrazine first in ethanol, then in toluene was unsuccessful.

This work was supported by the Russian Foundation for Basic Research (grant 14-03-00311 and 15-33-20187-mol_a_ved).

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Synthesis and functionalization of a new heterocyclic system 1-R-5,10-dihydro[1,2]diazepin[4,5-*b*]indol-4(3*H*)-on

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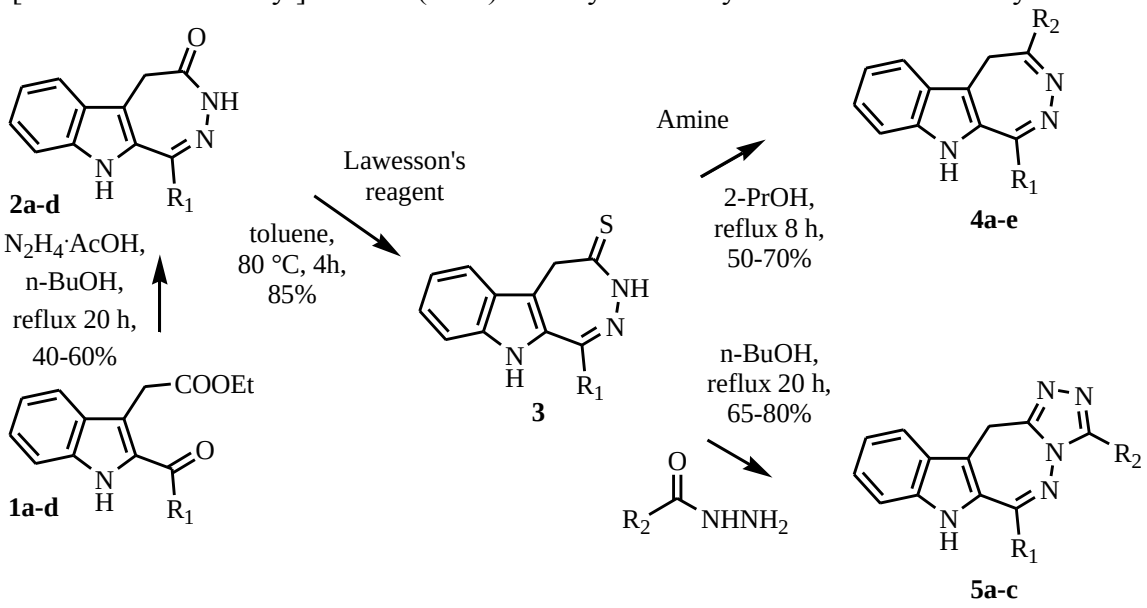
The 1,2-diazepine moiety is considered a prominent skeleton in medicinal chemistry, and many biologically active compounds, such as those with anti-inflammatory, anticonvulsant, antianxiety, antidepressive, sedative, psychoactive, and hypnotic activities, possess this important core. Herein, a facile synthetic route for a new 1,2-diazepines derivatives - 1-R-5,10-dihydro[1,2]diazepin[4,5-b]indol-4(3H)-ons starting from ethyl[2-aroyl-1*H*-indol-3-yl]acetates with good isolated yields is reported.

Convenient preparative procedures have been developed for the synthesis of previously unknown 1-R-5,10-dihydro[1,2]diazepino[4,5-b]indole-4(3H)-ones (**2a-d**) by cyclization of ethyl[2-aroil-1H-indol-3-yl]acetates (**1a-d**) with hydrazine hydrate under acid catalysis.



1, **2** R_1 = **a** 4-Cl-C_6H_4, **b** 4-Me-C_6H_4, **c** 3-OMe-C_6H_4, **d** 2-thienyl;
3, **4**, **5** R_1 = 4-Me-C_6H_4; **4** R_2 = **a** morpholine, **b** piperidine, **c** pyrrolidine, **d** N-Me-piperazine, **e** $N(Me)_2$; 5 R_2 = Aryl, Hetaryl

Some possible functionalization routs of new derivatives have been demonstrated for the compound **2b**. Thionation of the C=O moiety in the diazepine core was carried out by heating of **2b** derivative with Lawesson's reagent in toluene. Further nucleophilic substitution in diazepine-4-thione **3** proceeds under mild conditions at reflux in isopropanol with secondary amines to form 4-amino derivatives **4a-e**. Diazepine-4-thione **3** reacts with an appropriate amount of hydrazides by reflux in n-butanol. New triazolodiazepines **5a-c** have been obtained in a good yield.

The structures of all compounds have been confirmed by NMR ^1H and ^{13}C spectroscopy as well as chromato-mass-spectrometry.

Supramolecular [2+2] cross-photocycloaddition reactions of styrylpyridine derivatives

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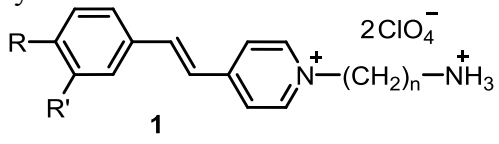
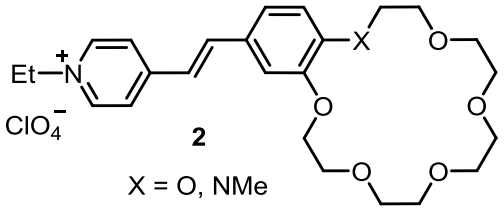
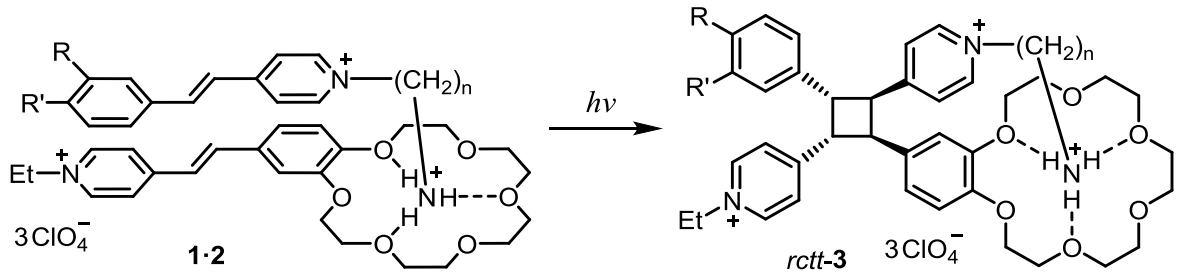
We elaborated the synthesis of styrylpyridine derivatives **1** having an ammonioalkyl substituent in the pyridine residue [1–3]. It was demonstrated that in MeCN the primary ammonium group of **1** can coordinate with the crown-ether moiety of dye **2**, which results in pseudodimeric complex **1·2**. In this complex the styrylpyridinium cations are arranged one above the other owing to stacking interactions. The stability constants of complexes **1·2** were measured by spectrophotometry and NMR spectroscopy.

It was found that the styrylpyridinium cations in complex **1·2** can undergo stereospecific [2+2] photocycloaddition reaction which produces cyclobutane **3** as the only *rctt* isomer. The quantum yield of this photoreaction was measured as a function of the substituents on the benzene ring of **1**. The structures of dyes **1**, complexes **1·2** and cyclobutanes *rctt*-**3** were studied by X-ray diffraction.



R = H, Cl, OMe, SMe, NO_2, NMe_2
R' = H, Cl, OMe; *n* = 2, 3





This work was supported by the Russian Science Foundation (project No. 14-13-00076), the Russian Foundation for Basic Research (grant No. 16-03-00267) and the Russian Academy of Sciences (Branch of Chemistry and Material Sciences).

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Investigation of the reaction of 6-(5-bromo-3,4-dihydropyrimidin-4-yl)--1*H*-perimidine with 2,4,6-trimethyl-1,3,5-triazine in PPA

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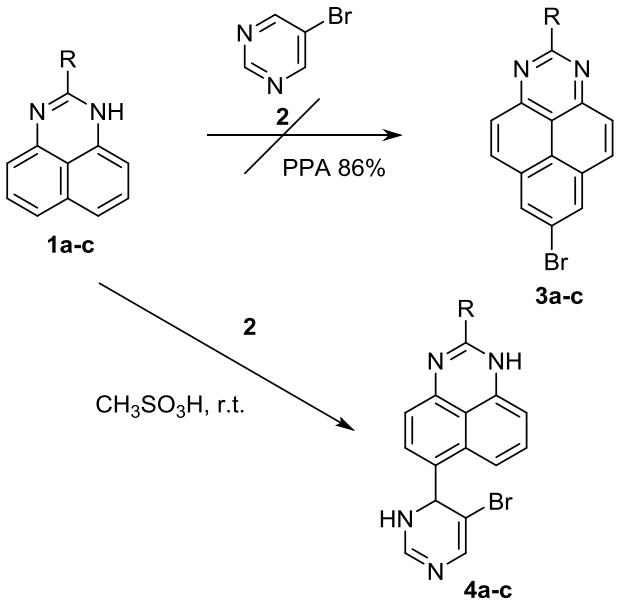
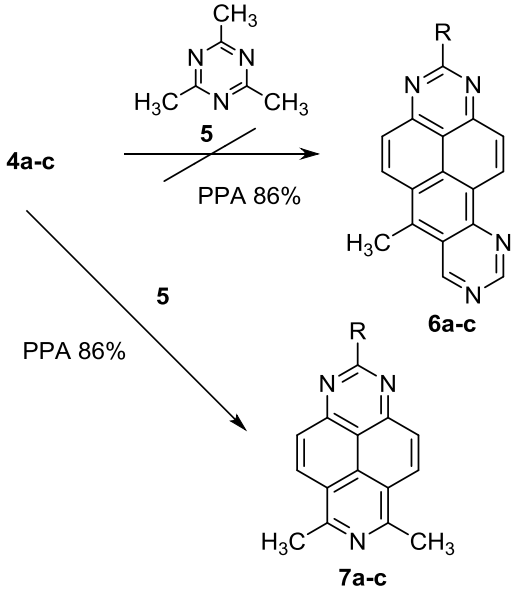
Recently in our laboratory a method of synthesis of 6-(5-bromo-3,4-dihydropyrimidin-4-yl)-1*H*-perimidines **4** was discovered [1]. These compounds were isolated as sole products in a reaction of 1*H*-perimidines **1** with 5-bromopyrimidine **2** in methanesulphonic acid. At the same time, the desired *peri*-annulation leading to the synthesis of 7-bromo-1,3-diazapyrenes **3** did not occur (**Scheme 1**):



Scheme 1 (R=H,Me,Ph)



Scheme 2 (R=H,Me,Ph)

We proposed that the following reaction of compounds **4a-c** with *simm*-triazine could end up with an annulation of quinazoline ring and lead to obtaining of quinazolino[6,7,8-gh]perimidines **6**. We used readily available 2,4,6-trimethyl-1,3,5-triazine **5**. Unexpectedly, synthesized earlier [2] 2-R(H)-6,8-dimethyl-1,3,7-triazapyrenes **7** were isolated as major products (**Scheme 2**).

This project received financial support from the Ministry of Education and Science of the Russia in the framework of the State Assignment to the Higher Education Institutions (grant №4.1196.2017/PP).

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Domino-reaction of α-cyanophenylacetonitrile with *o*-hydroxybenzaldehydes

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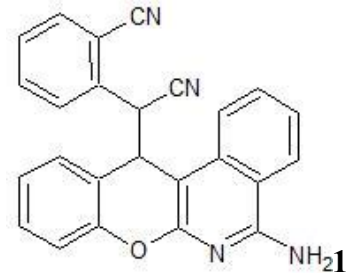
The development of effective methods for the synthesis of original bioactive compounds on the basis of domino- and multi-component processes is a challenging task of synthetic and pharmaceutical chemistry.

Examples of stereoselective reactions catalyzed by L-proline and occurring with high enantiomeric and diastereomeric excesses are widely known. We carried out a three-component reaction of homophthalonitrile and salicylic aldehyde in alcohol with the addition of 30 mol % of L-proline. The reaction mixture was refluxed for 30-45 hours, the precipitate formed was filtered off, washed with alcohol and air-dried. In this case, chromene **1-6** was formed in a yield of 60-94% and a diastereomeric excess of 90%.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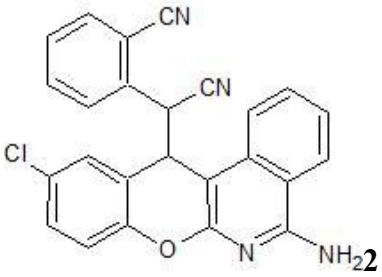
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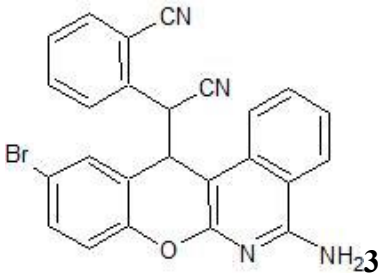
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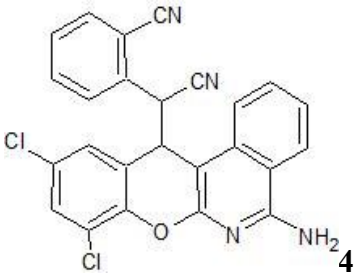
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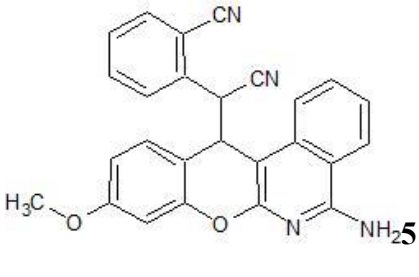
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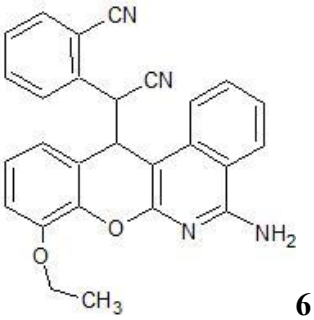
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Magnesium iodide catalyzed Friedel-Crafts alkylation of indole with α-ketoesters and imines

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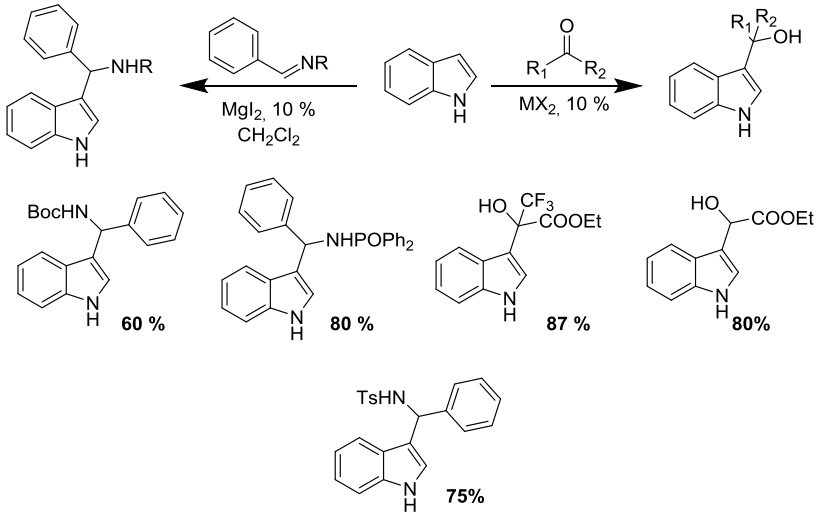
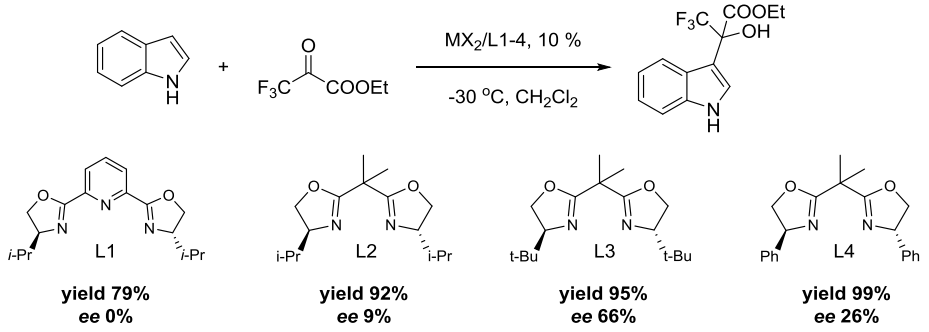
Addition of indole to C=O and C=N double bonds is an important reaction in synthesis of valuable compounds for pharmaceutical industry. It is known, that such reactions are catalyzed by salts and complexes of copper, zinc, titanium and scandium [1-3]. We had first show that the reactions of indoles with imines and α-ketoesters are catalyzed by magnesium iodide (scheme 1).



Scheme 1.

In addition, we had firstly studied the asymmetric addition of indole to methyl 3,3,3-trifluoropyruvate in presence of magnesium iodide complexes with bisoxazoline (Box) and pyridinebisoxazoline ligands (Pybox) (scheme 2)



Scheme 2.

This work was supported by the Russian Scientific Foundation (grant № 14-23-00186).

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Synthesis, structure and spectral properties of cyanine dyes containing terminal ammonium groups and photoactive supramolecular complexes based on them

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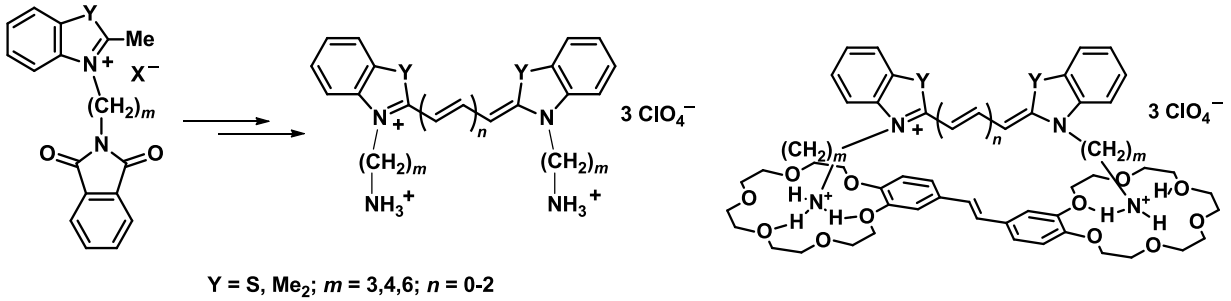
Self-assembled photoactive supramolecular systems formed by non-covalent interactions attract considerable attention. Cyanine dyes can be employed as light-sensitive components for the design of such supramolecular systems.

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 dyes with macroheterocyclic molecules containing electron-donating oxygen heteroatoms to form supramolecular complexes. Complexation was studied using absorbtion, luminescence and ^{1}H NMR spectroscopy.



The formation of supramolecular complexes of different stoichiometry was discovered. Their stability constants were determined.

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 RSF (project № 14-13-00076) and RFBR (project № 15-03-01883).

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Design and synthesis of novel BODIPY-based fluorimetric dual-mode chemosensor for mercury(II) cation and HS^- anion

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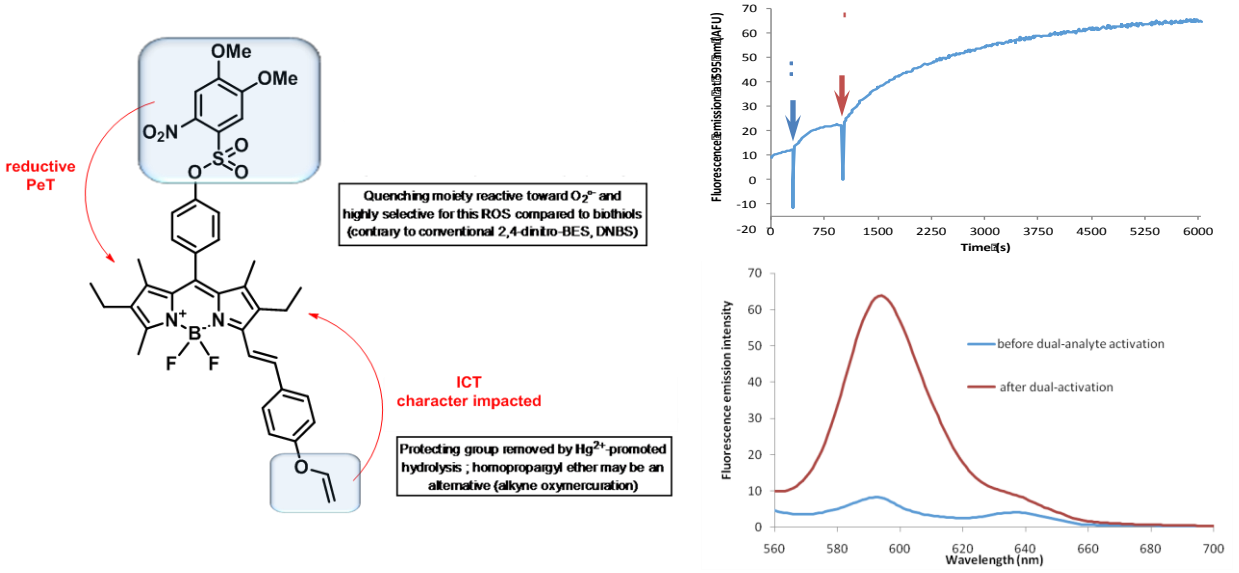
The multi-analyte detection has recently emerged as a valuable strategy in fluorescence sensing and imaging [1]. It entails the simultaneous monitoring of several (bio)chemical targets with a single probe, which leads to increased efficiency in a wide range of applications. Namely it appeals to improvement of therapeutics and diagnostics for medicine; the environmental monitoring of industrial wastes; noninvasively diagnose disease stages at the molecular level; molecular recognition and switching; drug delivery; molecular data-storage etc [2].

We have designed and synthesized a new 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) derivative that can act as a simultaneous dual "Off-On" sensor of biological biothiols and heavy metal cations. It represents bis-phenolic monostyryl-Bodipy dye whose the two OH groups are masked with 2,4-dinitrobenzenesulfonyl (DNBS) and vinyl quenching groups. The mechanism of its action implies thiolysis of the sulfinyl group of the weakly fluorescent DNBS-BODIPY by biological biothiols and simultaneous respond to mercury(II) cation through vinyl-BODIPY Hg(II)-mediated oxymercuration. The efficiency of this new dye as a dual sensor was probed in mixture of phosphate buffer (PB, 100 mM, pH 7.5) and CH_3CN (9:1, v/v) through sequential addition of aq. solutions of $HgCl_2$ and NaHS. The increase in the fluorescence intensity confirmed the ability of this dye to detect thiols and mercury (II) cations, with a view to application under physiological conditions.



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Solvent-free CuAAC polymerization catalyzed by N-heterocyclic carbene copper(I) complexes

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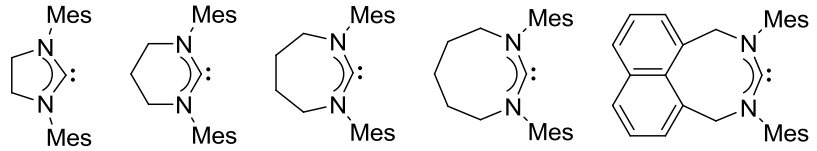
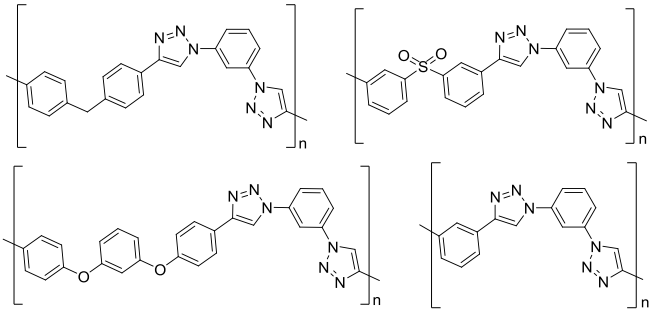
Derivatives of 1,2,3-triazole system, among which different types of 1,2,3-triazole-containing polymers, draw increasing attention because of its thermal stability in broad pH range on one hand and amide-triazole bioequivalence on the other. The main approach to 1,2,3-triazole system synthesis is copper-catalyzed azide-alkyne cycloaddition (CuAAC). Among different catalytic systems suitable for CuAAC copper(I) complexes with N-heterocyclic carbenes deserve special attention [1].

NHC are increasingly widely used as supporting ligands for transition metal catalysts due to its high donor and steric properties [2]. Simple and efficient approach for tuning of carbene properties is variation of a ring size of the NHC. Expanded-ring carbenes (er-NHCs) surpass their five-membered ring counterparts in stereoelectronic properties. These ligands are stronger donors and their steric bulk can be tuned in a wider range. Various copper(I) complexes with er-NHC were shown to be efficient catalysts in CuAAC reaction. However, there are no examples of application of er-NHC copper(I) complexes for 1,2,3-triazole-based polymers synthesis.



SIMes **THP-Mes** **THD-Mes** **HHD-Mes** **NaphtDHD-Mes**

In this study different (er-NHC)CuBr complexes were tested in polymerization reaction between organic bisazides and terminal bisacetylenes under solvent-free conditions. Exploiting the most efficient catalytic system a series of 1,2,3-trirazole-based polymers were obtained.



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Chiral macrocycles with BINAM moiety as fluorescent chemosensors

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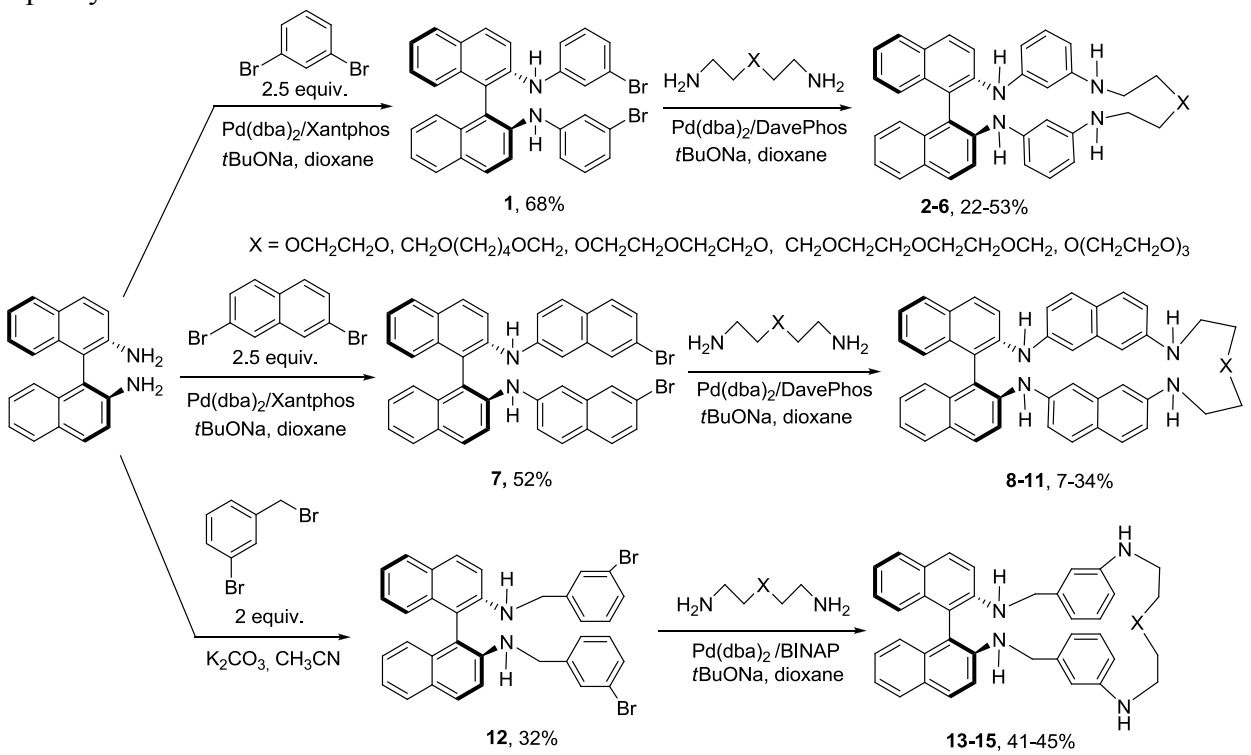
Macrocyclic compounds containing *C2*-chiral fragment of (*S*)-1,1'-binaphthalene-2,2'-diamine (BINAM) and aromatic spacers like 1,3-disubstituted benzene, 2,7-disubstituted naphthalene, oxadiamine linkers with different number of oxygen atoms were synthesized *via* Pd(0)-catalyzed amination reactions [1]. The syntheses of the *N,N'*-diaryl substituted BINAM **1** and **7** were run in the presence of $Pd(dba)_2$/Xantphos (Xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxantene), and macrocyclization reactions were catalyzed by $Pd(dba)_2$/DavePhos or $Pd(dba)_2$/BINAP (DavePhos = 2-dimethylamino-2'-dicyclohexylphosphinobiphenyl, BINAP= 2,2'-bis(diphenylphosphino)-1,1'-binaphthalene). The best yield of the macrocycles **2-6** with the phenylene spacer reached 53%, those with naphthalene spacer **8-11** – 34%, and those with benzyl spacer **13-15** – 45%.

Macrocycle **5** containing phenylene spacer and trioxadiamine linker possesses the fluorescence with the emission maximum at 490 nm, and in the presence of (*S*)-(+)-2-phenylglycinol a certain enhance of the emission with the hypsochromic shift of the maximum was observed. No changes were noted either in the presence of its isomer, (*R*)-(-)-2-phenylglycinol, or in the presence of other chiral amino alcohols like (*S*)- and (*R*)-2-amino-3-methyl-1-buthanol (L-and D-valinol), (*S*)-2-amino-1-propanol, (1*S*)-(2*R*)-2-amino-1,2-diphenylethanol.



This work was supported by the Russian Foundation for Basic Research (grant № 15-03-04698).

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New multicomponent condensation of ethylcyanoacetate with benzaldehyde and acetylacetone in the presence of sodium hydroxide

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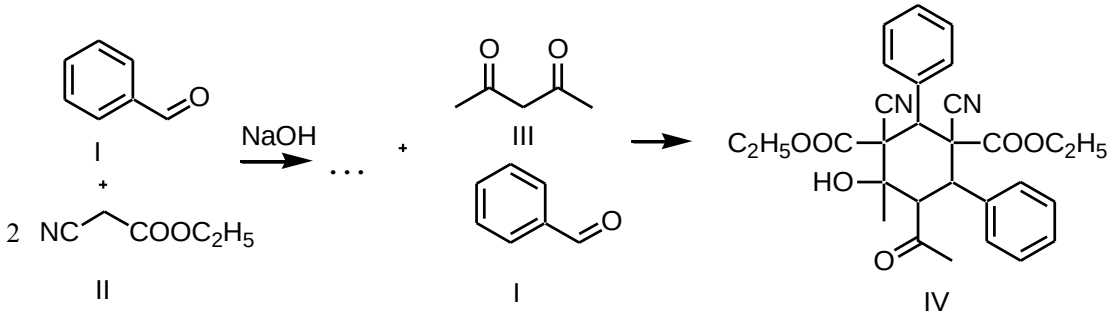
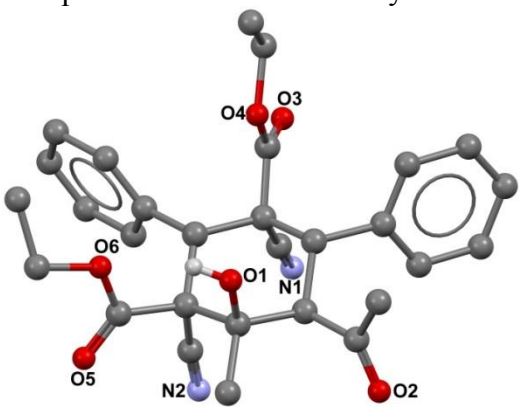
Multicomponent condensation is one of the rapidly growing fields of modern combinatorial chemistry. Multicomponent reactions are reactions in which three or more simultaneously added reagents converge to form a final product through a chain of consecutive elementary transformations. Among the variety of reagents used in the multicomponent condensation reactions particularly notable derivatives of cyanoacetic acid the success of those are summarized by review [1].

For the first time multicomponent condensation reaction of benzaldehyde with ethylcyanoacetate and acetylacetone in the presence of sodium hydroxide-which is not described in the literature was found by us. Reaction was carried out in ethanol at room temperature. Different sequence of reagent introduction to the reaction environment were carried out: in the beginning benzaldehyde (I) were mixed with ethylcyanoacetate (II) in molar ratio 1:2 accordingly in the presence of sodium hydroxide, then a mixture consisting from equimolecular quantities of benzaldehyde and acetylacetone (III) were added. As a result of reaction diethyl 5-acetyl-2,6-dicyano-3-hydroxy-3-methyl-1,2,3,6-tetrahydro-[1,1'-biphenyl]-2,6-dicarboxylate (IV) were obtained with a yield of 57 %.



The structure of synthesized compound were determined by RSA method, which is given below



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Synthesis of 3,9-alkyl-5-morpholin-4-yl-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]-2,7-naphthyridin-8(9*H*)-ones

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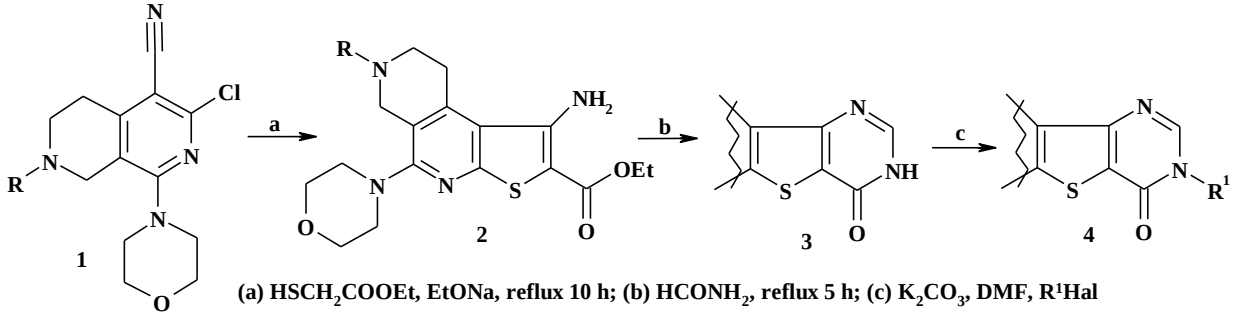
The combination of 2,7-naphthyridine ring with various heterocycles in one molecule, each of which carries some useful features, in the resulting polycyclic compounds in some cases may lead to new chemical and biological properties, which in turn opens up wide opportunities and perspectives to find new drugs. Taking into account that thieno[2,3-*b*]pyridines have a wide spectrum of biological activity as evidenced by the literature data [1], and by the results of our investigations [2], in the presented work we have synthesized new heterocyclic systems simultaneously having in their structure the above mentioned heterocyclic systems.

7-Alkyl-3-chloro-4-cyano-1-morpholin-4-yl-5,6,7,8-tetrahydro-2,7-naphthyridines **1** were used as starting compounds, in which the presence of two vicinal functional groups can provide the opportunity for a number of cyclization reactions [3]. The reaction of compounds **1** with ethyl mercaptoacetate resulted in the formation of ethyl 7-alkyl-1-amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-*c*]-2,7-naphthyridine-2-carboxylates **2**. The latter **2** were subjected to the cyclization by the action of formamide according to the Niementowski reaction, leading to the formation of the representative of new heterocyclic system: 3-alkyl-5-morpholin-4-yl-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]-2,7-naphthyridin-8(9*H*)-ones **3** (Scheme 1).

In the next step the regioselective *N*-alkylation of pyrimido[4',5':4,5]thieno[2,3-*c*]-2,7-naphthyridin-8-ones **3** with various alkyl halides in the basic medium was performed with formation of corresponding 3,9-alkyl-5-morpholin-4-yl-1,2,3,4-tetrahydropyrimido[4',5':4,5]-thieno[2,3-*c*]-2,7-naphthyridin-8(9*H*)-ones **4**.



(a) $HSCH_2COOEt$, EtONa, reflux 10 h; (b) $HCONH_2$, reflux 5 h; (c) K_2CO_3, DMF, R^1Hal

1–**3.** R = alkyl; **4**. R = alkyl, R^1 = alkyl; Hal = Cl, Br, I.

This work was supported by the RA MES State Committee of Science, in the frames of the research project (grant № 15T-1D221).

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Synthesis of 1*H*-pyrrolo[2,3-*b*]quinoline framework *via* Fischer reaction

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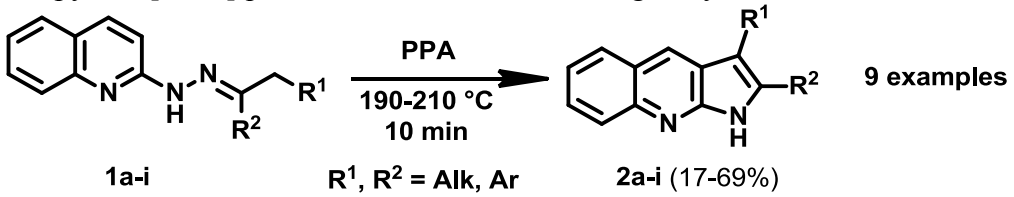
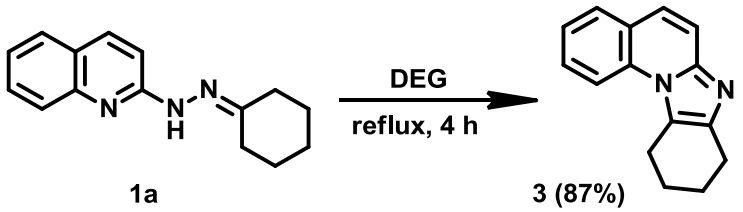
Pyrroloquinolines and their derivatives exhibit significant physicochemical properties and biological activities, in particular, they are the structural fragments of indoloquinoline [1] and marinoquinoline [2] alkaloid series. At the present time, there are no any universal synthetic approaches for the synthesis of pyrrolo[2,3-*b*]quinolines, as the Fischer reaction in the case of indoles. The Fischer cyclization may be successfully used in the synthesis of pyrrolo[3,2-c]- and [2,3-c]quinoline frameworks [3,4].We propose conditions (PPA, 190-210 °C, 10 min) for cyclization of 2-quinolylhydrazones of various ketones **1a-i** to produce the corresponding 2,3-disubstituted pyrrolo[2,3-*b*]quinolines **2a-i** in moderate to good yields.



The structure of starting carbonyl compound and its propensity to enolization affect the yield of pyrrolo[2,3-*b*]quinoline derivatives. Surprisingly, the use of thermal cyclization conditions (heating in diethylene glycol (DEG) for a few hours) leads to the 2,3-disubstituted imidazo[1,2-a]quinoline **3** in high yield.



This work was financially supported by the RFBR (grant № 17-03-00134).

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An ultrafast stage of the [2 + 2] photocycloaddition of styryl dyes mediated by cucurbit[8]urils

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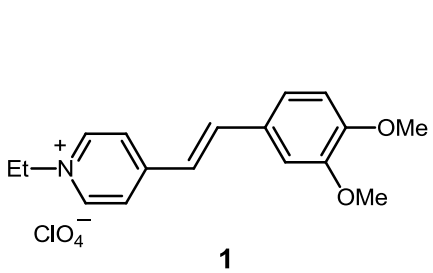
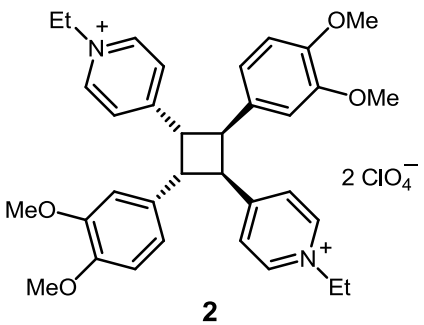
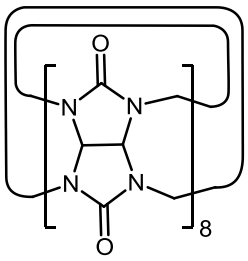
The [2 + 2] photocycloaddition of styryl dye, 4-[(E)-2-(3,4-dimethoxyphenyl)ethenyl]-1-ethylpyridinium perchlorate (**1**), mediated by 1:2 host-guest complexes with cucurbit[8]urils (CB[8]), was studied by means of fluorescence upconversion techniques. The quenching of florescence has been observed that leads to cyclobutane (**2**). The lifetime of 14.5 ps for excited **1** in aqueous solution and 3.8 ps for that in the presence of 0.5 equiv. of CB[8] were extracted from the fluorescence decay curves. The rate constant of such a quenching that was estimated by the classical Stern-Volmer formula is close to the diffusion control limit for bimolecular reactions.



1



2



CB[8]

The results of quantum-chemical calculations confirmed that in the ground state the geometry of reactants inside the cavity does not fit the topochemical principles and it requires a marked displacement to get a reaction-ready structure. The pre-organisation motion of excited **1** along a direction almost parallel to cucurbituril's axis was suggested on the basis of the measurements of time-resolved fluorescence anisotropy in the range of 1-5 ps.

