DIAZO N_2 2021

VI International Symposium «The Chemistry of Diazo Compounds and Related Systems»

Saint Petersburg, Russia, September 6-10

BOOK OF ABSTRACTS

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Book of abstracts contains theses of plenary, keynote, invited, oral and poster presentation, with were presented on The 6th International Symposium «**The Chemistry of Diazo Compounds and Related Systems**». The Symposium «The Chemistry of Diazo Compounds and Related Systems» was held in Saint Petersburg (September 6–10, 2021) as the satellite ivent of **Mendeleev 2021**, the XII International Conference on Chemistry for Young Scientists.

Abstracts are presented in the author's edition.

The 6th International Symposium «The Chemistry of Diazo Compounds and Related Systems»

The chemistry of diazo compounds and related systems is one of the most actively developing areas of organic chemistry, which is due to the high reactivity of such compounds and their wide use in the synthesis of natural and bioactive compounds. According to the Scopus database, about 2000 scientific articles have been published on the diazo topic over the past decade. In terms of publications on this topic for the entire time, the Russian Federation is in fifth place (about 200 publications), and St. Petersburg State University is in fourth place among organizations in the world (Figure 1). And what is the reason for this?

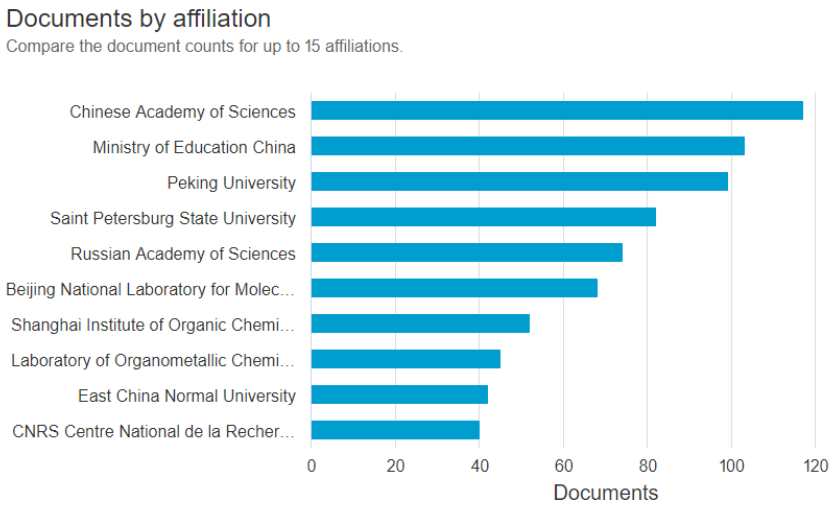
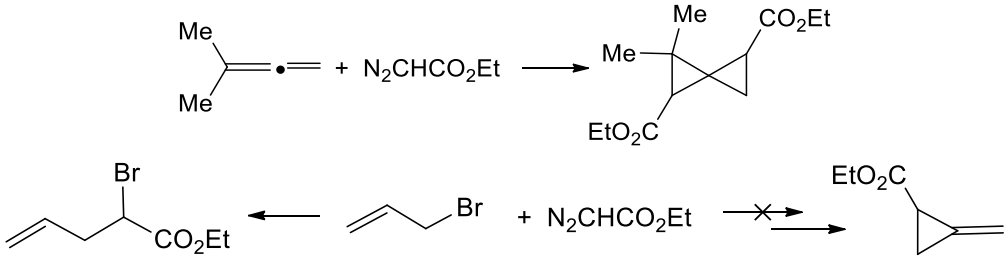
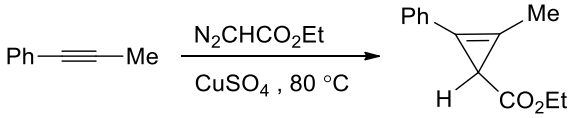


Figure 1. Statistics from Scopus on “diazo” documents

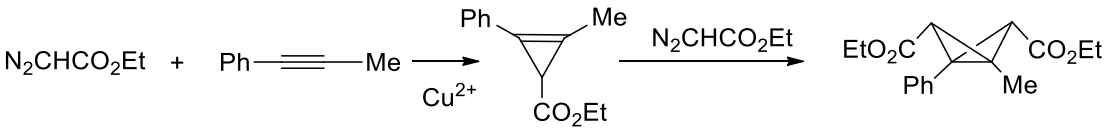
The first studies of diazo compounds in St. Petersburg University are associated with the name of Ivan Aleksandrovich Diakonov. He was born in St. Petersburg in 1911. In 1940, he defended his PhD thesis «To a problem of the formation of semicyclic double bonds at three-membered ring» under the supervision of academician Alexey Evgrafovich Favorskiy, famous Russian organic chemist. In 1959, he defended his doctoral dissertation on the topic "Research in the field of aliphatic diazo compounds and unstable cyclopropane derivatives". In 1960, he became a professor and headed the Department of Organic Chemistry at the Faculty of Chemistry of the St. Petersburg University. I. A. Diakonov is known for the pioneer works in the field of small ring compounds, aliphatic diazo compounds and carbenes. Developing of A.E. Favorsky ideas, I.A. Diakonov for the first time has assumed the formation of a bivalent carbon atom (carbene) as the intermediate under catalytic or photolytic decomposition of aliphatic diazo compounds. He demonstrated that this spieces are capable to add to the C=C bond to give cyclopropane derivatives and also to insert into the allylic or benzylic C–Hal bonds.



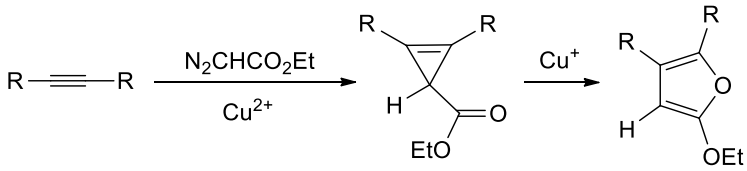
For the first time, he developed the synthesis of cyclopropene derivatives in the reaction of carbenes with alkynes. Independently, R. Breslow (Columbia University) obtained similar results. They used different catalysts: Diakonov - cupric sulfate, Breslow - copper powder.



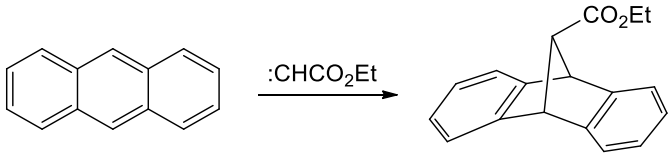
In further reaction of cyclopropenes with carbenes, bicyclo[1.1.0]butane derivatives were obtained, and the stereochemistry of its derivatives was studied.



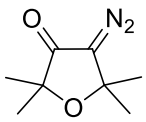
Diakonov also studied an isomerization of cyclopropene carboxylates or ketones to furan derivatives.



It is noteworthy that the first example of a 1,4-cycloaddition of ethoxycarbonylcarbene was found by Diakonov in the reaction of ethyl diazoacetate with anthracene.



I.A. Diakonov is the author of more than 100 publications, including some reviews on the carbene chemistry, cyclopropenylium cation, and valence isomerization, as well as monograph on the aliphatic diazo compounds. The diazo chemistry was further developed by the Diakonov's students and PhD students. Under his supervision, 16 PhD theses were defended. Many of his PhD students continued their research work in the St. Petersburg University.



A new direction in the chemistry of diazocarbonyl compounds appeared in the university in the 1960s, after Irina Kirillovna Korobitsina (1919–1990) moved to the university. In Leningrad, the PhD thesis of her first graduate student - Lyudmila L. Rodina - was devoted to the synthesis of diazo compounds of a new class - diazoketones of the tetrahydrofuran series. Then, many previously unknown carbo- and heterocyclic diazoketones were obtained, their properties and possible practical application were studied in detail. Another graduate student, Valeriy A. Nikolaev defended his candidate and doctoral dissertations on the methods for the synthesis of polyfunctional diazodicarbonyl compounds and the study of their chemical properties.

That's why it is not surprising that the symposium on the chemistry of diazo compounds is a traditional event for our university.

Previous symposium, the 5th International Symposium "The Chemistry of Aliphatic Compounds: Advances and Outlook" was held in St Petersburg in June 2011. It was dedicated to the 100th anniversary of the birth of Ivan Alexandrovich Dyakonov (Figure 2). More than 100 participants including 20 foreign scientists from 9 countries took part in that event. The world's leading scientists were the plenary speakers, among them are D. F. Taber (USA), V. V. Fokin (USA), V. Gevorgyan (USA), N.S. Zefirov (Moscow State University), M. Platz (USA), W. Brinker (Austria), H. Heimgartner (Switzerland), A.D. Dilman (IOC, Moscow), K. Maruoka (Japan), G. Mloston (Poland), V.A. Nikolaev (St. Petersburg State University), A.F. Khlebnikov (St. Petersburg State University), S.N. Osipov (INEOS), etc. The main organizers of previous excellent symposium were professor Rafael R. Kostikov (1938-2017), who was a PhD student of Diakonov, professor Valerij A. Nikolaev, professor Lyudmila L. Rodina, professor Mikhail A. Kuznetsov, and PhD student Olesya Galkina.

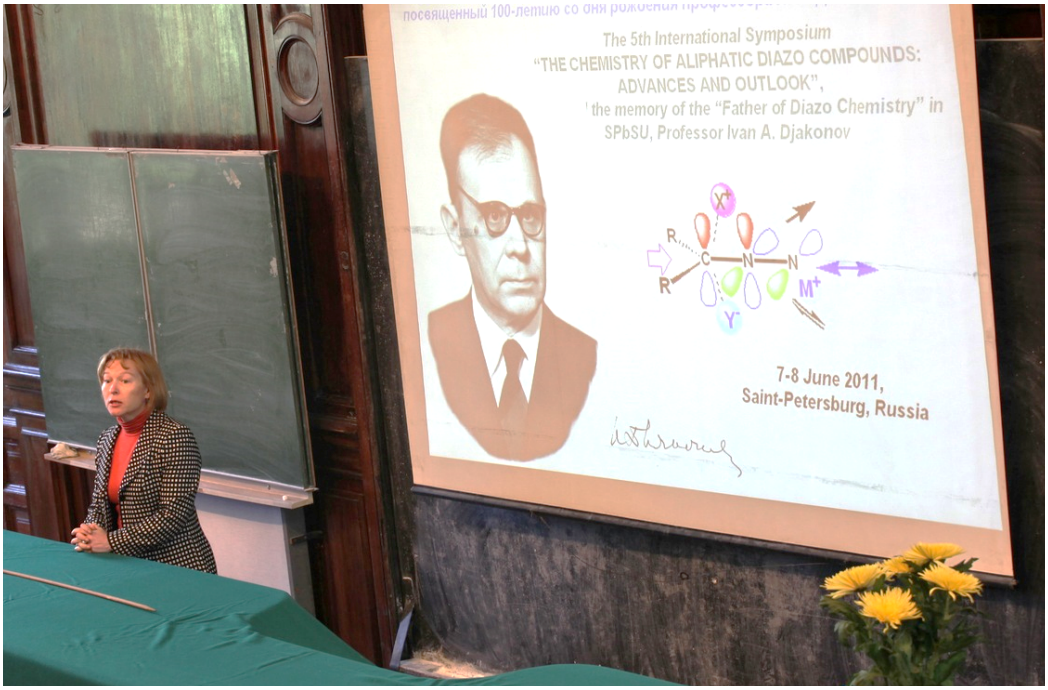


Figure 2. Opening ceremony of the previous symposium, June 2011

This year St. Petersburg University holds the 6th International Symposium «The Chemistry of Diazo Compounds and Related Systems». Compared to the previous symposium, the scientific program of current symposium was expanded to some other fields related to diazo compounds. In particular, diazirines, carbenes, transition metal carbenes, nitrenes, diazonium salts, diazenes, triazenes, heterocyclic precursors of diazo compounds, such as triazoles and thiadiazoles. There will be 7 plenary lectures of 40 minutes, 6 keynote lectures of 30 minutes, 6 invited lectures of 25 min, 30 oral presentations of 15 min, and 42 poster presentations. Due to difficult epidemiological situation, the event will be performed in a mixed format, in person and remotely.

On behalf of the organizing committee, I would like to thank all participants of the symposium for the interest to our meeting, all organizers of this symposium, especially Mariia M. Efremova and Vladimir N. Mikhaylov, and, of course, our sponsors.

I wish you that the symposium was useful for you, that you find new ideas, new friends, and new collaborations. I also hope that the guests of St. Petersburg will be able to get acquainted with the sights of our wonderful city.

Sincerely,
Chairman of the Symposium
Head of the Department of Organic Chemistry SPBU
Dr. Nikolai V. Rostovskii

PLENARY REPORTS

REACTIONS OF DIAZO COMPOUNDS AND AZIDES WITH THIOAMIDES AND ENAMINES

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Reactions of thioamides with nitrogen-rich 1,3-dipoles, such as diazo compounds and azides, have been known for a long time already [1]. However in last decades the use of metal catalysts [2-3], organocatalyst [4] as well as highly electrophilic heterocyclic and sulfonyl azides [3-6], allowed the development of new methods for the synthesis of 1,2,3-thiadiazoles and 1,2,3-triazoles and other heterocycles, enamines and dienamines [4]. Moreover, a new methodology in organic synthesis, based on generation and subsequent transformations of diazo compounds was created. Efforts of Japanese and Russian researchers led to new click-type reaction of sulfonyl azides with thioamides, capable of producing different sorts of *N*-sulfonyl amidines [7-10].

In addition, new reactions of diazo compounds and azides with thioamides, enamines and diamino acrylonitriles including ring transformations of 1,2,3-thiadiazoles and 1,2,3-triazoles will be presented in the lecture.

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CYCLOADDITION REACTIONS WITH VINYLDIAZO COMPOUNDS AND THEIR APPLICATIONS

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The transition metal catalyzed vinylcarbene approach to cycloaddition is remarkably effective and versatile [1-3]. These reactions use the three-carbon unit of the vinyl carbene to undergo highly chemoselective, regioselective, and stereoselective [3+*n*]-cycloaddition reactions (*n* = 1,2,3,4,5]. Dipolar metallo-vinylcarbenes generated from silyl-protected enoldiazo compounds are exceptionally effective. Products from these reactions are cycloalkenes bound on one side to an electron-donating group and on the other side to an electron-donating group and can be named “donor-acceptor cycloalkenes”. Their reactions, some of which are traditional, afford opportunities for the synthesis of diverse chemical structures with high optical purity.

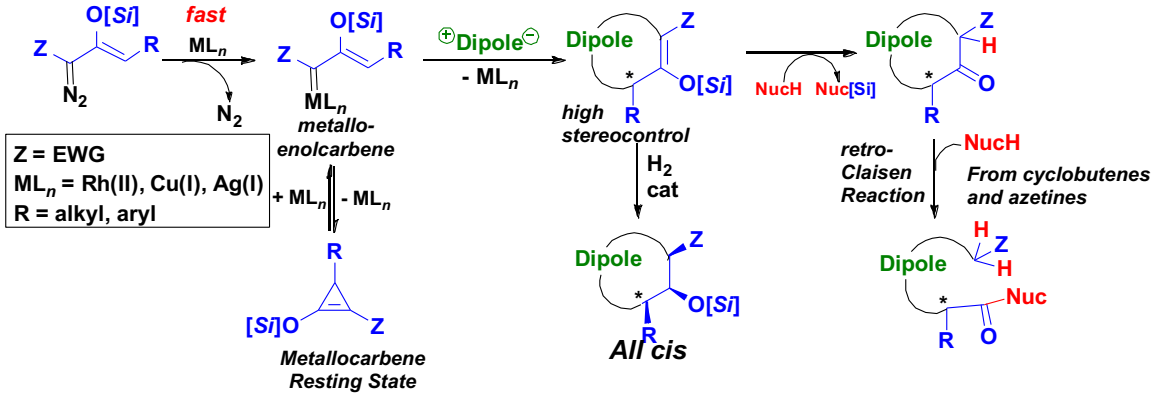

Figure 1. Silyl-protected Enoldiazo Compounds in Cycloaddition Reactions and Their Applications.

[3+*n*]-Cycloaddition reactions have been extended to 3-aryl- and 3-alkyl-analogues of enoldiazoacetates. Their applications include the synthesis of a broad range of carbocyclic and heterocyclic compounds, and their applications range from the formation of highly stereocontrolled multifunctionsal structures to nucleophilic ring opening reactions that access diverse peptide, glutaric acid, and monosubstituted succinic acids.

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Acknowledgements. This work was supported by the U.S. National Science Foundation.

METAL CARBENES THROUGH AROMATIVE DECARBENATIONS AND CYCLOISOMERIZATIONS

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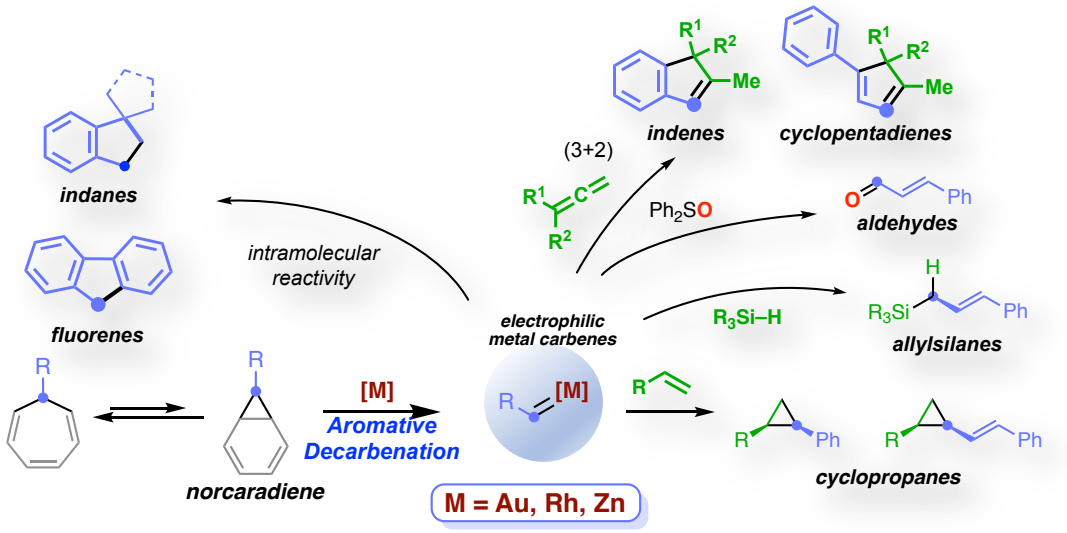
The gold(I)-catalyzed cycloisomerization of 1,n-enynes and the aromative decarbenation via a retro-Buchner reaction lead to the generation of similarly highly reactive species.[1,2] Related rhodium(II) and zinc(II) reactive species can also be generated by the aromative decarbenation of cycloheptatrienes.[3,4]



Progress on the development of synthetic applications proceeding through these electrophilic metal carbenes and new methods for their generation will be presented.

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Acknowledgements. This work was supported by Ministerio de Ciencia e Innovación (PID2019-104815GB-I00) and the European Research Council (Advanced Grant No. 835080).

EMPLOYMENT OF *N*-CONTAINING REACTIVE SPECIES IN SYNTHESIS OF HETEROCYCLES AND BEYOND

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In past two decades, our group was involved in the development of novel efficient transition metal-catalyzed methodologies for synthesis of multisubstituted carbo- and heterocycles, as well as in synthesis and C–H functionalization of diverse types of aliphatic molecules. Mostly, these methods involve employment or intermediacy of diazo compounds, heterocyclic precursors of diazo compounds, carbenes, transition metal carbenes, diazenes, diazonium salts, and other reactive species. Our earlier works involve thermal initiation of the reactions. Lately, we also developed several light-induced transition metal-catalyzed and transition metal-free methods. The scope of these transformations will be demonstrated and the mechanisms will be discussed.

ARYLDIAZONIUM SALTS, LIGHT AND GOLD COMPLEXES

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Only after two papers from 2000 had demonstrated the full potential of gold catalysis for organic transformations by a high increase of molecular complexity,[1,2] homogeneous gold catalysis was developed to a versatile tool for organic synthesis.[3,4] For a long time the field was exclusively focusing on electrophilic and nucleophilic species, radical intermediates were not involved, but this changed in 2013.[5]

The reaction of gold catalysts, not involving any photosensitizers or photoredox catalysts, can include dinuclear gold(I) catalyst and mononuclear gold(I) catalyst. Apart from the synthesis of different heterocycles (Figure 1), the use of these principles also allows a number of C-C coupling reactions, which in a formal sense can also address C,H bonds.[6]

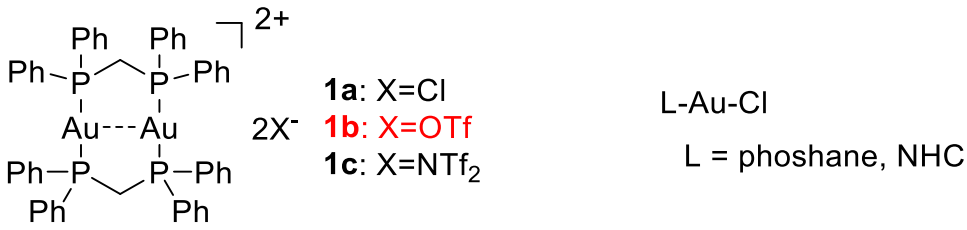

Figure 1. Catalyst for photochemical reactions of gold.

The lecture will cover photochemical conversions of mononuclear gold(I) complexes with aryldiazonium salts. This includes detailed mechanistic studies, computational studies and the use in synthesis.

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Acknowledgements. This work was supported by the Deutsche Forschungsgemeinschaft and the Landesgraduiertenförderung Baden-Württemberg.

DICHLORODIAZADIENES - NEW VERSATILE BUILDING BLOCKS

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It was shown that the reaction with hydrazones catalyzed by copper salts is of a more general nature, and N-substituted hydrazones can also be involved in it. As a result, we have developed a new reaction for the formation of carbon-carbon bonds of N-monosubstituted hydrazones with polyhaloalkanes with the formation of 1,2-diazabut-1,3-dienes. This highly efficient copper-catalyzed conversion has broad synthetic capabilities and enables the process to be carried out in a much more convenient one-pot mode, starting with readily available aldehydes and hydrazines.