The work was supported by the Russian Scientific Foundation (project no. 14-13-00751) and (in part) by the Russian Foundation for Basic Research (project no. 15-03-01883).

Interaction of derivatives of 2-amino-5-(2-aryl-2-oxoethylidene)-4-oxo-1*H*-4,5-dihydrofuran-3-carboxylic acid with *o*-aminophenol

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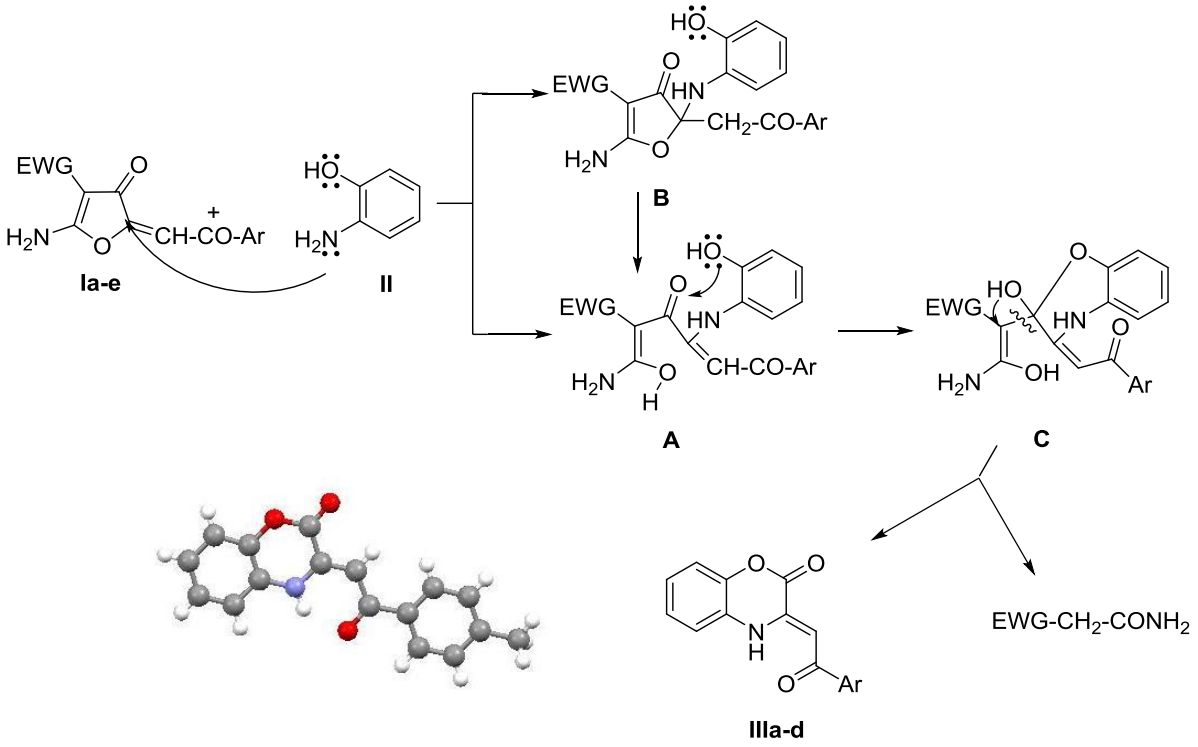
Nitriles and ethyl ethers of 2-amino-5-(2-aryl-2-oxoethylidene)-4-oxo-1*H*-4,5-dihydrofuran-3-carboxylic (**I**) [1] have been synthesized before have several reactivity centers are of organic synthesis interest.

We discovered, that interaction of 2-aminofurans (**Ia-e**) with *o*-aminophenol (**II**) in ethanol initiate formation of (Z)-3-(2-aryl-2-oxoethylidene)-3,4-dihydrobenzo[*b*][1,4]oxazin-2-ones (**IIIa-d**), which structure is confirmed by ^{1}H, ^{13}C, infrared spectroscopy data, and also X-ray spectral analysis method.



Ar=C_6H_5, EWG = CN, COOEt (Ia, Ib, IIIa); Ar = 4-$CH_3OC_6H_4$, EWG = COOEt (Ic, IIIb); Ar = 4-ClC_6H_4, X = COOEt (Id, IIIc); Ar = 4-$CH_3C_6H_4$, EWG = COOEt (Ie, IIId)

Possible scheme of compound **IIIa-d** formation includes Nitrogen-Amino **II** atom attack on Carbon C^5 Furan atom and NH_2 proton transfer to Oxygen Heterocycle atom or to Carbon Exocycle segment atom (**A** and **B** intermediates). Next **C** intermediate formation takes place and it decays to ethylcarbamoylacetate (EWG = EtOCO) or cyanoacetamide (EWG = CN) and benzo[*b*][1,4]oxazine (**IIIa-d**).

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Synthesis of 5-arylisatins

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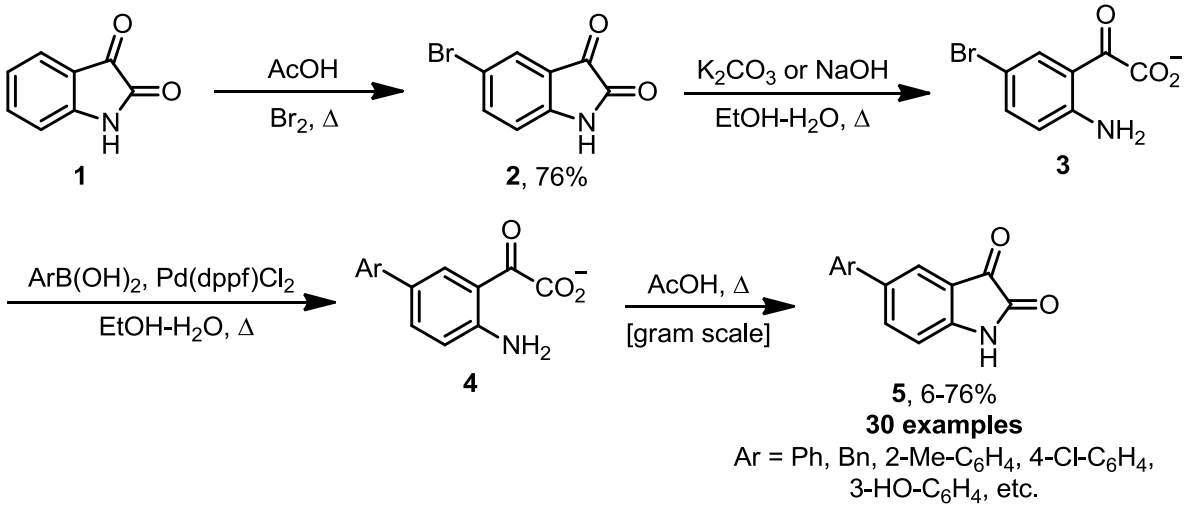
Isatin (indoline-2,3-dione) derivatives are widely used for the synthesis of various heterocyclic compounds which demonstrate different kinds of biological activity: antibacterial, antiprotozoal, antifungal, antiviral, anti-HIV, anticonvulsant and antihelminthic activities, influence CNS, participate in metabolism and stimulate the growth of plants [1]. In our research group, we have developed an efficient and practical technique for the synthesis of 5-aryl-substituted isatins employing palladium catalyzed Suzuki cross-coupling reaction as a key step.

Our synthesis commenced with the preparation of 5-bromoisatin **2** from commercially available isatin **1** by heating it with Br_2 in acetic acid. Then, 5-bromoisatin **2** was treated with inorganic base (K_2CO_3 or NaOH) in an ethanol–water mixture. After hydrolysis of initially formed *N*-anion (dark red color) an oxoacid anion **3** was obtained (transparent solution). At this point, arylboronic acids and palladium catalyst ($Pd(dppf)Cl_2$, 1÷5 mol.-%) were added to the reaction flask. Acidification of anions **4** with acetic acid furnished target compounds. As a result, a small library of 5-aryl-isatins **5** (30 examples) was synthesized.



In collaboration with scientists from Italy [2] the 5-aryl-isatine scaffold was identified to be a practical research tool for the design and realization of novel, potent and selective matrix metalloproteinases (MMPs) inhibiting agents, which could provide novel approaches to anticancer treatments.

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Synthesis of photo- and ionoactive 2-amino-1*H*-benzo[*d*]imidazole derivatives

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Heterocyclic iono(photo)active molecular switches of fluorescent activity are used to visualize cationic and anionic structures with a high degree of selectivity [1,2]. The alkylation of 2-amino-1*H*-benzo[*d*]imidazole **1** using 2-bromoethylphtalimide and subsequent hydrazinolysis led to the formation of 1-(2-aminoethyl)-1*H*-benzo[*d*]imidazol-2-amine **3** as well as various derivatives on its basis.

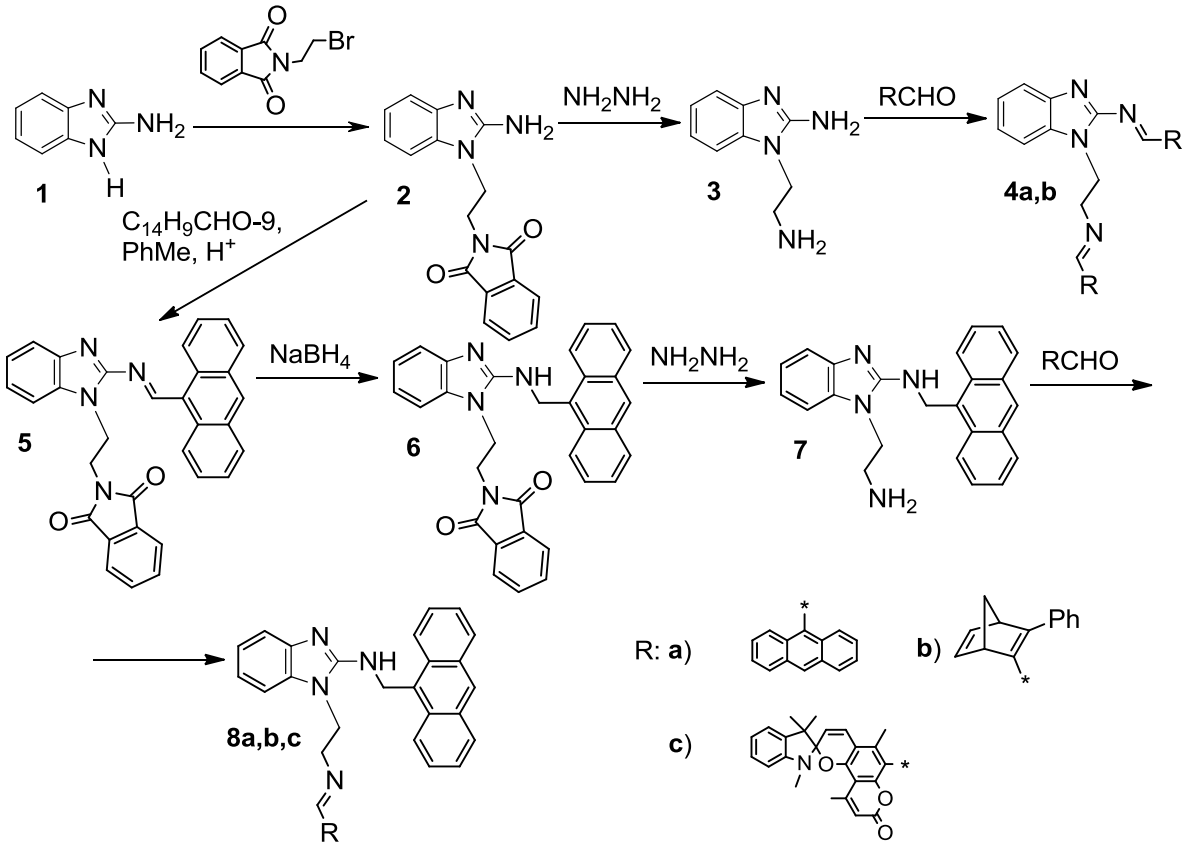

Photo- and ionochromic compounds **4**-**8** can be used as effective fluorogenic chemosensors for detection of *d*-metal cations and fluoride, cyanide and acetate anions.

This work was supported by the Russian Foundation for Basic Research (grant № 16-33-00439 mol).

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Synthesis of novel targeted molecules for the diagnosis and treatment of cancer: combination of cytostatics with metal complexes

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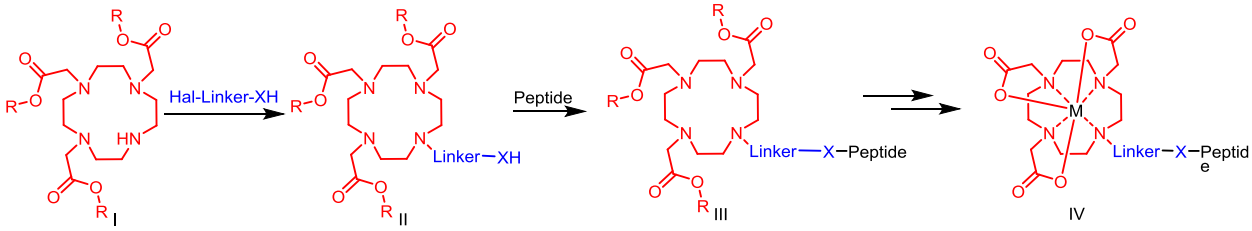
Targeted radionuclide therapy is one of the most intensively developing directions of nuclear medicine. Vector molecule as a part of radionuclide drug causes less collateral damage to normal tissues and allows targeted drug delivery to cancer cells. These metal complexes are widely used in SPECT (^{111}In and ^{68}Ga), MRI (^{86}Y and ^{157}Gd), PET (^{68}Ga, ^{64}Cu). Compounds of Tb^{3+}, Eu^{3+} and other lanthanides are used as fluorescent markers for the diagnosis of cancer and ^{90}Y and ^{177}Lu complexes are prospective agents for radionuclide therapy, making the modification of targeted cytostatic drugs an urgent task [1, 2].



R = Me, *t*-Bu
X = S, NH, O
M = ^{177}Lu, ^{157}Gd, Eu^{3+}, Tb^{3+}, ^{111}In, ^{68}Ga, $^{86/90}$Y, ^{64}Cu

The conjugation of a vector molecule to a chelate should not affect the biological activity of the drug, and chelating fragment should retain the ability to form highly stable complexes with metal ions. This can be achieved by covalent binding of the chelator **I** with a biologically active molecule through a linker. A number of DOTA-based bifunctional chelators **II** were synthesized by varying the linker (using carbon chains of various lengths, with different terminal functional groups). Methods for coupling chelating agents **II** with short peptides synthesized in previous works [3-5] were designed to obtain conjugates **III**. The complexation of these conjugates **III** with metal ions leads to targeted radionuclide drugs **IV**.

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Rare earth metal complexes with 5,5′-bitetrazolate dianion

Kirilenko N.Yu.[1], Chesnokov G.A.[1],Topchiy M.A.[2], Korotina E.V.[2], Krut'ko E.B.[2], Minaeva L.I.[3], Khrustalev V.N.[3], Muravyev N.V.[4], Grishin L.I.[4], Nikiforova A.S.[4], Utochnikova V.V.[1], Asachenko A.F.[2,3], Nechaev M.S.[1,2]

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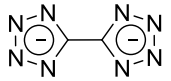
Nitrogen-rich, N-heterocyclic ligands, such as tetrazoles, have various points of interest. The ligand molecules themselves can be perceived as high-energy materials or nitrogen-generating agents. Complexes of rare earth elements (REE) with tetrazole-based ligands are interesting in view of the special spectroscopic, electronic and magnetic properties that can be expected for such compounds. It is, therefore, surprising that there is only one report on rare earth elements complexes of 5,5′-bitetrazole dianion (BT^{2-}, **1**) [1]. It was found that there are at least three different structural types in lanthanide series for $Ln_2BT_3{\bullet}xH_2O$.



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In our work missing rare earth metals complexes with BT^{2-} were synthetized through a modified procedure and their structures were determined by XRD. The structural types for the entire series are:

1) $[Ln_2(BT)_3(H_2O)_{12}]{\bullet}2H_2O$ for La and Ce;
2) $[Ln(BT)(H_2O)_7]_2(BT){\bullet}6H_2O$ for Pr, Nd, Sm, Eu and Gd;
3) $[Ln(H_2O)_8]_2(BT)_3{\bullet}4H_2O$ for Tb, Dy, Ho, Er, Tm, Yb, Lu and Y.

Luminescence properties of Eu and Tb compounds were investigated. For $[Eu(BT)(H_2O)_7]_2[BT]{\bullet}6H_2O$ it was found that the ratio of the europium bands depends on the excitation wavelength. It means that there is ligand to metal and metal to ligand energy transfer. Lifetimes of exited states were determined for Eu and Tb compounds and their deuterated analogs. From these data coordination numbers of metals were calculated. The results were in agreement with structures, determined by XRD.

Thermogravimetric studies were performed for REE 5,5′-bistetrazolates. For all studied compounds three stages of decomposition were observed. The obtained data reveal that the order of 1st stage mass loss on TGA-temperature curves is the same as its order in periodic table.

Recently the metal salts with high nitrogen content were proposed as additives to energetic formulations. So ammonium perchlorate (AP) and cyclotetramethylene-tetranitramine (HMX) combustion catalysis by synthetized rare earth element 5,5′-bistetrazolates were studied. No influence on HMX decomposition mechanism was observed, but AP decomposition was strongly influenced by addition of synthetized REE compounds.

This publication was financially supported by the Ministry of Education and Science of the Russian Federation (the Agreement number 02.a03.21.0008).

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New route to benzoxazoles based on annulation induced transformations of 1,2,3-triazoles

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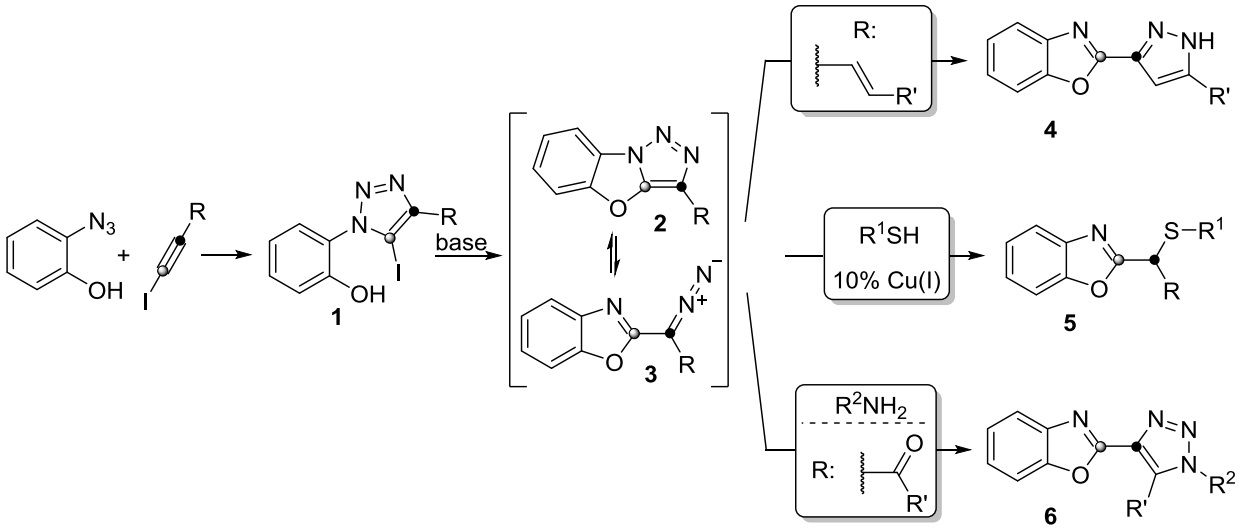
Benzoxazoles are an important class of heterocyclic compounds because this fragment is a well-known pharmacophore. A variety of natural and synthetic molecules containing benzoxazole moiety were shown to exhibit anticancer and antibacterial effects. Besides, benzoxazoles are used in agriculture and production of fluorescent dyes.

We have developed a new synthetic approach to benzoxazoles based on intramolecular nucleophilic substitution reaction in 5-iodo-1,2,3-triazoles **1**. Annulation of a new aromatic ring to 1,2,3-triazole induces tautomeric equilibrium between fused triazole (**2**) and highly reactive diazobenzoxazole (**3**). We have investigated a possibility to trap diazo tautomer **3**.

Intramolecular electrocyclization of vinylsubstituted iodotriazoles **1** provides pyrazolylbenzoxazoles **4** with almost quantitative yields. The similar reaction with imines, obtained *in situ* from aliphatic and aromatic amines, affords 2-triazolyl- substituted benzoxazoles **6**.



Annulation-tautomerization cascade with subsequent diazo trapping with thiols was promoted by $Cu(Ph_3P)_3Br$ and Et_3N in dioxane at 100 °C. Using our method we have obtained previously unknown benzoxazole derivatives **5** in good yields (52–84 %) by reaction of iodotriazoles with various thiols. The structure of new compounds was confirmed by ^1H and ^{13}C NMR spectroscopy and their composition – by MALDI-TOF mass spectrometry and elemental analysis. The mechanistic details of the domino reaction were investigated and all crucial intermediates were isolated and characterized.

Synthesis of indole-5,6-dicarbonitrile derivatives and modeling of their ^{13}C NMR spectra using DFT GIAO approach

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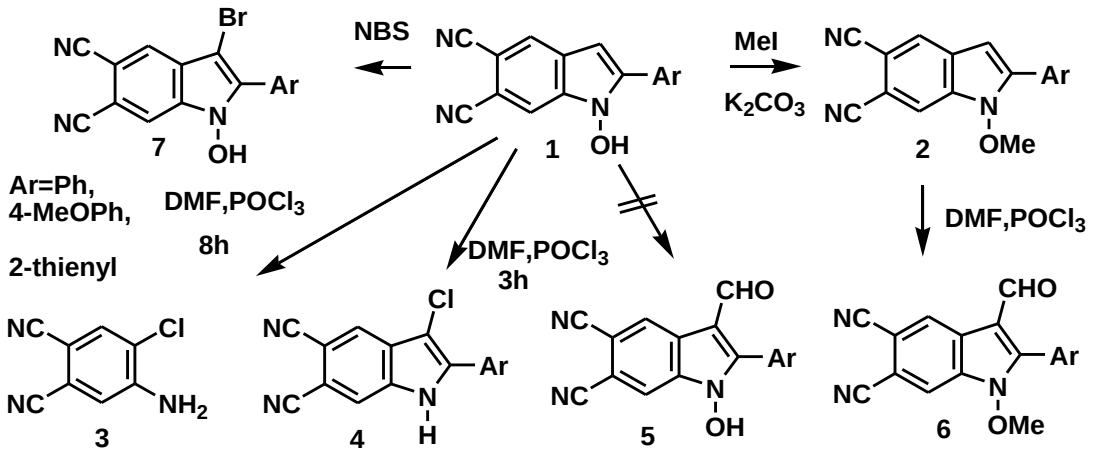
Various derivatives of indole-5,6-dicarbonitriles are potent inhibitors of the human MAO-A and MAO-B enzymes [1]. In some reactions based on 1-hydroxyindoles **1**, structures of reaction products are not always predictable. For example, a mixtures of 3-chloroindoles 4 were obtained instead of indole carbaldehydes **5** under Vilsmier-Haak reaction conditions (80°C, 3h). Unexpectedly, 4-amino-5-chlorophtalonitrile **3** was isolated as a main product of the Vilsmier-Haak reaction after 8h. Because structures of indole products can't be established only from ^{1}H-NMR and EI-mass spectra, X-ray analysis and ^{13}C NMR spectra should be used for an unambiguous determination of the reaction product structures.



In this work, ^{13}C NMR spectra calculated at the B3LYP/6-31+G* level of theory were in good accordance with real ^{13}C NMR spectra for all indole carbons except carbon atom with attached chlorine atom. For example, in ^{13}C-nmr spectrum of compound **3b** (Ar=4-MeOPh) signals of indole carbons are (C2) 142.3; (C7a) 134.1; (C4) 127.4; (C3a) 124.7; (C7) 115.6; (C6) 104.4; (C5) 103.8; (C3) 97.3, and calculated values are (C2) 142.4; (C7a) 130.6; (C4) 125.7; (C3a) 123.1; (C7) 113.8; (C6) 104.7; (C5) 104.7; (C3) 95.7. Calculated chemical shifts of carbons with attached chlorine atom are downshifted by 5-6 ppm from real ^{13}C shift and more complex calculation methods should be used.

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Synthesis of novel high functionalized triazole-linked calix[4]resorcinols *via click*-reaction

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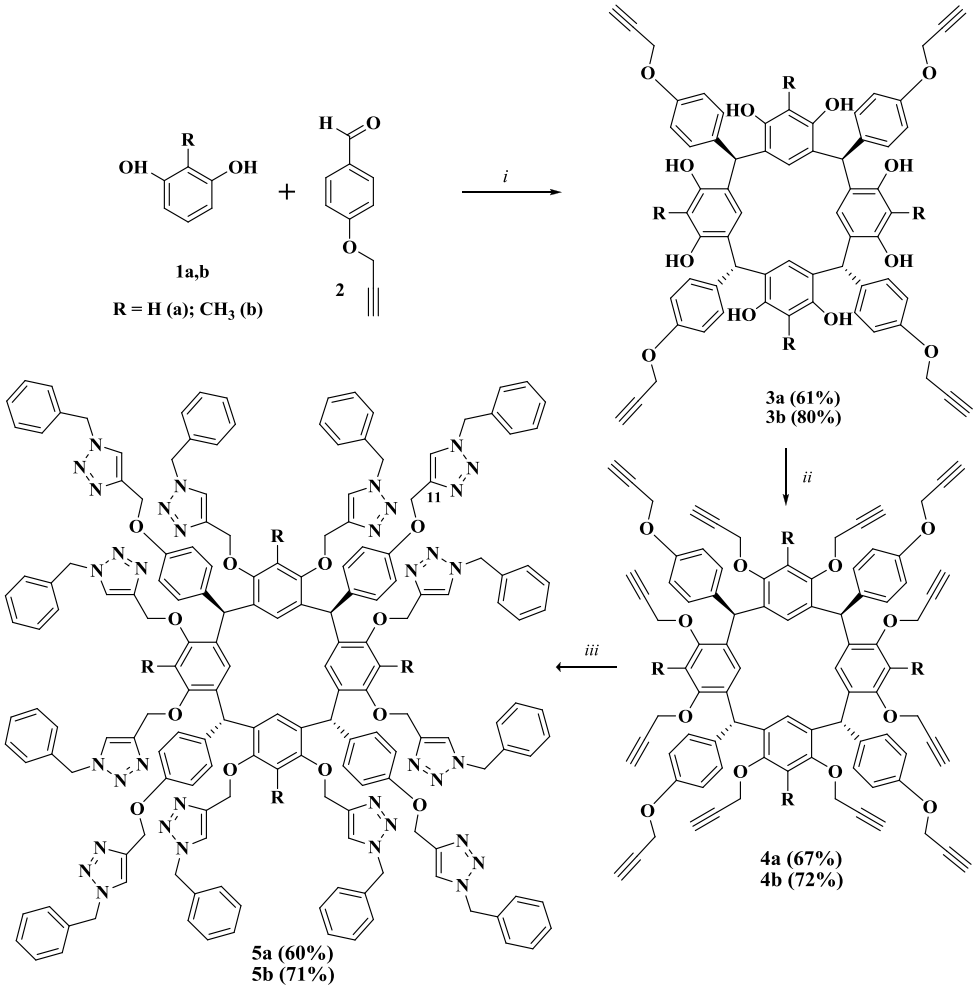
There is a growing interest of researchers in 1,2,3-triazole derivatives due to a broad variety of their properties. We synthesized new triazole-modified calix[4]resorcinols using one of the most popular methods for the preparation of 1,2,3-triazole derivatives, namely, *click*-reaction of calix[4]resorcinols containing 12 alkyne terminal groups with benzyl azide.



Scheme 1. Synthetic route to high functionalized triazole-linked calix[4]resorcinols

Reagent and conditions: *i*, CF_3COOH, $CHCl_3$, reflux; *ii*, $BrCH_2C{\equiv}CH$, K_2CO_3, MeCN, reflux; *iii*, BnN_3, sodium ascorbate, $CuSO_4{\cdot}5H_2O$, THF/H_2O, reflux.

This work was supported by Russian Foundation for Fundamental Research (Grant No. 16-03-00201-a).

Synthesis benzazecines with allene fragment from 1-phenylethynyltetrahydroisoquinolines and terminal alkynes

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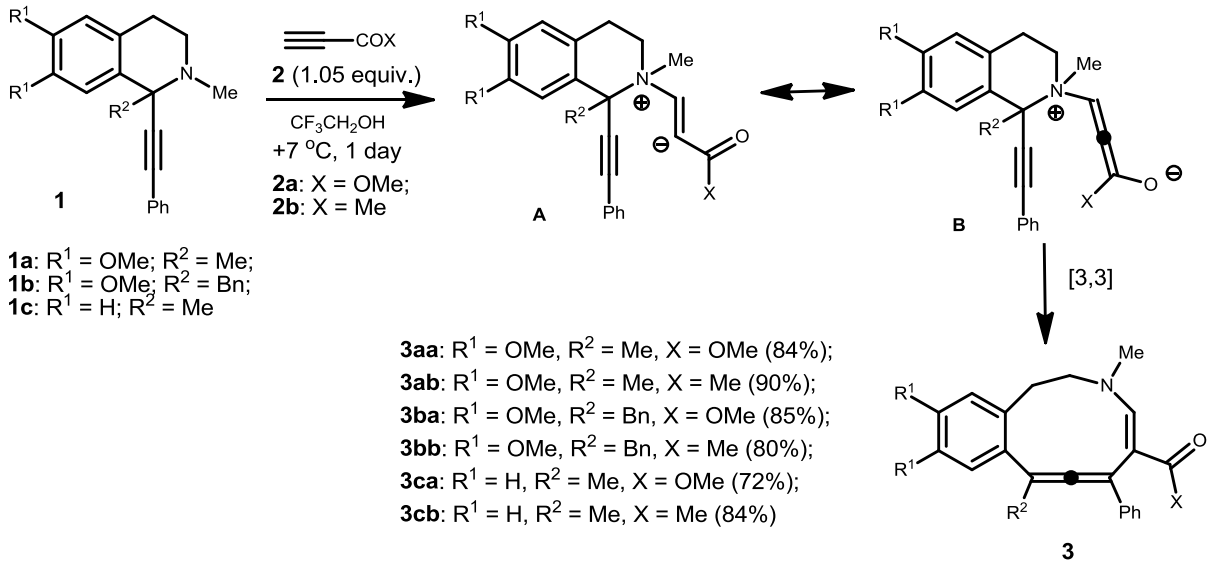
For the last 30 years allenes have been becoming popular among chemists. Methods for their synthesis, chemical properties as well as biological activity have attracted a great interest. For example, the most common among carotenoid, fucoxanthin, which is found in brown algae, possesses allene moiety and can be used as a promising agent for the treatment of diabetes and cancer [1].

In the literature there are only a few examples of the preparation of cyclic allenes with heteroatoms in the ring [2, 3], so this fact makes our research more important.. We have developed a regioselective method for the synthesis of benzazecines **3** with allene system in high yields. Cyclic allenes **3** were obtained from 1,1-disubstituted tetrahydroisoquinolines **1** and activated terminal alkynes **2** in trifluoroethanol at +7 °C. We also used methyl propiolate and acetylacetylene as activated alkynes. The reactions proceeded rather fast (3-24 hours). After evaporation of the solvent, the products were purified by recrystallization (EtOAc–hexane mixture), or in some cases by column chromatography.



This work was supported by the Russian Foundation for Basic Research (grant № 17-03-00605; 17-53-540001).

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Tandem aza-Cope/Mannich reactions for stereoselective synthesis of (3a*RS*,7a*RS*)-octahydro-1*H*-pyrrolo[3,4-*c*]pyridines

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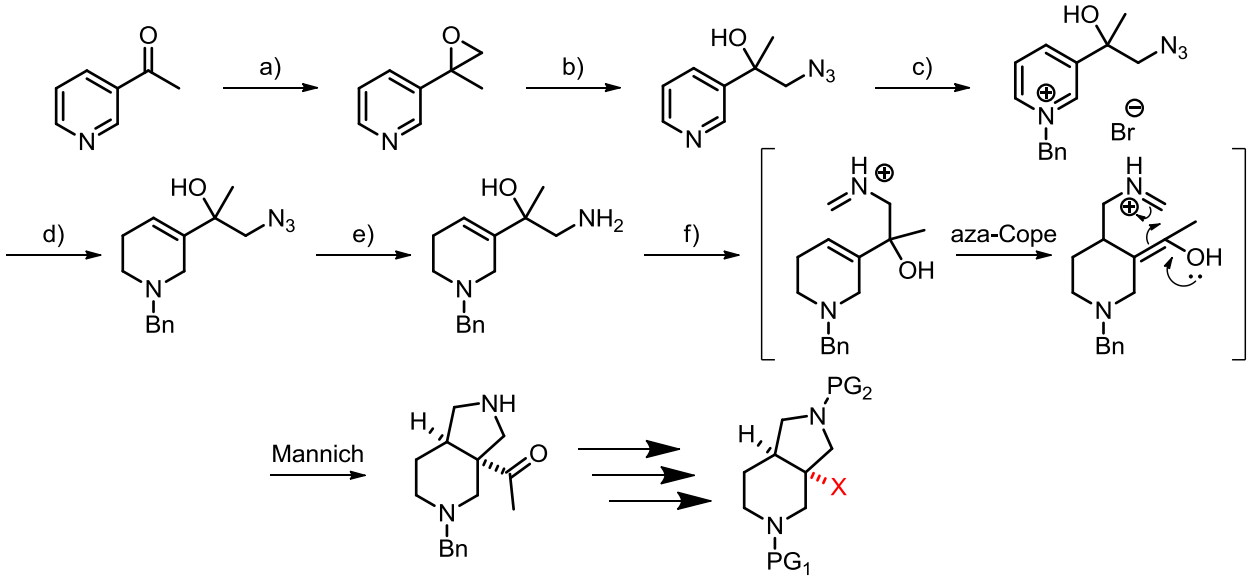
The search for novel small molecule scaffolds, rich in sp3 configured centers, and linking units in organic and medicinal chemistry is an ongoing challenge [1]. Saturated heterocycles with greater sp3 character have many advantages in terms of solubility, toxicity and ability to adopt complex structural shapes. New methodologies need to be developed to allow the efficient synthesis of these relatively complex scaffolds. Using aza-Cope/Mannich cascade reaction [2] we developed a new route to allow access to *cis*-fused 1-(3a*RS*,7a*RS*)-5-benzyloctahydro-1*H*-pyrrolo[3,4-*c*]pyridin-3a-yl)ethanone. Designing of different octahydro-1*H*-pyrrolo[3,4-*c*]pyridines bearing miscellaneous substituents at C3a position is now in development.



a) NaH, $Me_3S(I)O$, DMSO, THF; b) NH_4Cl, NaN_3, MeOH, 60^0C, 56% over 2 steps; c) BnBr, MeCN, 55^0C; d) $NaBH_4$, MeOH, -20^0C, 48% over 2 steps; e) $LiAlH_4$, THF, 0^0C, 94%; f) CH_2O_{aq}, CSA, THF, 45%

This work was supported by the Russian Foundation for Basic Research (grant № 14-03-01114).

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Synthesis of new fluorophores based on 2-methyltetrahydroquinazoline *N*-oxide

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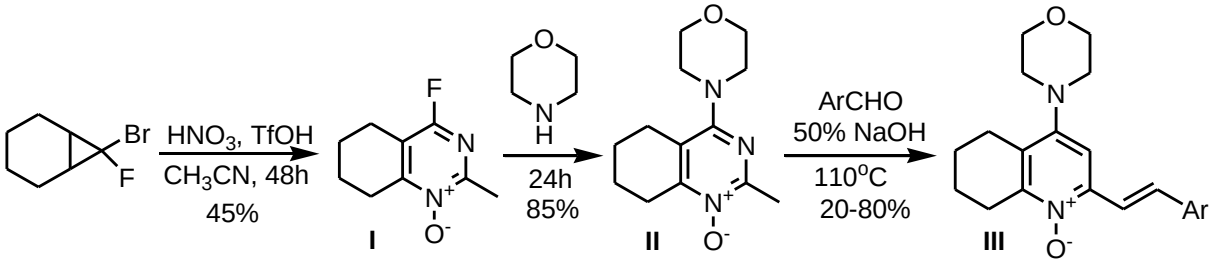
Pyrimidine represents a highly π-deficient aromatic heterocycle, which can therefore be used as electron withdrawing part in push-pull structures for intramolecular charge transfer (ICT). An effective ICT along the scaffold of the molecule can also induce luminescence properties. Such materials find widespread application in photonics, electronics and bioresearch. Pyrimidine *N*-oxide is even more π-deficient heterocycle that makes its derivatives promising exploration target. Nevertheless, the information about synthesis, application and photo-physical properties of pyrimidine *N*-oxide derivatives is quite limited due to low synthetic accessibility of these compounds.

Recently, an effective approach leading to easily functionalizable 4-fluoropyrimidine *N*-oxides **I** was found in our laboratory [1]. In present work, we describe synthesis and photo-physical study of new fluorophores **III** based on tetrahydroquinazoline *N*-oxide core.



Ar = Ph (**a**); 2,5-dimethylphenyl (**b**); 4-methoxyphenyl (**c**); 4-ethoxyphenyl (**d**); 3,4,5-trimethoxyphenyl (**e**); 4-formylphenyl (**f**); 4-(diethoxymethyl)phenyl (**g**); 4-(2-phenylvinyl)phenyl (**h**); -CH=CH-Ph (**i**)

A series of previously unknown heterocyclic compounds **III** was synthesized from tetrahydroquinazoline *N*-oxide **I** via aromatic nucleophilic substitution of fluorine and subsequent condensation of 4-aminosubstituted heterocycles **II** with aromatic aldehydes in basic conditions.

It was found that absorption wavelengths maxima for the compounds obtained were located in visible region (384–416 nm); the emission wavelengths maxima were located in range 527–560 nm (except for compound **IIIf**). The best result was obtained for tetrahydroquinazoline **IIIf**, containing an aldehyde function in *p*-position of phenyl fragment, that redshifts the longest-wavelength emission maximum to λ_{em} = 600 nm, nearer to therapeutic window (700–950 nm) and could be used for further design of new fluorescent probes for medical imaging.

This work was supported by the Russian Foundation for Basic Research (grant 17-03-00831-a) and the Presidium of RAS (Program N 8).

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Short and efficient preparation of highly substituted pyrimidines

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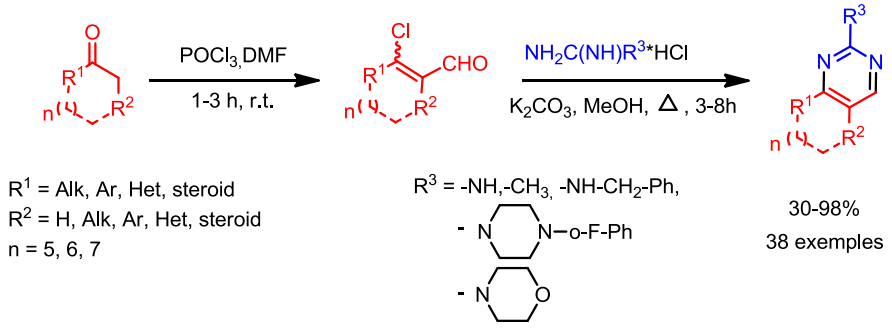
Pyrimidines represent important building block in natural products, agrochemicals, pharmaceuticals, and functional materials.[1] Especially, due to their special biological and pharmacological activities, pyrimidine scaffolds are widely present in numerous drug molecules such as vitamin B1, anti-inflammatory, antimicrobial, and antimalarial agents, antineuropathic pain drugs.[2] A number of synthetic approaches have also been developed for the synthesis of pyrimidines through the cascade condensation of amidines with 1,3-dicarbonyl derivatives or α,β-unsaturated ketones.[3] However, most of the methods mentioned above suffered from drawbacks such as harsh reaction conditions and starting materials that require multistep synthesis. Therefore, a simple and effective method for the synthesis of pyrimidines from simple and readily available starting materials still remains highly desirable.

We have developed a novel and efficient two step protocol for the synthesis of structurally important pyrimidine derivatives *via* Vilsmeier-Haack reaction/annulation/aromatization processes from commercially available guanidines/amidines and enolizable ketones. Various ketones including the symmetrical and asymmetrical, acyclic and cyclic, aromatic ketones, were involved in reaction with the Vilsmeier-Haack reagent providing corresponding β-chlorovinyl aldehydes. Treatment of the former with guanidines/amidines in the presence of base resulted in series functionalized pyrimidines in yields up to 98%.



Unlike previous processes, the present practical method avoids the requirement of an anaerobic procedure, uses inexpensive reagents, tolerates an array of functional groups. This simple, additive-free methodology was successfully applied for the efficient synthesis of heterosteroids and semi-synthesis of the anticancer drugs - Imatinib and Motsetinostat starting from readily available starting materials.