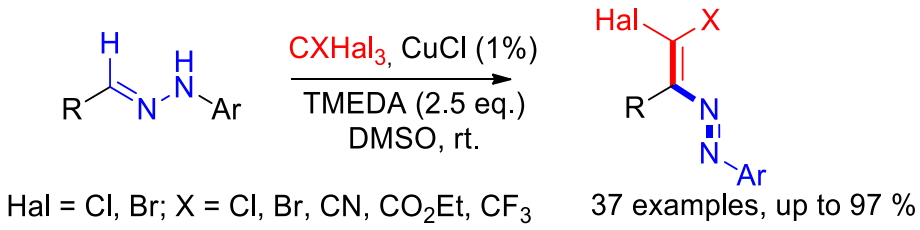

Figure 1.

The synthetic importance of the obtained halogenated azadienes was demonstrated in their reactions with O-, N-, S- and C-nucleophiles, which opened access to a number of valuable acyclic and heterocyclic products.

Mechanistic studies have shown that this copper-catalyzed conversion takes place in a radical way. At present, our laboratory is conducting further research into synthetic applications of the obtained halogenated azadienes.

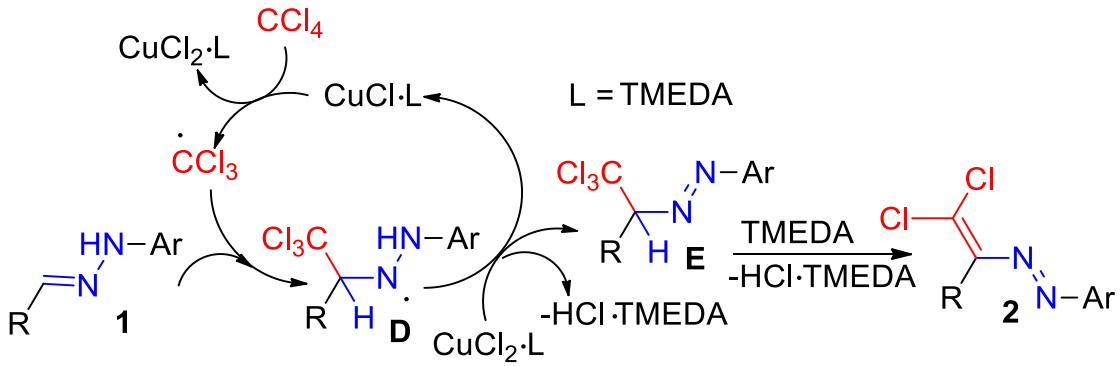

Figure 2.

CARBENE PRECURSORS AS CROSS-COUPLING PARTNERS

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In the past decade, a new type of transition-metal-catalyzed reaction of diazo compounds has been established, in which the diazo compounds (or their precursors *N*-tosylhydrazones) have been used as the cross-coupling partners in C-C single bond or C=C double bond formations. The transformations so far developed in this area can be summarized in the Figure 1. This type of carbene-based coupling has been proved to be general: various transition-metals including Pd, Cu, Rh, Ni, Co and Ir are effective catalysts; the scope of the reaction has also been extended to the substrates other than diazo compounds; and various cascade processes have also been devised based on the carbene migratory insertion.[1-6] The most recent advances in this area will be presented in this lecture.

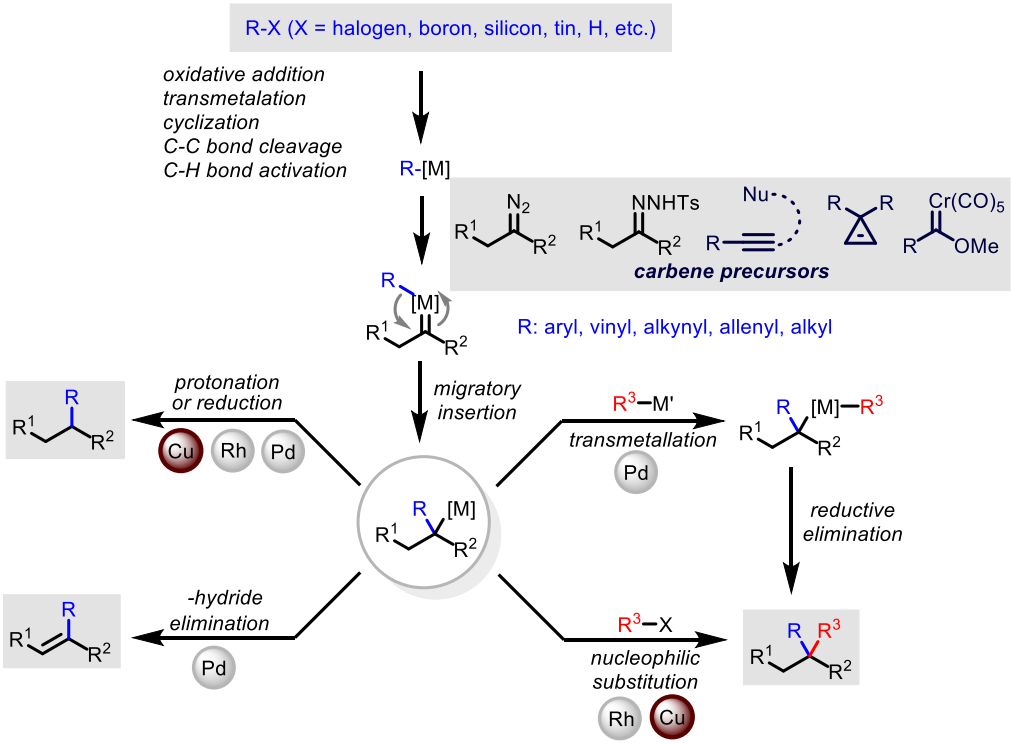

Figure 1. Summary of carbene-based cross-coupling reactions

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Acknowledgements. This work was supported by National Natural Science Foundation of China (NSFC) and Ministry of Science and Technology of China.

KEYNOTE REPORTS

THE DEVELOPMENT OF OXIDATIVE METHODS TO ACCESS *N*-ARYL NITRENES AND *N*-ARYL NITRENOIDS FROM NONACTIVATED ANILINES

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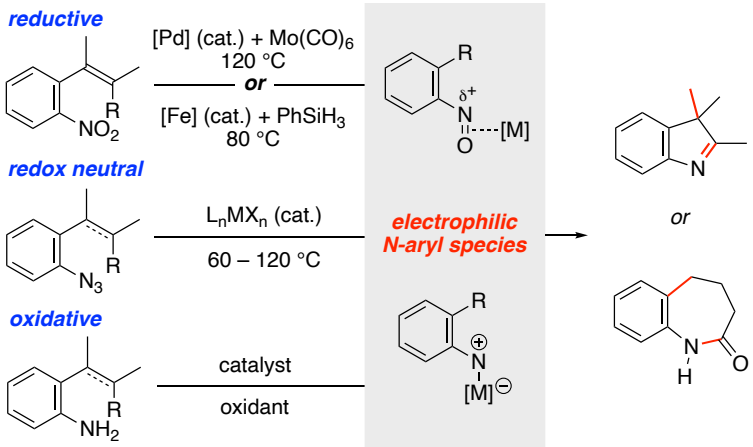

Figure 1.

Our research program is centered on the development of new methods to construct *N*-heterocycles by leveraging the reactivity embedded in electrophilic *N*-aryl nitrogen reactive intermediates. We established that transition metal complexes catalyze the synthesis of *N*-heterocycles from aryl azides through a site-selective C–H bond amination that occurred through a unique electrocyclization-migration of metal *N*-aryl nitrenes. We showed that similar reactivity could be unlocked from nitrosoarenes through a metal-catalyzed reduction of nitroarenes using $Mo(CO)_6$ or $PhSiH_3$ as the stoichiometric reductant. We were curious if these reactivity patterns could be unlocked from nonactivated anilines through oxidation, and we report our work towards identifying the optimal catalytic conditions to in situ generate *N*-aryl nitrenoids and exploit their reactivity to construct *N*-heterocycles.

REACTIVITY OF DIAZO COMPOUNDS UNDER VISIBLE-LIGHT IRRADIATION

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The application of visible light in organic transformations is of growing interest. In this line, both elimination of expensive and toxic metal catalysts and the use of visible light for activation of diazo compounds is extremely attractive. Photochemical reactions engaging various precursors of carbenes have been investigated over the years.[1] Although UV-light-induced carbene generation is well known, only recently it became also clear that the introduction of a donor group to diazoacetates enables their photolysis under blue light irradiation.[2]

We have shown that visible light-induced decomposition of diazo compounds allows reaction with various propargyl reagents giving allenes through the [2,3]-sigmatropic rearrangement. But α-diazo compounds can also be involved in photoredox reactions as efficient alkylating reagents of carbonyl compounds.[3,4,5]

Photoalkylation of electron-rich aromatic compounds with diazo esters leads to C2 alkylation of indoles and pyrroles.6 While for diazo compounds exhibiting strong absorption within the wavelength region of the light used for irradiation, the regioselectivity of the alkylation reaction alters from C2 to C3.

In terms of safety, 1,3,4-oxadiazolines constitute a valuable alternative to diazo compounds.[6] Under blue light irradiation, they also generate carbenes that we engaged in the cyclopropanation of electron-deficient olefins.

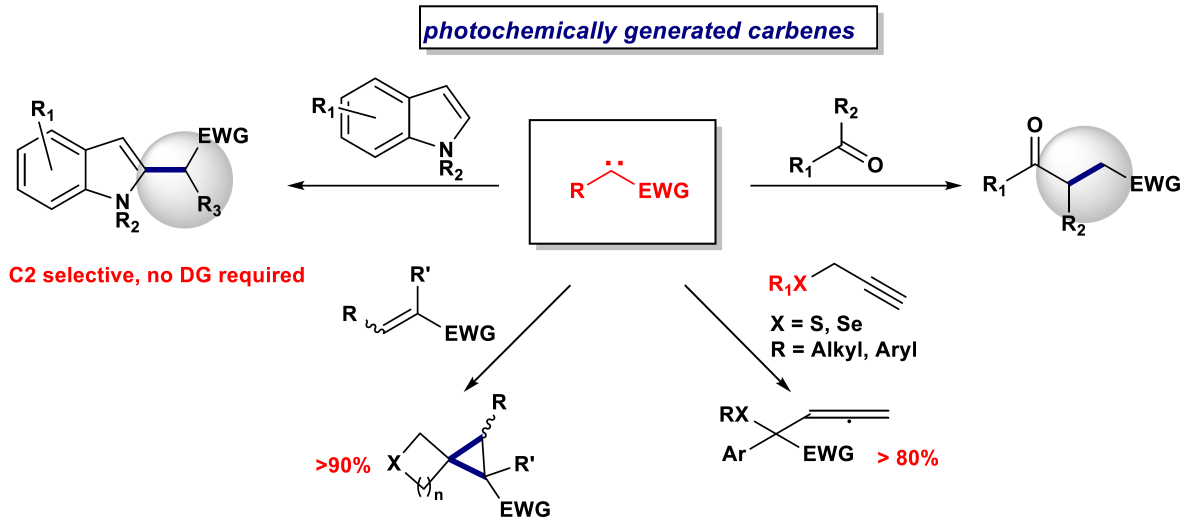

Figure 1. Reactions of photochemically carbenes.