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A facile synthesis of benzo[*d*]-3-aza-deca-4,6,7-triens

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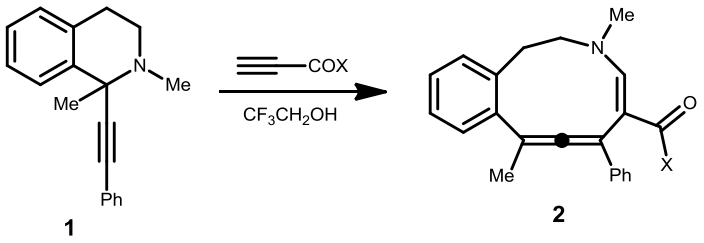
Azecine fragments have been found in a number of natural products. The well-known alkaloids protopine and allocryptopine [1] were isolated from plants of the families Berberidaceae, Papaveraceae, Fumariaceae, and Rutaceae. Both compounds play important roles in protecting plants from biotic stress and also exhibit several biological effects in mammals.

Only a few synthetic methods for condensed azecines have been published. They all are based on difficulty accessible starting materials and can hardly be considered common.

We have developed a regioselective method for the synthesis of benzo[*d*]-3-aza-deca-4,6,7-triens **2** with allene system in high yields. Cyclic allenes **2** were obtained from 1,1-disubstituted tetrahydroisoquinolines **1** and activated terminal alkynes in trifluoroethanol at +7 °C. We also used methyl propiolate and acetylacetylene as activated alkynes. The reactions proceeded rather fast (3-24 hours).



1 **2**

2a X = OMe (72%)
2b X = Me (84%)

This work was supported by the Russian Foundation for Basic Research (grant № 17-03-00605; 17-53-540001)

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5'-Aryl substituted 2,5-bis(3-decyl-[2,2'-bithiophen]-5-yl)-1,3,4-oxadiazoles. Synthesis and optical properties

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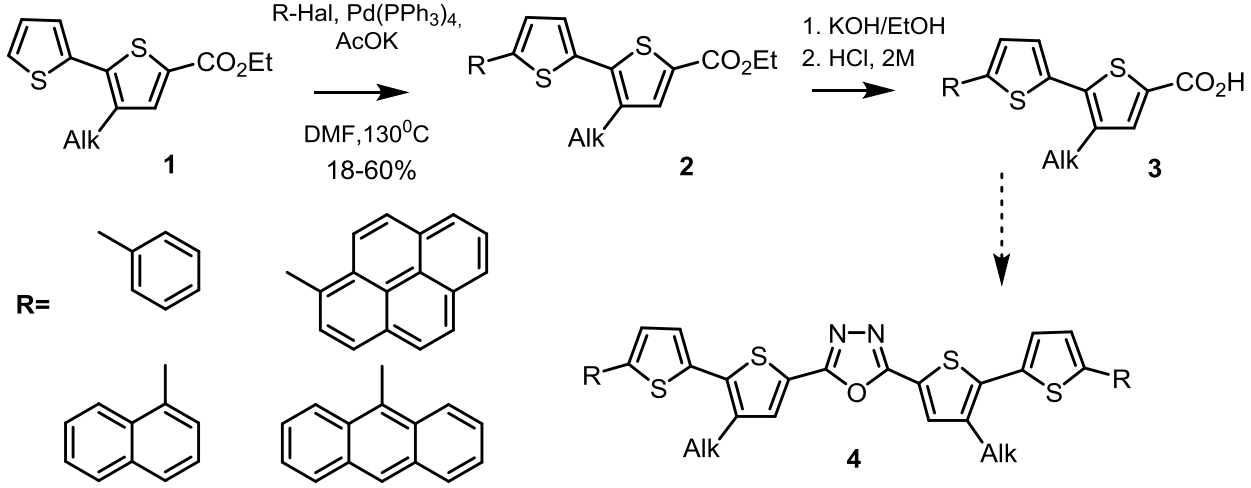
Bis bithiophene substituted 1,3,4-thiadiazoles, 1,3,4-oxadiazoles and 1,2,4-triazoles are promising components of active layers in various electronic devices such as organic light emitting diodes and field effect transistors because they combine special optical and electrochemical properties [1,2]. New photoluminescent 5'-aryl substituted 2,5-bis(3-decyl-[2,2'-bithiophen]-5-yl)-1,3,4-oxadiazoles were prepared by palladium catalyzed coupling from readily available compounds such as ethyl 3-decyl- [2,2'-bithiophene] -5-carboxylate and aryl halides. In our previous papers [3] we proposed an easy and efficient method for the preparation of alkylbithiophenes derivatives **1**, which were used as precursors of **2**. Optical properties of new donor−acceptor compounds **4** were investigated. Arylsubstituted ethyl 3-decyl- [2,2'-bithiophene] -5-carboxylate **3** were used as starting material for the preparation of conjugated derivatives of 1,3,4-oxadiazoles **4** which are promising materials for organic electronics.



This work was supported by the Russian Foundation for Basic Research (grant №16-33-00340 mol_a, 15-43-04313a) and the Ministry of Education and Science of the Russian Federation (the Agreement number 02.a03.21.0008)

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Synthesis of new oligomers containing 1,3,4-oxadiazole and bithiophene units

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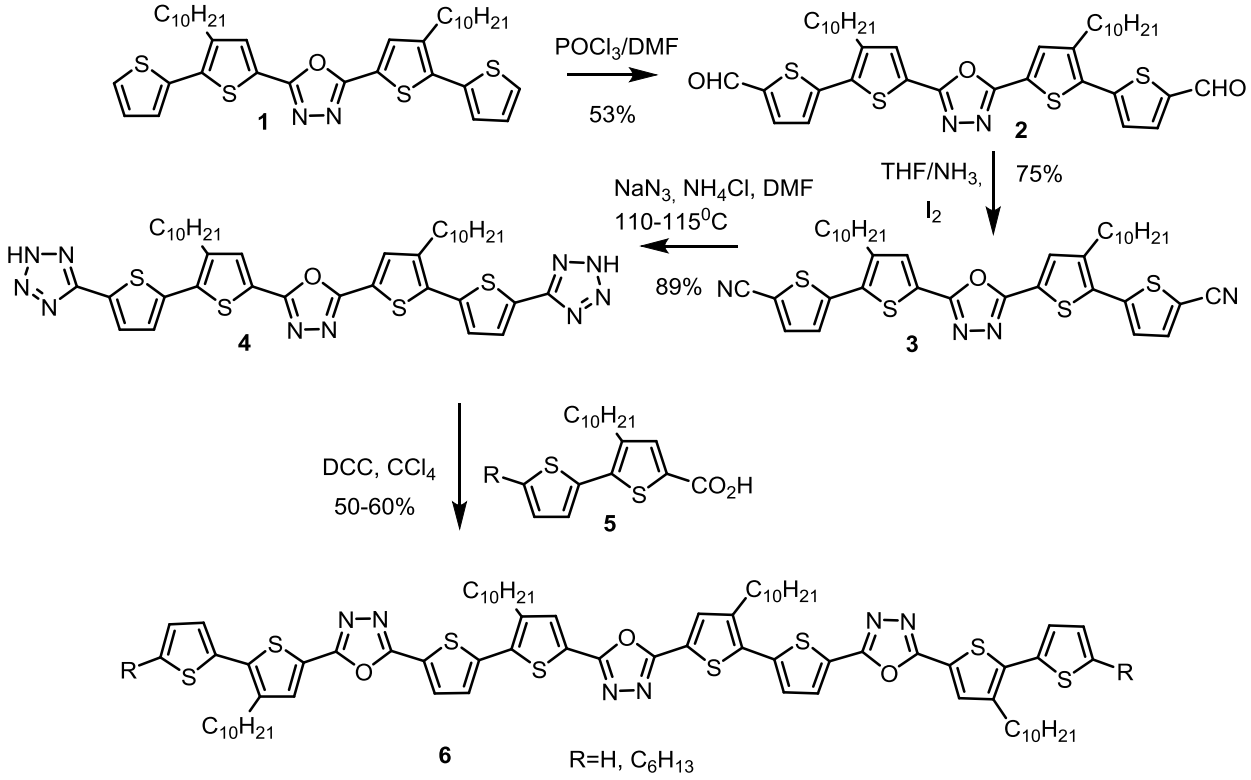
Recently, we have developed a simple method for the preparation of linear D-A-D compounds with one or two central 1,3,4-oxadiazole units [1-2] in conjugated chain. These compounds were used as components of organic LEDs [3]. Here we present a new approach for the synthesis of oligomers 6 consisting from eleven π-conjugated thiophene and 1,3,4-oxadiazole units as promising molecules for organic electronics. These compounds were synthesized through consistent functionalisation bis bithiophene substituted 1,3,4-oxadiazole 1 to formyl- (2), nitryl (3) and tetrazolyl (4) derivatives. The oligomers 6 were prepared by reacting of the tetrazolyl derivative 4 with building blocks 5 in the last stage.



This work was supported by the Ministry of Education and Science of the Russian Federation (the project number 4.1657.2017/ПЧ).

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New regioselective approach to 5-carboxy-1,2,3-triazoles based on Pd-catalyzed alkoxycarbonylation

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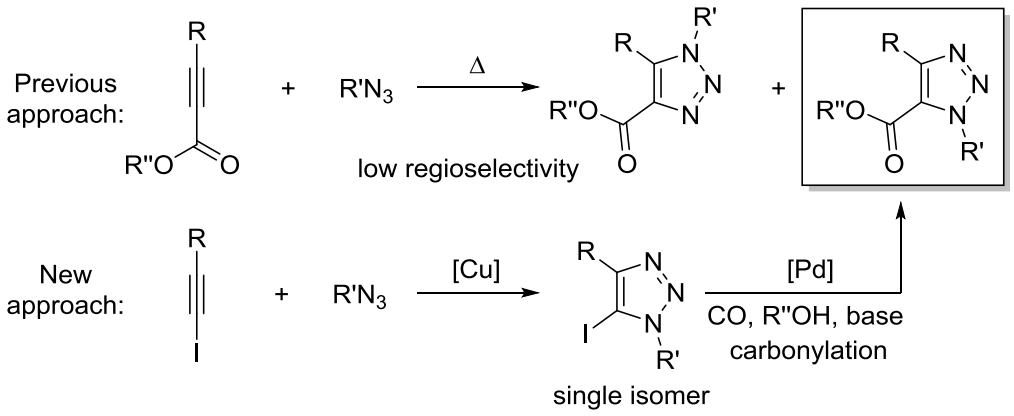
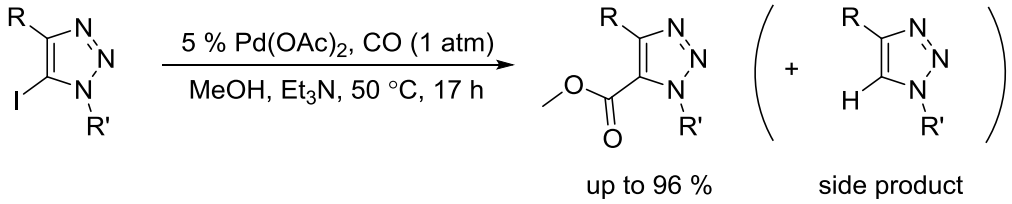
Various compounds containing 1,2,3-triazole moiety are of great importance in coordination and supramolecular chemistry, medicine, polymer and materials sciences. In particular, some 5-carboxy-1,2,3-triazoles were shown to be kinases inhibitors as well as to exhibit antiviral and antibacterial effects [1]. So far, the only synthetic route to these compounds was thermal [3+2]-cycloaddition of organic azides to propiolic acid derivatives. The main drawback of the method is low regioselectivity. Formation of two regioisomers diminishes yields of desired 5-carboxy-1,2,3-triazoles and complicates isolation of the products. Since 5-iodo-1,2,3-triazoles can be prepared from 1-iodoalkynes and azides under Cu(I) catalysis [2], the subsequent carbonylation reaction could became a new regioselective approach to 5-carboxy-1,2,3-triazoles.



We have shown that alkoxycarbonylation of 5-iodo-1,2,3-triazoles could be performed under mild reaction conditions with 1 atm of CO in the presence of 5 % $Pd(OAc)_2$. Various functional groups (ester, hydroxyl, ketone, nitro) were tolerated, and a number of 5-methoxycarbonyl-1,2,3-triazoles were obtained in good to excellent yields. The transformation appeared sensitive to steric effects, and bulky substituents led to decrease in reaction rate and/or yield.



This work was supported by RFBR (grant № 16-33-00801 mol_a).

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New anticancer drugs based on different types of spiro compounds: new results, biological testing

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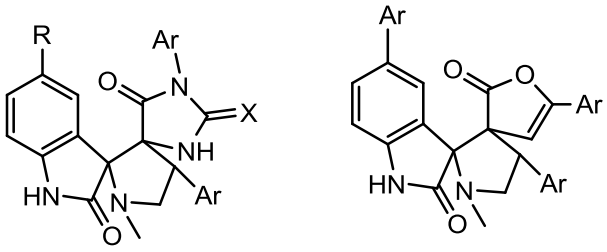
Compounds containing in its composition fragment of spiroindolinone are a new type of anticancer drugs, biological activity of this compounds based on the inhibiting protein p53-MDM2 interaction.

In this paper we developed synthetic methods for producing spiroindolinones containing oxazolone and tiogidantoin rings from available reagents by reaction of 1,3-dipolar cycloaddition. The resulting compounds were tested for biological activity on the cell lines PC3, LNCap, HCT p53 (+, +) and HCT p53 (-, -). Their toxicity is shown in micromolar concentration.



R = H, Cl, Br ; X = O, S, S(Me)

The structures of the compounds were shown by a full set of physical and chemical methods of analysis: ^{1}H NMR spectroscopy and HRMS.

This work was supported by the Russian Foundation for Basic Research (grant № 16-33-60166).

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Phenylacetylene complexation with cyclodextrins in solution

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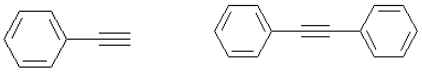
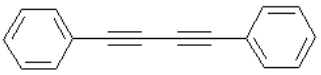
Cyclodextrins (CD) are natural macrocyclic oligosaccharides, composed of glucose residues. The outer surface is hydrophilic, the cavity is hydrophobic, allowing them to form water-soluble inclusion complexes "host - guest". The CD cavity significantly changes photophysical properties and reactivity of guest molecules.

In this study we investigate the complexation of acetylene derivatives 1-3 with α- and β-CD.



1 2



3

Absorption spectra of water solutions of 1 and 2 before and after the addition of cyclodextrines were analyzed, as well as after maintaining the solutions for several days.

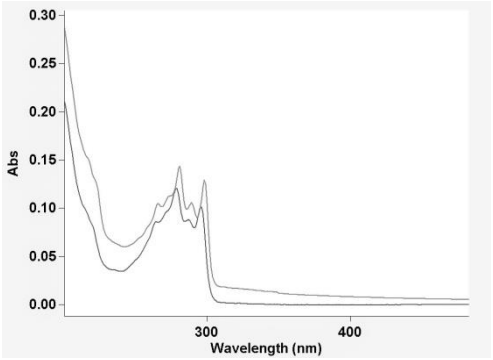


Figure 1. Absorption spectra of 2, Δλ under 3nm.

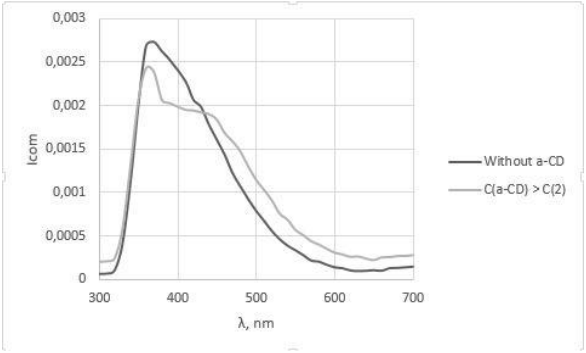


Figure 2. Fluorescence spectra of 2.

We analyzed changes in the absorption spectrum for the start and end points of the titration of the tolane solution in the presence of α-CD. Complexation constants of α-CD with tolan estimated by the spectrofluorimetric titration method, lg K=3,83.

Study of the formation of cyclodextrine-acetylene complexes may be used to describe the fundamental influence of homogeneous microenvironment on the properties of the material forming organic compounds.

This work was financially supported by the Russian Scientific Foundation (15-13-00163).

Highly asymmetric 1,9-disubstituted dipyrrins via nucleophilic substitution by aromatic amines

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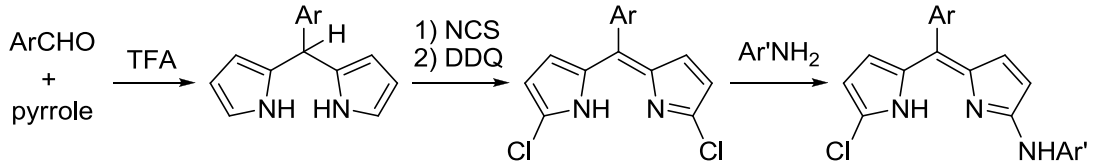
A number of novel dipyrromethene ligands bearing peripheral functional groups were synthesized using S_NAr substitution reaction with N-nucleophilic agents. The resulting dipyrromethenes in free base form and their boron fluoride (BODIPY) derivatives are expected to be the sensors for transition metal ions. Besides, their metal complexes are expected to be useful in catalysis.

The synthetic route includes 3 steps (see the scheme below): a. acid catalyzed condensation of pyrrole and arylaldehyde resulting in dipyrromethane [1]; b. chlorination followed by oxidation to dipyrromethene; [2]; c. nucleophilic substitution reaction. The latter is a novel reaction investigated for dipyrromethene substrates by the authors of present work [3]. Substitution of chlorine atoms by N-nucleophiles react yielding asymmetric mono-aminosubstituted dipyrromethenes only. Neutral and protoneted forms of the products have beem characterized by ^{1}H NMR; acid-base properties werestudied by UV-Vis titration method. Ligands exibit two absorbtion bands and weak fluorescence. The nature of this phenomenon is under investigation.



The synthesis of new BODIPYs based on these asymmetric dipyrrins has been performed and their optical properties were studied in various solvents.

Financial support of Russian Foundation for Basic Research (Grant No. 17-03-01267) is gratefully acknowledged.

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Synthesis of benzimidazolephanes

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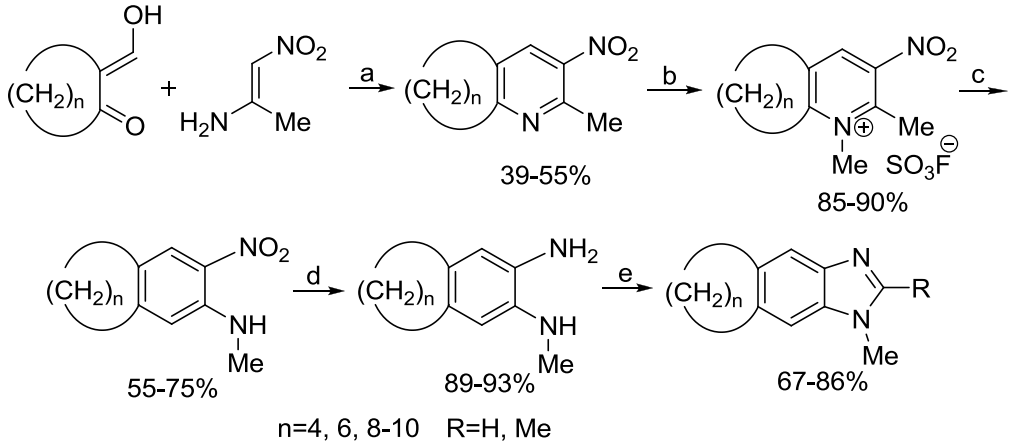
Benzimidazole is one of biologically significant heterocycles. Benzimidazole nucleus is included in the structure of vitamin B_{12}.Several benzimidazoles belong to a new class of universal non-natural nucleobases that are capable to complementary binding with any natural nucleobase [1].

The first benzimidazole alkaloids (Kealiiquinone, Kealiinine A, B and C) were isolated from sponge *Leucetta chagosensis* in the last two decades [2].

Benzimidazole derivatives have a broad spectrum of biological activity. Many examples of widely used classes of drugs containing the benzimidazole ring system are known [3,4].

In the present work we report a synthesis of benzimidazolephanes obtained on the basis of products of quaternary pyridinium salt recyclization.



(a) AcOH, 70°C , 24 h; (b) $MeSO_3F$, DCE, 25°C, 120 h; (c) $MeNH_2/H_2O$, 50-60°C, 5 h;
(d) $N_2H_4 \cdot H_2O$, Ni-Raney, EtOH, 70°C; (e) RCOOH, HCl, Δ, 3 h

The structure of the compounds obtained was confirmed by ^{1}H and ^{13}C NMR spectroscopy.

This work has financially supported by the Russian Foundation of Basic Research and Ministry of Edukation of Omsk Region (grant № 16-43-550144/16 p-a).

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Alkyne-induced transformations of tetrahydropyridene ring annulated with cromone system.

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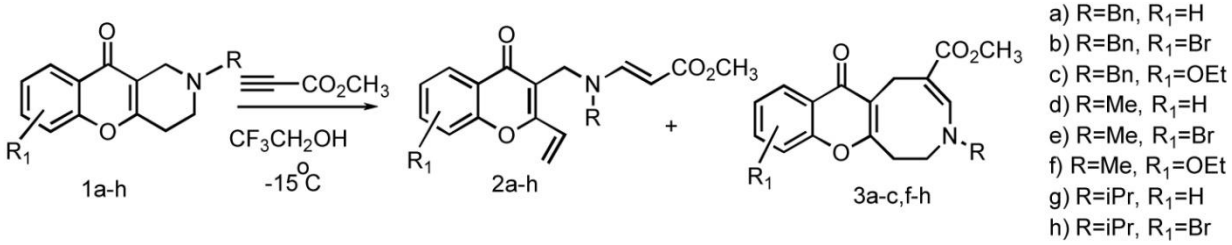
2-Arylchromones, also known as flavones, belong to the one of the most widespread classes of organic compounds in nature. However, 2-vinyl-substituted chromones are much less common, and only some of them, including, for example hormothamnione, were isolated from blue-green algae. Earlier, we have shown, that reaction of N-substituted chromeno[3,2-c]pyridines with activated alkynes in methanol at room temperature leads to tetrahydropyridine cycle opening yielding vinyl-substituted chromones. Considering that such compounds have high cytotoxic activity [1], the synthesis of 2-vinylchromones is rather actual.

Continuing our research in this direction, we have found, that analogues reactions of chromeno[3,2-c]pyridines **1** in trifluoroethanol at 15ºC below zero yield, beside 2-vinylchromones **2,** new azaheterococycles – chromeno[3,2-d]azocines **3**.



The structures of all synthesized compounds have been proved by complex of spectral methods. Compounds **1**, **2** have been additionally characterized by electronic adsorption spectroscopy and spectrofluorimetry. The structure of chromeno[3,2-d]azocines **3c** was confirmed by a single crystal X-ray analysis.

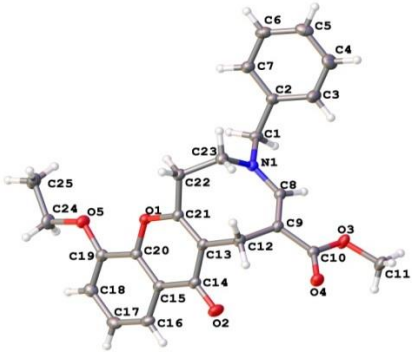


Figure 1. Molecular structure of **3c**

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.

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Investigation of the reaction of 1-(1*H*-perimidin-6-yl)ethan-1-one with 5-bromopyrimidine in Eaton's Reagent

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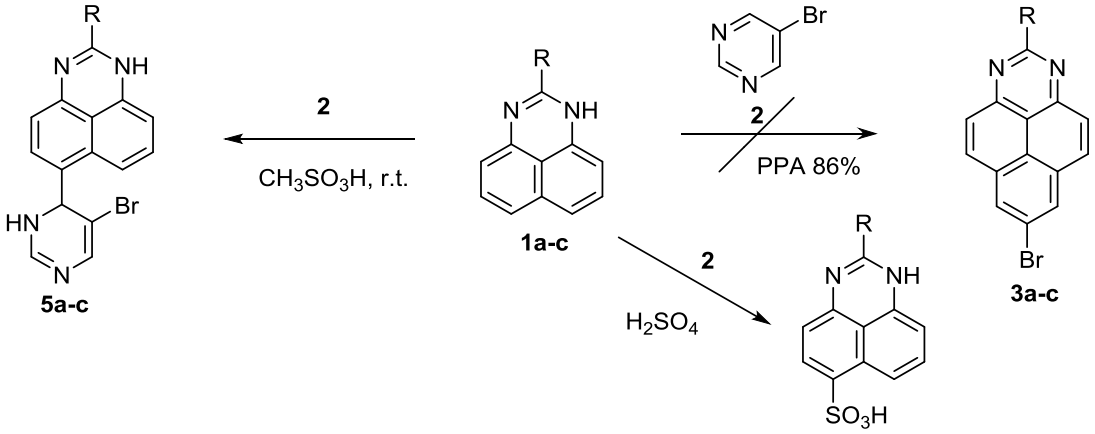
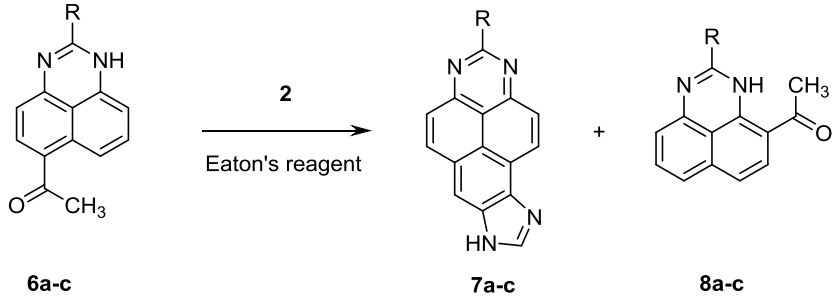
In continuation of our works on perimidines reactivity in reactions of *peri*-annulation of carbocyclic ring to 1*H*-perimidines **1**, we decided to carry out the synthesis of 7-bromo-1,3-diazapyrenes **3**. Unexpectedly, a reaction of 5-bromopyrimidine **2** with compounds **1a-c** in 86% PPA did not was not successful. Trials to carry out this reaction in sulfuric acid gave products of sulfurization **4**, while in methanesulfonic acid we obtained corresponding 6-(5-bromo-3,4-dihydropyrimidin-4-yl)-1*H*-perimidines **5** [1] (**Scheme 1**):



Scheme 1 (R=H,Me,Ph)

On the next stage of the reaction investigation we made an attempt to fulfill a reaction of ketones of perimidine row with 5-bromopyrimidine in the presence of Eaton's reagent. As a result of the reaction of acyl derivatives **6a-c** with pyrimidine **2**, corresponding 7*H*-imidazo[4',5':4,5]benzo[1,2,3-*gh*]perimidines **7** were obtained along with ketones **8,** by-products of thermodynamic rearrangement of acyl group (**Scheme 2**):



Scheme 2 (R=H,Me,Ph)

This project received financial support from the Ministry of Education and Science of the Russia in the framework of the State Assignment to the Higher Education Institutions (grant №4.1196.2017/PP)

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Antioxidant activity of sterically hindered *o*-quinones in reaction KO_2, in the process of lipid peroxidation in vitro

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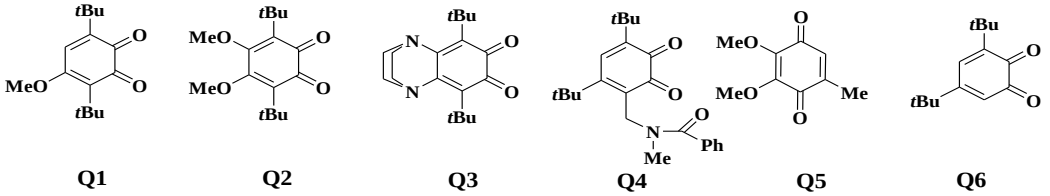
Quinones are redox-active molecules that play a vital role in biological systems; particularly these compounds participate in the oxidative phosphorylation, in reaction of electron transfer in respiration chain of mitochondria. Depending on the conditions, quinones may act as antioxidants and protect cells against reactive oxygen species (ROS) or act as prooxidants generating toxic intermediates [1]. In the present work we have investigated the reaction of sterically hindered *o*-quinones **Q1**-**Q4**, **Q6** and *p*-benzoqinone **Q5** with KO_2 and studied lipid peroxidation of rat (Wistar) brain homogenate in the presence of the compounds **Q1**-**Q5**.



Q1 **Q2** **Q3** **Q4** **Q5** **Q6**

A possibility of the reaction of quinones with superoxide radical anion or *o*-semiquinone radical (SQ) with oxygen is largely determined by the values of the cathode potential of the transition quinone/semiquinone relatively to the transition oxygen/superoxide anion radical.

$$SQ^{\bullet -} + O_2 \rightleftharpoons Q + O_2^{\bullet -}$$

On the base of electrochemical data quinone scan be divided into two groups: the first consists of **Q1**, **Q4**, **Q6** with reduction potentials shift to anodic region, while the second group includes **Q2** and **Q3** with higher reduction potentials. The methods of UV-visible and EPR spectroscopy were applied for the study of the interaction of quinones with potassium superoxide in DMF in the presence of cis-dicyclohexano-18-crown-6. Compounds of the first group with more anodic potentials react with KO_2 with formation of blue colored solutions. There are broad absorption bands of 650-900 nm were observed in UV-vis spectra, which characterizes the π-π * and n-π* transitions in the *o*-semiquinone radical anions. These data are confirmed by EPR spectroscopy. Radical anion species are stable under aerobic conditions. Among the compounds of **Q2** and **Q3** only **Q3** participates in the reaction with KO_2 because its reduction potential is shifted to the anode region compared with **Q2**.

Quinones **Q1**-**Q4** show low antioxidant effect on the process of enzymatic and non-enzymatic (ascorbate-dependent) lipid peroxidation in rat brain homogenate of reducing the concentration of TBARS as compared to blank experiment. In the presence of *p*-benzoquinone **Q5** the increase of oxidation products was observed that indicates the intensification of the process of lipid peroxidation.

This work was supported by the Russian Foundation for Basic Research (grant № 16-33-00027, 15-03-02967 a), Russian President Grant (MK-5285.2016.3).

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Antioxidant activity of sterically hindered bis-catechol thioethers

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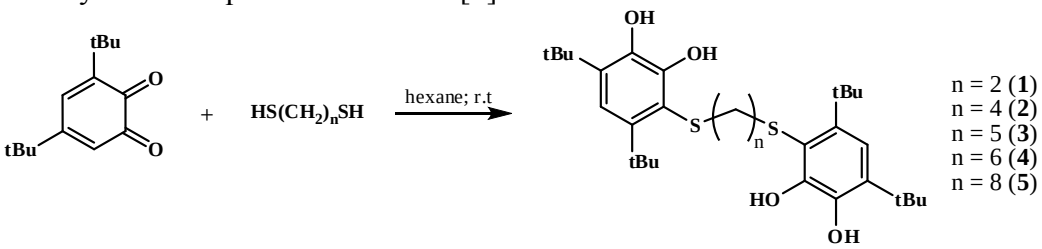
The functionalized sulfur-containing catechols, quinones and metal complexes based on of these compounds have different bioactivity. The synthesis of novel thioethers with sterically hindered catechol fragment is of interest in terms of anti/prooxidant properties research and as new prospective ligands in coordination chemistry. Current research is focused on the synthesis of new bis-catechol thioethers (**1-5**) and evaluation of their radical scavenging and antioxidant activity in a reaction with 2,2-diphenyl-1-picrylhydrazyl radical (DPPH), in oleic acid autooxidation. There are various methods for introducing thioether group into catechols (hydroquinone) structure, but we have used the well-known Michael addition of the dithiols to 3,5-di-*tert*-butyl-*o*-benzoquinone in hexane [1].



The introduction of compounds **1-5** into a solution containing DPPH radical results in a decrease in the intensity of the absorption maximum at 517 nm. The value of EC_{50} was determined at the equilibration in 90 – 160 min depending on the compound used. The values of EC_{50} of the target compounds are varying from 5.4 to 15.0 μmol and comparable with the data for α-tocopherol that is the evidence of the high antiradical activity of compounds.

Additives of the compounds (**1-5**) results in the inhibition of oleic acid autoxidation process at 333 K. However, the effect of bis-pyrocatechols to change hydroperoxide concentration is different from the action of the ionol and α-tocopherol. In the presence of compounds (**1-5**) the reduction of the level of LOOH was initially observed, while the concentration of hydroperoxide remained practically unchanged. The observed LOOH concentration decrease indicates that the bis-catechol thioethers can be considered as inhibitors of radical chain process, and hydroperoxides destructors as well. The analysis of the results in the effectiveness of inhibiting (EI %) of oleic acid auto-oxidation in the presence of test compounds shows that the value of this parameter for bis-pyrocatechols (**1-5**) is slightly higher than the α-tocopherol (80.5 ± 2.1%), and it is varying from 82.0 to 87.5%.

The antioxidant effect of the synthesized thioethers is caused by the following factors: 1) the thioethers can form a stable radical during the hydrogen atom transfer in the reaction with DPPH, LOO-radicals; 2) the presence of two sterically hindered catechol fragments determines the neutralization of a larger number of radical species; 3) the presence of thioether groups increases the activity of these compounds in relation to hydroperoxides.

This work was supported by the Russian Foundation for Basic Research (grant № 16-33-00027), Russian President Grant (MK-5285.2016.3).

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Reactions of 1,1-difluoroorganozinc reagents

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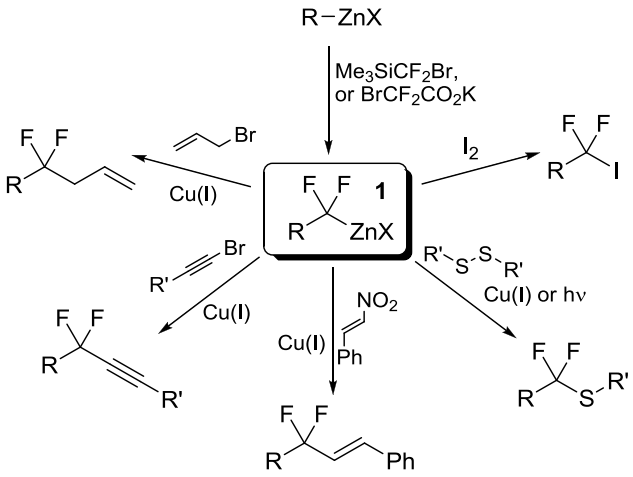
Organozinc compounds have emerged as valuable reagents for transition metal catalyzed cross-couplings and nucleophilic addition reactions [1]. Recently we reported an efficient method toward 1,1-Difluoroorganozinc reagents (**1**) by reaction of organozincs with difluorocarbene precursor, such as Me_3SiCF_2Br [2] or $BrCF_2CO_2K$ [3]. Fluorinated organozinc reagents typically exhibit low reactivity towards various electrophiles. Thus, **1** without any catalysis react only with halogens and protic acids [2]. But in presence of Cu(I) salts **1** undergo coupling with allylic halogenides [4] and 1-bromoalkynes [5]. Reaction with nitrostyrenes provides product of nitro group substitution [6]. Disulphides react with **1** using copper catalysis or under irradiation with visible light [7].



This work was supported by the Ministry of Science (project MK-6724.2016.3) and Russian Foundation for Basic Research (project № 16-29-10661).

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Thermolysis of 5-substituted 4-(trichloroacetyl)-2,3-furandione in the presence of cyclic ketones

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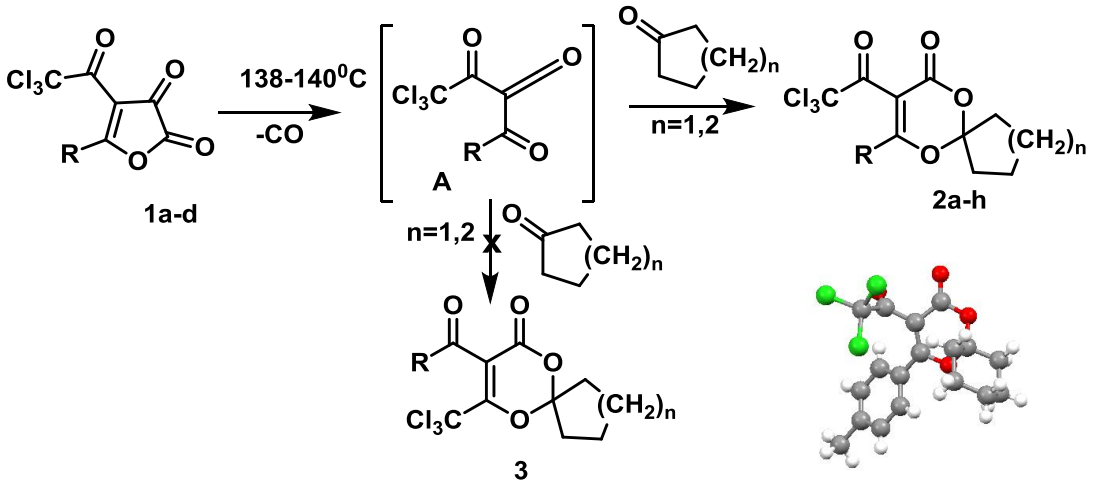
It is well known that 4,5-disubstituted furan-2,3-diones are thermally unstable. Heating of these compounds at 130–140 °C (ca. melting point) leads the formation of corresponding acylketenes via decarbonylation. Acylketenes generated in such a way are able to react with various dienophiles [1-3].

Heating of mixtures of furan-2,3-diones **1** and carbonyl compounds in a high-boiling aprotic solvent at 138–140°C (i.e., at a temperature corresponding to decarbonylation of initial furandiones) for 15–20 min led to formation of the corresponding [4+2]-adducts whose spectral parameters did not allow us to choose between two alternative isomeric structures **2** and **3** (Scheme 1). We unambiguously identified the cycloaddition products as substituted spiro-1,3-dioxin-4-ones **2** by single-crystal X-ray analysis.

Scheme 1.



2: R= C_6H_5, n=1 (a); R= C_6H_5, n=2 (b); R=4-MeC_6H_4, n=1 (c); R=4-MeC_6H_4, n=2 (d); R=4-MeOC_6H_4, n=1(e); R=4-MeOC_6H_4, n=2(f); R=2-thienyl, n=1 (g),R=2-thienyl, n=2 (h).

The structure of compound **2** was established by elemental analysis, IR, ^{1}H-NMR, ^{13}C-NMR, and single-crystal X-ray analysis.

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Recyclization of 4,5-dihydroisoxazole-5-carboxylates into 5-unsubstituted 3,4-diaryl-isoxazoles

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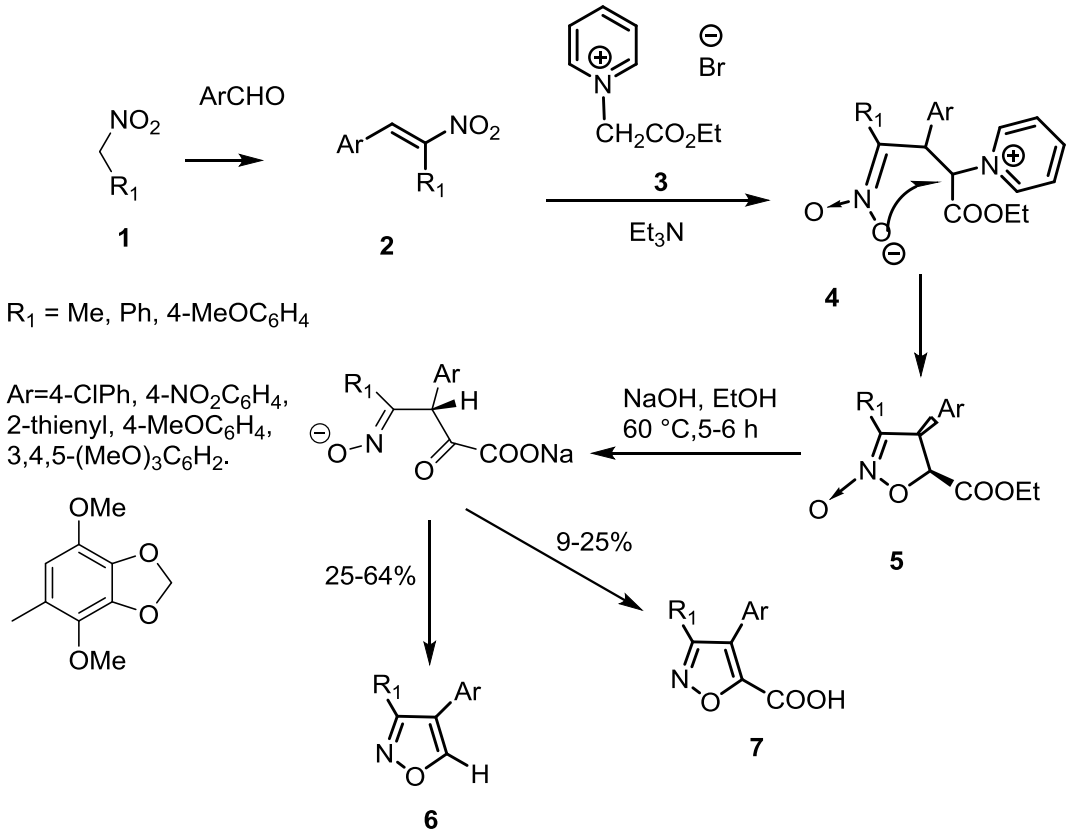
Some of ortho-diaryl-substituted heterocycles have good antitumor activity [1]. In this work, isoxazoline-N-oxides **5** were obtained in moderate yields by reaction of pyridinium salt **3** and nitrostilbenes **2** which were prepared by condensation of substituted nitromethanes **1** with aromatic aldehydes in good yields. We found that 3,4-diarylisoxazoles **6** are main products of a recyclization of isoxazoline-N-oxides **5** under basic conditions in ethanol. The corresponding isoxazole-5-carboxylic acids **7** can be separated from a complex reaction mixture in poor yields (is some cases less than 5%).



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Catalytic stereoselective formation of C-C and C-N bonds in target-oriented synthesis

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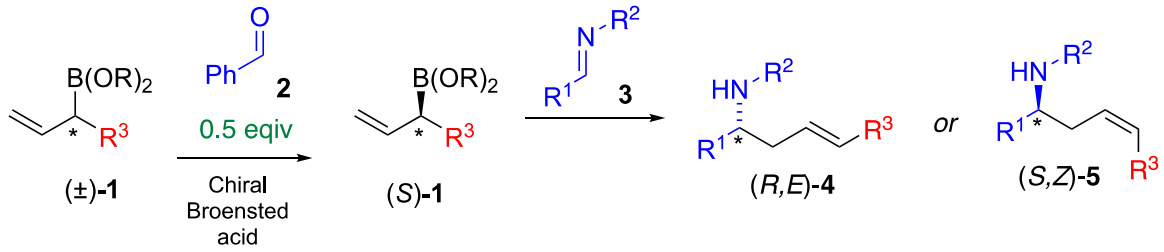
Chiral amines are powerful pharmacophore groups due to their favourable physico-chemical properties that include inherent capability of hydrogen bonding and a wealth of relevant, well-understood structural information. Homochiral amines and their derivatives belong to the class of strategic building blocks for pharmaceutical, agrochemical and fine chemical development [1].

Scheme



Herein, we present a novel solution to attaining high stereoselectivity in the allylation of imines with secondary allylboronates (Scheme). The method is based on our recently developed kinetic resolution of chiral racemic allylboronates (±)-**1** [2], which are readily synthesised from simple precursors [3,4]. Conditions of the kinetic resolution catalysed by chiral Brønsted acid TRIP were optimised to afford highly enantioenriched boronates (*S*)-**1**. DFT calculations at TPSSh/cc-pvtz//B3LYP/6-31g(d,p) level of theory were performed on the system to elucidate the origin of the stereodifferentiation [2]. In developing allylation of imines **3** with allylboronates (*S*)-**1**, it was important to ensure that the reaction is stereoselective, i.e. that chirality of the reagent is efficiently transferred into the product and that its selectivity is controlled with respect to the alkene geometry to give either **4** or **5**. In the case of aldehydes, the factors governing stereoselectivity of this process are reasonably well understood. In imines, substitution on the nitrogen brings an additional element of complexity – the steric size of the substituent. Therefore, the method is focused on the allylation of the in situ generated NH imines **3** (R^2 = H) [5], where the steric arrangement of the transition state should resemble that of aldehydes. Details of the development of stereoselective addition of (*S*)-**1** to imines to furnish selectively (*S,Z*)-**5** will be presented.

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5-Phenyl substituted pyrrolidino[60]fulleride of bis(toluene)chromium and 3'–(aryl)indolizidino[1',2':1,2][60]fullerenes

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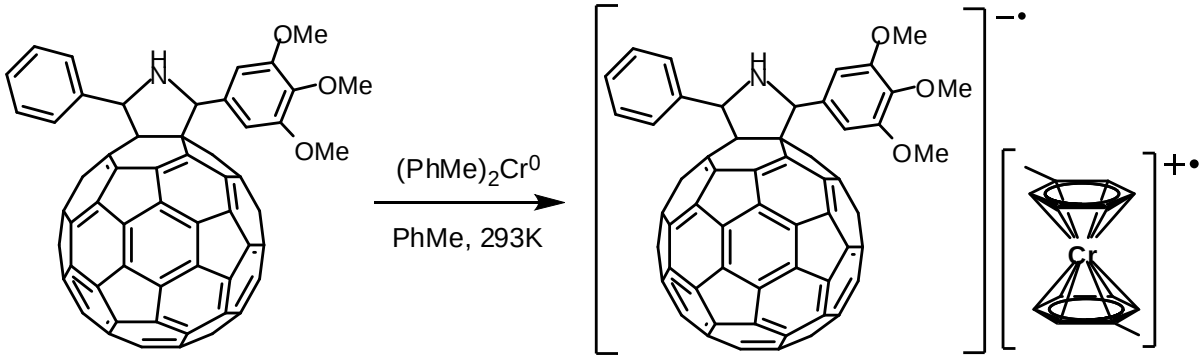
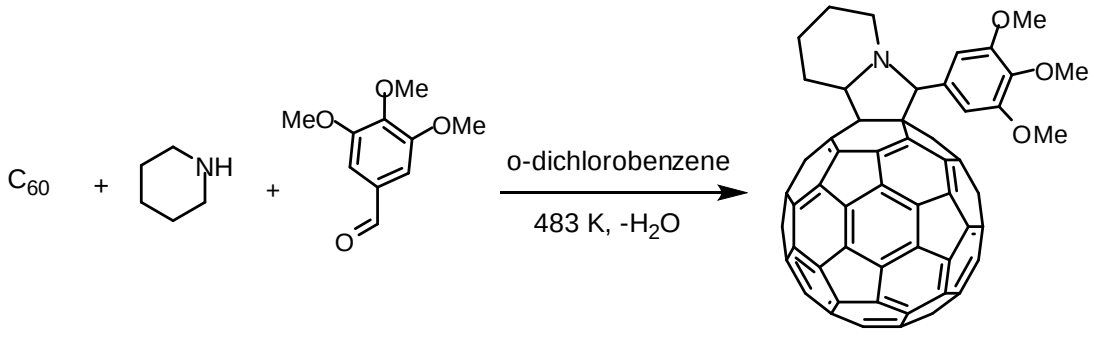
2'–(3,4,5–trimethoxyphenyl)–5'–phenylpyrrolidino[3',4':1,2][60]fulleride of bis(toluene)chromium (**1b**) has been obtained from the reaction of 2'–(3,4,5–trimethoxyphenyl)–5'–phenylpyrrolidino[3',4':1,2][60]fullerene (**1a**) with $(PhMe)_2Cr^0$ in PhMe at 293 K as a brown precipitate. The ion-radical salt fulleride **1b** is insoluble in hexane, sparingly soluble in toluene, soluble in THF.



1a **1b**

3'–(3,4,5–trimethoxyphenyl)indolizidino[1',2':1,2][60]fullerene (**2a**) has been obtained by heating of C_{60} with piperidine and 3,4,5–trimethoxybenzaldehyde in ortho-dichlorobenzene (with molar ratio C_{60} : piperidine : 3,4,5–trimethoxybenzaldehyde close to 1 : 4 : 15) at 483 K with thin-layer chromatography monitoring. After solvent evaporation in vacuo, the residue was washed by acetone, dried in vacuo and dissolved in toluene. Column chromatography over silica gel in toluene (with toluene as eluent) gave first unreacted C_{60} and then fulleroindolizidine **2a** as amorphous brown solid (yield 30%).



2a

Indolizidinofullerene **2a** is insoluble in hexane, sparingly soluble in acetone, soluble in $CHCl_3$. The UV/vis spectroscopy of **2a** in decaline solution at 290 K shows absorption bands at λ = 705, 693, 672, 431, 327, 309, 256, 210 nm typical for 1,2 fullerene derivatives. The ^1H NMR spectra show low nitrogen lone pair inversion rate on the NMR time scale, indicate the energetically high conformational inversion barrier of indolizidino moiety in **2a** at 295 K in $CDCl_3$ solution. All reactions were carried out under an inert atmosphere.

This work was supported by RSCF (№ 14-13-00832).

Design of magnetic materials from verdazyl radicals via amide bond

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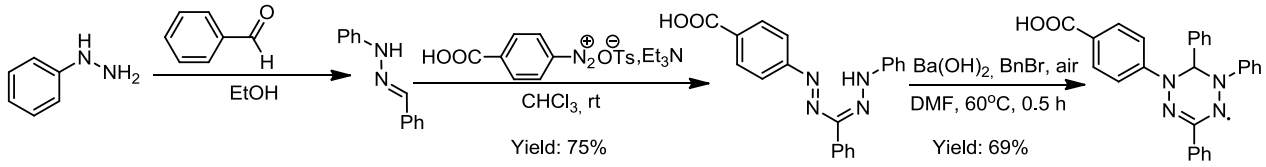
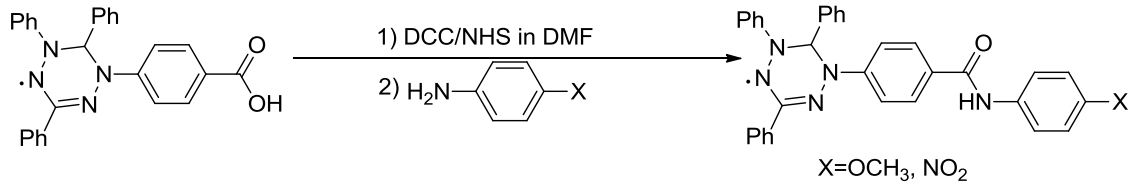
Radicals are widely studied due to their interesting magnetic properties [1]. In order to use radicals for obtaining magnetic materials, these organic species should be stable under ambient conditions [2]. Verdazyls are a class of stable radicals where an electron is delocalized onto the carbon-nitrogen six-membered heterocycle. Moreover, stable verdazyls have some important advantages: they are air and water stable, remain monomeric in solution and in solid state, can be handled and stored individually without decomposition [3].

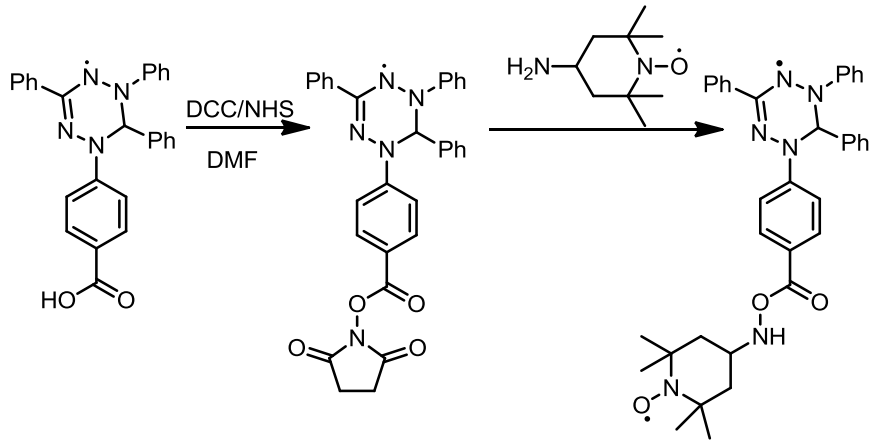
In this work, we have developed a convenient procedure for the synthesis of verdazyl radical bearing -COOH group:



The reaction of obtained radical with different amines was used as a model to optimize the conditions for further applications.



We suggest using this verdazyl radical as a building block for constructing different hetero-biradicals.



This work was supported by Ministry of Education and Science of Russian Federation (project no. 4.5924.2017)

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Recyclization of pyrrolo[1,2-*c*][4,1]benzoxazepinetriones under the action of binucleophiles

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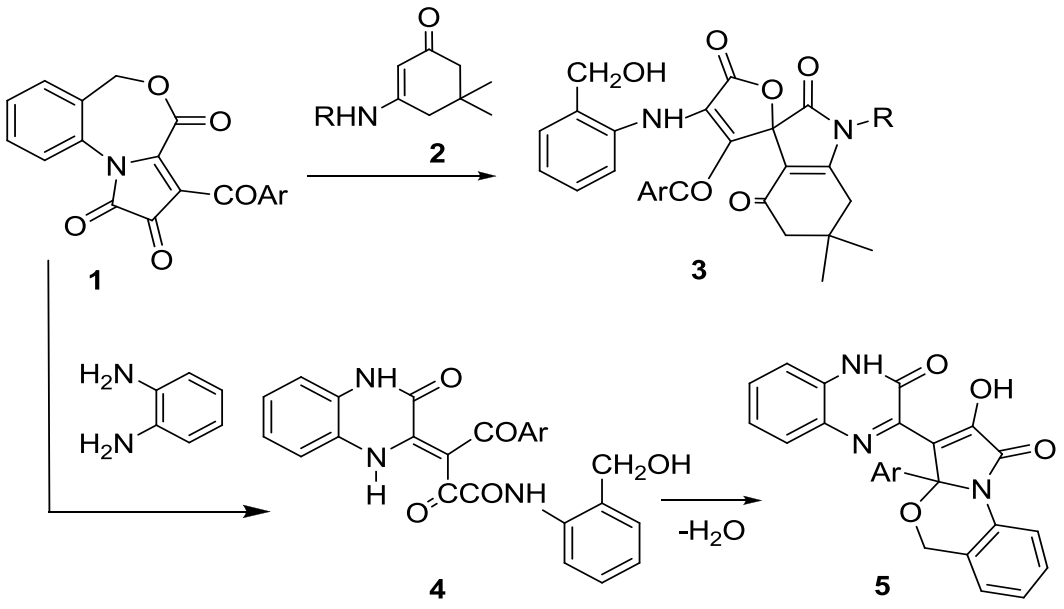
Spiro-heterocyclizations of pyrrolo[1,2-*a*][1,4]benzoxazine-1,2,4-triones under the action of enamines and *o*-phenylenediamine proceed through attack of nucleophilic groups of binucleophile on the carbon atoms in the positions *3a* and *4* with the cleavage of the oxazinone ring at the C^4–O^5 bond. The reactions of pyrrolo[1,2-*a*][4,1]benzoxazepine-1,2,4-triones with enamines and *o*-phenylenediamine has not been investigated before.

We have synthesized new hetareno[*e*]pyrrole-2,3-diones, 3-aroylpyrrolo[1,2-*c*][4,1]benzoxazepine-1,2,4-triones **1**, and studied their reactions with 3-arylamino-5,5-dimethylcyclohex-2-en-1-ones **2** and *o*-phenylenediamine. The reactions were carried out by heating the reactants in boiling anhydrous chloroform for 5-20 min. As a result, we isolated 1'-substituted 3-aroyl-4-[2-(hydroxymethyl)phenylamino]-6',6'-dimethyl-6',7'-dihydro-5H-spiro[furan-2,3'-indole]-2',4',5(1'H,5'H)-triones **3** and (*Z*)-4-aryl-N-[2-(2-hydroxymethyl)phenyl]-2,4-dioxo-3-[3-oxo-3,4-dihydroquinoxalin-2(1*H*)-ylidene]butanamides **4** respectively. The formation of compounds **3** occurs apparently due to the primary addition of the NH group of enamines **2** to the lactam carbonyl group in the position *1* of compounds **1** with the opening of the pyrroledione ring at the C^1–N^{11} bond and the subsequent closure of a pyrrolone ring via the intramolecular nucleophilic addition of the C^2H group of enamines to the ketone carbonyl group with the formation of a hemiacetal hydroxy group. This OH group attacks in its turn the lactone carbonyl group C^4=O with the opening of the oxazepine ring at the C^4–O^5 bond and the intramolecular closure of a furan ring. Presumably, compounds **4** are formed as a result of nucleophilic attack by the amino groups of *o*-phenylenediamine on the C3a and C4 atoms of **1** and subsequent opening of the oxazepine ring at the C^4–O^5 and C^{3a}–N^{11} bonds. Compounds **5** are formed as a result of double intramolecular cyclization of compounds **4**.



This work was supported by Ministry of Education and Science of Russian Federation.

Role of supramolecular nanostructures in mechanisms of catalysis with Ni or Fe heteroligand complexes

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The self-assembled systems and self-organized structures mediated by transition metals are briefly considered in connection with increasing research interest in chemical transformation with use of these systems. We successfully used for the first time method of atomic force microscopy (AFM) to research the possibilities of formation of supramolecular structures due to intermolecular H-bonds based on heteroligand complexes of nickel and iron: **{**$Ni^{II}(acac)_2 \cdot L^2 \cdot$**L^3}** **(«A») (**$L^2$ =MP, HMPA, **MSt (M = Na, Li),** His (His=L-Histidine)**, L^3=PhOH, Tyr (Tyr=L-Tyrosine),** $Ni_2(OAc)_3(acac)MP \cdot 2H_2O$ **(«B»)** (MP = N-methylpirrolidone-2), $Fe^{III}_x(acac)_y$(18-crown-6)$_m(H_2O)_n$ («C»). Complexes "A"−"C" are effective catalysts for oxidation of alkylarens with molecular oxygen to hydro peroxides, and also structural and functional models of Ni(Fe)-Acireductone Dioxygenases (Ni(Fe)-ARD) and Fe-Acetylacetone Dioxygenase (Fe-Dke1). We assumed that the stability of the complexes «A»−«C» as the alkylarens oxidation catalysts could be associated with the formation of stable supramolecular structures due to intermolecular H-bonds [1]. And different activity of Ni (or Fe)-ARD towards common substrates (Acireductone (1,2-Dihydroxy-3-keto-5-methylthiopentene-2) and O_2) in the methionine salvage pathway, as one of the reasons - with self-organization of catalysts into various macrostructure due to intermolecular H-bonds. These assumptions were confirmed by our AFM studies. We demonstrated with AFM the self-organization of Ni and Fe heteroligand complexes «A»−«C» in macrostructures due to H-bonding on special prepared surface of modified silicone [2].

The received AFM data point to the very probable stable supramolecular nanostructures appearance based on heteroligand **complexes** «A»−«C» due to intermolecular H-bonds in the real catalytic ethyl benzene oxidation with dioxygen, catalyzed by «A»−«C».

Self-organization of iron complexes in form, resemblimg the shape of the micro fiber tubes of yubuline (such as in the case of complexes $Fe^{III}_x(acac)_y 18C_{6m}(H_2O)_n$) can promote O_2 activation ($Fe^{II}+O_2 \rightarrow Fe^{III}–O_2^-$), the first stage in the mechanism of Fe^{II}ARD action, and subsequent regioselective addition of activated oxygen to the Acireductone ligand, and the reactions leading to methionine.

The formation of multidimensional forms (in the case of Ni-ARD) may be one way of controlling Ni(Fe)-ARD activity. We also suggest that, in the case of Ni-ARD. Tyr moiety, if it participates in the mechanism, can affect the activity of Ni-ARD. The first time we observed the formation of nickel triple complexes **{**$Ni^{II}(acac)_2 \cdot L^2 \cdot$**L^3},** modeling the active site of Ni-Acireductone Dioxygenase (L^2=MP, His (His=L-Histidine), L^3=PhOH, Tyr), and of self-organized macrostructures based on **{**$Ni^{II}(acac)_2 \cdot L^2 \cdot$**L^3}** due to intermolecular H-bonds (AFM, **UV-spectroscopy**). These facts testify in favor of the inclusion of Tyr moiety as a regulatory factor in the mechanism of action of Ni-ARD.

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Preparation of polyimides with crown ethers for sorption materials

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Over the past few decades a lot of research has been devoted to the use of crown ethers for the extraction of alkali metals including Cs. Due to the matching of the size of the cation Cs^+ and the cavity of the crown ring dibenzo-21-crown-7 is used as an extractant of Cs. Though a given crown ether tends to form its most stable complexes with ions having diameters comparable to that of its opened cavity, it can also form complexes with ions of larger size.

Therefore, the preparation of sorption materials based on polyimide matrix with dibenzo-21-crown-7 for the extraction of radioactive Cs^+ was considered topical. Thereunder, the experimental samples were synthesized by our research group. Their structures are shown in the Figure 1.

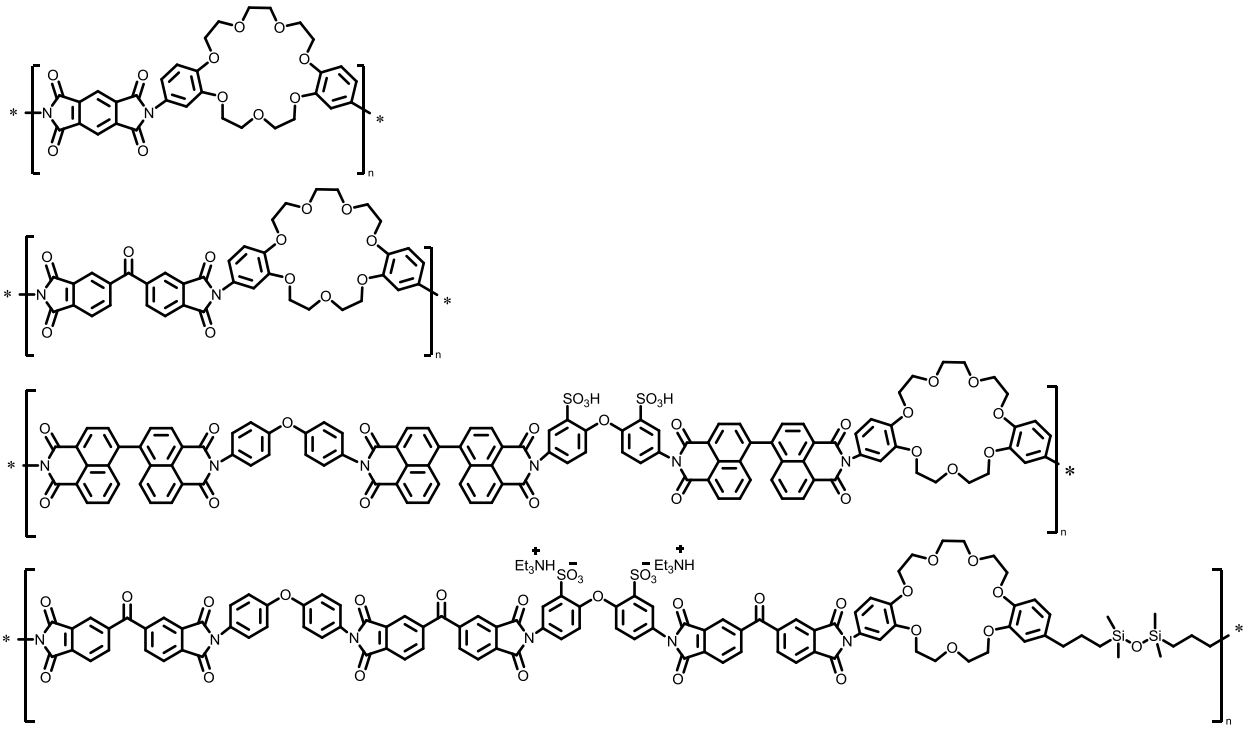

Figure 1 – Experimental samples of polyimides with dibenzo-21-crown-7.

The sorption ability of the presented polyimides with crown ethers was studied. Various metal cations, such as Cs^+, Co^{2+}, Cu^{2+} were used for this **research.**

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Synthesis of arylsemicarbazones of esters and amides possessing potential anticonvulsant activity

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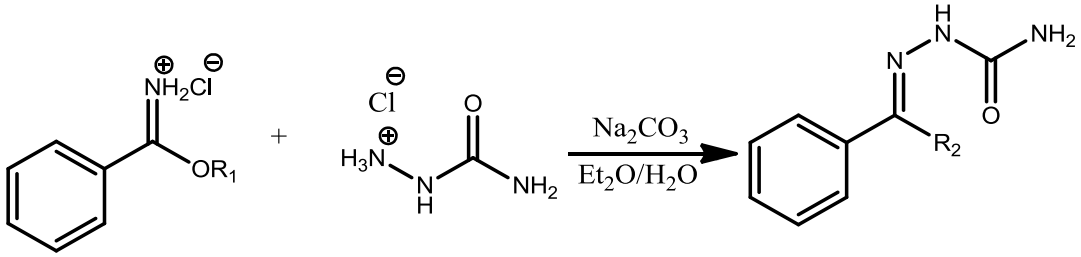
Several papers are dedicated to anticonvulsant properties of aromatic aldehydes and ketones semicarbazones. Dimmock et al. [1] reported anticonvulsant activity of some arylsemicarbazones. These observations support the theory that one large hydrophobic group, e.g. aryl ring, and two electron donating atoms of semicarbazone group are required for protection in the maximal electroshock **(**MES**)** anticonvulsant screen, which is claimed to identify compounds with efficacy against generalized tonic-clonic ("grand mal") seizures. After oral administration to rats, a number of compounds displayed significant potencies in the MES screen (ED_{50} of 1-5 mg/kg) accompanied by very high protection index [2, 3].

Recently Magedov, Smushkevich and Usorov described synthesis of ethyl N-(aminocarbonyl)benzenecarbohydrazonate [4] (Scheme 1), which needs further investigations.

In this work, arylsemicarbazones of esters and amides, which may have higher anticonvulsant activity, have been successfully synthesized. N-(aminocarbonyl)-benzenecarbohydrazonamide has been obtained in the reaction of methyl benzocarboxyimidate hydrochloride with semicarbazide hydrochloride.



R_1 = Et, Me

R_2 = Et, NH_2

Scheme 1. semicarbazones synthesis

Atomic charges of these compounds were calculated in HyperChem and the calculation results were compared with previously published data. On this basis, it can be concluded that semicarbazones of esters and amides can have high anticonvulsant activity. Similar results shows the way2drug service in the study of the PASS method.

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Some chemical transformations of furo[2,3-*f*]isoindoles

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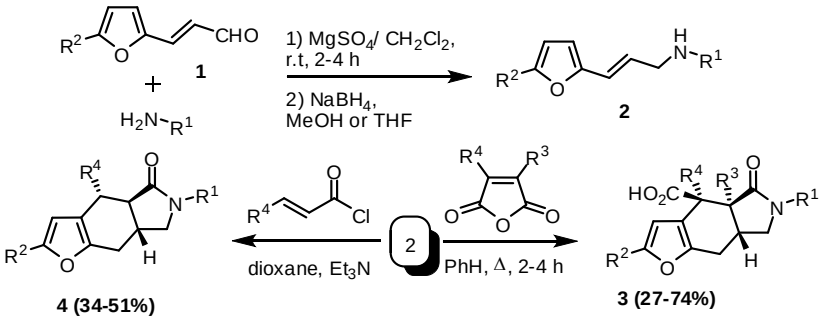
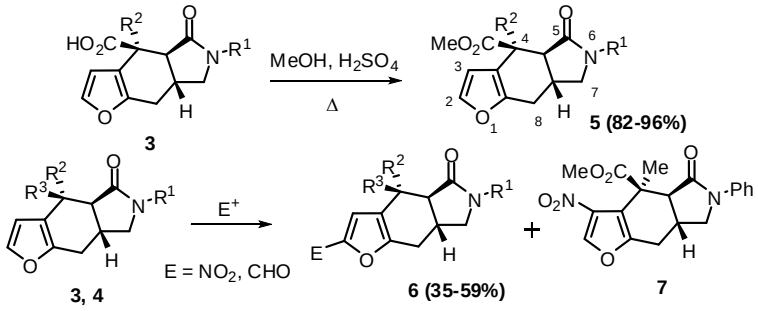
As it has been previously shown by our groups, the interaction of 3-(furyl)allylamines with α,β-unsaturated acid anhydrides leads to the formation of furo[2,3-*f*]isoindoles – the aza-analogs of pinguisane-type sesquiterpenes. 3-(2-Furyl)allylamines **2**, easily available in two steps from furylacroleins **1** and primary amines, were used in the tandem *N*-acylation / intramolecular [4+2]-cycloaddition reaction with maleic anhydrides and cinnamoyl chloride, as a result various hexahydro-4*H*-furo[2,3-*f*]isoindoles **3,4** were synthesized efficiently under mild conditions [1, 2].



R^1=H, Me, Et, Pr, D, TMS; R^2=Ph, Bn, Pr, i-Pr, Cyclopropyl, Allyl, $(CH_2)_2Ph$, $(CH_2)_2C_6H_3$-3,4-$(OMe)_2$, C_6H_4-4-OMe; R^3=H, Me; R^4=H, Me, Ph

Very limited information was found on the chemical transformations of furoisoindoles. Some possible directions of modification of the obtained hexahydro-4*H*-furo[2,3-*f*]isoindoles **3,4** are presented in the scheme. The esterification of carboxylic acids **3** in the presence of sulfuric acid yields the methyl esters **5** in good yields.



R^1=Ph, Bn; R^2=H, Me, Ph; R^3=CO_2H, CO_2Me, H

Furo[2,3-*f*]isoindoles having no substituent at position C-2 were subjected to nitration and formylation. The reactions were regioselective, and the corresponding 5-nitro and 5-formyl derivatives **6** were formed in moderate yields. In one case the nitration of ester **5** (R^1=Ph, R^2=Me) formed the mixture of 2-nitro- **6** and 2-nitro furoisoindoles **7** with total yield 35 %.

This work was supported by the Russian Foundation for Basic Research (grant № 16-33-00389, 16-03-00125).

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Synthesis of 1-aminophosphonates based on different siloxane frameworks

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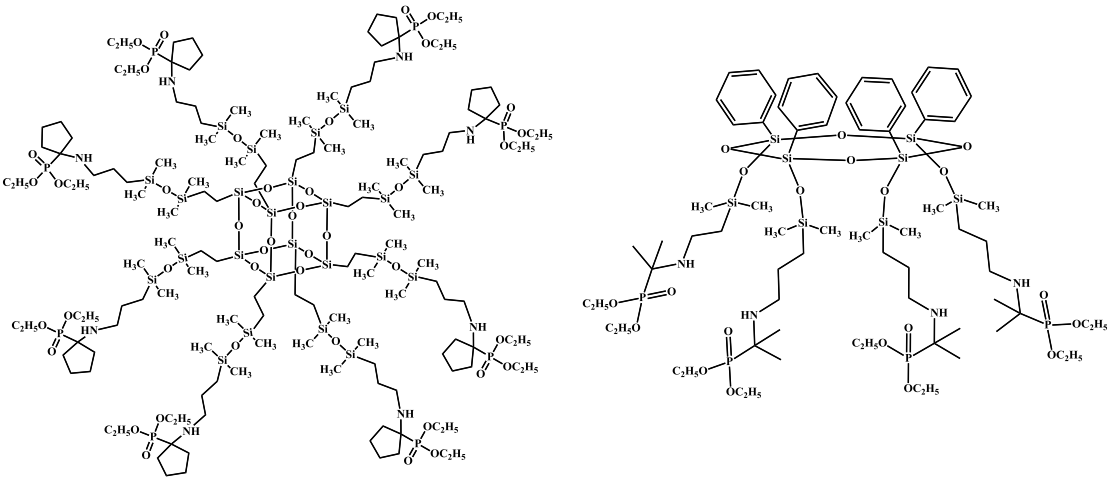
The development of hybrid materials bearing multifunctional silicone fragments is a promising research area. The introduction of various fragments able to selectively bind, recognize and transfer biologically important subjects into the siloxane structures makes it possible to obtain new materials with useful properties. Polyfunctional organophosphorus compounds, e.g., 1-aminophosphonates, are attractive for such a research. They have found application in industry, agriculture and medicinal chemistry.

In this regard, we have studied the combination (covalent cross-linking) of the hybrid functional model, methylsiloxane, and 1-aminophosphonate fragment [1,2].



Scheme 1. 1-aminophosphonates based on oligomeric silsesquioxane frame

The introduction of the amino group to the siloxane structure by hydrosilylation reaction is proposed by initial deactivation of a lone-electron pair at the nitrogen atom with a bulky substituent. The reaction conditions were optimized for the amino derivative. The Kabachnik Fields reaction was carried out without intermediate isolation of amino derivative. The synthesis of 1-aminophosphonate derivatives of methylsiloxane oligomer has been performed. The proposed methodology allows introducing 1-aminophosphonate fragment in different siloxane skeleton, excluding them destruction.

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Synthesis and antibacterial activity of N-(2-(2-(2-acylamidoethoxy)ethoxy)ethyl)eremomycin-carboxamides

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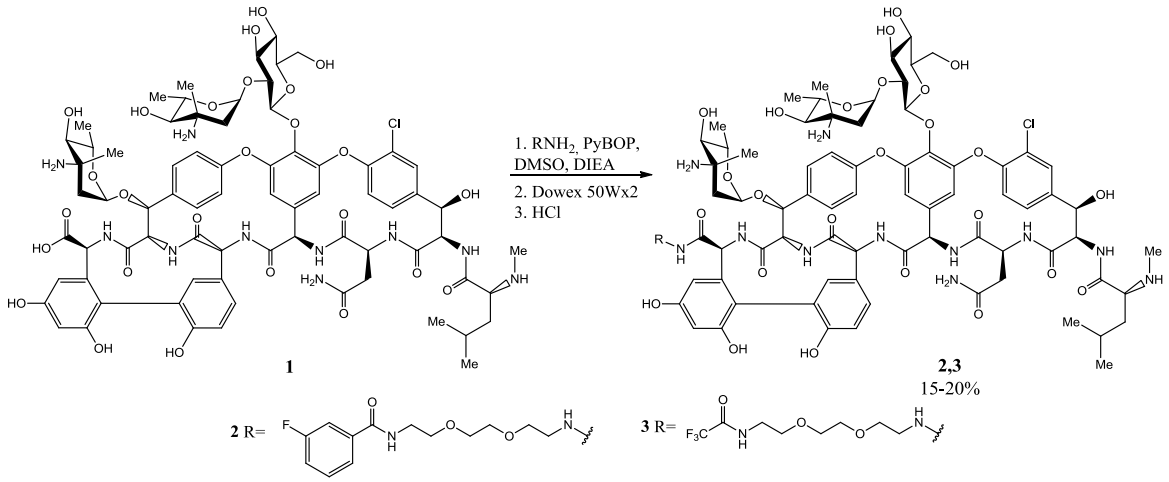
Eremomycin (**1**) is a natural glycopeptide antibiotic produced by *Nocardia orientalis* discovered in 1979 by G.F. Gause. Though eremomycin has higher activity than vancomycin and other natural glycopeptides, it has low activity against some resistant strains as GISA (Glycopeptides Intermediate-resistant *S. aureus*) and VRE (Vancomycin Resistant *Enterococcus*). Thereby, the searching of new semi-synthetic eremomycin derivatives which could circumvent bacterial resistance is a perspective direction for the development of new antibacterial agents.

One of the most promising ways of modification of glycopeptides is a transportation of C-terminus of the peptide core into carboxamide group [1]. Also well known that activity of glycopeptide antibiotics can be increase by the introduction of hydrophobic substituent [2]. Taking into account these data, the new eremomycin carboxamides **2-3** from eremomycin and corresponding N-(2-(2-(2-aminoethoxy)ethoxy)ethyl)acylamides were obtained. The condensation was carried out by PyBOP as a condensing agent in the presence of the base (DIEA) in DMSO. Crude products were purified by ion exchange chromatography on a Dowex 50Wx2 resin.



In vitro antibacterial activity of new glycopeptides **2**, **3** has been evaluated. Both derivatives **2, 3** were 2 to 4 times more of active against reference strains *S. aureus* and *E. faecalis* and up to 50 times more potent against some sensitive clinical isolates of *E. faecalis* and *E. faecium* than «gold-standard» vancomycin. With regard to against of glycopeptides intermediate - resistant strains these derivatives also has activity 8 times better activity than vancomycin. However, this new modification of **1** didn't show a significant increasing of activity of semi-synthetic derivative **2, 3** against GRE strains, although they are superior of vancomycin's activity in several times.

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4-(1,2-Dihydrobenzo[f]isoquinolin-4-yl)- and (3,4-dihydroisoquinolin-1-yl)-1,2,5-oxadiazol-3-amines: novel amino substrates for modified Pictet–Spengler reaction

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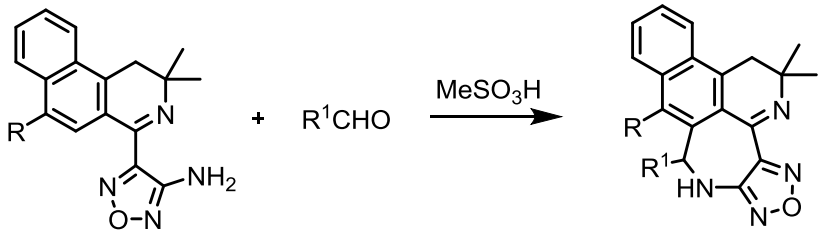
In this work we report the use of 4-(1,2-dihydrobenzo[f]isoquinolin-4-yl)- and (3,4-dihydroisoquinolin-1-yl)-1,2,5-oxadiazol-3-amines as amino subsrates for Pictet-Spengler (P-S) type reaction. Condensation of 4-(1,2-dihydrobenzo[f]isoquinolin-4-yl)-1,2,5-oxadiazol-3-amine **1** with aliphatic aldehydes or aryl aldehydes having electron-withdrawing substituents at room temperature in the presence of $MeSO_3H$ affords novel oxadiazolo[3',4':6,7]azepino[3,4,5-ij]benzo[f]isoquinolines **8** in excellent yields (76-89%). Reactions of **1** with aryl aldehydes containg electron-donating groups do not occur.



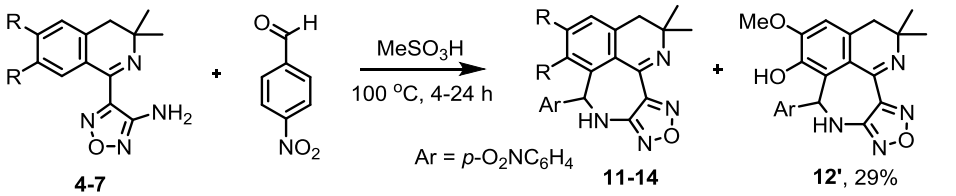
1-3 **8-10**

1: R = OMe; **2**: R = Me; **3**: R = H

Conditions: rt, 1.5-48 h (for **8**); 100°C, 7 h (for **9**), 100°C, 16 h (for **10**)

8: R=OMe (R^1 = 4-$O_2NC_6H_4$ (89%); 3-$O_2NC_6H_4$ (76%); 4-BrC_6H_4 (87%); 4-FC_6H_4 (76%); *i*-Pr (78%); cyclohexyl (80%); **9**: 82% (R = Me, R^1 = 4-$O_2NC_6H_4$); **10**: 64% (R = H, R^1 = 4-$O_2NC_6H_4$)

P-S type condensation with 1,2-dihydrobenzo[*f*]isoquinolines 2, 3 and 3,4-dihydroisoquinolines 4, 5, requires heating at 100 °C providing novel oxadiazolo[3',4':6,7]azepino[3,4,5-*ij*]benzo[*f*]isoquinolines 9, 10 and oxadiazolo[3',4':6,7]azepino[3,4,5-*ij*]isoquinoline 11, 12, respectively, in good to excellent yields (44-82%). 3,4-Dihydroisoquinoline 5 affords oxadiazolo[3',4':6,7]azepino[3,4,5-*ij*]isoquinoline 12 along with *O*-demethylated product 12'. There is no P-S reaction when compounds 6, 7 are used.