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DIAZO-FUNCTIONALIZED REACTIVE HETEROCYCLES: VERSATILE TOOLS IN SYNTHESIS

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Synthetic strategies based on diazo-functionalized reactive heterocycles make it possible to obtain new nitrogen-containing heterocyclic assemblies and fused heterocyclic systems. The developed synthetic approaches use the orthogonal stability and reactivity of functional groups and rings in compounds containing a diazo function and a heterocyclic ring such as azirine, isoxazole, and pyrrole. The use of diazo-function transformations (DAT), such as intermolecular and intramolecular Buchner reactions (Inter/IntraMBR) and others, together with transformations of the azirine (ART) and isoxazole (IRT) rings, for the synthesis of heterocycles is discussed [1-6].

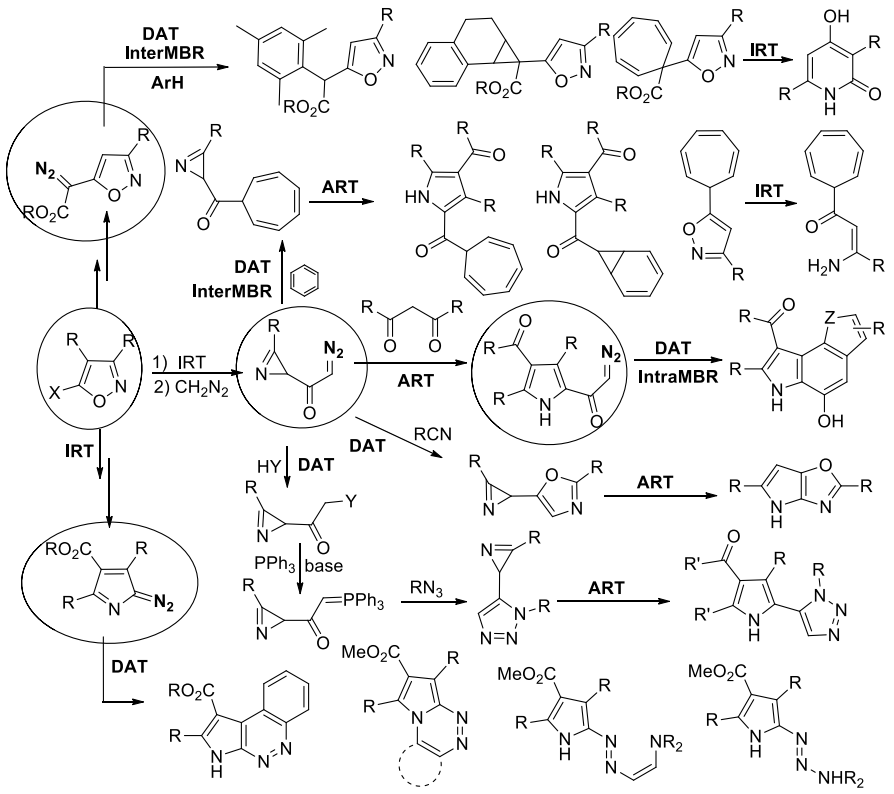

Figure 1.

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MEDICINAL CHEMITRY APPLICATIONS OF DIAZO COMPOUDS: SELECTED EXAMPLES

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In this talk, we will focus on the medicinal chemistry projects that have stemmed from innovation in diazo chemistry in our labs.

Using the usual arsenal of diazo function transformations (primarily, the X-H Rh cabenoid insertion), one can reach into diverse areas of biotarget perturbation as exemplified by the recently developed thrioredoxin reductase inhibitors [1], metallo-β-lactamase inhibitors [2], carbonic anhydrase inhibitors [3] as well as trace amine associated receptor agonists and free fatty acid binding protein ligands [4].

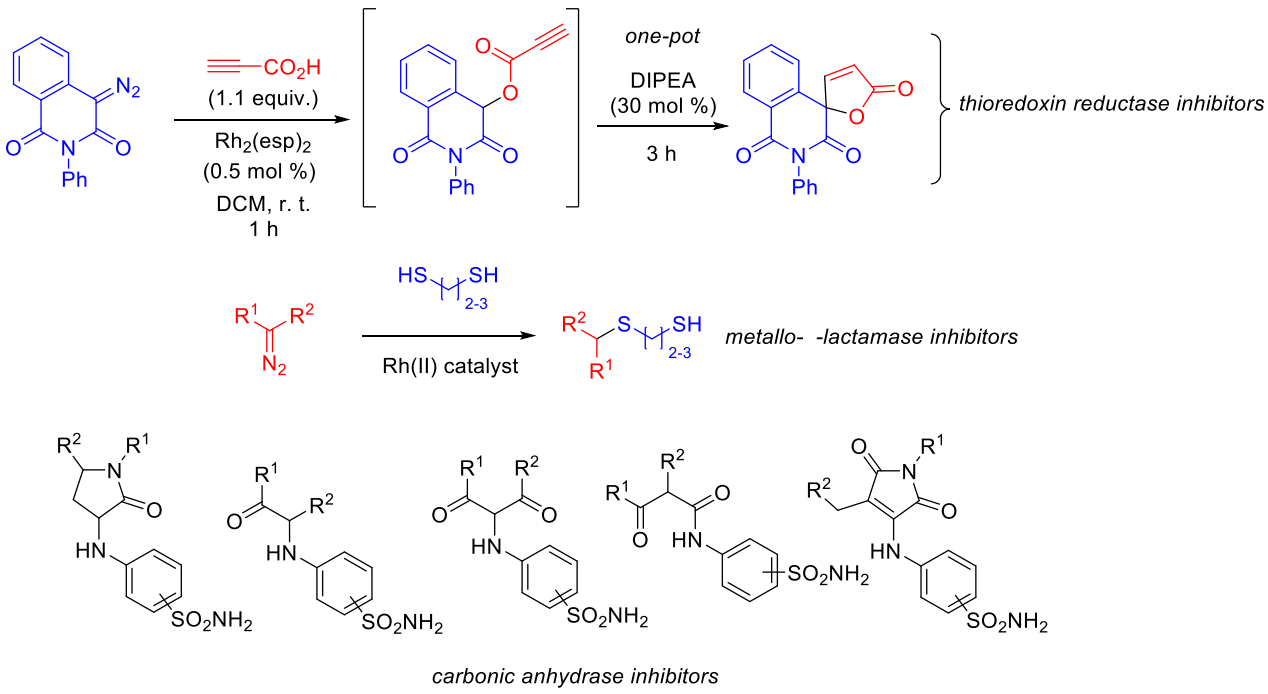

Figure 1. Areas of research covered in the talk

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DIAZO-DERIVED RHODIUM CARBENES AS USEFUL TOOLS FOR RING-EXPANSIONS AND ANNULATIONS IN AZIRINE, AZOLE AND PYRROLE SERIES

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Transition metal-catalyzed reactions of diazo compounds are widely used in the synthesis of various acyclic compounds, carbo- and heterocycles. They proceed through the intermediate formation of transition metal carbenes that are capable of reacting with various π-systems, the lone pairs of heteroatoms, or undergoing rearrangements. The interaction of a metal carbene with a heteroatom of a heterocycle often triggers important processes leading to the replacement of atoms in the ring or the change of its size. The report discusses the latest advances in the rhodium catalyzed synthesis of N-, N,N-, N,O-, and N,N,O-heterocycles from diazo carbonyls and readily accessible heterocyclic compounds [1,2].

The use of diazo compounds as C1 synthons in above catalytic reactions enable the one-atom ring expansion of some three- and five-membered heterocycles. These reactions underlie the synthesis of 1,2-dihydroazetes from azirines, 2*H*-1,3-oxazines from isoxazoles, 1,2-dihydropyrimidines from pyrazoles and 2*H*-1,3,5-oxadiazines from 1,2,4-oxadiazoles (Figure1). Diazo compounds can also be successfully used as C1 synthons in the synthesis of pyrrolin-3-ones from azirine-2-carbaldehydes. 2-Acyl-2-diazoaceatets are involved as C1 synthons in the straightforward synthesis of 3,4-epoxypyrrolines from 2-haloazirine-2-carboxylates via “azirine ring opening/tandem cyclization” sequence. Another diazo strategy for the formation of pyrroline derivatives, e.g., 3-alkoxy-4-pyrrolin-2-ones, implies the use of diazo carbonyls as C2 synthons in the denitrogenative transannulation of 1,2,3-triazoles. [2+1+1] Assembly of spiro β-lactams from azirines and diazo esters is the first example of the transformation of one heterocycle into another using two different diazo compounds, one of which acts as a C1 synthon, and the other one – C2 synthon. Finally, the unprecedented synthesis of 1*H*-pyrrolo[1,2-*c*][1,3]oxazin-1-ones from 2-aroylpyrroles demonstrates the ability of diazomalonates and aryldiazoacetates to deliver at once two non-adjacent atoms in the target heterocycle. The mechanisms of all mentioned reactions are discussed.

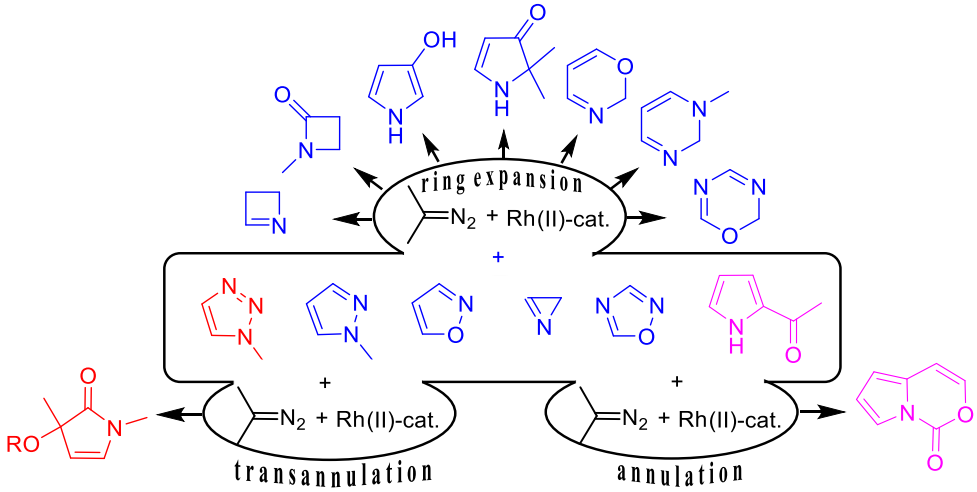

Figure 1. Rhodium carbene-mediated ring expansion and annulation reactions of azirines, azoles and pyrroles.