4-7 **11-14** **12'**, 29%

4: R+R = -OCH_2CH_2O-;
5: R= OMe; **6**: R = Me; **7**: R =H

11: R+R = -OCH_2CH_2O- (4 h, 80%)
12: R= OMe (5 h, 44%)
13: R = Me (24 h, 0%); **14**: R =H (24 h, 0%)

This work was supported by the Russian Foundation for Basic Research (grant № 16-03-00561)

The investigation of conversion of benzylidenemalonitrile Michaels alkylation product

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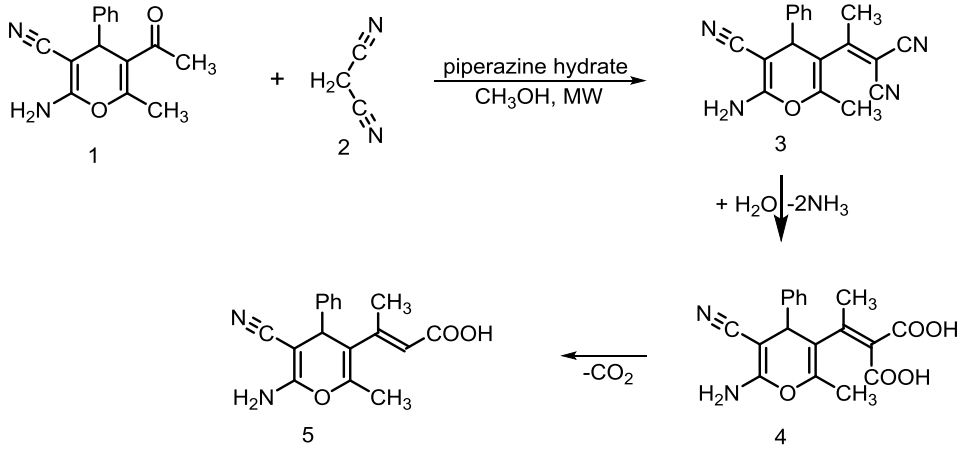
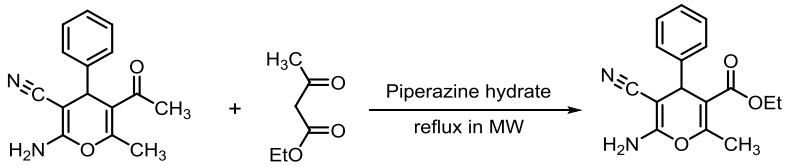
It is possible to find information about obtaining of corresponding pirane derivatives by reflux of benzylidenemalononitrile with acetoacetanylide in the presence of piperidine catalyst in ethanol [1]. So as other authors have shown synthesis of corresponding alkylation products by reflux of ethyl ether of nitrile acetic acid and malononitrile with the product of Knoevenagel condensation in ethanol with triethylamine [2].

But in presented work, in contradiction to known, in methanol media, using piperazine hydrat as base we, synthesized 5-acetyl-2-amino-6-methyl-4-phenyl-4h-pyran-3-carbonitrile by Michael addition with benzylidenemalononitrile. We think, compound (3) obtained by decarboxylation in microwave and in ethanol media, and in presence of piperazine hydrate, can be fall under aminolysis by action of systems water. Synthesized diacid converted to corresponding unsaturated acid (5).



1 2 3 4 5

In the same conditions, by interaction of benzylidenemalononitrile and acetoacetic ether we observed substitution of methyl group of acetyl fragment by etoxy group, corresponding to literature information.



The reactions were monitored by *thin*-layer chromatography method. Structures of synthesized compound were confirmed by ^{1}H and ^{13}C NMR spectroscopy and rentgen spectroscopy.

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Unusual rearrangement of 2-azabicyclo[2.2.1]heptenes under the action of DMAD

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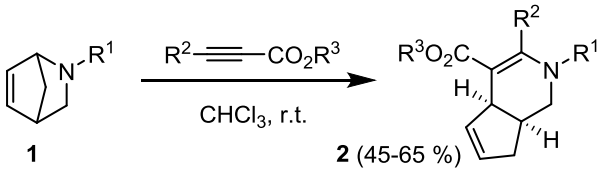
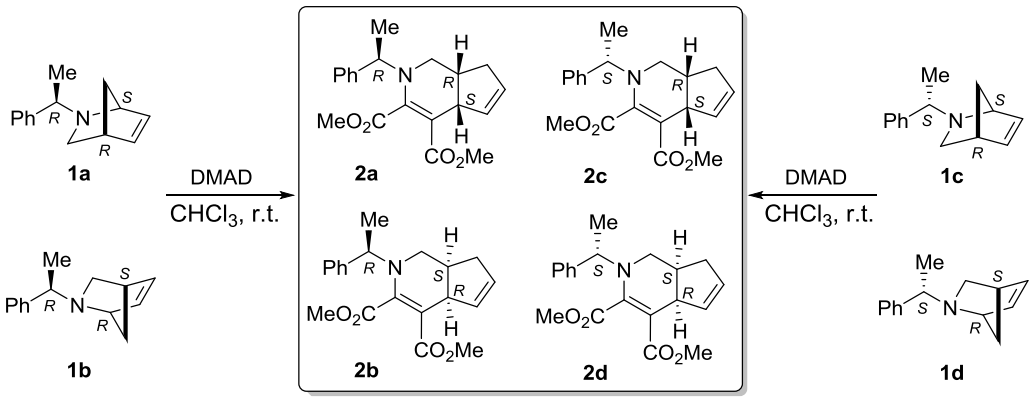
2-Azabicyclo[2.2.1]heptene derivatives are commonly used in stereoselective synthesis of analogues of natural products. Alkyl substituted azanorbornens (**1**), obtained by the multicomponent aza-Diels-Alder reaction of the corresponding primary amines, formaldehyde and cyclopentadiene, react with activated alkynes unusually. The reaction is followed by the aza-Claisen rearrangement [1] to form derivatives of cyclopenta[*c*]pyridine (**2**) in yields up to 65%. Pyridines **2** are potentially interesting as synthons for preparation of various biologically active compounds.



R^1 = Me, *i*-Pr, $C_{12}H_{25}$, Cyclohexyl, Cyclopentyl, Cyclopropyl, Allyl, Bn, (*S*)-1-Phenylethyl, (*R*)-1-Phenylethyl
R^2 = H, CO_2Me, CO_2Et; R^3 = Me, Et

In case of using of the optically active phenylethylamines, two isomeric pairs of 2-azabicyclo[2.2.1]heptenes (**1a-d**) [2] have been obtained after the aza-Diels-Alder reaction. These isomeric pairs were conversed into cyclopenta[*c*]pyridines (**2a-d**) by the interaction with DMAD. All the isomers **2a-d** have been isolated in the enantiopure form.



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Supramolecular complexes of bis(aza-crown)dienones with alkanediammonium cations

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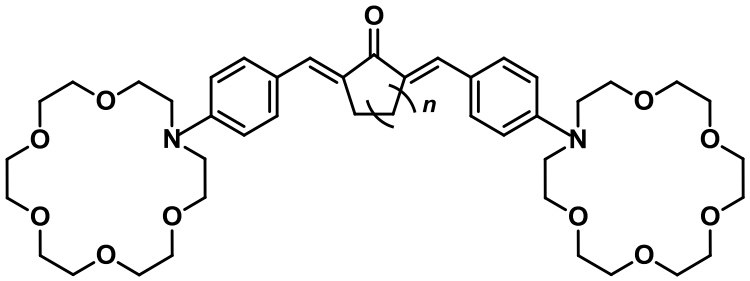
During the last two decades, considerable research interest has been devoted to the design of crown ether substituted chromophores. These compounds were mainly studied for their photochromic and fluorescence properties. In order to elucidate the possibility to construct photoactive supramolecular systems based on dienones we synthesized symmetrical dienones substituted with two aza-crown ethers. 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.

The formation of complexes **1a** and alkanediammonium ions **2** is caused by interaction of the ammonium groups **2** with the crown ether moieties of the dienone **1a**. The complexation induces considerable changes in the absorption spectra of the dienone **1a**. The stability constants of the formed complexes were determined.



1: n = 1(**a**), 2(**b**)

2: $^{+}H_3N(CH_2)_nNH_3^{+}$ $2ClO_4^{-}$; n =1-12

It was shown that in dilute solution bis(aza-crown)dienone **1a** 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 dienone binding sites. The dienone forms 1:2 complexes with short alkanediammonium ions (n = 1-5) and high stable 1:1 complexes with long ions.

The results of this study can be used for the targeted design of photoactive supramolecular assemblies and optical molecular sensors.

This work was supported by the Russian Science Foundation (project № 14-13-00076).

Synthesis of substituted 3-polyfluoroalkylpyrazol-4-amines

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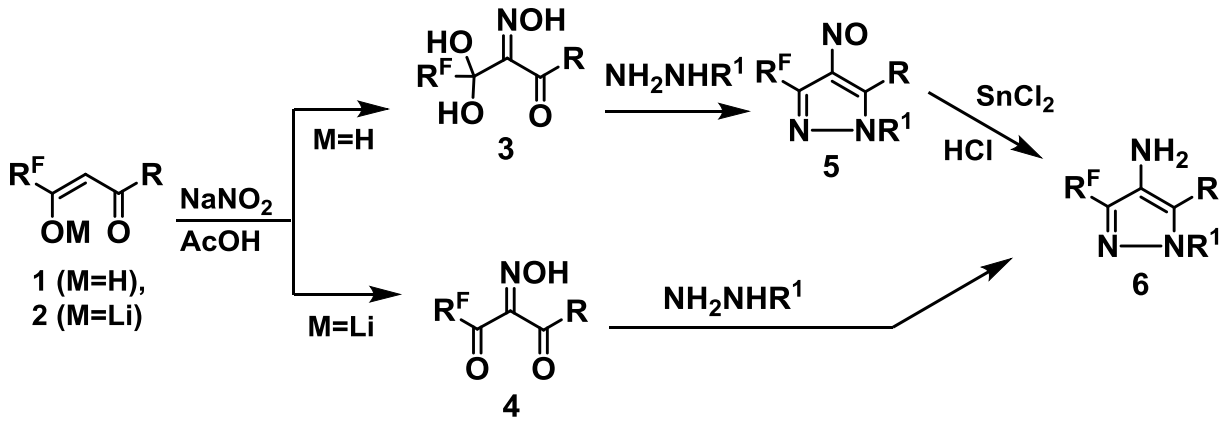
Fluoroalkyl-containing pyrazoles appear to be important building blocks for the synthesis of bioactive compounds and a variety of mono- and polynuclear coordination compounds. Introduction of substituents into the pyrazole ring expands significantly their synthetic potential. For example, 5-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-4-amine is the key compound for the synthesis of novel 3-trifluoromethylpyrazole-1,2,3-triazole hybrids, which proved to be promising antimyco-bacterial compounds with a low cytotoxicity [1].

In this communication we wish to report on the synthesis of 1-R^1-5-R-3-(polyfluoroalkyl) substituted pyrazol-4-amines **6** starting from the readily available 1,3-diketones **1** and their lithium enolates **2**. It has been found that synthetic pathways to 4-aminopyrazoles **6** are different, depending on either 1,3-diketones **1** or lithium salts **2** have been used as the starting materials.



R^F = polyfluoroalkyl; R = Alk, Ar;
R^1 = H, Ph

All steps to prepare pyrazoles **6** are simple, and yields of the target products are in the range of 70-95%. Products **3**-**6** have been characterized by the data of elementary analysis, GC-MS, IR, ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy.

This work was financially supported by Federal Program for Support of Leading Scientific Schools (grant SS-8922.2016.3) and the Russian Science Foundation (grant 16-13-10255).

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Transformations of 1-aroyl-3,4-dihydroisoquinolines as a method for the synthesis of Schiff base

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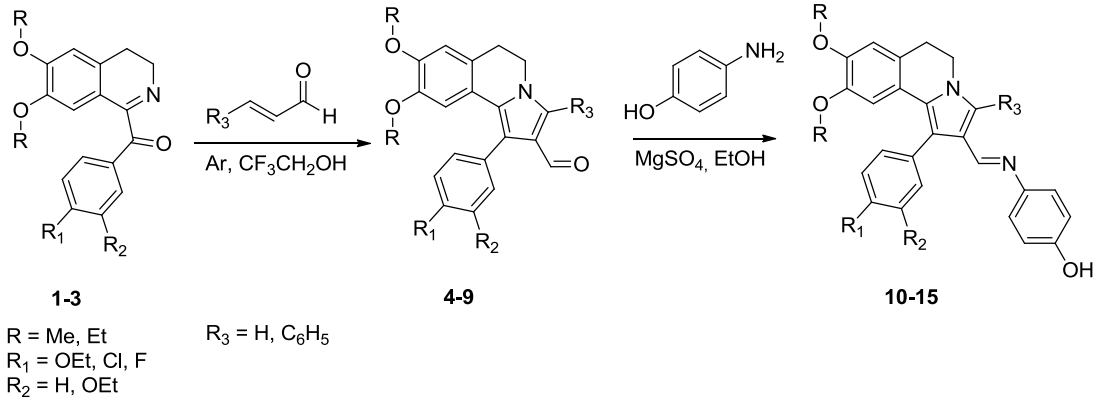
One of the beneficial area of modern organic chemistry is a synthesis of aromatic heterocycles systems, containing pyrroloisoquinoline fragment. Considerable interest has been directed towards these polyaromatic natural products primarily due to their broad-spectrum biological activities with multiple underlying intracellular targets. [1] Alkaloids, including a 5,6-dihydropyrrolo[2,1-*a*]isoquinoline moiety, exhibit antitumor and antileukemia activity, inhibit tubulin polymerization and displays an affinity for estrogen receptors [2].

In this research, the aim was to synthesize Schiff base via transformation of pyrrolo[2,1-*a*]isoquinolines. On the first step, isoquinolines **1-3** reacted with aldehydes in trifluoroethanol to provide pyrrolo[2,1-*a*]isoquinolines **4-9**.

Scheme 1



The reaction of pyrrolo[2,1-*a*]isoquinolines **4-9** with 4-aminophenol in the presence of magnesium sulfate provided Schiff base **10-15** with good yields. This work was supported by the Russian Foundation for Basic Research (grant № 17-03-00605).

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Self-assembly through hydrogen bonding, spectral properties and structure of supramolecular complexes of thiamonomethyncyanine containing terminal ammonium groups with cucurbiturils

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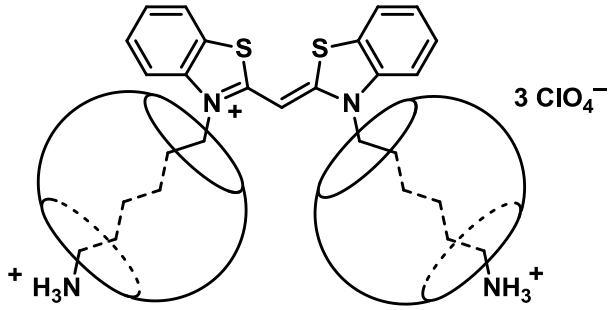
The "host-guest" complexes of macrocycles with organic molecules, in which the guest molecule has a chromophoric moiety, are of particular interest for supramolecular photochemistry.

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 thiamonomethyncyanine dye 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.



Complex formation of cyanine dyes with cucurbiturils was studied by electronic and ^{1}H NMR spectroscopy methods. The formation of supramolecular complexes of different stoichiometry was discovered. Their stability constants were determined.

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 RSF (project № 14-13-00076) and RFBR (project № 15-03-01883).

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Direct α-iodination of carboxylic acids using iodine chloride

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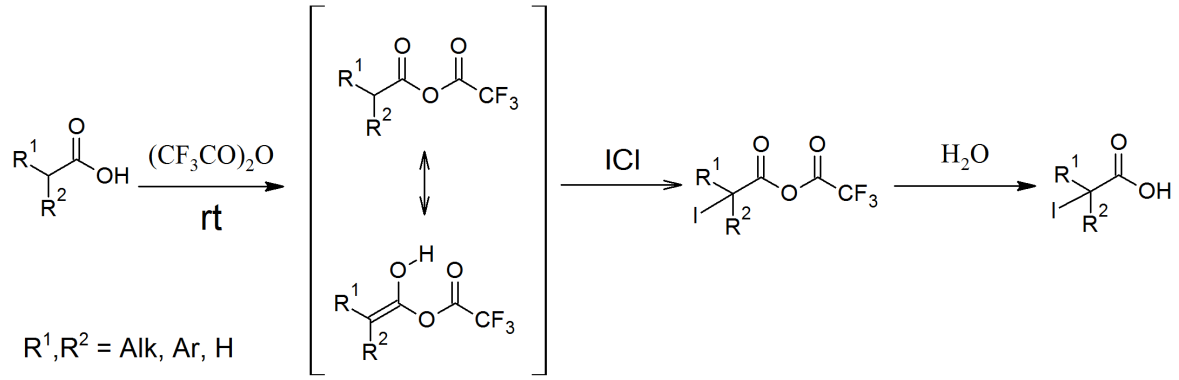
Direct metal-free α-iodination of carboxylic acids via formation of mixed anhydrides with trifluoroacetic acid, using iodine chloride, gave the corresponding α-iodo carboxylic acids in good to high yields.

Recently we have reported direct α-bromination method [1] of different carboxylic acids. Using the same approach to α-iodination of carboxylic acids with I_2 failed to give desired product. However, α-iodo carboxylic acids can be prepared replacing halogen with sodium iodide [2]. Harpp *et al.* [3] reported that the reaction of acyl halide with iodine gave the α-iodoacyl halide. Rathke and Lindert [4] described a convenient method for the preparation of α-iodo esters using lithium ester enolate and iodine. Horiuchi and Satoh [5] reported the direct α-iodination of carboxylic acids using iodine-copper (II) acetate in acetic acid. However, this method gives small yield of products, since the reaction proceeds only at high temperature and the forming HI reacts with the corresponding iodocarboxylic acid to give initial carboxylic acid.

In the present research, we would like to report that the α-iodination of carboxylic acid via formation of mixed anhydride with trifluoroacetic acid, using iodine chloride, gave α-iodo carboxylic acid at room temperature (scheme 1) in good to high yield.



Scheme 1. Carboxylic acid α-iodination reaction protocol

This is the first time that direct metal-free carboxylic acids α-iodination has been successfully accomplished at room temperature. It is also noteworthy that this reaction affords a new synthetic method for α-iodo carboxylic acid, more convenient the method used heretofore.

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Synthesis and biological activity of 33-dehydrooligomycin A

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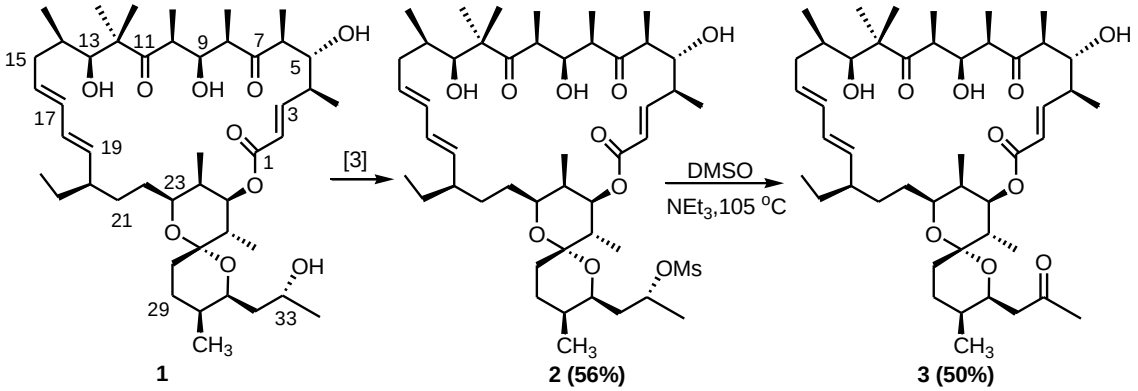
The macrolide antibiotic oligomycin A (**1**), produced by actinomycetes *Streptomyces*, is a well-known inhibitor of F_0F_1 ATP-synthase, which is regarded as a molecular target for new drugs in the treatment of tumors and infections. In micromolar concentrations, oligomycin binds to F_0 c-subunit, blocks proton translocation and disrupts bioenergetic metabolism [1].
Novel semi-synthetic derivatives with a pointed modification of the functional groups in the molecule of oligomycin A (**1**) would be valuable for SAR studies, validation of intracellular targets and depicting the mechanism of F_0F_1 ATP-synthase functionality. Of interest is the development of modifications of the side-chain propanol of oligomycin A as a hydroxyl group of this moiety plays a key role in the inhibition of F_0F_1 ATP-synthase by oligomycin A [2]. Based on this point, we synthesized and evaluated 33-dehydrooligomycin A (**3**). The new derivative **3** was prepared by the Kornblum oxidation of 33-O-mesyloligomycin A [3] (**2**). Treatment of **2** with triethylamine in DMSO at 105°C for 3-4 h led to 33-dehydrooligomycin A (**2**) in good yield.



1 **2 (56%)** **3 (50%)**

Biological data of the 33-dehydrooligomycin A (**3**) have been evaluated. The antimicrobial properties of the new derivative **3** were similar or approximately twice as weak as the native compound **1**. It should be noted that this transformation of oligomycin A led to increased activity against the leukemia cell line K562 and decreased cytotoxicity against non-malignant human fibroblasts. This indicated the expediency of in-depth evaluation of the spectrum of antiproliferative activity and antitumor properties of 33-dehydrooligomycin A (**3**). Additionally, the introduction of a reactive ketone group at position 33C of oligomycin A opened new opportunities for further synthetic and research studies.

This work was supported by the Russian Science Foundation (agreement № 15-15-00141).

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Advances of ^{77}Se NMR spectroscopy in analysis of chiral organic compounds

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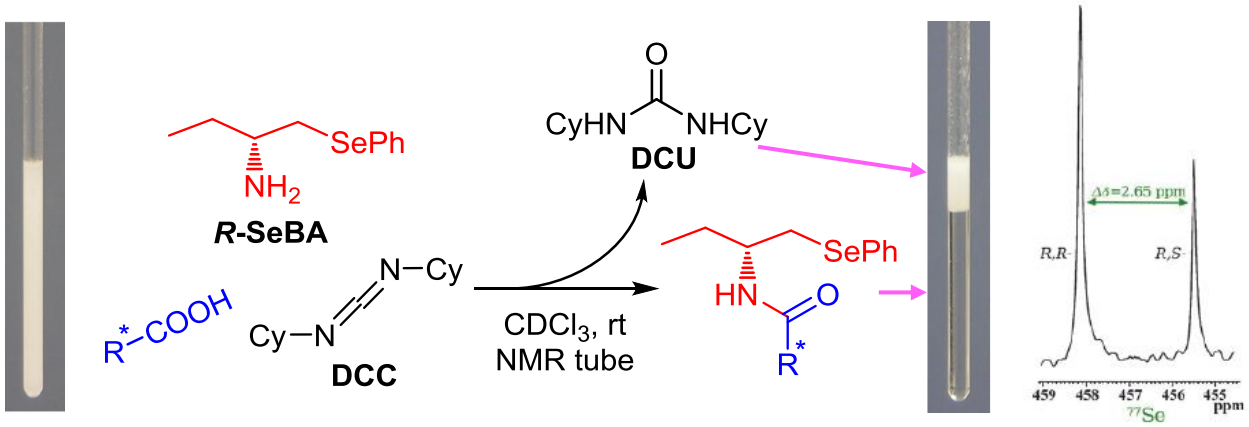
Nowadays NMR spectroscopy has become a powerful tool for analysis of chiral organic compounds [1]. Use of derivatization methods which don't require time and reagent consuming isolation and purification steps or various chiral solvating agents allows quick differentiation of enantiomers in NMR spectra [2].

Recently we have developed a simple procedures of derivatization of chiral alcohols, amines [3, 4] and carboxylic acids [5] using Se-containing chiral probes directly in NMR tube suitable for 1D and 2D NMR measurements without purification or isolation steps (scheme 1). ^{77}Se NMR spectra are superior in assignment of signals because only peaks of selenium-containing diastereomers are present. Large NMR scale of ^{77}Se nuclei excludes signals to overlap that makes it possible to determine enantiomeric purity of even as little as 0.01 mg of chiral samples with high accuracy.

Remarkable correlation between difference of ^{77}Se chemical shifts of diastereomers and structure of analyzed chiral compounds was found. Thus preliminary structure elucidation of complex molecules can be performed using simple 1D NMR experiment.



Scheme 1. DCC-promoted "in tube" derivatization of chiral carboxylic acids with chiral probe *R*-SeBA.

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The study of antioxidant properties of new synthetic porphyrin

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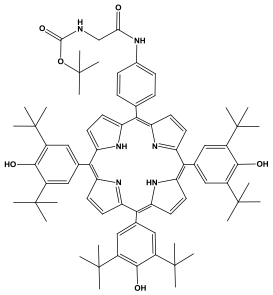
The porphyrins play a significant role in the oxidation processes in living organisms. Recently various synthetic porphyrins were found to possess the activity as photosensitizers and antioxidants [1]. The electrochemical methods are widely used to evaluate the antioxidant activity of the compounds [2]. We have studied the electrochemical properties of the synthetic porphyrin containing both the antioxidant phenol group and amino acids residues. The interaction of porphyrin with an electrochemically generated $O_2^{\bullet-}$ in aprotic solvent CH_2Cl_2 at a platinum electrode and the inhibitory activity in the peroxidation of oleic acid at 37° C for 5 h was studied.



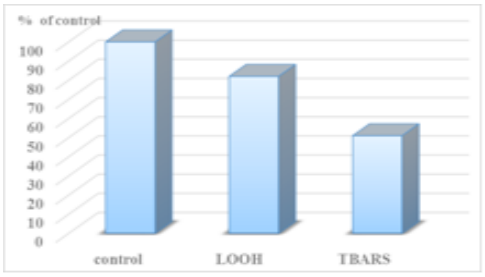


Fig. LOOH and TBARS in oleic acid in the presence of 1 mM porphyrin at 37°C (5 h, air)

Electrochemical studies were performed by cyclic voltammetry method in a three-electrode cell using an IPC-pro potentiostat. Porphyrin is oxidized in CH_2Cl_2 on Pt-electrode in a reversible two stage way at a potential 1.05 V and 1.21 V respectively. The reversibility of the oxidation indicates that the stable intermediates are formed and therefore antioxidant effect might be expected. Interaction of porphyrin with an electrochemically generated $O_2^{\bullet-}$ demonstrates an increase of the cathode and anode peaks of oxygen reduction and appearance of the peak in the anode region (E_{pa} = - 0.2 V). This suggests that the porphyrin acts as a proton donor in the reaction with $O_2^{\bullet-}$. We studied the peroxidation of *cis*-9-octadecenoic (oleic acid) by molecular oxygen, which is the model process of lipid peroxidation. This process involves the formation of primary oxidation products hydroperoxides (LOOH) and secondary products of lipid peroxidation - carbonyl compounds, which react with thiobarbituric acid (TBARS). The inhibitory activity of porphyrin is well pronounced: reduction in the level of LOOH by 20% is observed, while the level of TBARS decreases by 50% (Fig.).

Thus, the study confirms that the combination of several redox-active centers (2,6-di-tert-butylphenol, porphyrin ring and amino acids residues in porphyrin structure allows one to predict a certain biological antioxidant activity.

This work was supported by the Russian Foundation for Basic Research (grant № 16-03-00334).

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Recyclization of trifluoroacetylchromenes to trifluoromethylchromenols

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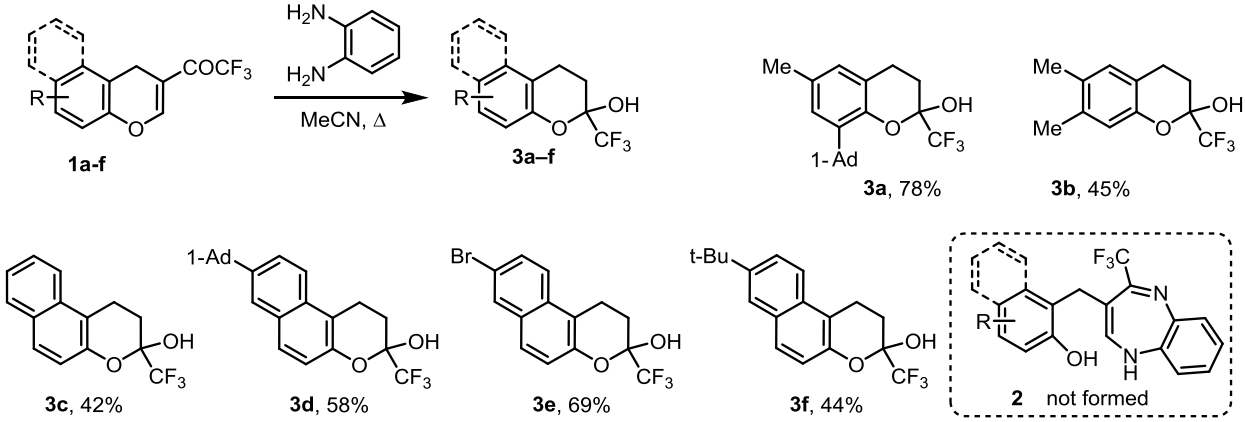
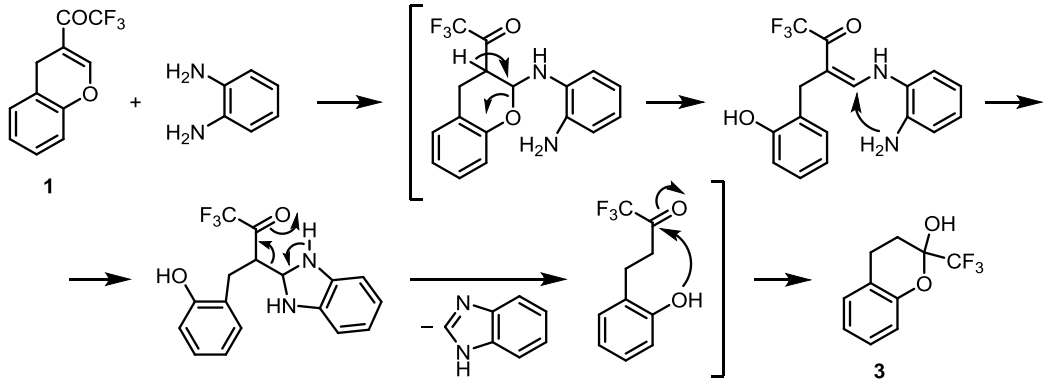
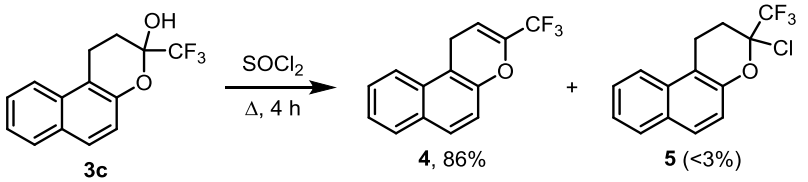
One of the obvious approaches to the preparation of trifluoromethyl-substituted benzodiazepines is the reaction between 1,3-dicarbonyl compounds or their synthetic equivalents and *o*-phenylenediamine. We expected that the reaction 3-trifluoroacetyl-4*H*-chromenes **1a,b** or 2-trifluoroacetyl-1*H*-benzo[*f*]chromenes **1c**–**f** as structural analogues of β-alkoxyvinyl(trifluoromethyl)ketones with *o*-phenylenediamine also can give the respective benzodiazepines **2**. However, the reaction produced only 2-(trifluoromethyl)chroman-2-ols **3a,b** and 3-(trifluoromethyl)-2,3-dihydro-1*H*-benzo[f]chromen-3-ols **3c**–**f** long with benzimidazole.



The proposed rearrangement mechanism included the following steps: aza-Michael reaction – addition of one of the *o*-phenylenediamine amino groups to chromene **1**, a retro-oxa-Michael reaction – opening of dihydropyran ring, repeated aza-Michael reaction, a retro-Mannich reaction accompanied by elimination of benzimidazole, and hemiketalization.



Refluxing the chromenol **3c** with excess of thionyl chloride allowed to obtain chromene **4** in 86% yield. The content of by-product **5** in the reaction mixture was less than 3%.



This work was supported by the Ministry of Education and Science of the Russian Federation (the Agreement number 02.a03.21.0008).

The reaction 1,4,5,8-tetra- and 1,4,5-triaminonaphtalene with aliphatinc nitrocompounds

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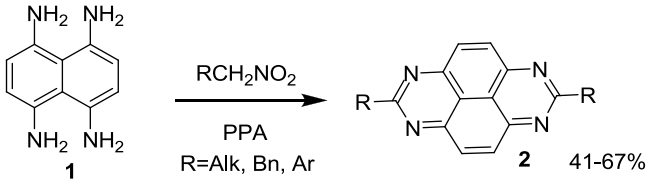
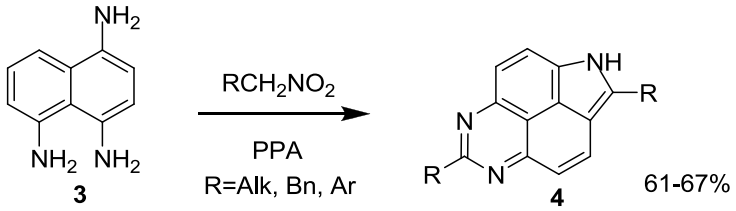
There are dozens of works devoted to the development of methods of synthesis polynuclear aromatic and heteroaromatic compounds, such as poliazapyrenes and similarly structured systems. Low availability of such compounds is determined, primarily by the lack of convenient methods of *peri*-annulation of carbocyclic and heterocyclic nuclei to phenalenes and azaphenalenes. The development of *peri*-annulation methodologies, namely, the search for new reagents, reagent systems and conditions conduce to the construction of both new and previously known heterocyclic systems.

Recently [1] in our laboratory, a new method for annulation of five-membered nitrogen-containing heterocycles on a basis of reaction of *ortho*-substituted anilines with nitroalkanes was shown. This method gives good yields of benzoxazoles and benzoimidazaoles in mild conditions.

Increasing the distance between the amino groups, such as using of *peri*-substituted naphthalene may provide a method of annulation of six-membered heterocycles. Indeed, the reaction of 1,4,5,8-aminonaphthalene with nitroalkanes in PPA leads to corresponding 2,7-disubstituted 1,3,6,8-tetraazapirenov. Sequential addition of two nitro compounds leads to the formation of tetrazapirenes with two different substitutients.



Indeed, the reaction of 1,4,8-triaminonaphthalene with nitroalkanes in PPA leads to corresponding 2,6-disubstituted 1,5,7-triazacyclopenta[cd]phenalenes. Sequential addition of two nitro compounds leads to the formation of 1,5,7-triazacyclopenta[cd]phenalenes with two different substitutients [2].



This work was supported by the Russian Foundation for Basic Research (grants № 16-03-00177a and 16-33-00483 мол_а).

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Self-assembly of fluorescent nanoparticles based on ammonium derivatives of thiacalix[4]arene in water

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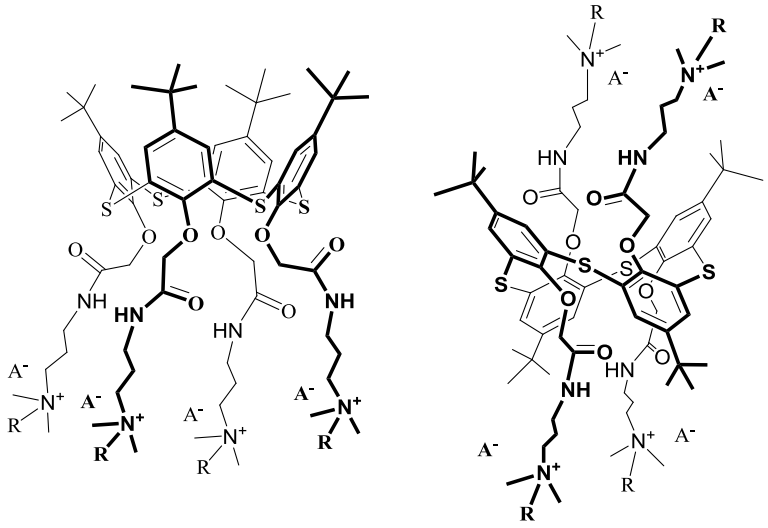
Design and synthesis of artificial receptor structures an important part of modern organic chemistry. One of the platforms used to create molecules-"hosts" is (thia)calix[4]arene.

The aim of this work is the synthesis and study of aggregation and fluorescent properties of the water-soluble ammonium derivatives of *p-tert*-butylthiacalix[4]arenes containing chiral amino acid fragments of *L*-tryptophan at the lower rim of the macrocycle, in *cone* and *1,3-alternate* conformation.



New derivatives of *p-tert*-butylthiacalix[4]arene tetrasubstituted at the lower rim with chiral amino acid L-tryptophan fragments in *cone* and *1,3-alternate* conformations were obtained. The structure of the compounds was confirmed by a complex of physical methods (^{1}H and ^{13}C NMR, IR spectroscopy and mass spectrometry), and the structure was confirmed by elemental analysis.

The methods of dynamic light scattering, fluorescence spectroscopy, transmission and scanning electron microscopy demonstrated the ability of the obtained compounds in *cone* and *1,3-alternate* conformations to form fluorescent nanoparticles in water.

This work was financially supported by the Ministry of Education and Science of the Russian Federation on the program to improve the competitiveness of Peoples' Friendship University of Russia (RUDN University) among the world's leading research and education centers in the 2016-2020

Hybrid antibiotics based on protein kinase inhibitors with some antimicrobial agents: synthesis and biological properties

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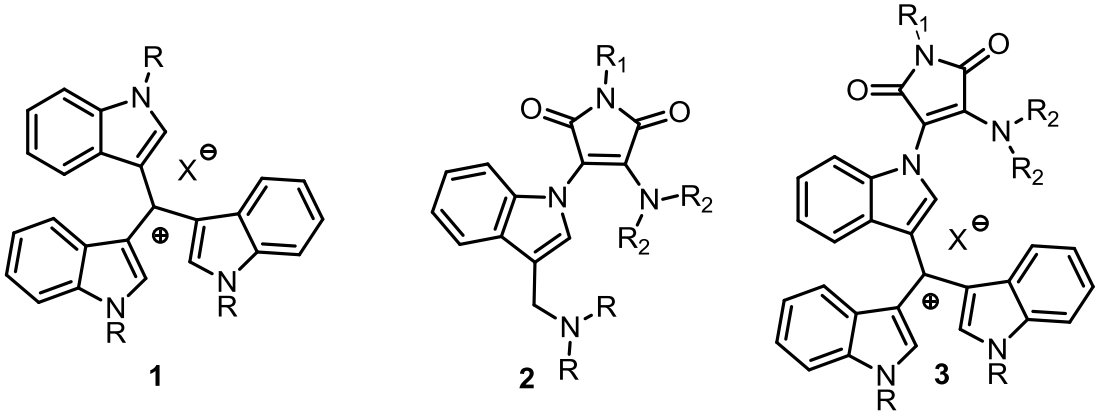
Development of new antibiotics is now possible either by search of new naturally occurring biologically active compound or by means of total synthesis [1,2]. Recently we synthesized tris-(1-alkylindol-3-yl)methyllium salts(**1**), which showed high antibacterial and antifungal activity [2,3], and 4-substituted 3-[3-dialkylaminomethyl)indol-1-yl]maleimides (**2**), which are capable of inhibition of vital protein kinases [4]. It seems promising to combine these two classes into hybrid molecules (**3**) in an attempt to make more active compound bearing both pharmacophore fragment simultaneously.



1 **2** **3**

R = Alkyl, R_1 = H, CH_3, R_2 = Alkyl, Aryl

X = $MeSO_3^-$, Cl^-

25 Compounds of the structure **3** were synthesized and tested for antibacterial and antifungal activity. Some of them turned out to be active against mycelial fungi, yeasts and bacteria, including antimicrobial-resistant strains.

The study was carried out with the support of the Russian Science Foundation (project №16-15-10300)

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Transformation of α-halogen-1,5-diketones with thiosemicarbazide

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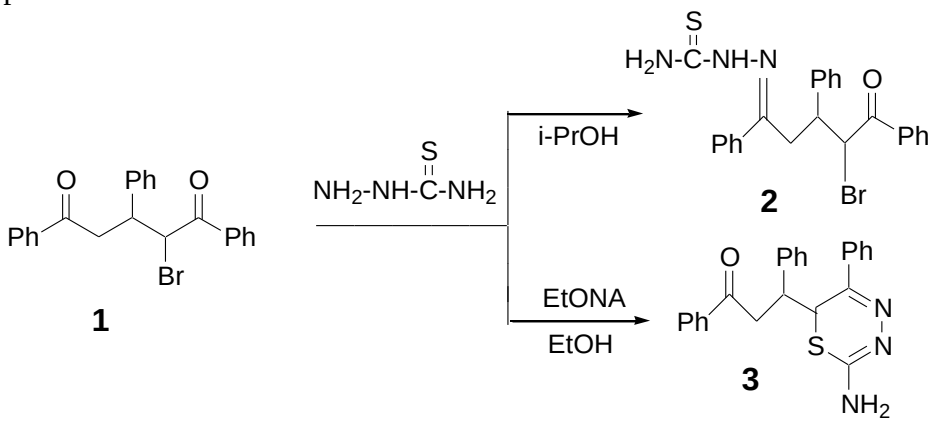
Currently, revealed the fact of huge significance α-galogencarbonyl compounds in the synthesis of 5-and 6-membered N,S-containing heterocycles.

It is known [1], that condensation of the thiosemicarbazide with α-galogenketones leads to 3,4-thiadiazines, the last outs are usually high, but, depending on the nature of the original reagents, from nature of solvent and temperature, can be derived by-products 3-aminothiazols.

We found that in reaction of 2-bromo-1,3,5-triphenylpentan-1,5-dione 1 with thiosemicarbazide in absolute *i*-PrOH 2-bromo-1,3,5-triphenylpentane-1,5-dion thiosemicarbazone 2 is formed with the release of 69%.

3-(2-Amino-5-phenyl-4H-1,3,4-thiadiazine-6-yl)-1,3-diphenylpropane-1-one 3 it was obtained by boiling diketone 1 with thiosemicarbazide in the presence of EtONa in absolute ethanol. Output is 57%.



Cyclization of the bromopentane-1,5-dione 1, under the influence of thiosemicarbazide in the absence of a catalyst does not occur, and the place has a competing cyclization process condensation with the participation of diketone propanonyl fragment with formation of thiosemicarbazone 2.

Structural fragment involved in reactions with thiosemicarbazide in the presence of catalyst (EtONa) is a system of α-bromo-ketone.

The structure of compounds 2 and 3 is confirmed on the basis of the data of IR and NMR spectroscopy.

This work performed on the Ministry of science and education job 2014/203, project code 1255.

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Synthesis of novel nonsymmetric diarylethenes containing 2-amino-1,3-thiazole bridging fragment

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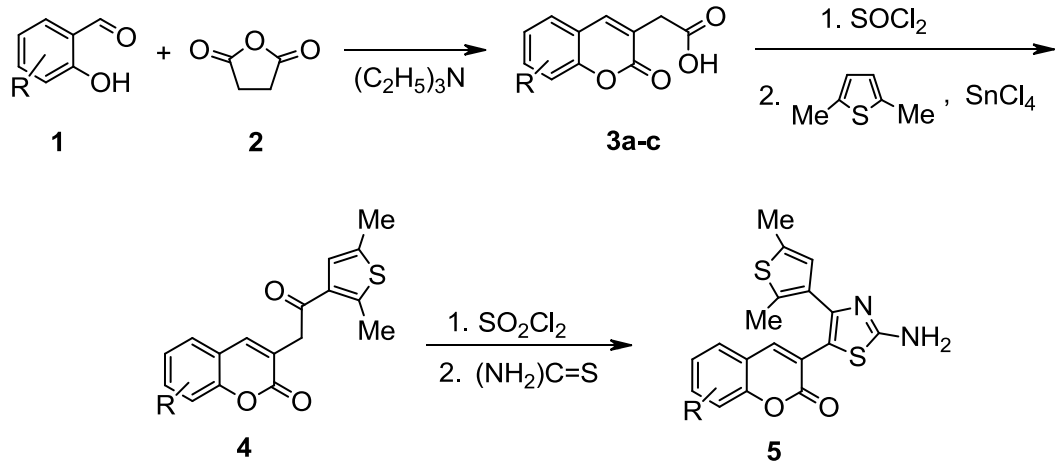
Dihetarylethenes, capable of photoinduced reversible electrocyclic rearrangements associated with changes of spectral and fluorescent properties, in recent years have caused a steady interest due to their possible use as promising materials for photonics and molecular electronics [1-3]. In the most part of cases, they are symmetric systems. With the purpose to extend the range of structural types of dihetarylethenes and to study their reactivity and photochromism, we synthesized novel nonsymmetric diarylethenes containing the thiophene and benzopyran-2-one moieties as hetaryl residues and 2-aminosubstituted 1,3-thiazole as bridging fragment.



1 **2** **3a-c** **4** **5**

By interaction of substituted salicylic aldehydes **1** with succinic anhydride **2** were synthesized novel coumarin acetic acids **3a-c**. Their interaction with 2,5-dimethylthiophene led to ketones **4a-c**, treatment of which with sulfuryl chloride and thiourea gave rise to diarylethenes **5a-c**. The obtained nonsymmetrical dihetarylethenes exhibit photochromic and fluorescent properties.

This work was supported by Grant of President of Russian Federation (No. MK-6738.2016.3).

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Study on mono- and bis-phenylazacrown-ether coordination systems, bridged by linear styrene motif

Pod'yacheva E.S.,[1] Nuriev V.N.,[1] Moiseeva A.A.,[1] Vatsadze S.Z.,[1]
Mamedova S.F.[2], Gromov S.P.[1,3]

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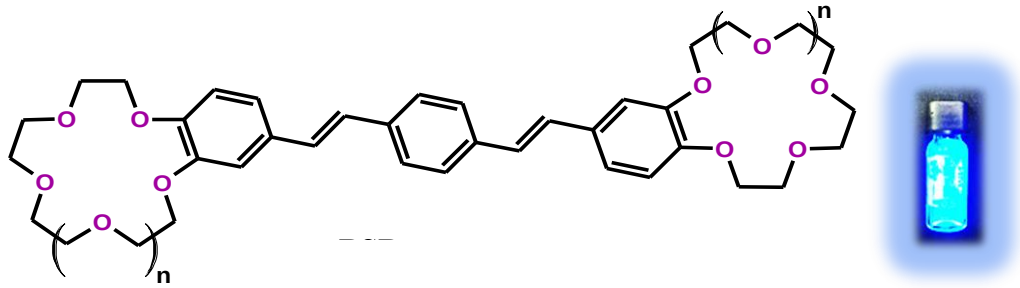
The linear derivatives of oligostyrenes, that exhibit high quantum yields of fluorescence, have received much attention for molecular sensor creation, imaging applications and constructing of the optoelectronic materials [1]. The attachment of the extended conjugated system to the benzocrown-ether receptor units dramatically influences on the spectral and photochemical properties and also allows fine tuning of these properties by using appropriate metal or ammonia ions [2]. We have recently started the comprehensive study of the convenient routes to obtain linear bis-crown-containing bis-styrylbenzenes (BSB). For this aim, a simple way to produce this family of key building blocks useful for creating supramolecular ensembles was elaborated starting from bisymmetrical synthone.



X-ray diffraction and electron spectroscopy study of the structure and spectral properties of BSB-ligands and their «host-guest» complexes with alkali and alkaline-earth metal cations show high affinity of such systems to self-assembling into bis-sandwich aggregates. Electrochemical study proves the possibility for such system to form even more complicated supramolecular ensembles, which might be controlled by light.

This work was supported by the Russian Scientific Foundation (project 14-13-00076).

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Eight-component condensation with isophorone under the condition for the synthesis of iminothiohydanthion

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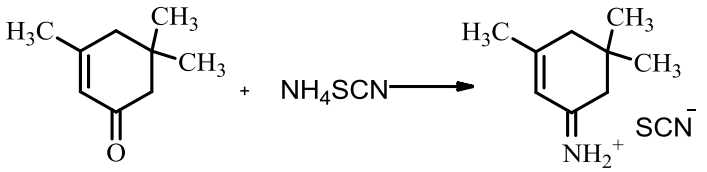
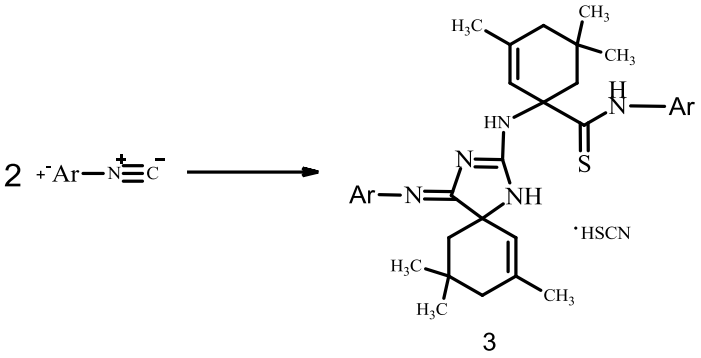
Previously it was shown that by using of ammonia or methylamine in four-component condensation - isocyanide, keton, amine, HSCN – instead of the expected iminothiohydantoin a product of eight-component condensation 8CC was obtained [1, 2].

The most probable factors that determine the direction of the abnormal reaction, are high basicity of amine and small steric hindrance for the formation of intermediates leading to 8CC.

In the present study, we investigate the possibility of 8CC with isophorone **1**, NH_4SCN and $ArN^+ \equiv C^-$ in the following reaction:



1 2



3

Ar = -Ph-CH_3, -Ph-OCH_3

The structures of obtained products were confirmed by spectral studies.

The obtained product 8CC **3** possess reactive groups suitable for the further chemical modifications to obtain the original bioactive compounds.

References

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Synthesis and thermal rearrangements of the spirocyclic derivative of the bicyclo[1.1.0]butane

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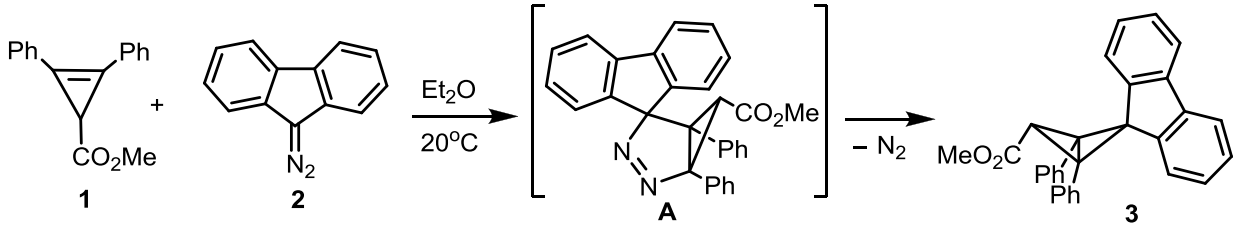
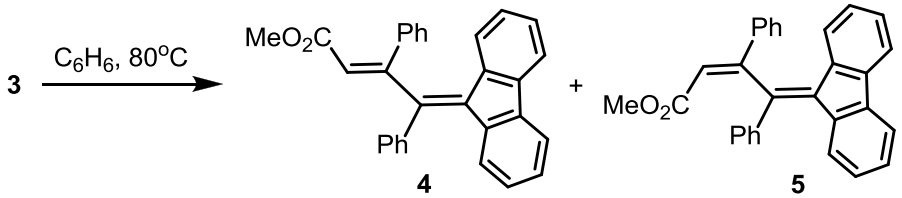
It is known [1–5] that thermal or photochemical deazotation of 2,3-diazo-bicyclo[3.1.1]hex-2-ene derivatives (homopyrazolenines) obtained in the reaction of 1,3-dipolar cycloaddition of diazoalkanes to cyclopropenes in some cases is a convenient method for creating a core of functionally substituted bicyclo[1.1.0]butanes.

We carried out the reaction of cyclopropene **1** with 9-diazofluorene **2** (diethyl ether, 20 °C, 5 d, darks) and obtained crystalline spirocyclic bicyclobutane **3** as the only product with the *exo*-arrangement of the methoxycarbonyl substituent.



We associate the origin of bicyclobutane **3** with the low thermal stability of the intermediate homopyrazolenine **A**, which experiences spontaneous deazotation under the experimental conditions.

Unlike related 1,3-diphenyl-substituted bicyclobutanes [5–7], which undergo reversible *endo*, *exo*-isomerization at 80–120 °C, compound **3** at reflux in benzene gives products **4** and **5** in the ratio 1 :4 under bicyclobutane-butadiene isomerization. After reflux in toluene only diene **5** is formed.



The reason of the low thermal stability of bicyclobutane **3** is seen in the large strain of its framework is created by the spirocyclic fragment of fluorene.

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Interaction of α-furyllactams with allyl bromide

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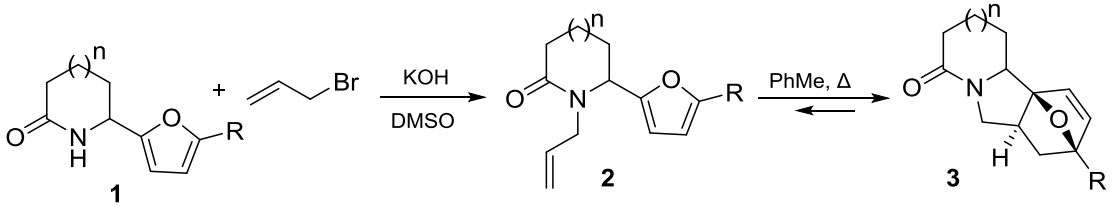
During the last decade, we have systematically studied the [4+2] cycloaddition between α,β-unsaturated acid anhydrides and furfurylamines, aimed at developing new approaches to the synthesis of isoindoles annelated with other heterocycles [1, 2].

α-Furyllactams possessing 6, 7, or 8-membered rings (**1**) can be easily alkylated with allyl bromide at room temperature to produce N-alkyl derivatives (**2**). Their boiling in toluene leads to formation of dynamical mixtures of the open forms (**2**) and the cyclic adducts (**3**).

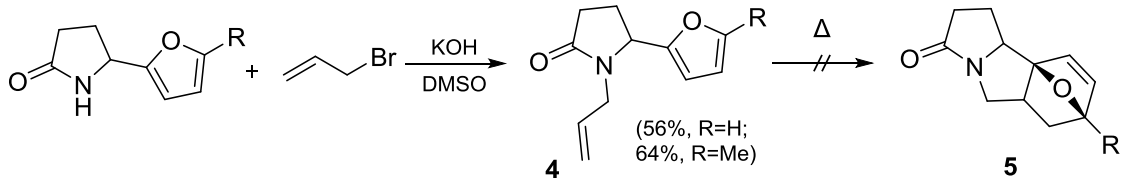


n	**2** / **3***	Total yield, %	R
1	28:72	62	H
2	35:65	71	H
3	32:68	65	H

n	**2** / **3***	Total yield, %	R
1	21:79	56	Me
2	26:74	59	Me
3	34:66	65	Me

* the ratio of tautomers **2** and **3** was established for solutions in $CDCl_3$ at 25 °C.

α-Furylpyrrolidones (**4**) do not turn into cyclic derivatives (**5**) even in boiling *o*-xylene.



This work was supported by the Russian Foundation for Basic Research (grant № 16-03-00125).

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Devrivatives of hetareno[*e*]pyrrole-2,3-diones, displaying biological activity

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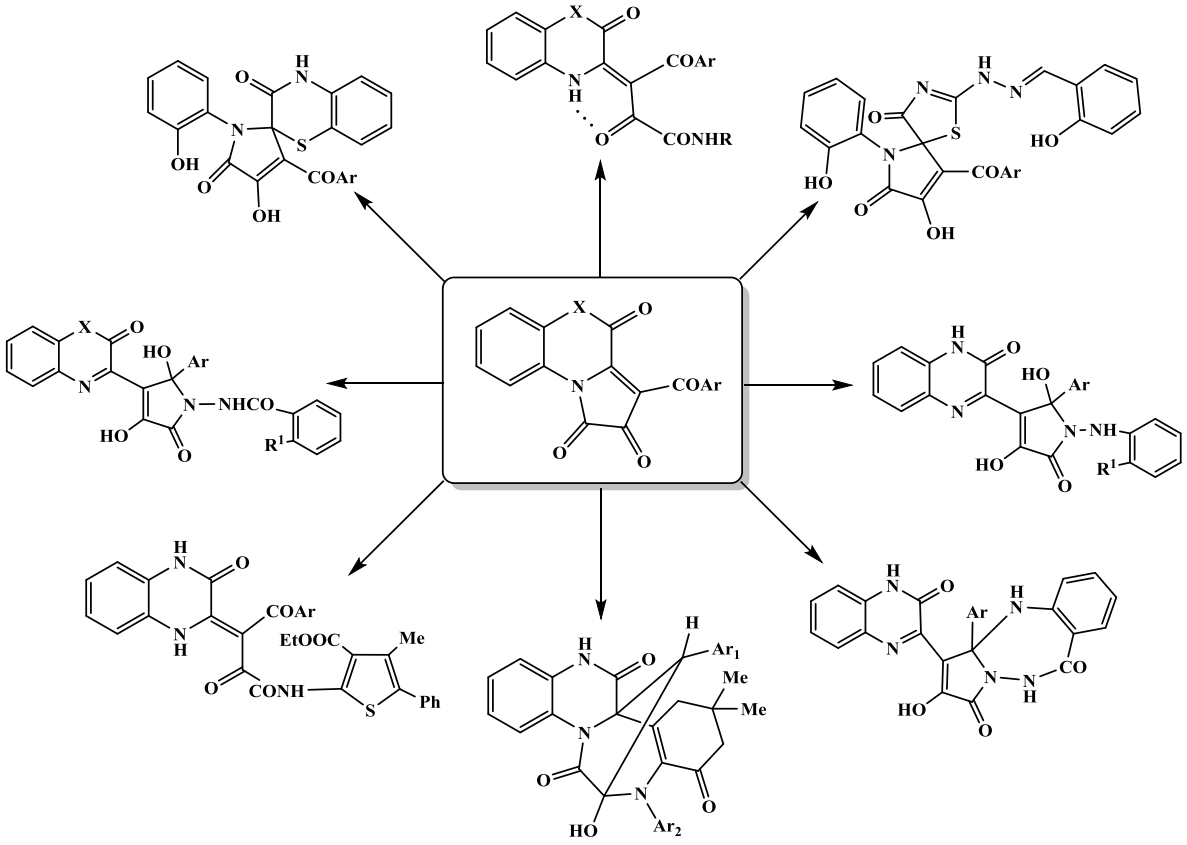
Heterocyclization and heterorecyclization with different binucleophiles are efficient and convenient methods of the synthesis of five-, six- and seven-membered azaheterocycles, condensed, bridged and spiro-bis-heterocyclic systems. Among synthesized compounds were found structures close to natural metabolites, like heterocyclic derivatives of acylpyruvic acid.



Antimicrobal, antifungal, antioxidant, antihypoxic, antidiabetic, anti-inflammatory and analgesic activities of synthesized compounds were studied. Most of them display low toxicity and significant biological activity.

This work was supported by the Russian Foundation for Basic Research (grant № 14-03-96005-p).

Synthesis of new 1,2,4-triazolo[3,2-b]-1,3-thiazine-7-ones containing sterically hindered phenol fragment

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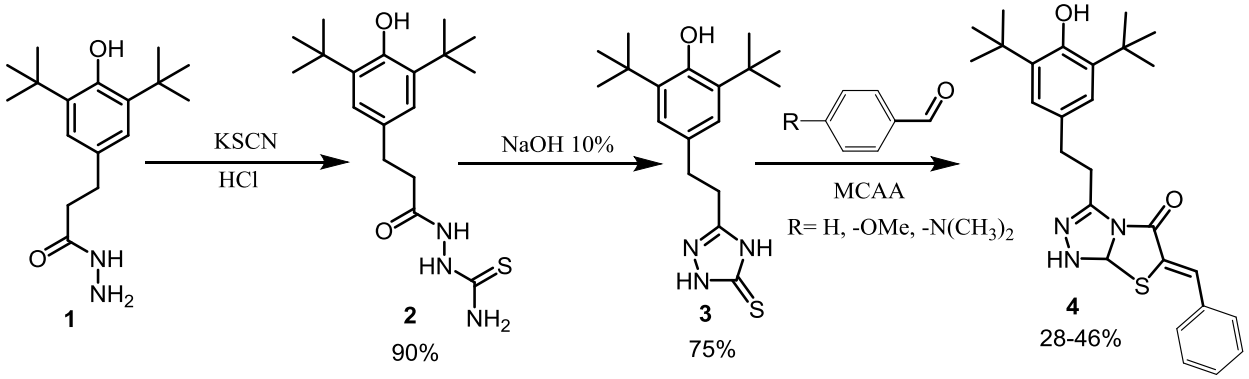
Among the compounds containing a 1,2,4-triazole moiety a large number of substances that exhibit biological activity has been revealed and such substance are used as antifungal, antispasmodic, antibacterial, neuroleptics. In addition, they are used in agriculture (herbicides, fungicides) [1]. Among compounds of these series of particular interest are 1,2,4-triazolo[3,2-b]-1,3-thiazine-7-ones, because of their high anti-inflammatory activity [2]. At the same time, to create new compounds having complex utilitarian properties, including the ability to inhibit the oxidation processes, it is appropriate to combine in the same molecule heterocycle and fragment of sterically hindered phenol, because of well-known high efficiency antioxidant phenolic compounds.

The key intermediate in the preparation of 1,2,4-triazolo[3,2-b]-1,3-thiazine-7-ones is 1,2,4triazol-5-thione **3**. It was obtained from 1-acylhydrazide **1** by action of potassium thiocyanate and subsequent heterocyclization of 4-acylthiosemicarbazide **2**. The treatment of 1,2,4triazol-5-thione **3** with chloroacetic acid and substituted or non-substituted benzaldehydes in the presence of sodium acetate, acetic acid and acetic anhydride gave the fused ring products **4**.



Target compounds, presumably, will have a broad spectrum of biological activity and low toxicity. The composition of the substances set by elemental analysis, and structure of the synthesized compounds were confirmed by FT-IR spectroscopy methods, 1H NMR spectroscopy and mass spectrometry.

References

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New hydrogenated six-membered azahetrocycle derivatives of phosphonic acid as perspective bioactive compounds

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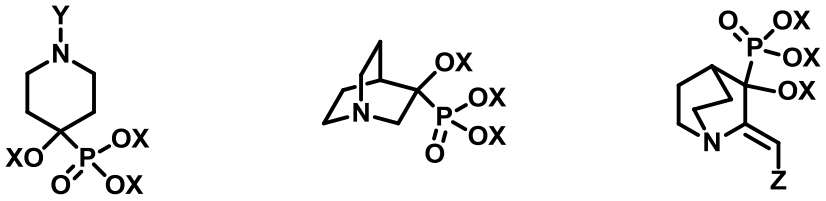
Functionalized organophosphorus acids and their derivatives with heterocyclic moieties are of great interest as effective chelating ligands and perspective bioactive substances with various properties [1]. These acids are well-known biomimetics of hydroxyl (amino)carbonic acids and natural pyrophosphates, and some of them such as zoledronic, risedronic, and minodronic acids are widely used in medicine. We have synthesized the new functionalized phosphonic acids and their derivatives including six-membered azaheterocycles *via* addition of tris(trimethylsilyl) phosphite to nitrogen-containing six-membered heterocyclic ketones. Trimethylsilyl-containing organophosphorus compounds easily react with methanol excess or with sodium methylate in methanol giving water soluble acids or their sodium salts in high to excellent yields [2,3].



X = H, Me_3Si, Na **Y = H, Me, Bn, Ac, Ms**

Z = 4-BrC_6H_4, 4-$MeOC_6H_4$, 4-$Me_2NC_6H_4$, Fc

The resulting compounds are the perspective biologically active substances and polydentate ligands with versatile properties as well as the promising precursors for multitarget drug discovery.

This work was financially supported by the RFBR (grants numbers 15-03-00002 and 17-03-00169).

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The C-3 acylation of 1-hydroxyindoles

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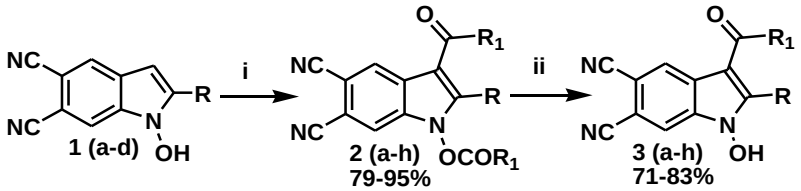
1-Hydroxyindole derivatives have attracted significant interest as valuable synthetic intermediates and due to their diverse pharmacological activities, including antiprolifirative and antibacterial properties. Several synthetic approaches towards these heterocycles have been developed, including the reductive cyclization of (o-nitrobenzyl)ketones or o-nitrostyrenes and the oxidation of NH-indolines. Recently we reported substituted 1-hydroxyindole-5,6-dicarbonitriles to be monoamine oxidaze inhibitors [1, 2], and these results have stimulated further studies of this class of compounds. In particular, attention was drawn to the corresponding 3-acyl derivatives since 3-acylindoles are known as universal building blocks for the synthesis of a variety of heterocyclic ring systems.

Presenty, the most used procedures for the C-3 acylation of indoles are various Friedel-Crafts acylation and Vilsmayer-Haack reactions. However, for 1-hydroxyindoles the C-3 acylation has not been described although it is known for O-substituted derivatives of 1-OH-indoles. The reaction of 2-aryl-1-hydroxyindole-5,6-dicarbonitriles **1 (a-d)** with acetic, propionic or butyric anhydrides with use of a 3.6-fold molar excess of $BF_3 \cdot Et_2O$ afforded 1-acyloxy-3-acyl derivatives **2 (a-h)** in high yields.



(i) **1** (2 mmol), $(R^1CO)_2O$ (2 ml), $BF_3 \cdot Et_2O$ (7.2 mmol), 65-85 °C, 5-20 min;
(ii) a) **2** (2 mmol), K_2CO_3 (4 mmol), EtOH (10 mL), 60-70 °C, 30 min; b) HCl

Propionic and butyric anhydrides reacted similarly to Ac_2O, though the reaction required longer reaction times (20 min) and higher temperature (85 °C). Additionally, isolation of the corresponding propanoyl and butanoyl derivatives 3e-h was more troublesome since they were initially formed as oils which crystallized slowly.

Simply heating **2 (a-h)** in EtOH at 60-70 °C in the presence of K_2CO_3 for 30 min. was sufficient for hydrolysis of the O-acyl groups in **3 (a-h)** to yield 3-acyl-1-hydroxy derivatives 4a-h. The structure of the synthesized compounds **2 (a-h)**, **3 (a-h)** were confirmed by the data of IR, NMR spectroscopy and mass spectrometry. The structure of 3-acyl-1-hydroxyindoles **3** was unequivocally confirmed by single crystal X-ray diffraction study for compound **3c** (Fig 1.).

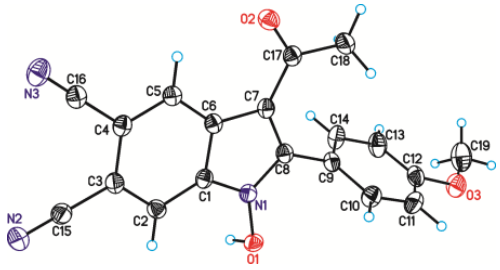


Figure 1. General view of compound **3c** with 50% probability displacement ellipsoids and the atom-numbering scheme.

References

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Catalytic asymmetric crotylation: method development and application in total synthesis

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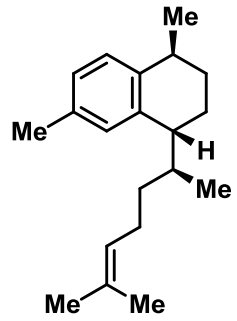
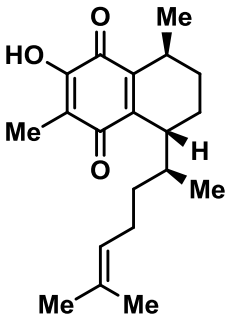
Secondary metabolites **1**-**4** isolated from marine soft coral *Pseudopterogorgia elisabethae* exhibit a wide range of useful biological properties, which include anti-tubercular, anti-inflammatory, antimicrobial and analgesic activities [1]. The analgesic properties are superior to industry standards such as Indomethacin. As a result, partially purified gorgonian extracts are used in commercial skin care products [2].



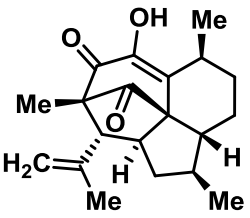
1

(-)-erogorgiaene



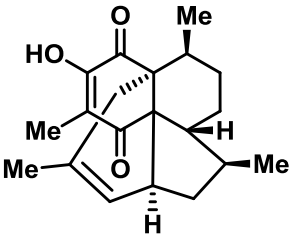
2

(+)-elisabetadione



3

(-)-elisapterosin B



4

(-)-colombasin A

Herein, we present a novel general strategy for a scalable enantioselective total synthesis of diterpenes **1** and **2** [3], where the key stereochemistry defining steps are asymmetric crotylation, anionic oxy-Cope rearrangement and cationic cyclisation. Preliminary biological evaluation of these compounds will be presented.

This work was supported by the Russian Science Foundation (grant 15-13-00092)

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Derivatives of phosphoncarboxylicacids

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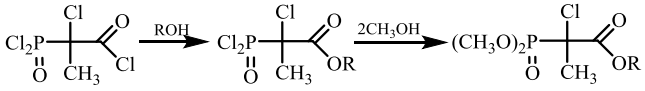
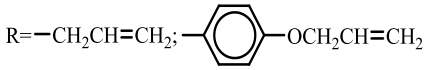
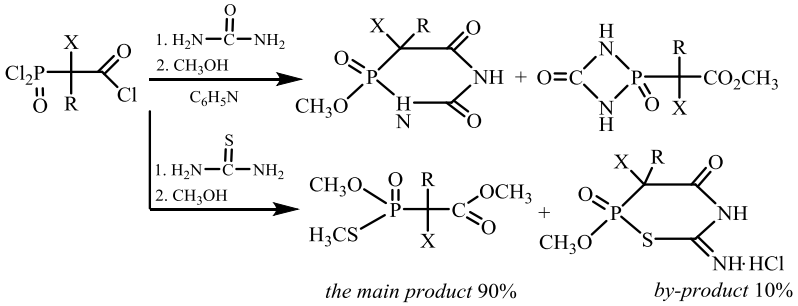
Corresponding C-allyl and phenyl esters were obtained by the interaction of trichloro anhydrides of phosphoncarboxylicacids with allyl alcohol and phenols. Synthesized esters with methanol leads to production of P,P-dimethyl esters of the corresponding acids.





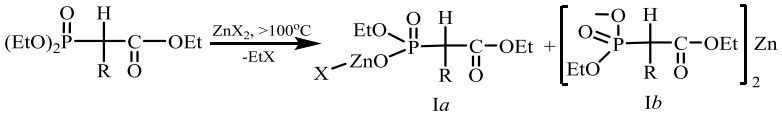
Interaction of trichloro anhydrides of phosphoncarboxylicacids with bidentate reagents (urea, thiourea etc.) results in obtaining phosphon barbiturates both in the presence and in the absence of tertiary amines [1]. Thiourea reacts with indicated trichloroanhydride and substitution products including nitrogen and sulfur atoms are found:



the main product 90% *by-product* 10%

R=X=H; R=CH_3; X=Cl

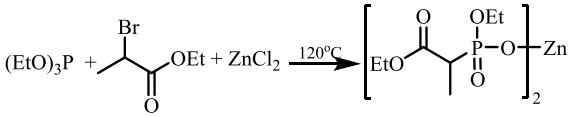
Triethyl esters of phosphoncarboxylicacids interact with $ZnCl_2$, $Zn(OCOCH_3)_2$ at room temperature forming molecular compounds, which enter into Arbuzovs reaction at temperature above 100°C and zinc phosphonates (I*a*-*b*) have been formed:



I*a* I*b*

R=H, CH_3; X=Cl, $CH_3COO^{\ominus}$

Indicated zinc phosphonates can also be prepared by condensation of trialkylphosphites with halogen carboxylic acid esters in the presence of $ZnCl_2$ at 120-130°C.



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Synthesis of 1-tetrazolyl substituted 1,2,3,4-tetrahydroisoquinolines via azido-Ugi reaction and investigation of their reactivity with activated alkynes

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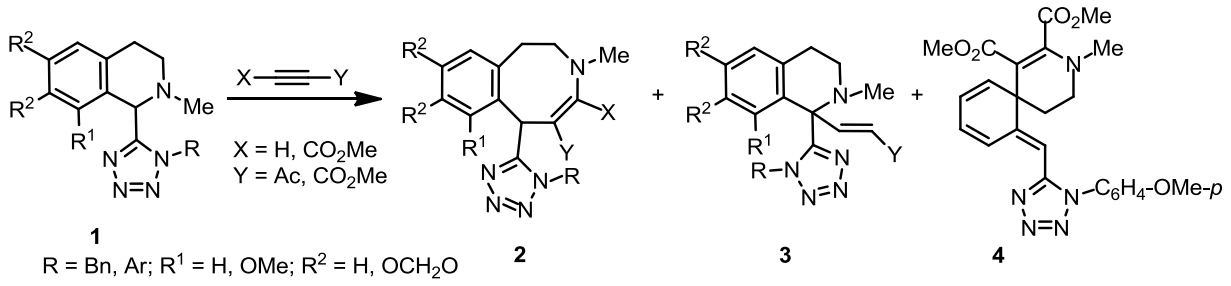
Compounds with the tetrazole moiety were shown to exhibit a cytotoxic activity [1], and their derivatives may be useful for development of antiviral and anticancer drugs.

1-Tetrazolyl substituted isoquinolines **1** were obtained in high yields from corresponding 3,4-dihydroisoquinolinium salts, isonitriles and sodium azide via three-component Ugi azido-reaction. The reactivity of isoquinolines **1** towards activated by electron-withdrawing groups alkynes in trifluoroethanol and acetonitrile has been studied. 6-Tetrazolyl substituted benzazocines **2**, 1-vinyl substituted isoquinolines **3** – the products of Stevens' rearrangement and 3-azaspiro[5.5]undeca-1,7,9-trien **4** were isolated from multicomponent reaction mixtures by column chromatography.



The structures of all compounds were confirmed by spectral data. The structure of 3-azaspiro[5.5]undeca-1,7,9-trien **4** was also confirmed by X-ray diffraction study.

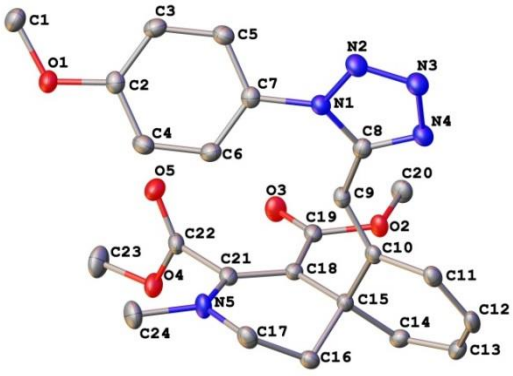


Fig 1. The structure of compound **4**.

This work was supported by the Russian Foundation for Basic Research (grant № 17-53-540001).

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New simple approach to the synthesis of 1,3,6,8-tetraazapyrenes

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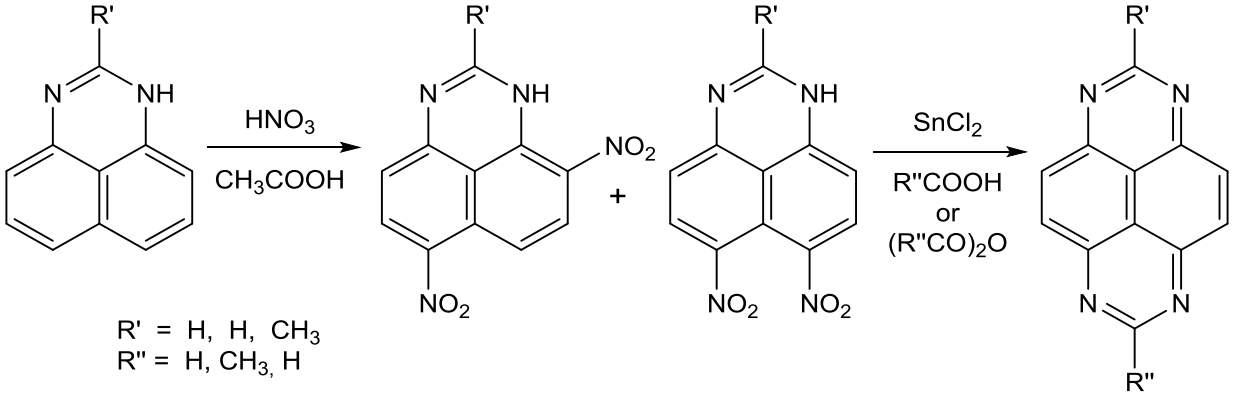
Azapyrenes have been molecules of interest due to both theoretical aspects such as aromaticity, thermodynamic stability, the mechanism of electrophilic and nucleophilic substitution, stability of radical-ions and the results of applied studies [1]. The change of the biological activity with insertion of nitrogen atoms to a pyrene ring is of undoubted interest.

1,3,6,8-Tetraazapyrenes also known as pyrimido[4,5,6-*gh*]perimidines have already been under research by our group concerning their method of synthesis [2].



It is well known that 1*H*-perimidine is nitrated by concentrated HNO_3 in the medium of acetic acid with formation of *mono*- and further *di*-nitration products [3] shown on the scheme. Their separation is cumbersome because the reaction mixture involves several compounds. We have found that reduction of a reaction mixture with $SnCl_2$ with simultaneous cyclization into corresponding 1,3,6,8-tetraazapyrene in the medium of formic acid or acetic anhydride guarantees formation of the desired product which is easily separated from the rest of the reaction mixture because of its polar nature.

Separation includes careful solvent selection for the recrystallization as well as straightforward filtration through a silica pad with solvents of different polarity. We plan to extend this methodology to different examples including cyclizations with aldehydes what allows to obtain a wider selection of derivatives.

This project received financial support from the Ministry of Education and Science of the Russian Federation in the framework of the State Assignment to the Higher Education Institutions (grant № 4.1196.2017/PP).

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Unexpected result of the reaction of 6-(5-bromo-3,4-dihydropyrimidin-4-yl)-1*H*-perimidine with nitrobenzene

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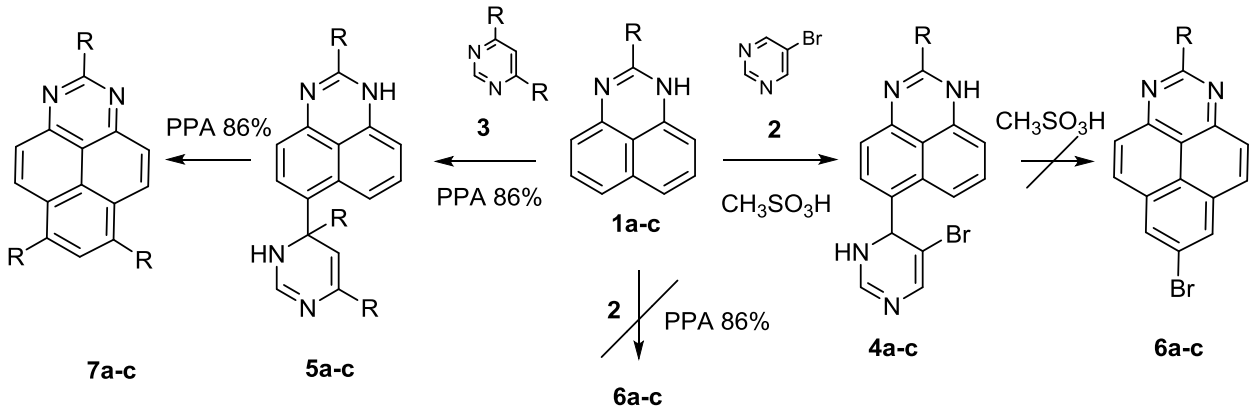
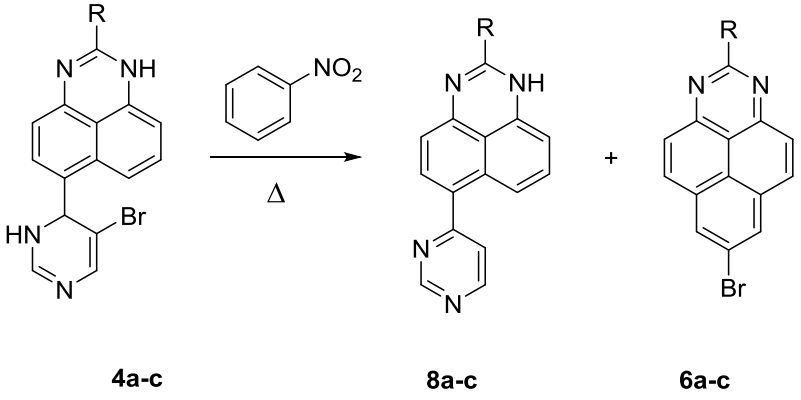
Earlier we found a reaction [1] leading to the synthesis of 6-(5-bromo-3,4-dihydropyrimidin-4-yl)-1*H*-perimidines **4**. Noteworthy, that unlike 4,6-substituted pyrimidine **3**, a reaction with 5-bromopyrimidine **2** stops on a stage of alkylation of 1*H*-perimidines **1** and *peri*-annulation of carbocyclic ring does not occur (**Scheme 1**):



Scheme 1 (R=H,Me,Ph)

Trying to oxidize obtained dihydroderivatives **4** we fulfilled the reaction of the latter with nitrobenzene. Along with the expected products **8** of a dehydrogenation reaction (yields 60-65%), 7-bromo-1,3-diazapyrenes **6** were isolated with yields 30-35% (**Scheme 2**):



Scheme 2 (R=H,Me,Ph)

This project received financial support from the Ministry of Education and Science of the Russia in the framework of the State Assignment to the Higher Education Institutions (grant №4.1196.2017/PP)..