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

INVITED REPORTS

STEREOSELECTIVE FUNCTIONALIZATIONS OF YLIDES DERIVED FROM METALLOCARBENES

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Transition metal-catalyzed functionalization of *α*-diazocarbonyl compounds has found widespread application in stereoselective synthesis of complex frameworks because of their ability to produce reactive metallocarbene intermediates. These metallocarbenes are capable of delivering variety of useful transformations,[1] which includes traditional reactions like cyclopropanation, X–(C)H insertion and ylides. Recently, three component approach [2] and functionalization of nitrogen analog of *α*-diazocarbonyl compounds, *viz. α*-diazoimines [3], with various coupling partner has been studied extensively. In this presentation, our recent efforts in the synthesis and transition metal catalyzed stereoselective functionalization of *α*-diazocarbonyl compounds and its nitrogen analog *via* in-situ generation of ylides will be discussed.[4]

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PHOTOCHEMICAL REACTIONS OF DIAZOALKANES AND NITRENE PRECURSORS IN ORGANIC SYNTHESIS

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Carbenes and nitrenes are important reactive intermediates and possess exquisite reactivity to conduct organic synthesis under mild conditions. Most commonly, transition metal complexes are used to access and to control the reactivity of such intermediates, which constitutes today one of the key strategies for their application in synthesis.

Despite the intense color of diazoalkanes, their application in photolysis reactions remained restricted to studies in physical organic chemistry for many years. Only recently, several groups independently reported on their advances on the application of such photochemical carbene generation in organic synthesis via the photolysis of diazoalkanes [1-3]. Herein, we discuss our advances into this research area via free carbene intermediates [2-3]. We further discuss our recent findings of diazoalkanes under photochemical conditions. Specifically, photoexcitation of diazoalkanes opens up new pathways via photoexcited proton transfer reactions for the synthesis of fluorinated ethers, which represents a new reactivity of diazoalkanes [4]. More lately, we demonstrated that depending on the electronic properties of aryl/aryl diazoalkanes, different reaction pathways can be accessed via photolysis reactions under the otherwise identical reaction conditions [5] (Figure 1, a-b).

We commence with the discussion of photochemical reactions of iminoiodinanes to access nitrene intermediates. Depending on the photolysis conditions, either nitrene or nitrene radical anion intermediates can be accessed [6-7] (Figure1, c-d).

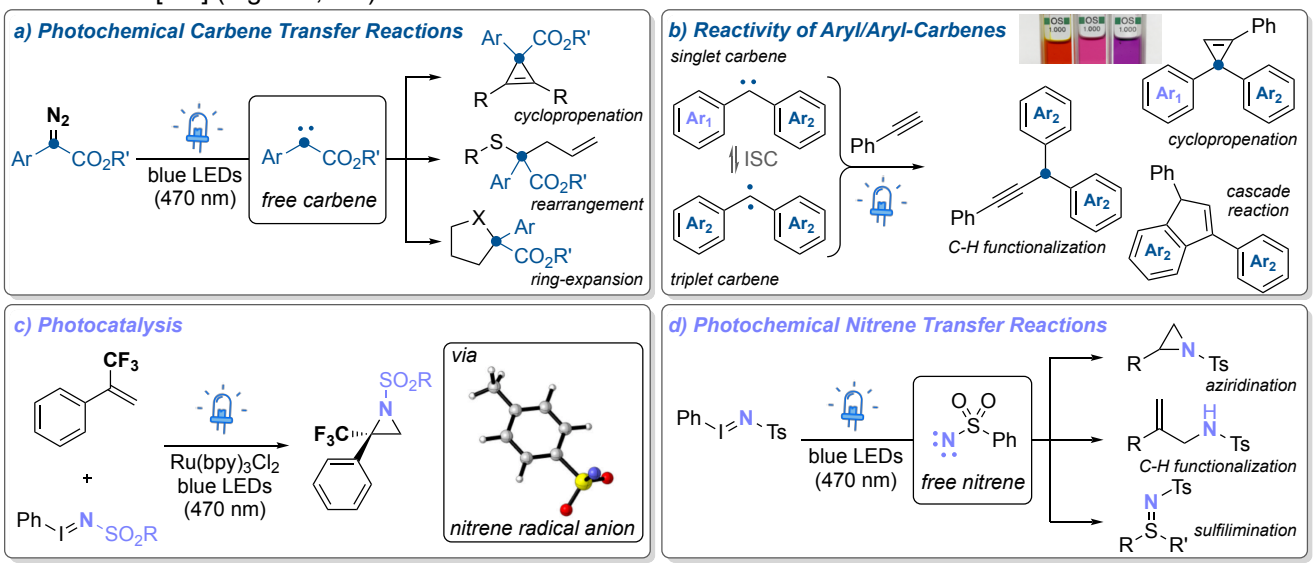

Figure 1. Photochemical reactions of diazoalkanes (top) and iminoiodinanes (bottom) in organic synthesis.

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ENHANCING THE SYNTHETIC UTILITY OF α-DIAZOCARBONYL COMPOUNDS BY LEVERAGING CONTINUOUS FLOW TECHNOLOGY

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The synthetic versatility of α-diazocarbonyl compounds is very clear, resulting in a wide range of transformations which cannot be readily effected through other methodologies, frequently employing mild reaction conditions, neutral pH and highly selective catalysts.[1] Nevertheless, their use in large scale organic synthesis, including for the production of Active Pharmaceutical Ingredients, is limited due to the hazards associated with their use; principally, the handling and storage of their precursors – diazoalkanes, sulfonyl azides *etc*. [2]

The advantages associated with continuous flow technology, including the potential to generate on demand and use hazardous reagents *in situ*, in line monitoring and effective heat transfer provide an unprecedented opportunity to enable the safe use of diazo compounds in synthetic processes where their use would have previously been discounted at an early stage on safety grounds.[3]

Enantioselective C–H insertions and aromatic additions with α-diazocarbonyl compounds, utilising a range of copper and rhodium catalysts, has been a focus of our research for many years [4] – herein, we describe progress in leveraging the advantages of synthesis in continuous flow to enhance the practical synthetic utility of this methodology. Development of a number of protocols for diazo transfer in flow [5] and harnessing the potential to telescope the generation of α-diazocarbonyl compounds with enantioselective transition metal catalysed C–H insertions and aromatic additions will be described. [6]

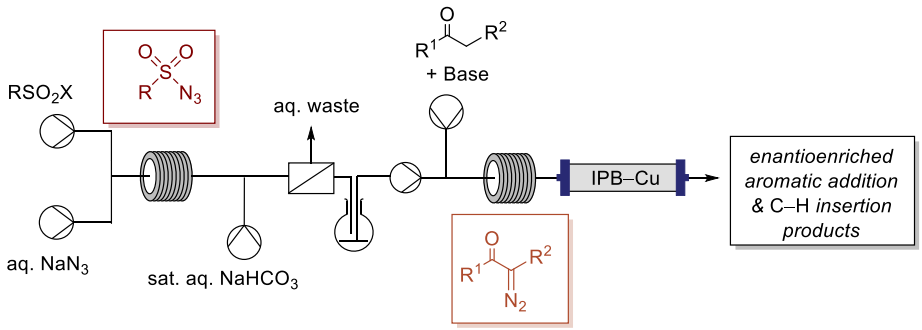

Figure 1.

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EXPANDED RING N-HETEROCYCLIC CARBENES – VERSATILE LIGANDS FOR LATE TRANSITION METAL HOMOGENEOUS CATALYSIS

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More than a decade our group deals with the chemistry of N-heterocyclic carbenes bearing expanded, six-, seven- or eight-membered ring, er-NHCs. For such carbenes, it is possible to vary the stereoelectronic properties in a wider range than for their five-membered ring counterparts. We have developed approaches for synthesis and isolation of carbenes and their late transition metal complexes (Cu, Ag, Au, Pd, Pt). Superior stereoelectronic properties of er-NHCs enabled us to develop highly efficient catalytic systems for important organic transformations such as C-C and C-N cross-coupling, addition of nucleophiles to acetylenes, CuAAC, CH borylation. In many cases the developed synthetic protocols are not only efficient, but also meet the requirements of green chemistry: water as solvent, solvent-free conditions, environmentally benign and affordable co-catalysts, and additives.

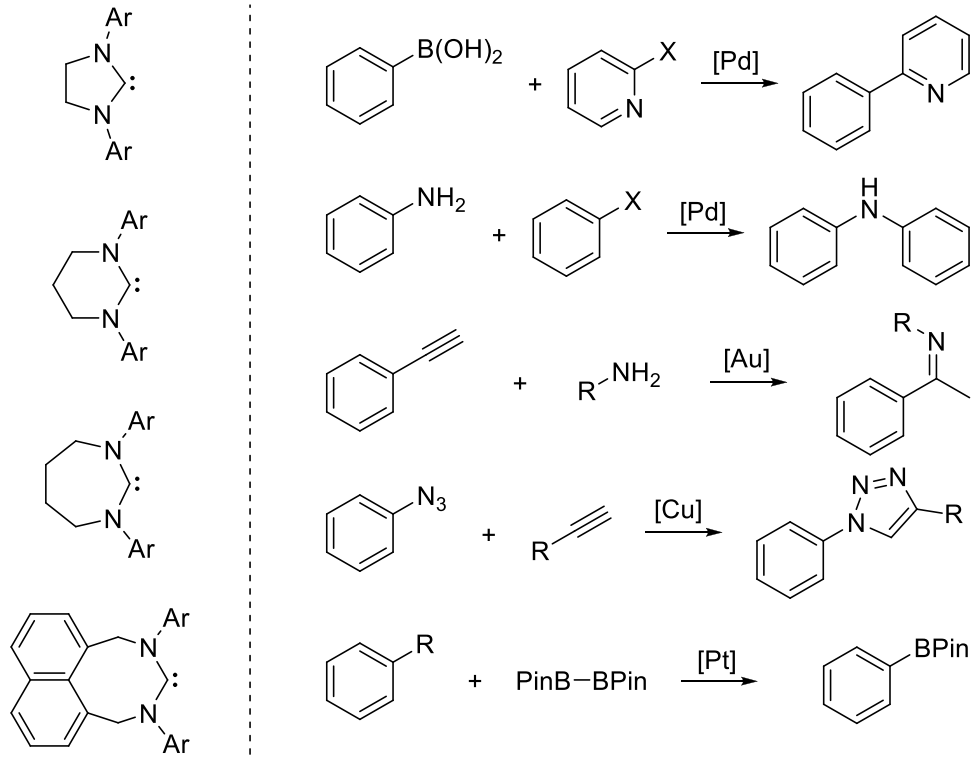

Figure 1.

Acknowledgements. This work was supported by the Russian Science Foundation (projects No 17-13-01076-П, 17-73-20023, 19-73-10185).

DIAZO COMPOUNDS AND DIAZIRINES: VERSATILE SYNTHETIC INTERMEDIATES FOR Si–H INSERTIONS AND CYCLOADDITIONS

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Recent work about the insertion reaction of diazo compounds into X–H bonds will be disclosed [1]. Copper and iron catalysis appear particularly efficient for the insertion reaction of diazo compounds into the Si–H bond. An asymmetric copper(I)-catalyzed Si−H insertion reaction of 1-aryl-2,2,2-trifluoro-1-diazoethanes will be presented. A C_2-symmetric copper(I) diimine complex enables the asymmetric insertion reaction to give enantioenriched (1-aryl-2,2,2-trifluoroethyl)silanes with enantioselectivities *up to* 96% *ee* [2]. An efficient synthesis of 3-trifluoromethyl-3-aryl-cyclopropenes *via* the cyclopropenation reaction of alkynes with photolytically-generated carbenes from diazirine compounds will be disclosed. This reaction is performed in continuous flow using readily available LEDs in mild reaction conditions. This new and efficient method describes the synthesis of 25 examples of 3-trifluoromethyl-3-aryl-cyclopropenes with yields *up to* 97%, achieved in continuous flow with 5 min residence time [3].