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A new synthesis of substituted 6-nitro-1*H*-pyrazolo[4,3-b]pyridines

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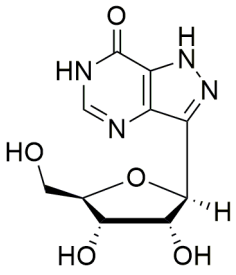
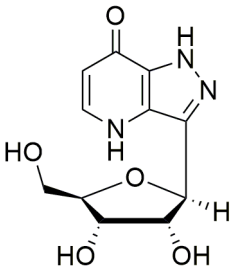


formycin B

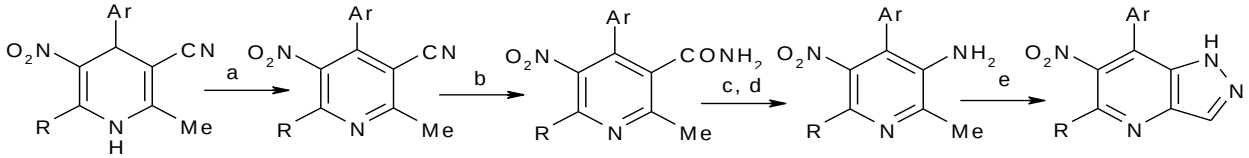


6-deazaformycin B

Naturally occurred C-nucleoside antibiotic formycin B possesses antiviral, antineoplastic and antiparasitic activities. But high toxicity of formycin B has restricted its use for clinical development. To decrease the toxicity of formycine, 6-deazaformycin B has been synthesized [1]. 1-Sulfonyl-pyrazolo[4,3-b]pyridines possess high anti-tumor activity as selective c-Met inhibitors [2]. Pyrazolo[4,3-b]pyridine-3-amine (VU0418506) showed high antiparkinsonian efficacy in preclinical studies [3].

The search through Reaxys and SciFinder databases shows that the main methods for synthesis of pyrazolo[4,3-b]pyridines are the reactions of 2-acetyl-(benzoyl-, formyl-)-3-halopyridines with hydrazine and 3-acylamino-2-methylpyridines with alkyl nitrites [1, 4]. The completion of pyridine ring to 4-aminopyrazole is more rarely used [5]. The syntheses of 6-nitro-*1H*-pyrazolo[4,3-b]pyridines have also been published: by cyclocondensation of nitromalonic dialdehyde with 4-aminopyrazoles and by acid-catalyzed transformation of the product of hetarylation of 5(4*H*)-oxazolones with 2-chloro-3,5-dinitropyridine [6, 7].

In this work we have solved the problem of availability of 3-amino-2-methyl-5-nitropyridines and have prepared 6-nitro-1*H*-pyrazolo[4,3-b]pyridines by intramolecular azo coupling reaction of pyridyl diazonium salts with CH-acidic methyl group.



(a) AcOH, $NaNO_2$,65^{0}C; (b) H_2SO_4, 100^{0}C, 1h; (c) $PhI(OAc)_2$, EtOH, Δ;
(d) NaOH, EtOH-H_2O, 70^{0}C, 24h; (e) $NaNO_2$, AcOH, DMSO, r.t., 48 h

R = Me, Ph; Ar = Ph, p-$MeOC_6H_4$, 2,4-$MeOC_6H_3$, p-ClC_6H_5, 2-Fu

This work was financially supported by the Russian Foundation of Basic Research and Ministry of Education of Omsk Region (grant № 16-43-550144/16 p-a).

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Electrosynthesis of *O*-, *S*-containing heterocyclic compound based on the use of activated hydrogen sulfide and 3-(12-oxo-11,12-dihydrochromeno[2,3-*b*]chromen-11-yl)chroman-2,4-dione

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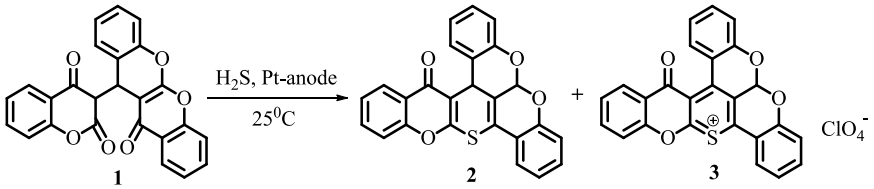
The natural and synthetic compounds which belong to the class 2*H*-chromen-2-one have a wide range of biological effect. They are the structural basis for the development of drugs with antibacterial, antimutagenic, antiviral, and other vasodilating properties. Lately the different substances which are anticoagulants produced by 2*H*-chromen-2-one's derivatives [1,2]. In the present work we studied the new synthetic metod to obtain the cyclization product of 3-(12-oxo-11,12-dihydrochromeno[2,3-*b*]chromen-11-yl)chroman-2,4-dione **1** with the participation of hydrogen sulfide. The reaction of compound **1** with H_2S was conducted in conditions of electrochemical one-electron oxidation stage of H_2S to the radical cation at a Pt-anode in organic solvents. Earlier the redox activation of H_2S was considered by us for the synthesis of other thiopyran structures without the using of mineral or organic acids [3,4].

The electrolysis of mixture a substrate **1** and H_2S was investigated in CH_3CN, CH_2Cl_2, CH_3CN/CH_2Cl_2 (1:1) for 2.0 h using the *n*-Bu_4NClO_4 as supporting electrolyte. The S-cyclization of compound **1** is possible due to the fragmentation of the radical cation of H_2S to proton and thiyl radical. This reaction proceeds in the mild condition according to the scheme:



1 **2** **3**

CH_3CN:	33,4%;	27,9%
CH_2Cl_2:	41,8%;	36,1%
CH_3CN/CH_2Cl_2 (1:1):	39,5%;	24,2%

The mixture of two products **2**, **3** was obtained after electrolysis. The thiopyran is able to oxidize at the electrolysis potential and this leads to forming of thiopyrilium salt. The current yield depends on the nature of organic solvent. The conversion of 3-(12-oxo-11,12-dihydrochromeno[2,3-*b*]chromen-11-yl)chroman-2,4-dione to sulfurcontaining heterocyclic compounds varies from 57.1 to 74.5 % in different organic media.

This work was supported by the Russian Foundation for Basic Research (grant № 16-03-00730).

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Catalytic Asymmetric Crotylation of Aldehydes.

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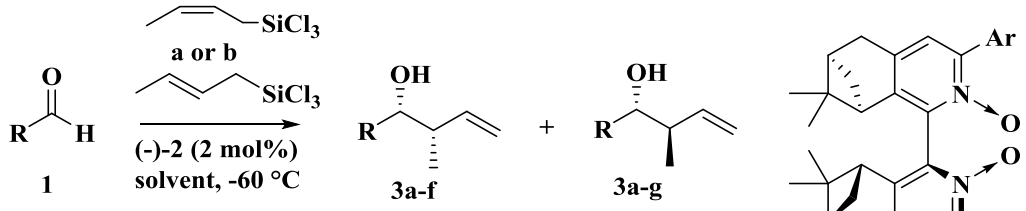
It is well documented that chiral bipyridine-*N*,*N*'-dioxides are highly efficient catalysts for asymmetric allylation of aldehydes with allyltrichlorosilanes.[1-8] However, none of these catalysts are commercially available and their syntheses either involve lengthy sequences or give low overall yield, which makes them unsuitable for larger scale applications. Therefore, we now designed a new axially chiral bis-N-oxide 2 that can be synthesized in just four easy steps from inexpensive starting materials.



1

a: R = Ph
b: R = 4-MeOC$_6$H$_4$
c: R = 4-ClC$_6$H$_4$
d: R = *(E)*-PhCH=CH
e: R = *(E)*-PhCH=CMe
f: R = *(E)*-PrCH=CH
g: R = PhCH$_2$CH$_2$

Ar=3,5-(CF$_3$)$_2$-C$_6$H$_3$

The efficacy of the new catalyst 2 was assessed in the asymmetric crotylation of model aldehydes 3a–f with crotyltrichlorosilanes *(Z)*-a and *(E)*-b. Bis-N-oxide 2 turned out to be an extremely efficient catalyst producing excellent enantio- and diastereoselectivities over a whole range of aldehydes tested. Brief screening of solvents identified dichloromethane as the optimal choice; propionitrile came a close second, while THF gave only modest enantioselectivities. Catalyst 2 proved particularly efficient with unsaturated aldehydes 3d–f, though with aliphatic 3g enantioselectivity dropped representing a common trend in the catalytic allylation with allyltrichlorosilanes.[1-8] Diastereoselectivity generally reflected the geometrical purity of the starting crotyltrichlorosilanes (Z)-a (Z/E 98:2) and (E)-b (E/Z 95:5). However, in propionitrile cinnamyl aldehydes 3d and 1e appeared to react slightly faster with (Z)-a giving the syn-enriched alcohols 3d and 3e, respectively.

This work was supported by the Russian Science Foundation (grant 15-13-00092).

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Aza-Cope Mannich reaction for stereoselective synthesis of novel tricyclic 3,5-epiminocyclohepta[*b*]pyridine scaffold

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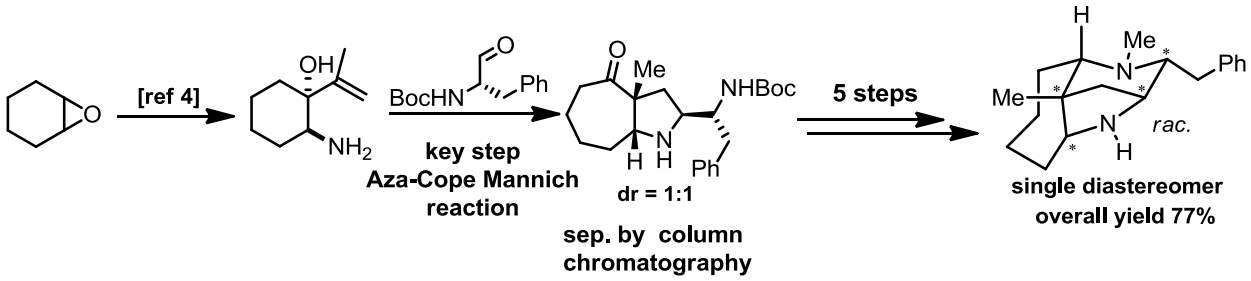
Tricyclic scaffolds with higher sp^3 character are of great interest nowadays [1] Such compounds exhibit higher structural complexity than more planar analogs, thereby making them more akin to natural products and better able to probe different regions of chemical space [2]. To create sp^3-rich collections of molecules, methodology needs to bedeveloped to allow the efficient synthesis of these relatively complex scaffolds. Common route to this challenge includes the use of natural products themselves as starting points for diversification [3]

We have recently described an approach founded on Aza-Cope Mannich reaction, which allows us to obtain diverse scaffolds that contain structural features similar to biologically active alkaloid natural products based on *cis*-cyclohepta[*b*]pyrrolidine motive:



Thus, this methodology enables to synthesize the target compound in 6 steps in a high overall yield (77%) with complete stereocontrol.

This work was supported by the Russian Foundation for Basic Research (grant № 14-03-01114).

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Synthesis of hybrid multicyclophanes based pillar[5]arene and p-tert-butylthiacalix[4]arene

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In recent years, the synthesis multicyclophanes is of great interest. Preparation of hybrid macromolecules based on a variety of macrocyclic platforms allow to create new materials that combine the properties of both one and the other class of macrocyclic compounds. In connection with this new multicyclophanes based pillar[5]arene and *p-tert*-butylthiacalix[4]arene were obtained.

In the course of the study it was synthesized a series of derivatives of substituted mono Pillar [5] arene containing in its structure amide and amino groups. Synthesized macrocycles as used in the preparation of terminal fragments multicyclophanes.

Was developed an approach to getting mixed multimacrocycles based pillar[5]arene and p-tert-butylthiacalix[4]arenes.

Hybrid macrocycles containing in its structure the nucleus - p-tert-butylthiacalix[4]arene in the 1,3-alternate conformation, and four fragments of pillar[5]arene connected via amide or ammonium spacers were synthesized.

Structure of hybrid multicyclophanes was described methods one-dimensional ^{1}H and ^{13}C NMR and IR spectroscopy, mass spectrometry MALDI .

Two-dimensional ^{1}H-^{1}H NMR NOESY spectrum of allows for cross-peaks corresponding set interacting spatially contiguous groups and their signals correlate ^{1}H NMR spectrum in which two protons resonating region macrocycles are overlapped with each other.

This work was supported by RFBR (№15-03-02877 A).

Synthesis of a new functionalized azaheterocycles from Schiff bases

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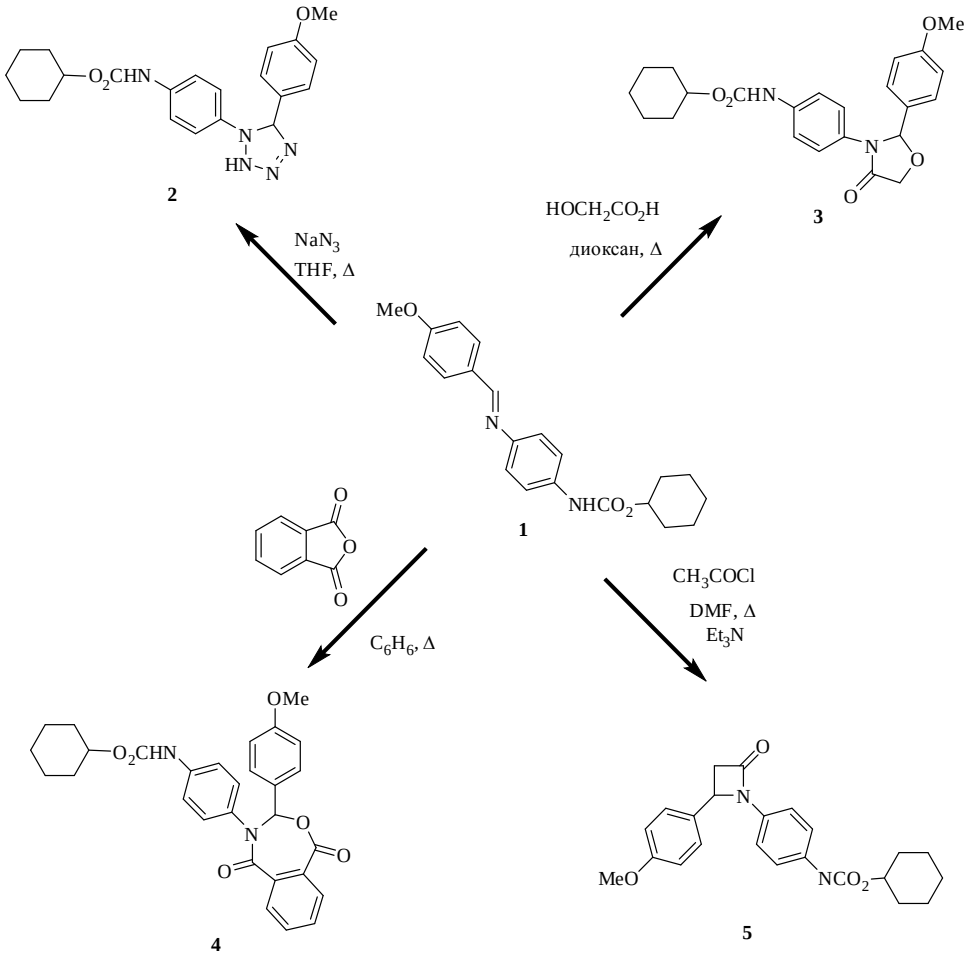
Schiff bases are important intermediates in the synthesis of new functionally substituted azaheterocycles. The development of research on the synthesis of new biologically active azaheterocycles with a carbamate function are potential prodrugs, we studied the reaction of imine **1** with sodium azide, glycolic acid, phthalic anhydride and acetyl chloride.



Optimal conditions for the reactions were found. Structure of the novel compounds was confirmed by IR, ^{1}H NMR spectroscopy, mass spectrometry and by elemental analysis.

This work was supported by the Ministry of Education and Science of the Russian Federation (grant № 115021010181).

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β-Carbolines: a new synthesis of norharmane, harmane and harmine

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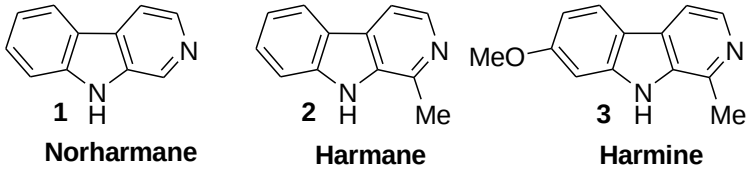
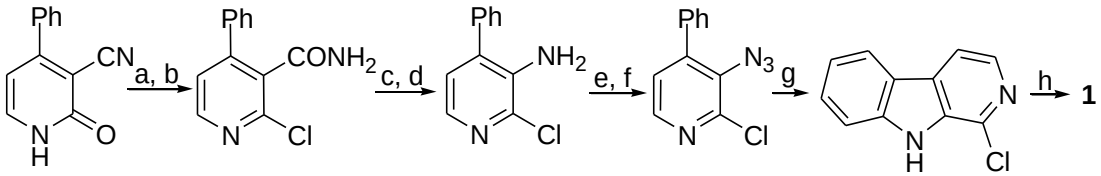
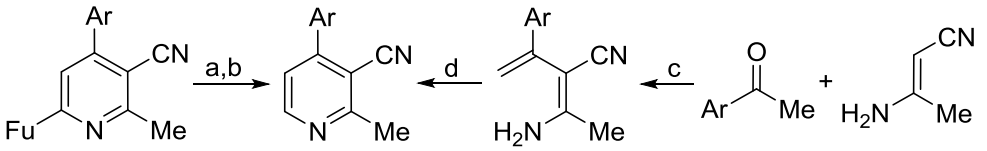
The extraordinary biological significance of compounds of the β-carbolines series is a powerful stimulus to motivation the development of new approaches to the synthesis of these compounds [1].

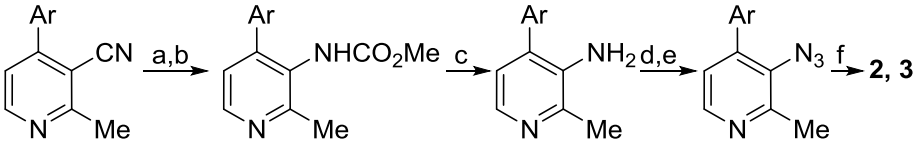




(a) $POCl_3$, DMF, Δ; (b) H_2SO_4, Δ; (c) MeONa, NBS, Δ; (d) H_2SO_4, Δ;
(e) 48% HBF_4, $NaNO_2$; (f) NaN_3; (g) *p*-xylene, Δ; (h) Zn, AcOH, Δ



(a) $KMnO_4$, r.t.; (b) Δ, $–CO_2$; (c) $TiCl_4$, NEt_3, r.t.; (d) $BtCH=N^+Me_2Cl^-$, r.t., 2N NaOH



(a) H_3PO_4, Δ; (b) MeONa, NBS, Δ; (c) NaOH, EtOH, Δ;
(d) 48% HBF_4, $NaNO_2$; (e) NaN_3; (f) *p*-xylene, Δ

The structure of the compounds obtained was confirmed by ^1H and ^{13}C NMR spectroscopy.

This work has financially supported by the Russian Foundation of Basic Research and Ministry of Edukation of Omsk Pegion (grant № 16-43-550144/16 p-a).

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Synthesis of substituted pyrido[2,3-*b*]indolizine-10-carbonitriles

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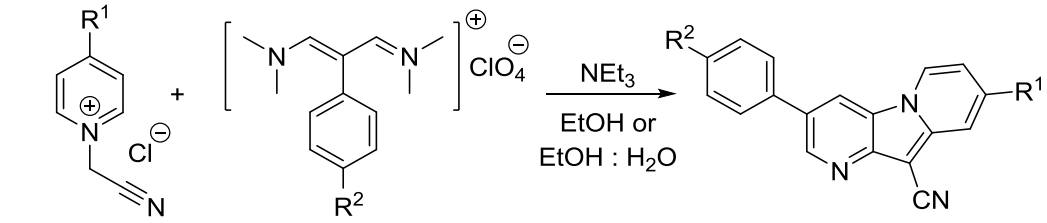
Generation of molecular complexity from simple starting materials is one of the actual goals of a modern organic chemistry. The synthetic procedures employed should meet the requirements for Eco-friendliness, safety and atom economy. Multicomponent reactions is a useful tool, which meets these requirements.

One of the directions of our today's work is the preparation of pyrido[2,3-*b*]indolizine-10-carbonitriles **3**, which may be synthesized through a multicomponent reaction of cyanomethyl pyridinium salt **1** with perchlorates **2**.



1 R1 = H, Me, Et, Ph **2** R^2 = H, Cl, F, NO_2 **3** (10 examples, 8-38%)

Variation of the reaction conditions showed, that the maximum yields may be achieved in EtOH (or EtOH – H_2O 5:1 mixture), employing Et_3N as a base. Presumably, due to high reactivity of perchlorates **2**, the reaction is still going with the formation of multicomponent mixtures, giving target compounds **3** with not higher than 40% yields.

This work was supported by the Russian Foundation for Basic Research (grant № 16-33-00640).

The effective electrosynthesis of triindolylmethane derivatives as new potential antibacterial drugs

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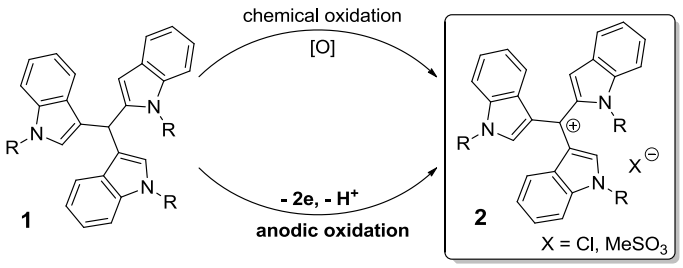
In the development of methods for the synthesis of new antimicrobial agents not only their biological activity, but also high efficiency, environmental safety and low cost of obtaining the target structures are essentially important [1].

Previously we described synthetic method of some salts series - derivatives of tris(1-alkylindolyl-3-yl)methyl **2** (see Scheme) with high antibacterial activity [2]. Oxidation of triindolylmethane **1** derivatives under prolonged bubbling air through the reaction mixture in the presence of activated charcoal and $MeSO_3H$ or by the action of $FeCl_3$ led to structures **2** [3, 4]. In further studies we found that in some cases the offered methods of synthesis are reproduced with difficulty, and the received products contain hardly separable impurities of heavy metals and resinous substances. In this regard, replacing of non-reusable and low-selective oxidants for cheap and available electric current was of interest.

As a result, we have developed a hitherto undescribed electrosynthesis of compounds **2** using Pt anode as the «green oxidizing agent». The process was carried out at oxidation potentials of corresponding triindolylmethanes **1** in the divided cell (supporting electrolyte – 6% $MeSO_3H$ in MeOH-THF) with formation of target products **2** in yields up to 80% and purity ~99%.



Thus, for the first time we established the principle possibility of effective atom economy electrosynthesis of new triindolylmethane salts **2** (R = Alk, cyclo-Alk etc.) having potential antibacterial activity.

This work was supported by the Russian Science Foundation (project No. 16-15-10300)

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Synthesis of 2-thiazolidin-4-one derivative from semicarbazone of chalcone and diethyl acetylenedicarboxylate

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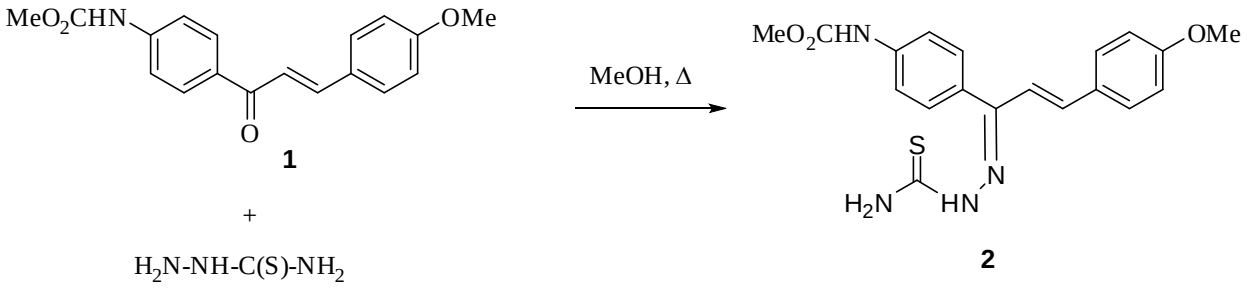
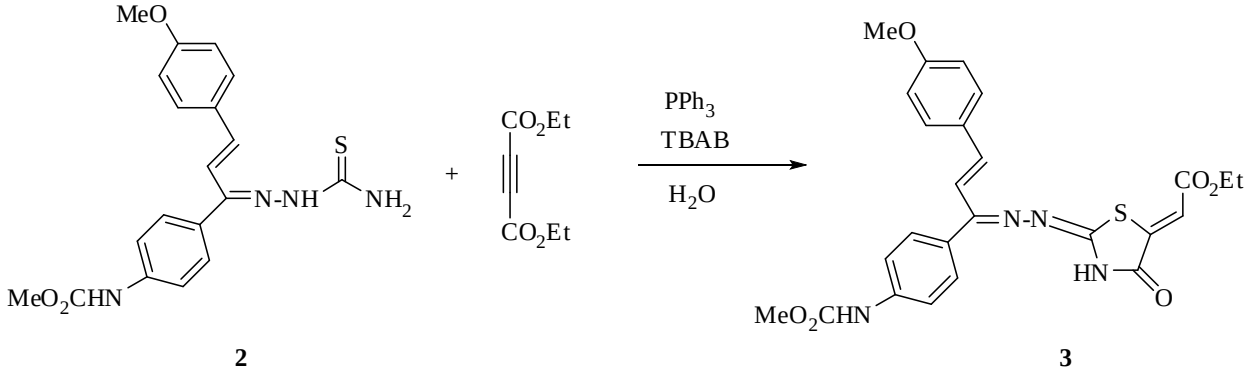
The 2-thiazolidin-4-one derivatives are important heterocyclic compounds of interest which is due to the wide spectrum of biological activity. Among them are found substances exhibiting antituberculosis, anticonvulsant, fungistatic activity. In this connection, the synthesis of new functionalized representatives of this class is of considerable interest.

We studied the possibility of obtaining thiosemicarbazone of methyl N-4-[(*E*)-3-(4-methoxyphenyl)-2-propenoyl]phenylcarbamate [1]. It is found that heating in a water bath equimolar amounts of chalcone **1** and thiosemicarbazide in methanol for 3 h leads to afford the corresponding thiosemicarbazone **2** in 91% yield.



Refluxing of equimolar amounts of compound **2**, diethyl acetylenedicarboxylate, TBAB in water in the presence of triphenylphosphine (0.1 mol%) for 2 hours leads to the preparation of 2-thiazolidin-4-one derivative **3** in 85% yield.



Structure of the compounds **2,3** is confirmed by IR, ^{1}H NMR spectroscopy, mass spectrometry and elemental analysis.

This work was supported by the Ministry of Education and Science of the Russian Federation (grant № 115021010181).

References

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Sequential three-component reaction of homophtalonitrile, *o*-hydroxybenzaldehyde and nitromethane

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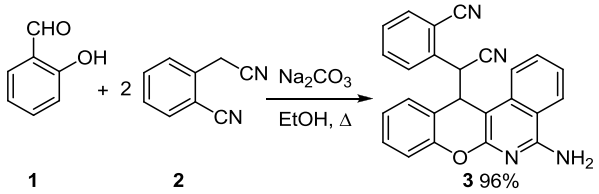
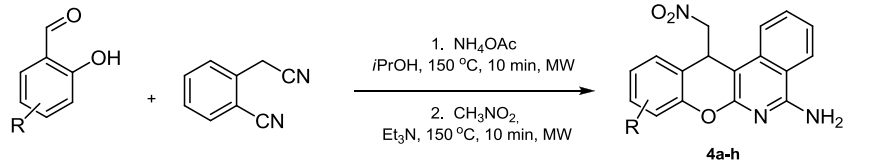
2-Aminochromene represents a favored class of heterocyclic compounds that exhibit a variety of biological activities[1-3] and are valuable platforms for drug discovery.

We found that refluxing *o*-hydroxybenzaldehyde **1** with homophthalonitrile **2** in EtOH in the presence of sodium carbonate induced a pseudo-three-component reaction that formed chromenoisoquinolinamine **3** in excellent yield.

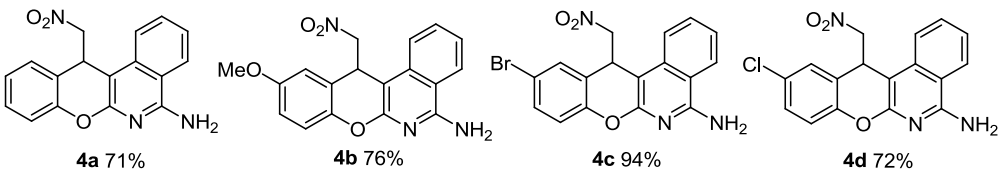


1 **2** **3** 96%

We hypothesized that adding a different CH-acid as the third reaction component would result in the synthesis of an analogous chromenoisoquinoline with a different substituent on the chromene ring. In fact, refluxing salicylaldehyde **1** and homophthalonitrile **2** with nitromethane in the presence of NH_4OAc in EtOH—H_2O (3:1) afforded three-component reaction product **4** in 18% yield (Scheme 2). It was found that nitroderivative could be obtained with the higher yield through the sequential procedure, by heating an *i*-PrOH solution of *o*-hydroxybenzaldehyde, homophthalonitrile, and NH_4OAc in a sealed container to 150°C in a microwave reactor, adding nitromethane and Et_3N, and heating again for 10 min at 150°C. The target compounds could be isolated by chromatography or with extraction. The developed method was used to study the synthetic limits of the reaction. As it turned out, a wide array of *o*-hydroxybenzaldehydes could be used to produce excellent yields of variously substituted chromenoisoquinolinamines **4a-f**.



4a-h

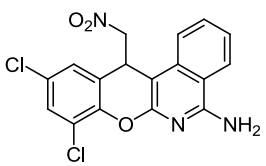


4a 71%

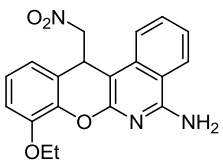
4b 76%

4c 94%

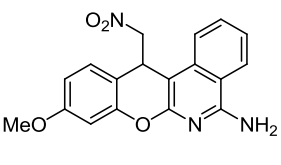
4d 72%



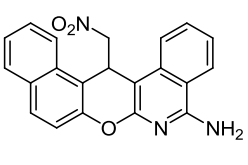
4g 82%



4f 73%



4e 46%



4h 20%

The work was supported by RFBR Grant 15-33-70034 mol_a_mos, and Grant MK-5319.2016.3 of the RF President for young scientists.

Synthesis of azithromycin - benzoxaborole conjugates and evaluation of their biological activity

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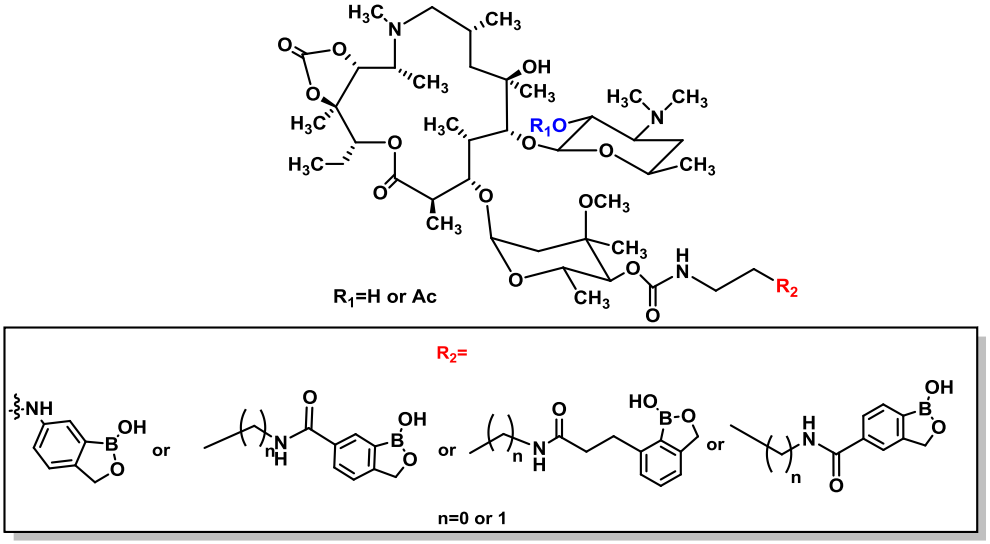
Although benzoxaboroles were first described in 1957 by Torssell, their applications in medicinal chemistry have only begun since 2006, when 5-flurobenzoxaborole (AN2690) was found to have antifungal activity by targeting fungal leucyl tRNA synthetase (LeuRS). Further investigations demonstrated that benzoxaboroles possess a variety of bioactivities, and were successfully used to obtain new types of hybrid molecules, particularly, for the synthesis of hybrid (dual-acting) antimicrobial and anti-parasite drugs [1, 2]. We developed method of synthesis and obtained series of azithromycin – benzoxaborole conjugates in which benzoxaborole fragment was attached to the 11-hydroxy group of antibiotic via aminoalkylcarbomoyl spacer. The reaction of azithromycin with ethylene carbonate gave 11, 12-cyclic carbonate of azithromycin, 2'-O-hydroxyl group was protected with an acetyl group by interaction with acetic anhydride in pyridine. The resulting intermediate was introduced into the reaction with propylenediamine or pentylendiamine what led to the opening of the 11, 12-cyclic carbonate ring and simultaneous splitting of the 2'-acetyl group. The obtained azithromycin derivative containing amino group was acylated by the benzoxaboroles that contain carboxylic group in the presence of DCC and HOBt. The structures of all target derivatives were supported by mass-spectrometry data (mass spectra, determined by high-resolution mass spectrometry with electrospray ionization (ESI) method and NMR spectroscopy method.



It was shown that the obtained hybrid antibiotics demonstrated wide spectrum of antibacterial activity, especially against susceptible *S. pneumonia* strain although the investigated modification didn't result in the overcoming of bacterial resistance in MRSA.

This work was supported by the Russian Foundation for Basic Research (grant № 16-34-60110).

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Synthesis and structure-activity relationship study of new antitumor anthra[2,3-*b*]furan-3-carboxamides

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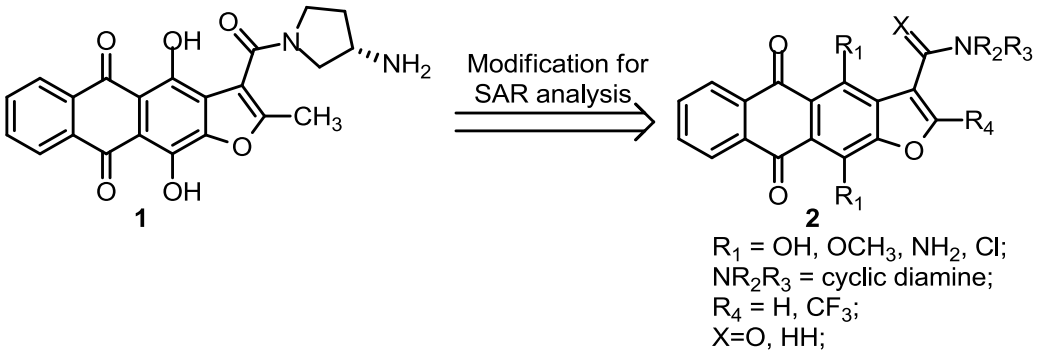
The linear pyrrole- and furan-containing anthraquinones bearing a cyclic diamine at the position 3 are the promising class for further development of anticancer agents [1,2]. The most potent amide derivative **1** with (*S*)-3-aminopyrrolidine in the side chain demonstrated a multiple action on cellular targets, including binding to DNA, poisoning of topoisomerases 1 and 2 and inhibition of protoncogenic oncogenic protein kinases [2].

In continuation of the study of anthra[2,3-*b*]furan-3-carboxamides we performed some structural modifications and synthesized a series of new analogs **2** for better understanding of structure-activity relationship. Testing of the antiproliferative properties on a panel of cancer cell lines revealed that new compounds inhibit the growth of tumor cells in a range from low micromolar to submicromolar concentrations. The most important finding is almost all of anthra[2,3-b]furan-3-carboxamides **2** overcome mechanisms of multidrug resistance that makes this class of compounds prospective for the search of new drug candidates.



This work was supported by the Russian Foundation for Basic Research (grant № 16-33-00908 mol_a).

References

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Synthesis of amino phosphonic acids of cyclopropane series – novel conformationally restricted analogs of γ-aminobutyric acid (GABA)

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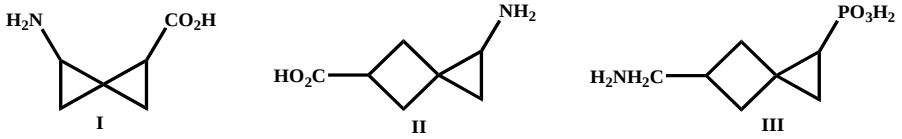
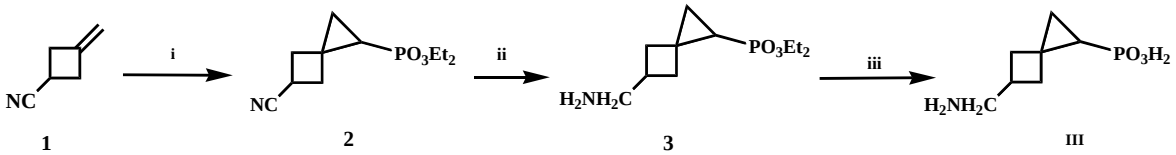
Currently, the actual problem of medicinal and organic chemistry is the development of methods for the preparation of non-natural polycyclic amino acids and their closest bioizosteric analogs [1]. Previously, we have developed the approach to the preparation of spirane amino acids **I** and **II**, which demonstrated a high anxiolytic and tranquilizing activity during biological properties testing [2, 3]. The aim of this work was to develop methods of synthesis of a new conformationally rigid bioizosteric phosphonic analog of GABA – the amino acid **III**.

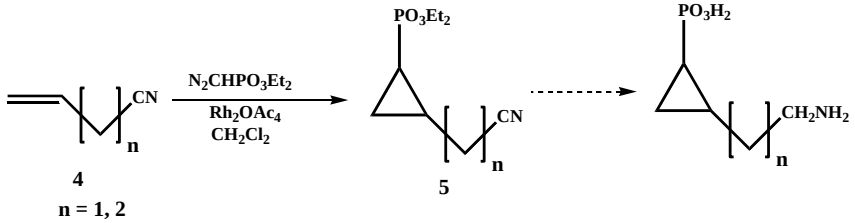


Amino acid **III** has been obtained according to a synthetic scheme included the (1) catalytic cycloaddition of diazophosphonic ester (DPE) to the double bond of 3-metylenecyclobutanecarbonitrile **1** in the presence of dirodium tetraacetate, (2) reduction of the nitrile group of the adduct **2**, and (3) cleavage of PO_3Et_2-group of amino phosphonate **3** under the action of TMSBr followed by treatment with propylene oxide in ethanol.



i: $N_2CHPO_3Et_2$, Rh(II), CH2Cl2; ii: [H]; iii: 1) TMSBr, CH_2Cl_2; 2) propylene oxide, EtOH.

Also we investigated the catalytic reactions of [1+2] cycloaddition of DPE to other unsaturated nitriles **4** and as a result cyanomethyl substituted cyclopropanephosphonates **5** were synthesized. The selection of reagent for the selective reduction of cyanophosphonates **5** to corresponding amino phosphonic esters is under the way now.



The work was supported by the RAS (Medicinal Chemistry' program №9).

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[3]. N.V. Yashin, A.V. Chemagin, T.S. Kuznetsova, N.S. Zefirov, M.E. Zapolsky. Pat. WO2012RU00146 20120229.

Synthesis of quinolines via acid-catalyzed cyclodehydration of 2-(tosylamino)chalcones

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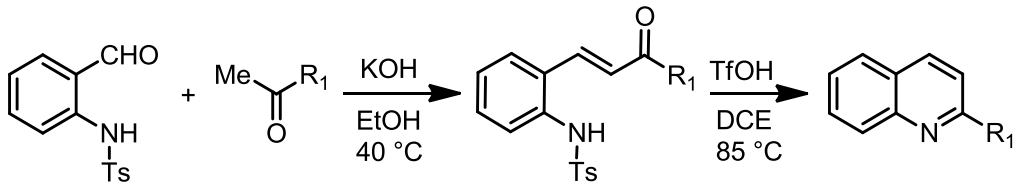
Quinoline skeleton is present in many natural and synthetic drugs (quinine, mefloquine, chloroquine, imiquimod) and other biologically active substances (e.g., herbicide quinmerac), organocatalysts and ligands for catalysis (cinchonine, cinchonidine, quinidine), dyes, and other valuable compounds. It is therefore not surprising that the development of new and modification of existing methods of synthesis of quinolines is an important and urgent task.

The classical Friedlaender, Skraup, Doebner–Miller, Conrad–Limpach, Pomeranz–Fritsch, Combes reactions and other approaches are used to synthesize quinolines. Despite the development of new approaches to the formation of the quinoline skeleton, Friedlaender reaction remains one of the most common and widely used methods for the synthesis of quinolines. This is an acid- or base-catalyzed condensation of *o*-acylarylamines with carbonyl compounds containing an active methylene group. However, the mechanism of the Friedlaender reaction is still a matter of discussion. To date, two alternative paths for the formation of quinolines have been proposed. These differ by the sequence of the C(3)–C(4) and C(2)–N(1) bonds formation.

In order to better understand the mechanism of Friedlaender synthesis, we studied the cyclodehydration of 2-(tosylamino)- chalcones to substituted quinolines.



We have developed an efficient method for the synthesis of quinolines from (*E*)-3-[(2-tosylamino)- phenyl]-1-(het)arylprop-2-en-1-ones. The reaction takes place as a result of acid-catalyzed cyclodehydration comprising the key step of (*E*,*Z*)-isomerization, and leads to the desired products in high yields. It should be noted that, unlike the Friedlaender synthesis, the developed method allows to isolate the intermediate 2-(tosylamino)-chalcones which can be easily modified. These products may be subjected to the subsequent cyclodehydration reaction, thereby increasing the spectrum of the resulting quinolines. The precursor chalcones were prepared by condensation of 2-(tosylamino)benzaldehyde with readily available ketones [1].

This work was supported by the Russian Foundation for Basic Research (grant № 16-03-00513) and Ministry of Education and Science of the Russian Federation (the Agreement № 02.a03.0008).

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3-Arylallylamines in the synthesis of isoindole containing heterocycles

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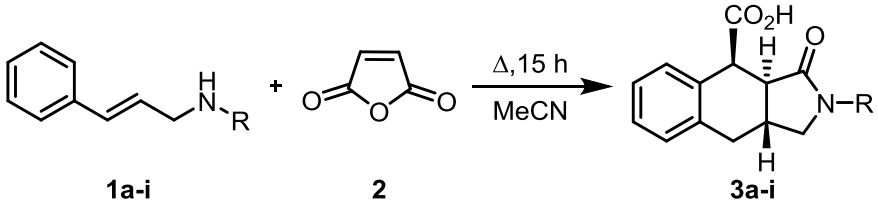
Last year our groups proposed the IMDAV approach [1, 2] to the synthesis of furo[2,3-*f*] isoindoles, which was based on the interaction of 3-(furyl)allylamines with α,β-unsaturated acid anhydrides.

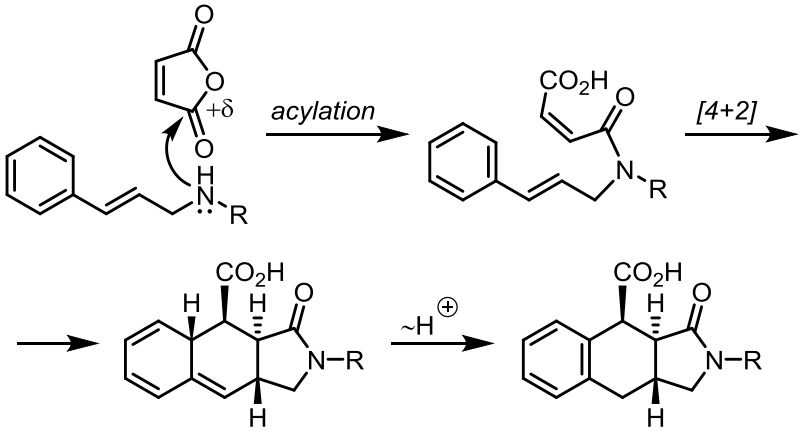
The present study is a further extension of these works and involves the reaction of readily accessible 3-(phenyl)allylamines (**1**) with maleic anhydride.



1a-i **2** **3a-i**

The interaction of the amines **1a-i** with maleic anhydride was carried out in boiling acetonitrile, benzene or toluene, but the best results were achieved in acetonitrile. In these conditions, the target benzo[*f*]isoindoles (**3**) were precipitated from the reaction mixture.

The mechanism of the IMDAV reaction includes three stages and proceeds *via* initial *N*-acylation / the subsequent intramolecular [4+2] cycloaddition / and final aromatization step, affords the tricycles **3a-i** with moderate yields.



a: R = Allyl (45%); **b**: R = *i*-Pr (28%); **c**: R = cyclopropyl (49%); **d**: R = *t*-Bu (30%); **e**: R = *n*-pentyl (40%); **f**: R = cyclopentyl (37%); **g**: R = Bn (50%); **h**: R =3,4-$(MeO)_2C_6H_4$-CH_2- (35%); **i**: R = 3,4-$(MeO)_2C_6H_4$-CH_2-CH_2- (38%).

This work was supported by the Russian Foundation for Basic Research (grant № 17-53-45016)

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Self-assembly and photochemical properties of supramolecular complexes of bis(18-crown-6)stilbene with alkanediammonium ions

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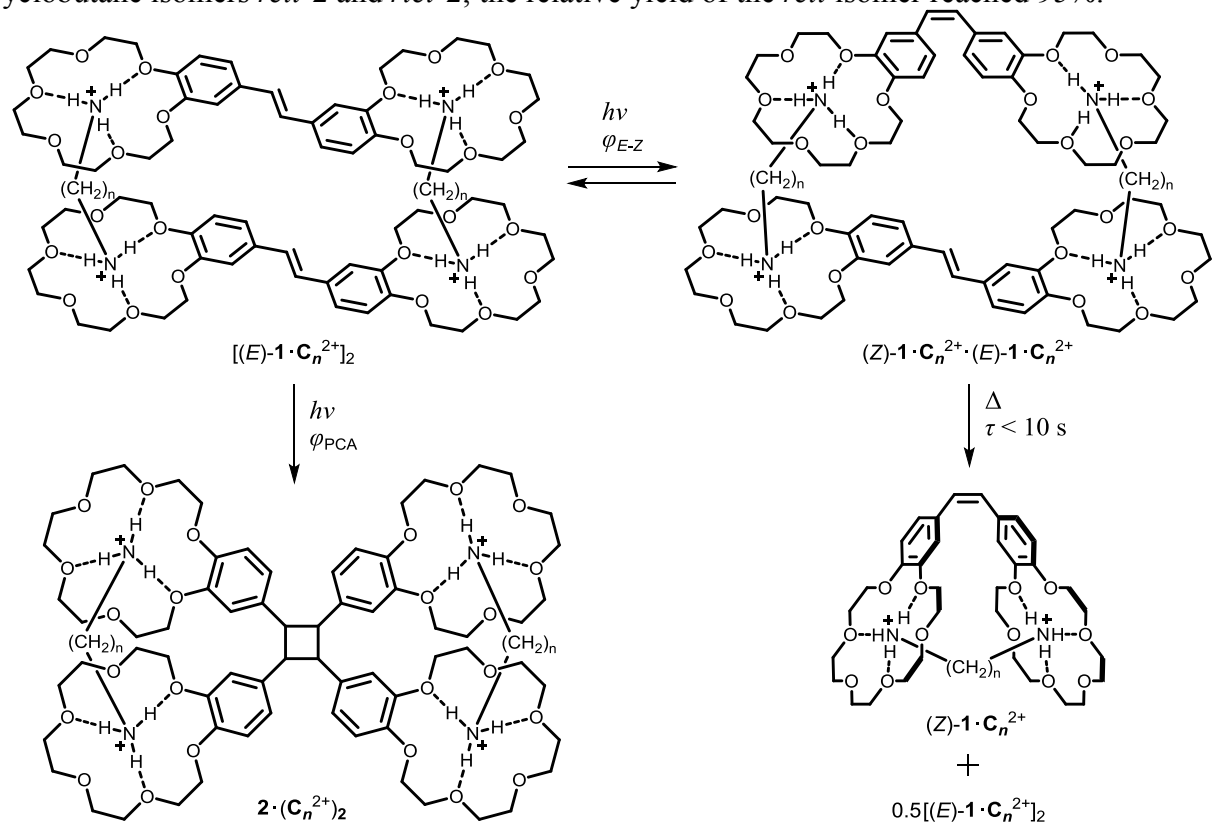
The *E* isomer of bis(18-crown-6)stilbene ((*E*)-**1**) is able to form pseudocyclic complexes of 2:2 composition (bis-pseudosandwich complexes) with alkanediammonium ions of the structure $^{+}H_3N(CH_2)_nNH_3^{+}$ ($\mathbf{C}_n^{2+}$), where n = 2–6. The photoirradiation of complexes [(*E*)-**1**·$\mathbf{C}_n^{2+}$]$_2$ in MeCN afforded the *Z* isomer of bis(18-crown-6)stilbene ((*Z*)-**1**) and two cyclobutane isomers *rctt*-**2** and *rtct*-**2**; the relative yield of the *rctt* isomer reached 95%.



It was demonstrated that with a decrease in the length of the polymethylene spacers in the 2:2 complex, the quantum yield of supramolecular [2+2] photocycloaddition (φ_{PCA}) increases from 0.02 to 0.27, while the quantum yield of the competing *E–Z* photoisomerization ($\varphi_{E\text{-}Z}$) decreases from 0.12 to 0.06. Spectrophotometric observations and density functional theory calculations revealed that (*Z*)-**1**, unlike the *E* isomer, is able to form pseudocyclic 1:1 complexes with $\mathbf{C}_n^{2+}$, n = 2–6, owing to the proximity of two crown ether moieties. The peculiar spectral properties of these complexes are associated with large torsion angles around the ethylene–benzocrown single bonds.

This work was supported by the Russian Science Foundation (project No. 14-13-00076).

Synthesis of tertiary amines with inhibitory activity

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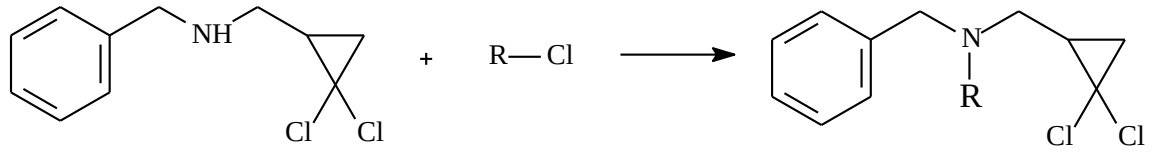
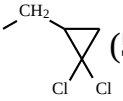
Amines containing *gem*-dichlorocyclopropyl fragment are widely used in organic synthesis and are used in various fields of science and technology [1]. It was found that similar compounds containing aminoalkyl groups have several advantages when they are used as inhibitors, surfactants and flotation agents [2].

We have proposed the synthesis of various tertiary amines **6-9**, containing a *gem*-dichlorocyclopropyl fragment based on the *N*-benzyl-1-(2,2-dichlorocyclopropyl)methylamine **1** obtained by previously known method [3]. *N*-alkylation of the compound **1** by allyl chloride **2**, 1,3-dichloropropene **3**, benzyl chloride **4**, 2-chloromethyl-*gem*-dichlorocyclopropane **5** in DMSO at 70°C (in case of allyl chloride at 30°C) during 6 h led to the formation of the desired products **6-9** with yields more than 60%.



1 **2-5** **6-9**

R = -CH_2-CH=CH_2 (**2, 6**); -CH_2-CH=CH-Cl (**3, 7**); -CH_2-Ph (**4, 8**);  (**5, 9**)

The obtained compounds **6-9** were examined for inhibitory activity relative to electrochemical corrosion processes for carbonic steel sample. In comparing the effectiveness of the compounds it is apparent that the compound **9**, containing two *gem*-dichlorocyclopropyl groups, has the most inhibitory activity in 1M HCl solution (more than 70%).

This work was supported by the President of the Russian Federation (RF President's scholarship for young scientists and graduate students SP-1960.2015.4).

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Transformations of 1-aroyl-3,4-dihydroisoquinolines via unsaturated ketones derivatives

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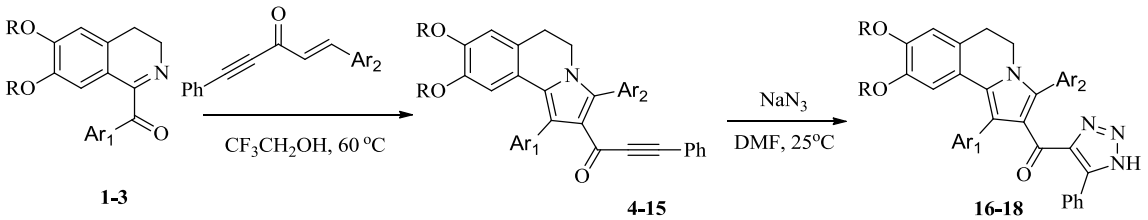
Pyrrolo[2,1-*a*]isoquinolines contain a heterocyclic system that is often encountered in natural products and synthetic compounds with various important pharmacological properties. Alkaloids, including a 5,6-dihydropyrrolo[2,1-*a*]isoquinoline moiety, exhibit antitumor and antileukemia activity, inhibit tubulin polymerization and displays an affinity for estrogen receptors [1].

In this research, we hypothesized that pyrrolo[2,1-*a*]isoquinolines could be synthesized using 1-aroyltetrahydroisoquinolines **1-3** and unsaturated ketones. The reactions occur under 2,2,2-trifluoroethanol heating for 4-6 days in the presence of a catalytic amount of glacial acetic acid. Derivatives pirroloisoquinolines isolated by crystallization from the reaction mixture in good yields.

Scheme 1



R=OMe,OEt
Ar_1=p-C_6H_4-Cl,p-C_6H_4-F,C_6H_3-3,4-di-OEt
Ar_2=p-C_6H_4-Cl,p-C_6H_4-Me,p-C_6H_4-OMe,Ph

After we have studied the reactivity of the triple bond in the obtained pyrrolo[2,1-*a*]isoquinolines **4-15**. Substituted triazole ring can be synthesized by cycloaddition of azides to unsaturated ketonic moiety in DMF at room temperature. The reactions were complete in less than 1 day; we obtained pyrrolo[2,1-*a*]isoquinolines **16-18** in high yields.

This work was supported by the Russian Foundation for Basic Research (grant № 17-53-540001).

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Novel synthetic approach to functionalized 4-nitro- and 4-aminoisoxazoles

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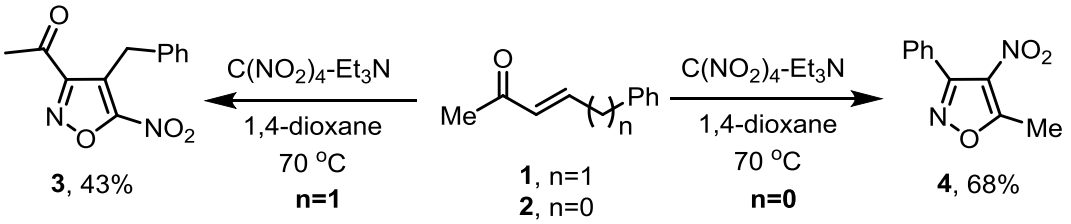
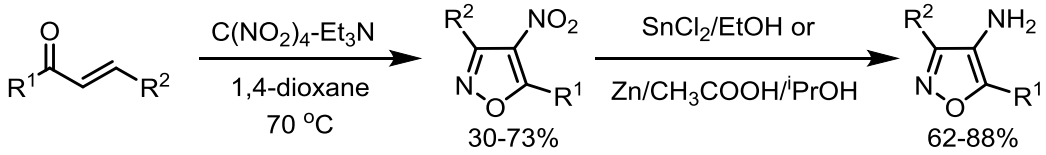
Recently we have developed the general synthetic approach to polysubstituted 5-nitroisoxazoles based on heterocyclization of electrophilic alkenes under the treatment of activated tetranitromethane (TNM) [1]. Using this methodology we elaborated convinient synthetic routes to isoxazole derivatives with variety of functional groups. However, studying the heterocyclization of phenyl substituted alkene **2** in standard conditions we unexpectedly found that this reaction results in 4-nitroisoxazole **4**.



Next we investigated a series of α,β-unsaturated ketones bearing aryl substituents under treatments of TNM-Et_3N complex. The starting electrophilic alkenes were obtained by the condensation of corresponding aldehydes with acetone or by Wittig reaction. It was demonstrated that heterocyclization of aryl substituted electrophilic alkenes affords 4-nitroisoxazoles in good isolated yields. Subsequent reduction of nitro group of heterocycles in known conditions [3] results in series of 4-aminoisoxazoles.



R^1 = Ph, Me
R^2 = Ph, 4-(MeO)-C_6H_4, 4-F-C_6H_4, 4-NO_2-C_6H_4, 2,6-Me_2-C_6H_3, 3,4,5-$(MeO)_3$-C_6H_2, 2-OH-C_6H_3, furyl, pyridyl

Thus, we accomplished the simple, universal and efficient synthetic method allowing obtain 4-nitro- and 4-aminoisoxazoles with a wide range of substituents from readily available starting materials. A number of heterocycles were synthesized using this method and their biological activity was estimated.

This work was supported by RFBR (Project 14-03-00469-a) and Presidium RAS (program No. 8P)

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Synthesis of dihydrobenzofurans by Lewis acid-induced rearrangement of 2-(*o*-hydroxyaryl)cyclopropane-1,1-dicarboxylates

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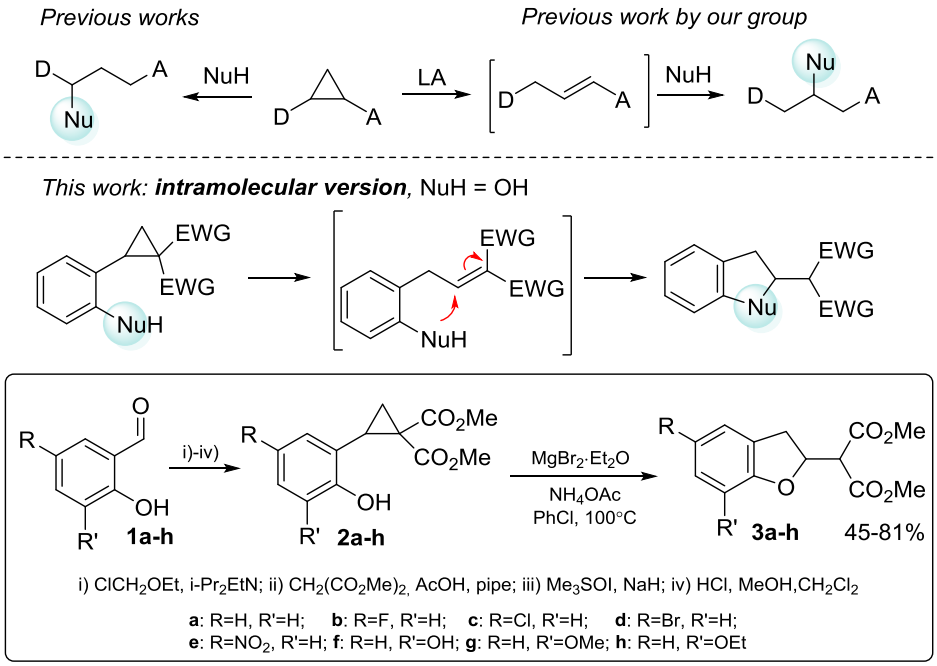
Donor-acceptor (DA) cyclopropanes are in demand for the synthesis of diverse molecular scaffolds due to variety of their reactivity. Recently we have found a brand new reaction of these cyclopropanes with nucleophiles. On the contrary to the typical nucleophilic ring openings of DA cyclopropanes affording 1,3-addition products, reactions of these substrates with nitroalkanes and malonate esters in the presence of magnesium halides led to products of the formal nucleophilic attack on the cyclopropane C(3) atom accompanied by the C(1)–C(2) bond breaking. These reactions proceed as domino process involving Lewis acid-induced isomerization of cyclopropane to alkene wherein double bond is conjugated to ester groups followed by Michael addition of the nucleophile to this alkene.



Here, we report the intramolecular version of this novel DA cyclopropanes nucleophilic ring opening wherein functional group at the *ortho*-position of donor aromatic substituent serves as nucleophilic moiety. We demonstrated that treatment of DA cyclopropanes **2a-h** with $MgBr_2 \cdot OEt_2$ points the simple way to 2,3-dihydrobenzofuran derivatives.

This work was supported by the Russian Science Foundation (grant № 14-13-01178).

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Spontaneous self-assembly of water-soluble anionic (thia)calix[4]arenes into fractal hybrid nanodendrites in presence Ag^+

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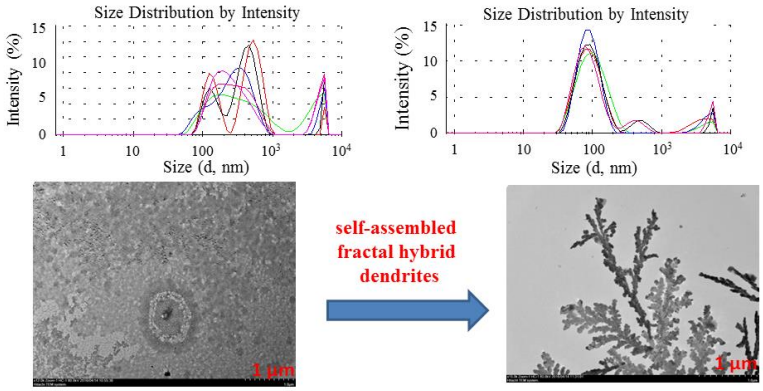
The synthesis of the stable, concentrated aqueous dispersions with desired physicochemical properties on the silver nanoparticles (AgNP) basis is a necessary step in the creation of nanostructural materials used in microelectronics, electrochemistry, and the synthesis opticoelectronic sensors pigments, etc [1]. Also, AgNP are often used to produce various materials with antibacterial properties [2]. Silver ions have a pronounced ability to inactivate viruses, smallpox and influenza A-1, B. It is active for some enterovirus, adenovirus, human immunodeficiency virus (HIV) [3]. The development of effective methods for the synthesis of original bioactive compounds on the basis of domino- and multi-component processes is a challenging task of synthetic and pharmaceutical chemistry. It was observed, the AgNP effects are determined by the size, concentration and dispersion stability [4]. Thus, creation of the stable, low-diversity, water-soluble AgNP has attracted the attention of researchers.

We report new approach to design AgNP with organic ligand based on new water-soluble *p-tert*-butyl(thia)calix[4]arenes, bearing *O*-3-propanesulfonate fragments at the lower rim. The simple preparation technology of stable, monodisperse AgNP in water is proposed.



The presence of the supramolecular associates in solutions at the critical micelle concentration of $1.65 \cdot 10^{-5}$ M were investigated in aqueous solution by a combination of different techniques. It found that macrocyclic platform decreases the CMC tenfold as compared with non-macrocycle analogues. Simple approach to design of stable monodisperse Ag-based nanoaggregates (near 95 nm) containing ionic Ag and organic ligand – thiacalix[4]arene sulfo derivative - is realized in water.

This publication was supported by the research grant of Kazan Federal University.

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The reaction 5-(hetarylmethyliden)-2,4,6-pyrimidin-2,4,6(1*H*,3*H*,5*H*)-trions with aldehydes and *L*-proline

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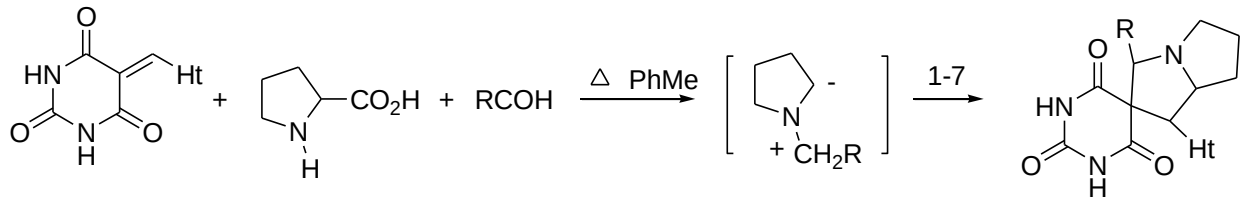
The reaction of 5-(hetarylmethyliden)-2,4,6-pyrimidin-2,4,6(1*H*,3*H*,5*H*)-trions **1-7** with the azomethineylide **A** generated from *L*-proline **8** and aldehydes **9,10** resulted in a series of previously unknown hetaryl hexahydro-1*H*-spiro[pyrimidine-5,2′-pyrrolizine]-2,4,6(3*H*)-triones **11-24** derivatives with a yield of 60-75%.



1-7 **8** **9,10** A **11-24**

Ht= 1-benzofuran-2-yl (**1**,**11**,**12**), 1-benzofuran-5-yl (**2**,**13**,**14**), 5-bromfuran-2-yl (**3**,**15**,**16**), 1,3-benzotiozol-2-yl (**4**,**17**,**18**), 2,1,3-benzooxodiazol-5-yl (**5**,**19**,**20**), 1,3-dimethyl-5-morpholinopyrazol-4-yl (**6**,**21**,**22**);
5-acetoxymethylfuran-2yl (**7**,**23**,**24**), R= H (**9**,**11**,**13**,**15**,**17**,**19**,**21**,**23**), 3-PhOC_6H_4 (10,**12**,**14**,**16**,**18**,**20**,**22**,**24**)

One can assume that during thermolysis *L*-proline **8** with aldehydes **9,10** corresponding azomethineylide **A** generated [1], resulting in the last process of 1,3-dipolarcycloaddition to molecules stabilized dipolarophile **1-7** desired products **11-24**.

The structure of the compounds set by IR spectroscopy, ^{1}H, ^{13}C NMR, mass-spectrometry, and elemental analysis data become. The report discussed the reaction mechanism.

The study was carried out under the financial support of the Ministry of Education and Science of the Russian Federation (grant no. № 01201259085), of the program «Development of innovative infrastructure in Russian high schools» (grant no. 13G637.31.00.38) using the research equipment of the scientific and educational center «Green Chemistry» of Astrakhan state university.

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Bacteriochlorine-naphtalimid conjugates for photodynamic therapy and fluorescent imaging of cancer

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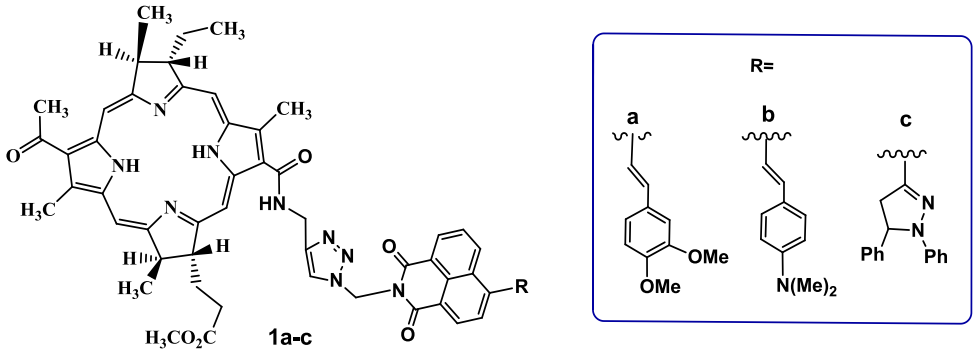
Photodynamic therapy (PDT) is known to be one of the gentle methods of treatment of cancer tumors. It is based on using a drug known as a photosensitizer, light and oxygen to destroy tumors and their surrounding vasculature. In lines of advance of the effectiveness of PDT, the design of theranostic agent for both photodynamic therapy and fluorescent tumor imaging seems to be a challenging task.

The aim of this work is the synthesis and photophysical study of conjugates which consist of two covalently bonded functional fragments: photosensitizer (bacteriochlorin) and fluorophore (**1a-c**). Excitation **1a-c** by the light with wavelength corresponding to the Q-band of bacteriochlorin would lead to formation of singlet oxygen responsible for cancer cell damage. Further excitation of fluorophore unit by the other light wavelength is expected to produce the strong emission signal, which could be used to monitor tumor responses to treatment. We choose 1,8-naphthalimide-based dyes as a fluorophore responded for the imaging effect because of strong emission in the visible region, large Stokes shifts and excellent photostability. Fluorophores were selected in a way to provide a minimum overlap between their emission spectra and the absorption spectrum of bacteriochlorin, which, as expected, would reduce the veracity of the energy transfer process.



In this work we propose a synthesis of **1a-c** conjugates by the click-reaction of azide-naphthalimide derivatives and bacteriochlorin-*e* containing a propargyl group. The conjugate **1b** was tested in vitro and it appears to be an effective theranostic agent, showing the absence of dark toxicity, as well as the ability to penetrate into tumor cells and to give a contrast image of them.

Photophysical studies revealed that the emission from the naphthalimide chromophore in all conjugates was quenched due to resonance energy transfer between the photoactive components. Its efficiency was evaluated by the experimental and computational methods. It is known, that one of the ways to minimize FRET-process is an extension of the spacer between the chromophores. So, we synthesized bacteriochlorin-naphtalimide conjugate with a polyglycol chain containing ten glycol motifs as a spacer. Studying of the spectral properties of this conjugate is our priority task.

We thank the Russian Foundation for Basic Research 16-13-10226 for financial support.

Anti-stress properties of 5-hydroxy benz imidazole – ambiol

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Antioxidants (AO), as substances that prevent the activation and the development of free radical oxidation processes, have found wide application in chemical, food, cosmetic, pharmaceutical industry, medicine and agriculture. One of the promising groups of synthetic antioxidants is the group of nitrogen-containing heterocyclic phenols, where belong the derivatives of 5 –hydroxy benzimidazole and in particular 2-methyl-4-dimethylamine-methyl-benzimidazole-5-ol-dihydrochloride – ambiol.

Stress factors lead to a shift of antioxidant–prooxidant balance towards increased production of reactive oxygen species (ROS), which causes the development of a number of pathological conditions due to damage components of the cell [1]. Mitochondria of animals, the chloroplasts and mitochondria of plants are the main sources of ROS in these conditions. It can be assumed that antioxidants should affect the generation of ROS by these organelles under conditions of stress, i.e. to have adaptogenic properties. The aim of our study was to investigate the influence of ambiol on the functional state of mitochondria of plant and animal origin.

To study the protective properties ambiol we had to develop a model, which simulating a stress, notably have to find conditions under which will increased ROS production by mitochondria, and thus will be activated LPO. We solved this problem by having developed a model of “aging” (the incubation of mitochondria in a hypotonic medium at room temperature), that was leading to activation of lipid peroxidation in the membranes of mitochondria of liver and pea seedlings. At the same time, the intensity of the fluorescence end products of lipid peroxidation (Schiff bases) increased by 3-4 times. Introduction abiol in the incubation medium of mitochondria led to a decrease in the fluorescence of LPO, and this decrease was dependent on the concentration ambiol in the incubation medium. In concentrations of 10^{-5}, 10^{-7} and 10^{-9} M ambiol reduced the fluorescence intensity of LPO products to a control level.

Changing of physic-chemical state of membranes of effect on the activity of enzymes of the respiratory chain of mitochondria. The drug at a concentration of 10^{-5} M and 10^{-6} M caused 2-fold increasing of the electrons transport rates in respiratory chain of pea seedling mitochondria in oxidation of NAD-dependent substrates. At the same time increased and the efficiency of oxidative phosphorylation, (the respiratory control rate (RCR) increased from 2.09 ± 0.06 to 3.00 ± 0.10 and the ratio of ADP / O from 2.00 ± 0.10 to 2.45 ± 0.2). The increase in the respiratory control rate was associated with an increase in the rates of oxidation of NAD-dependent substrates by pea seedling mitochondria in the presence of ADP by 47%.

When used as a substrate of succinate oxidation also observed to increase the efficiency of oxidative phosphorylation in the presence of the drug at the same concentration. However, in this case, the growth in the respiratory control rates occurred by reducing the rates of respiration in the presence of ATP, i.e., in a state of "peace" (V_4).

The obtained data may indicate the presence in the drug of anti-stress properties, which can be tested on pea seedlings in conditions of water deficiency. The water deficiency is more than 2.5 times inhibits growth processes, and the processing of pea seeds with abiol prevents the retardation of shoot growth of pea seedling. Based on obtained data we can conclude about the presence of anti-stress properties of ambiol drug.

References

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Regio- and stereoselective 1,3-dipolar cycloaddition of indenquinoxalinone-based azomethine ylides to β-nitrostyrenes

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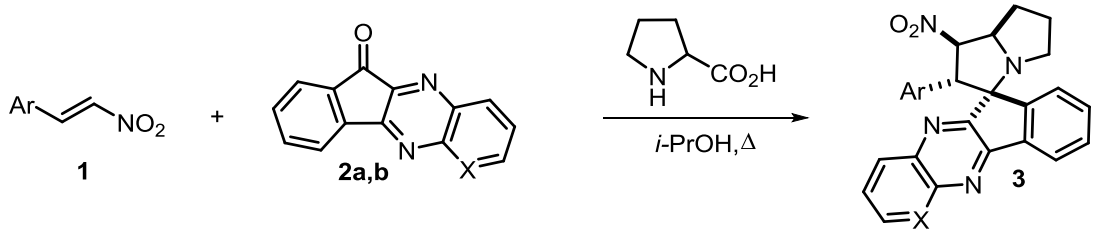
The 1,3-dipolar cycloaddition reaction of azomethine ylides with olefins is an efficient methodology for regio- and stereoselective synthesis of structurally complex pyrrolidines with a few chiral centers from relatively simple precursors.

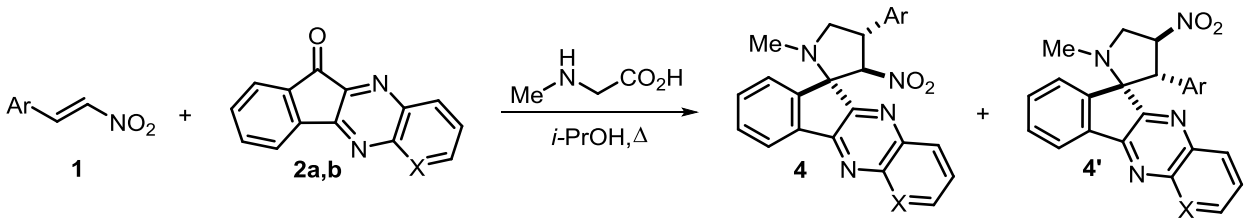
We studied the regio- and stereochemistry of [3+2] cycloaddition reaction of β-nitrostyrenes **1** with azomethine ylides from indenoquinoxalinones **2** (X = CH, N) and proline or sarcosine.

It was found that the 1,3-dipolar cycloaddition of azomethine ylides generated from indenoquinoxalinones **2** and proline at the double bond of the nitrostyrenes **1** leads to the *endo*-spiro[indeno[1,2-*b*]quinoxaline-11,3'-pyrrolizines] **3** in 48–94% yields as single regio- and stereoisomeric products.



Ar = Ph, 2-HOC_6H_4, 4-HOC_6H_4, 3-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 2,4-$Cl_2C_6H_3$

In similar reactions, involving nitrostyrenes **1** and azomethine ylides generated from indenoquinoxalines **2** and sarcosine, the *endo*-products **4** were obtained as mixtures containing 20-36% of the regiomer **4'** with 33–46% yields.



Ar = Ph, 3,4-$(MeO)_2C_6H_3$, 2,4-$Cl_2C_6H_3$

The structures of **3** and **4** were characterized by NMR, HRMS, IR and XRD data, stereochemistry of **4'** was confirmed by NOESY experiment.

This work was supported by the Russian Science Foundation (project № 14-13-00388).

Optical molecular sensors based on crown-containing dienones of cyclic ketones

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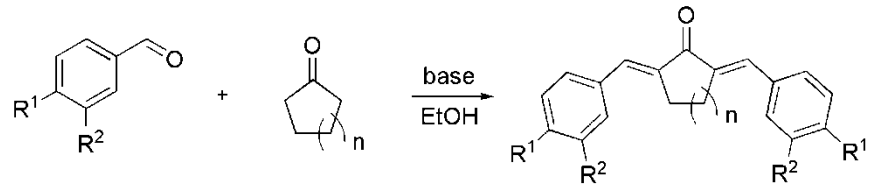
Cross-conjugated dienones of cyclic ketones are available substances, widely used in organic synthesis as a synthons for obtaining of different carbo- and heterocycles. These compounds have an ability to enter into photochemical reactions, can be used as a photosensibilizators and perspective as ligands in synthesis of coordination polymers [1].



n = 1, 2
R^1 = H, OMe, SMe, NMe_2, NEt_2, azacrown-ether, R^2 = H
R^1, R^2 = OMe, OEt, crown-ether

Crown- and azacrown-containing dienones, and dienones with different other donor groups were obtained by condensation of aromatic aldehydes with cyclic ketones in the presence of base. The structure of dienones were determined by NMR-spectroscopy methods, and confirmed by mass-spectrometry and elementary analysis data.

Clear-cut ability of obtained symmetrical crown- and azacrown-containing dienones to coordinate cations of alkaline metals and ammonium was observed. This ability characterizes by significant changes in absorption and fluorescence spectra, which allows considering them as a perspective optical molecular sensors.

This work was supported by the Russian Scientific Foundation (grant № 14-13-00076) and the Russian Foundation for Basic Research (grant № 16-03-00267).

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Combination of domino reactions for "one pot" synthesis of fused heterocycles

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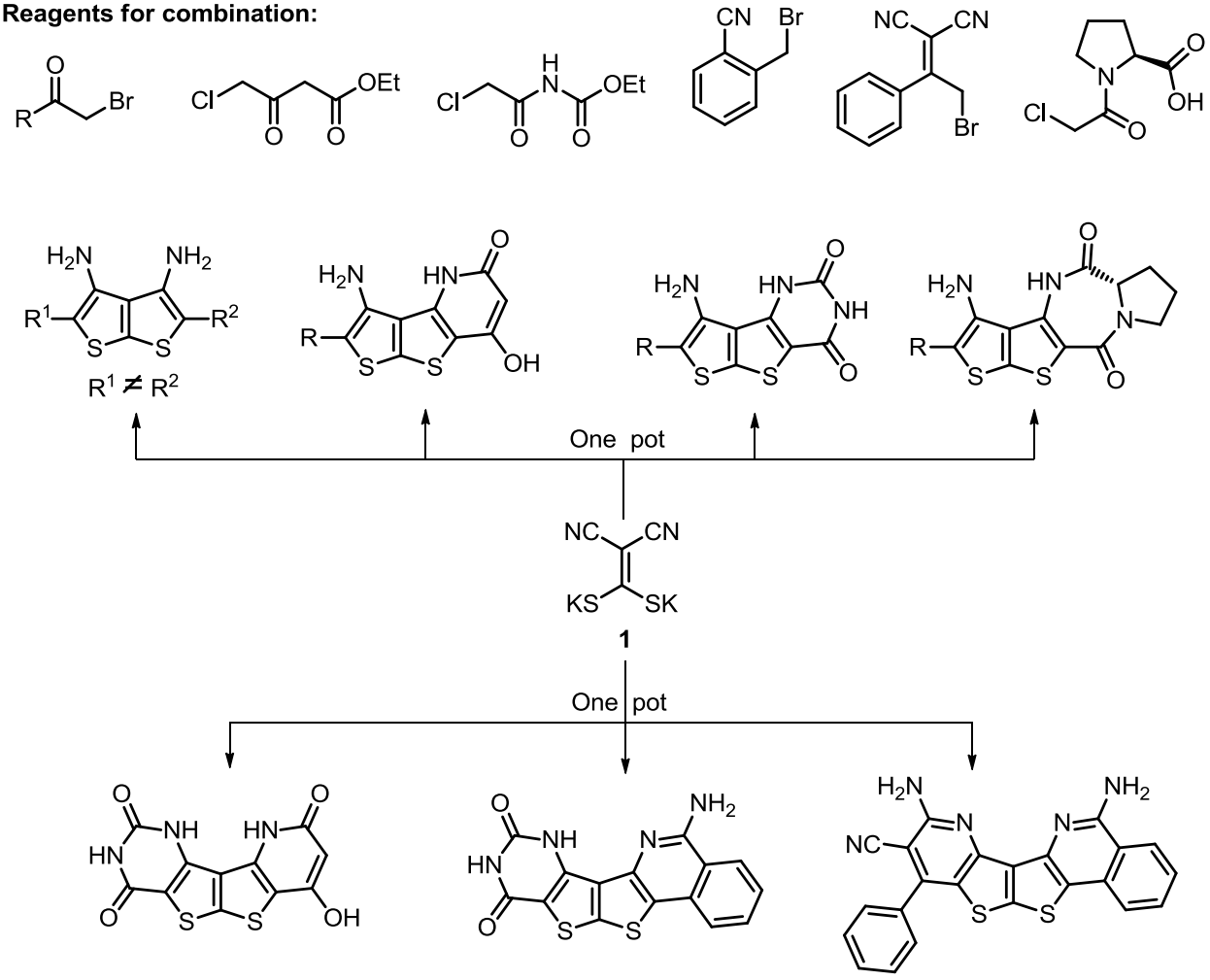
Domino reactions are widely used in organic synthesis [1], including preparation of heterocyclic compounds and biologically active molecules [2]. In this presentation we demonstrate the method of combination of two same or different domino reactions for synthesis of fused heterocycles. All reactions were carried out as "one pot" process, starting from polyfunctional salt **1**. The reactions used for combination ware domino types of: the S_N2 reaction → the Thorpe-Ziegler reaction, the S_N2 reaction → the Thorpe-Ziegler reaction → the Thorpe-Guareschi reaction and the S_N2 reaction → the Thorpe-Ziegler reaction → the hetero-Thorpe-Ziegler reaction.

Reagents for combination:



This is a convenient way for preparation of complex heterocyclic molecules from simple starting materials and it can be transferred to other systems by using of appropriate reagents.

References

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