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Acknowledgements. This work was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC) and the FRQNT Centre in Green Chemistry and Catalysis (CGCC).

RH(II)-CATALYZED DENITROGENATIVE INSERTION REACTIONS OF N-SULFONYL-1,2,3-TRIAZOLES

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The seek for the discovery and development of novel and efficient synthetic approaches for accessing heterocyclic scaffolds relevant for biological studies and medicinal applications is at the fore front of organic chemistry. In the past few years, transition-metal catalyzed denitrogenative ring opening of N-sulfonyl-1,2,3-triazoles and exploiting their reactivity in the constuction of other heterocyclic compounds gained a lot of interest. Various transition-metals like Rh, Cu, Ni and Pd were able to trap the α-imino-diazo intermediate and convert it into a highly reactive α-imino-carbenoid species, which shows reactivity similar to classical metal-carbenoids generated from diazoacetates. In addition, these species also display unique reactivity leading to a variety of novel reactions like transannulation, cycloaddition and insertion reactions. In this presentation, I would like to discuss our efforts to exploit the reactivity of Rh-azavinyl carbenoids in a variety of insertion and cyclization reactions to access various heterocyclic moieties like oxazolidinones, benzoxazinones and indigoids.

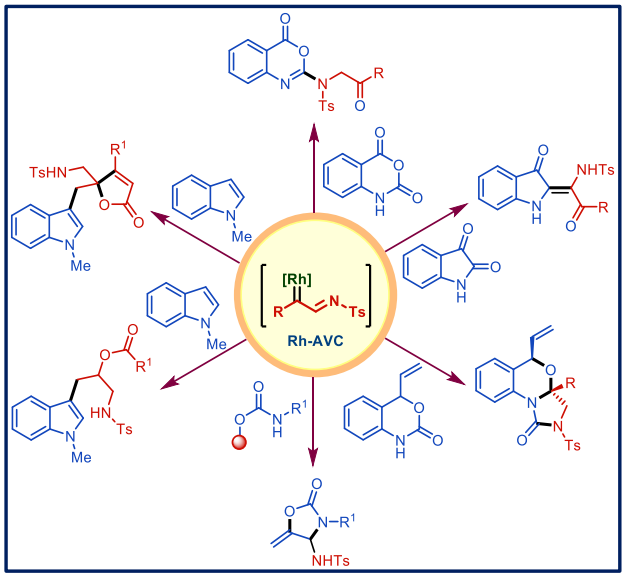

Figure 1. Rh(II)-catalyzed denitrogenative transformations of 1,2,3-triazoles

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Acknowledgements. This work was generously supported by Science and Engineering Research Board (SERB), India.

ORAL AND POSTER REPORTS

REACTIVITY OF DIAZO CARBONYL COMPOUNDS TOWARD 5-OXY-/5-AMINO-/5-SULFANYLISOXAZOLES

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As it was shown in our previous works, 5-alkyloxy/5-amino-4-halogenisoxazoles react with diazo esters to form 4-halogen-2-azabuta-1,3-dienes. On the next step, 4-bromo-2-azabuta-1,3-dienes can be successfully transformed to thermally and hydrolytically stable alkyl 2,3-dihydroazete-2,3-di-/2,2,3-tricarboxylates through their 1,4-electrocyclization and hydrodebromination reactions [1]. On the other hand, 4-chloro-2-azabuta-1,3-dienes are able to undergo the reductive ionic 1,5-*exo*-*trig*-cyclization to form 4-hydroxy-1*H*-pyrrole-3-carboxylic and 3-hydroxy-1*H*-pyrrole-2,4-dicarboxylic acids derivatives [2]. (Figure1)

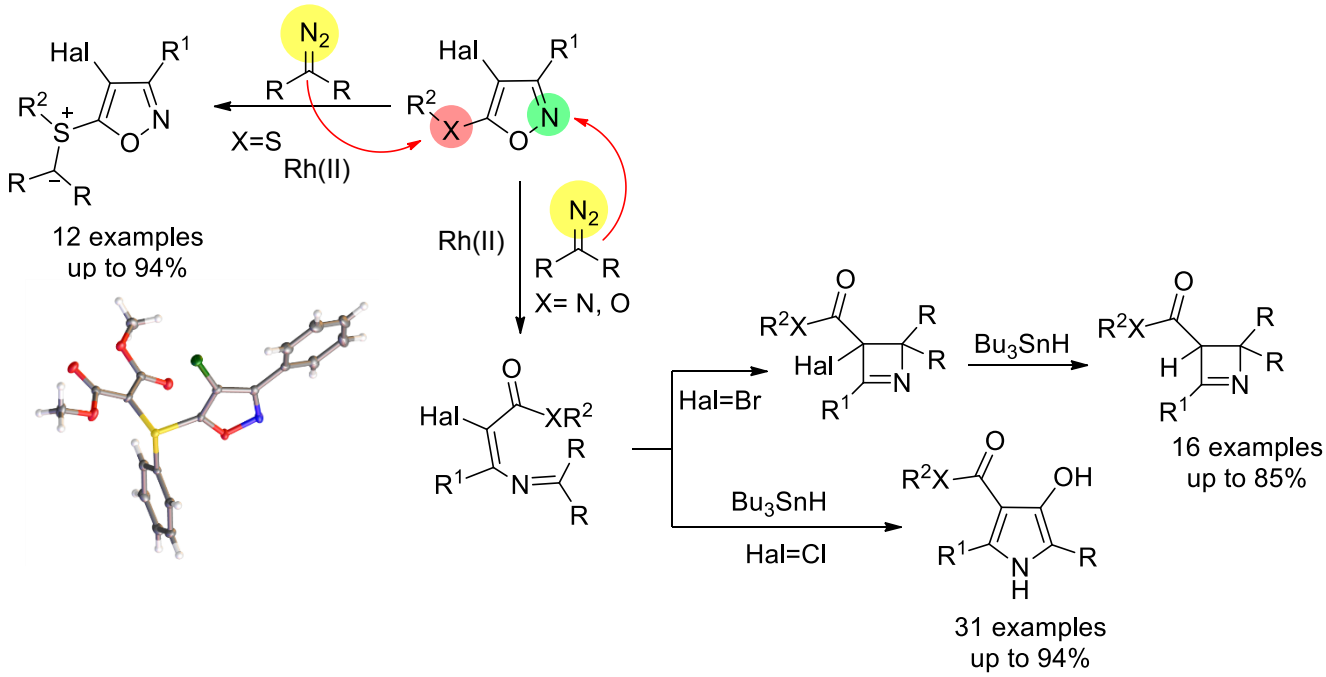

Figure 1. Possible reactions between isoxazoles and diazo compounds

Recently, we found that 5-R-sulfanyl isoxazoles react with rhodium carbenoids generated from diazo compounds in a different way. In this case, changing the reaction center in the isoxazole molecule from N-atom to R-sulfanyl group was observed. As the result of the reaction center changing is the formation of new isoxazolyl-substituted sulfonium ylides. The structure of ylides was confirmed by X-ray analysis data.

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

REARRANGEMENT OF THIAZOLO[3,2-*a*]PYRIDINES INTO TRIAZOLO[4,3-a]PYRIDINES INDUCED BY C=N BOND REDUCTION

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Thiazolo[3,2-*a*] and triazolo[4,3-*a*]pyrimidines are among the promising structural fragments for the development of drugs, including anti-cancer drugs [1]. The structure of these heterocycles resembles purine, which can be used in the construction of structures that actively bind to biological targets.

This work is devoted to the synthesis of triazolo[4,3-*a*]pyrimidine derivatives by reducing 2-arylhydrazone derivatives of thiazolo[3,2-*a*]pyrimidines in the new reduction system ($NaBH_4/V_2O_5$/EtOH) [2], as well as to the assessment of the cytotoxicity of the obtained compounds and the study in the crystal phase of new complexes obtained as a result of the interaction of 2-arylhydrazone derivatives of thiazolo[3,2-*a*]pyrimidines with d – and f – cations.

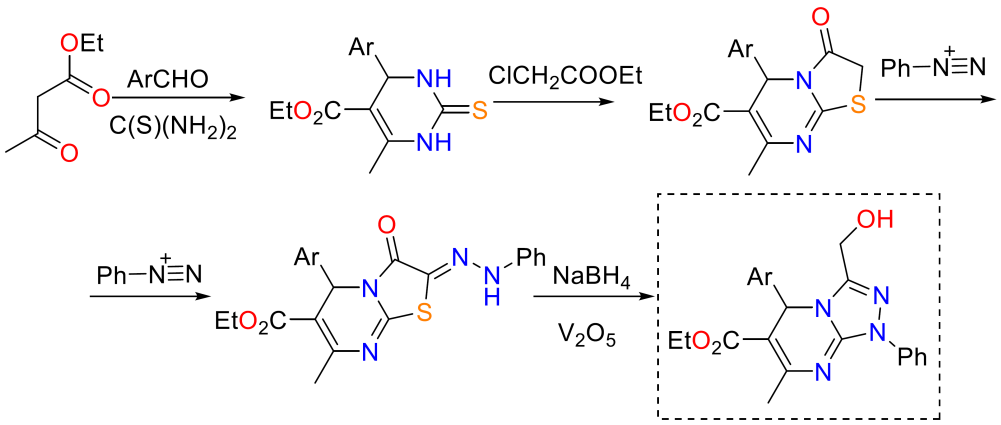

Figure 1. Reaction sequence for the preparation of triazolo[4,3-a]pyrimidine derivatives.

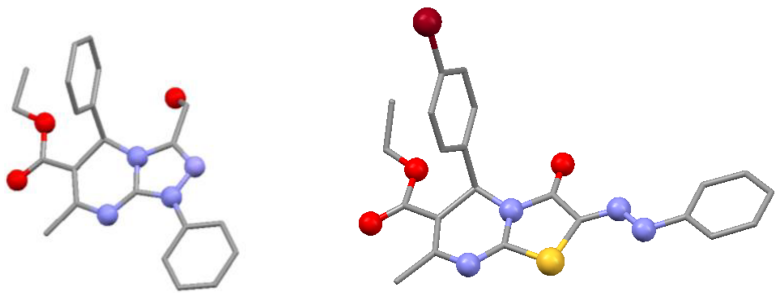

Figure 2. Crystal structure of derivatives of 2-(arylhydrazinylidene)[1,3]thiazolo[3,2-*a*]pyrimidines and 3-(hydroxymethyl)[1,2,4]triazolo[4,3-*a*]pyrimidine.

The structure of the obtained compounds was determined using mass spectrometry, X-ray diffraction analysis, IR and NMR spectroscopy.

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

SYNTHESIS OF TRIAZOLE-FUSED HETEROCYCLES WITH NEUROBLASTOMA DIFFERENTIATION ACTIVITY

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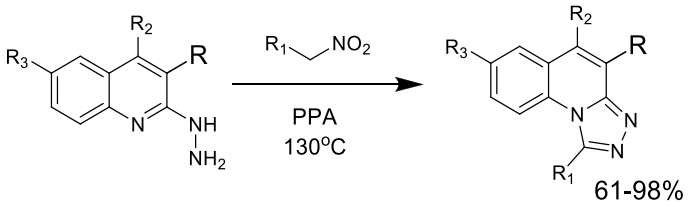
We discovered a reaction of nitroalkanes with 2-hydrazinylquinolines, 2-hydrazinylpyridines and bis-2,4-dihydrazinylpyrimidines in polyphosphoric acid (PPA) affording 1,2,4-triazolo[4,3-a]quinolines, 1,2,4-triazolo[4,3-a]pyridines and bis[1,2,4]triazolo[4,3-a:4',3'-c]pyrimidines, respectively. The reaction expands the scope of heterocyclic annulations involving phosphorylated nitronates, believed to be the electrophilic intermediates formed from nitroalkanes in PPA. Several of the synthesized triazoles showed promising anticancer activity by inducing differentiation in neuroblastoma cancer cells. Due to the urgent need for novel differentiation agents for neuroblastoma therapy, this finding warrants further evaluation of this class of compounds against neuroblastoma.



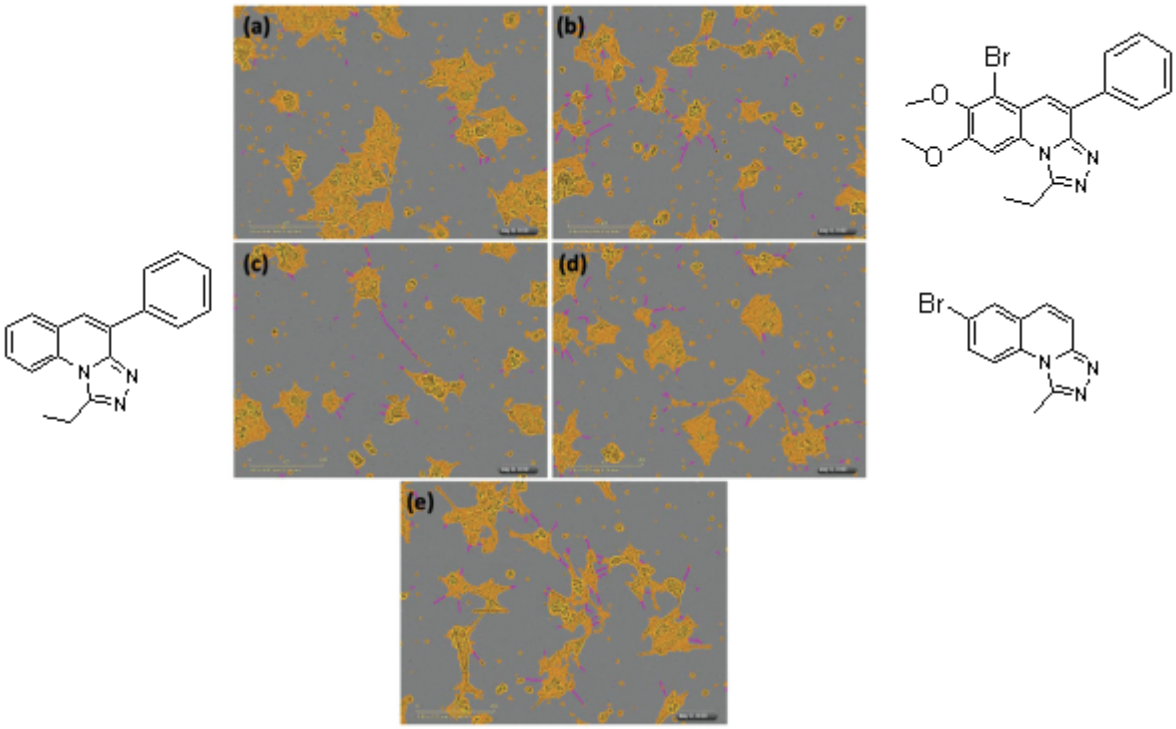


Figure 1. Compounds induce neurite outgrowth in BE(2)-C cells. Shown are representative phase-contrast images for cells treated with (a) DMSO control, (b) comp1 (25 μM), (c) comp2 (25 μM), (d) comp3 (25 μM) and (c) ATRA (2.5 μM) for 4 days. Neurites are highlighted in pink and cell bodies in yellow color.

Acknowledgements. This work was supported by the Ministry of Education and Science of the Russian Federation (grant #0795-2020-0031).

GENERATION OF NITRILE OXIDES AS A KEY MOTIVE FOR THE REACTIONS OF NITRO COMPOUNDS IN MEDIUM OF POLYPHOSPHORIC ACID

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One of the key topics of our team in recent years has been the reactions of electrophilically activated nitro compounds under the action of polyphosphoric acid. The approach brought us great results, the start of which was laid with the acetamimation reaction of arenes [1]. Recently, we noticed that in the course of such reactions it is possible to capture the corresponding nitrile oxides, which may indicate the possible participation of these particles as key electrophiles in such reactions (Figure 1). To gain a foothold in this methodology, we obtained a library of furoxans with various substitution profiles (Figure 2). The most interesting are furoxans with acyl substituents, as a number of such molecules have been shown as anti-cancer agents [2]. No less interesting is the interception of furoxans by other dipolarophiles, for example, acetylenes.

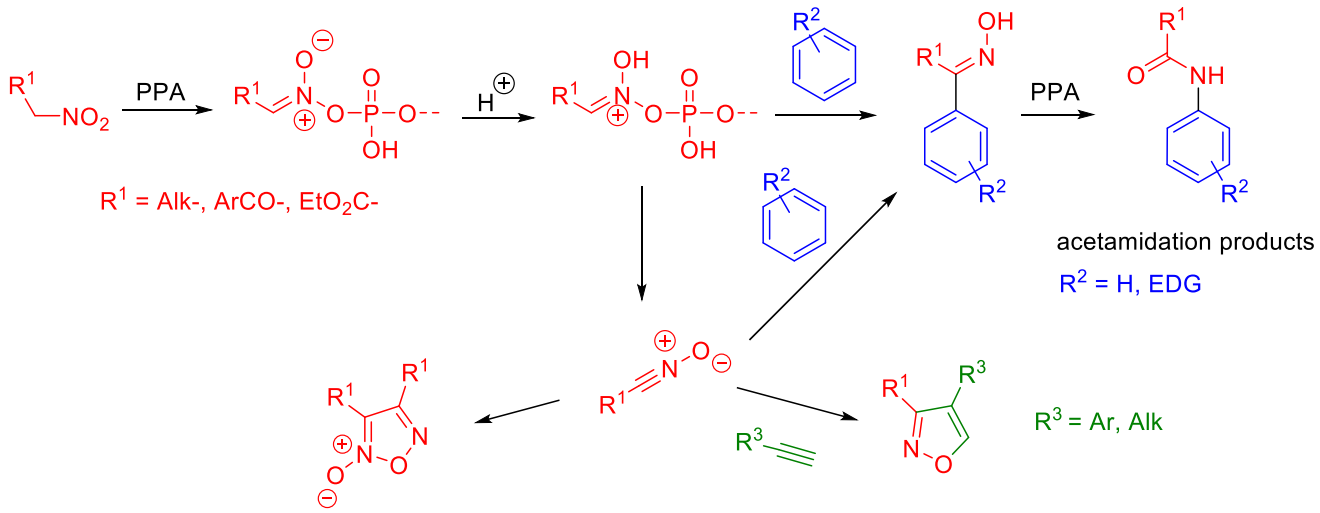

Figure 1. Key reaction routes considered in the report

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

QUANTUM-CHEMICAL MODELING OF AMINOCHLOROPYRAZOLE FORMATION REACTION BY THE ACTION OF THIONYL CHLORIDE ON AZIDOPYRAZOLE

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Pyrazole derivatives belong to aromatic heterocyclic compounds which are widely used in synthetic organic and medicinal chemistry [1]. *Ortho*-substituents in aryl azides play significant role in reducing the energy barrier for the formation of nitrenes due to the appearance of cyclic transition states [2]. Azidopyrazoles are precursors for the synthesis of biologically active small molecule inhibitors of factor Xa, which plays a central role in the blood coagulation cascade [3].

Recently, we have discovered the influence of the arrangement of the azide and carboxyl groups in the pyrazole ring on the course of the esterification reaction [4]:

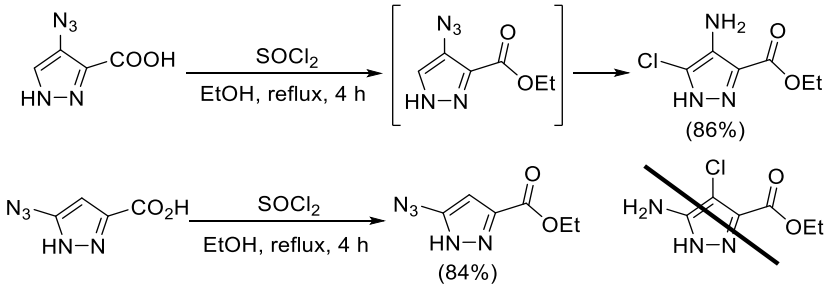

Figure 1. Experimental results of the esterification reaction.

We made an assumption about the acid-catalyzed destruction of the azide. A quantum chemical study of isomeric intermediates in the proposed mechanism of the discovered reaction was carried out for ethyl 3-azido-1*H*-pyrazole-5-carboxylate and ethyl 4-azido-1*H*-pyrazole-5-carboxylate (Figure 1) using the PBE1PBE/def2-TZVP calculations. [5].

The acidic destruction of azide leads to the formation of a nitrenium ion. For the 4-azidopyrazole system, a specific interaction of the ethyl carboxylate group and the nitrenium center with the formation of a bicyclic structure, which was not previously found in the literature, was proposed:

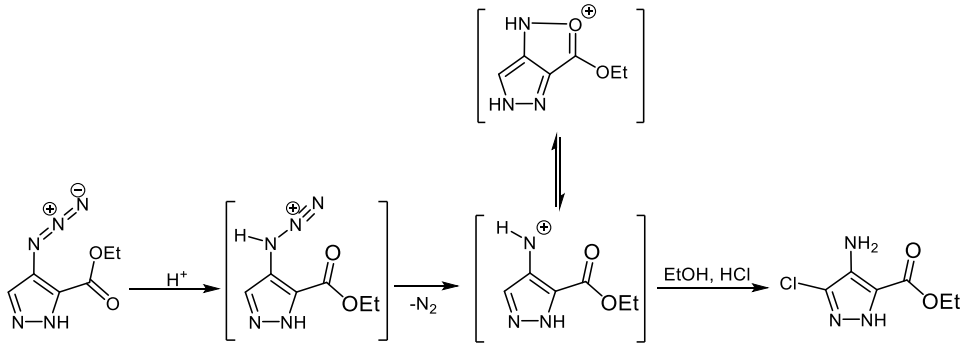

Figure 2. The proposed mechanism of the formation of 4-amino-3-chloro-1*H*-pyrazole-5-carboxylate.

Thus, fundamental differences in the reactivity of 3- and 4-azido-1*H*-pyrazole carboxylates were established and proved by the methods of computational chemistry. The directing effect of the carboxyl group on the reduction of the barrier of the elimination reaction of the nitrogen molecule during the decomposition of the azide is shown. The mechanism of the studied reaction is proposed.

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A ROUTE TO CYCLOPROPANES FROM ALKENE-TETHERED 5-IODO-1,2,3-TRIAZOLES

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Diazo compounds represent a well-known class of highly reactive valuable synthetic intermediates being utilized in the preparation of a great variety of functionalized molecules. Despite an apparent synthetic utility of diazo compounds, there are several drawbacks of their application regarding potential safety risks. Therefore, it is more preferable to use some stable substances capable of transforming to diazo compounds *in situ* upon a special treatment. Some types of 1,2,3-triazoles can serve as diazo precursors *via* electrocyclic ring-opening. In particular, the corresponding ring-chain tautomerism is well-established for *N*-sulfonyltriazoles and triazolopyridines. In the presence of transition metals or Lewis acids as well as under thermal or photochemical activation these compounds can be used for a generation of (metal) carbenes. This methodology is being extensively studied in the last few years and is successfully employed in design of efficient approaches to various structures, including pharmaceutically relevant and natural compounds.

Recently we developed the approach to various 1,2,3-triazole-fused heterocycles *via* intramolecular nucleophilic substitution in 5-iodotriazoles bearing a pendant nucleophilic group [1-4]. Due to the ring strain and the formation of aromatic system these compounds are prone to electrocyclic ring opening to form diazo compounds.

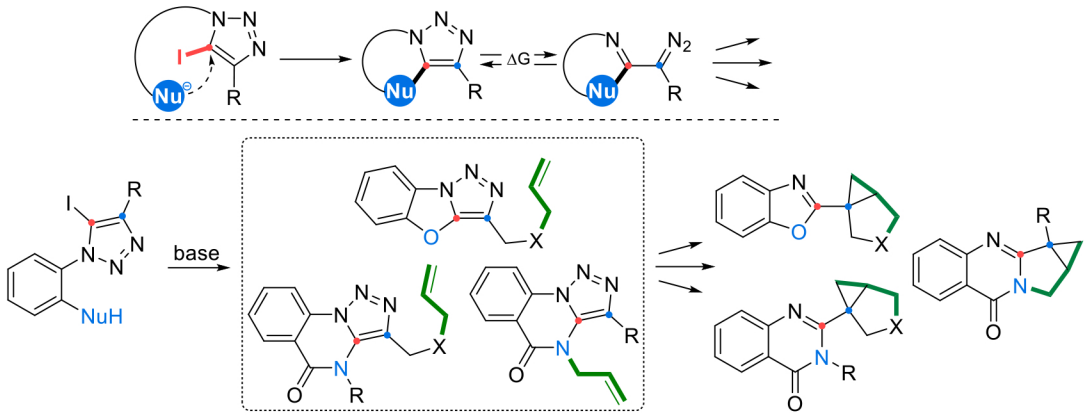

Figure 1.

Herein we utilized this approach to synthesize bicyclo[N.1.0]alkane derivatives comprising benzoxazole and quinazolinone motif. It was found that nucleophilic substitution in 2-(5-iodotriazolyl)phenols, containing double bond, affords bicyclo[N.1.0]alkane derivatives in good yields. The best yields were obtained in non-polar solvents, the formation of Δ^2-pyrazolines is predominant in trifluoroethanol in most cases.

The base-induced cyclization of 2-(5-iodotriazolyl)benzamides produces either bicyclo[N.1.0]alkane derivatives or triazoloquinazolinone derivatives depending on the position of double bond in molecule. Triazoloquinazolinones were shown to participate in Rh(II)-catalyzed intramolecular C-H insertion reactions.

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Acknowledgements. This work was supported by the Russian Science Foundation (project No 21-73-00161

STUDY OF THE PROPERTIES AND STABILITY OF ARENDIAZONIUM TRIFLATES, TOSILATES AND TETRAFLUORBORATES IN THE GAS PHASE BY THE MASS SPECTROMETRY METHODS

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Arendiazonium triflates $ArN_2^+TfO^-$ (ADTP) are more stable than tetrafluoroborate ($ArN_2^+BF_4^-$) and tosylate ($ArN_2^+TsO^-$) diazonium salts (DS) [1]. At the same time, ADTP show high reactivity in typical DS reactions in combination with high solubility, both in polar and non-polar solvents [2]. However, the behavior of the DS in the gas phase is almost unexplored region. Mass spectrometry methods are very rarely used in the chemistry of DS, while only some arendiazonium tetrafluoroborates have been investigated [3], and the influence of the nature of XDS counterions on the characteristics of DS mass spectra is unknown.

We investigated the properties of a series of DS $ArN_2^+X^-$ (X = TfO^-, TsO^-, BF_4^-) in the gas phase by mass spectrometry using electrospray ionization (ESI). All DS form salt cluster particles $(ArN_2^+)_nX^-_{n-1}$. It was revealed that in the gas phase, in addition to fragmentation processes, there is the generation of benzyne intermediates (derivatives of cyclohexa-1,3-dienine, RC_6H_3) followed by polymerization.

The comparative stability of a number of nitro-substituted DSs was studied at different fragmentation energies, and the curves of the dependence of the fragmentation degree on the energy in the collision cell were plotted. To describe the effect of the anion nature, the fragmentation of cluster particles containing two diazonium cations and an anion was investigated. As a result, the fact of a powerful stabilizing effect of anion on the stability of diazonium cations in clusters was revealed. In the initial mass-spectra and fragmentation spectra of cluster particles, lines corresponding to the loss of nitrogen are completely absent; the only way of fragmentation of salt cluster particles is the loss of a cation-anion pair, followed by the destruction of free diazonium cations (DC) at high collision energies. In this case, DCs in the cluster fragmentation spectra are observed up to energies of 40 eV, in comparison with free DCs, the destruction of which occurs completely already at energies less than 5 eV. The stabilization of diazonium cations in clusters depends on the nature of the anions and the following order of this stabilization is established: $TfO^- \approx TsO^- > BF_4^-$.

It is shown that the observed transformations and the regularities of the DS reactions in the gas phase are in agreement with the results of the quantum-chemical simulation of DFT B3LYP in the aug-cc-pvdz basis. The results obtained predict previously unknown DS reactions in the gas phase and open up new possibilities for their synthetic use.

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$GaCl_3$-MEDIATED INTERACTION OF DONOR-ACCEPTOR CYCLOPROPANES WITH DIAZO ESTERS

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The chemistry of cyclopropanes containing donor and acceptor substituents (DAC) has lately been attracting an increasing attention of scientists due to their exceptional synthetic potential. The push−pull effect of donor and acceptor substituents in DAC causes a strong polarization of the vicinal C−C bond, which enables its opening and implementation of processes involving this three-carbon synthon. Attempts to conduct direct formal (3+3)-cycloaddition under typical conditions result in the loss of a nitrogen molecule and formation of products of C–C coupling of both substrates — substituted alkenes and cyclopropanes. Moreover, the main pathways are determined by the addition of a diazo ester to 1,3-zwitterionic intermediates being generated, followed by carbocationic rearrangements and fragmentation [1].

A separate approach in the chemistry of DAC, in particular 2-arylcyclopropane-1,1-dicarboxylates (ACDC) **1**, involves the reactions that occur with 1,2-hydride shift in pre-generated 1,3-zwitterion **2** [2]. This process is very typical if anhydrous gallium trichloride is used.

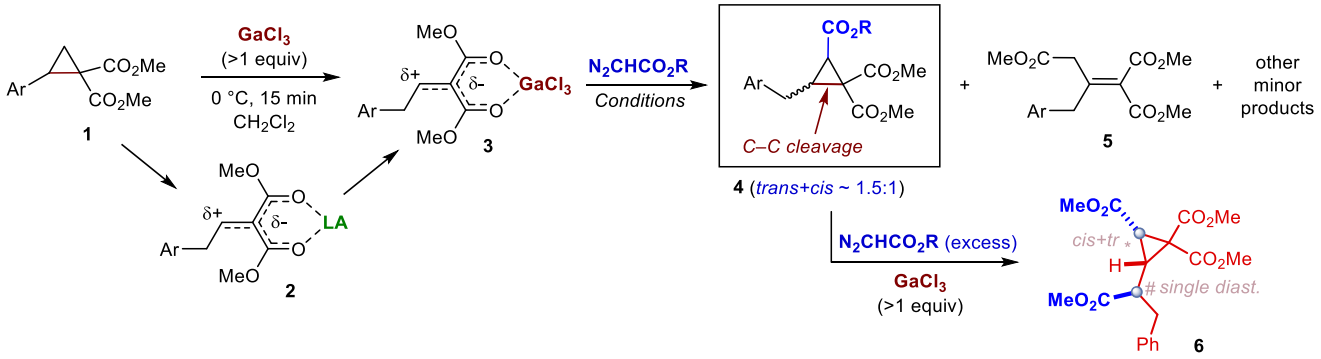

Figure 1. $GaCl_3$-Mediated interaction of donor-acceptor cyclopropanes with diazo esters

Herein we demonstrated a new ionic cyclopropanation process involving the addition of diazo esters to donor−acceptor cyclopropanes (DAC) activated by $GaCl_3$. The reactions occur via 1,2-zwitterionic gallium complexes **3** with elimination of nitrogen in all cases to give 1,1,2,3-tetrasubstituted cyclopropanes **4** as the main products [3]. Also, a number of related processes with the formation of various polysubstituted cyclopropanes, alkenes, and cyclobutanes, including products of multiple diazo ester addition, have been developed. It should be noted that both reaction pathways giving isomeric compounds **4** and **5** practically do not change, which does not allow one to obtain each of them selectively. Likewise, we failed to make the formation of cyclopropane **4** a stereoselective process (the ratio of *trans* and *cis* isomers remains at *ca*. 1.5:1 level). Obtained by the developed method tetrasubstituted cyclopropanes are themselves activated cyclopropanes such as DAC and can be used for further synthesis in this capacity. An activation of a three-membered ring in cyclopropane **4** in the presence of $GaCl_3$ leads to further C–C cleavage of the cyclopropane ring and subsequent reaction with 2nd MDA molecule giving compound **6**.The mechanisms of the occurring processes, as well as the structures and stereochemistry of a rich range of products formed, are discussed in detail.

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Acknowledgements. This work was funded by the Russian Foundation for Basic Research (RFBR) according to the research project № 18-33-01000 (mol_a).

α-DIAZOMETHANE SULFONAMIDE – NOVEL TYPE OF DIAZO REAGENT

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Diazo compounds have a unique role in organic chemistry, mainly as carbene precursors, but also their 1,3-dipole character is often used. By now, a large number of diazo compounds with an α-Heteroatom are known. However, despite synthetic versatility of diazo compounds and significant prominence of sulfonamide functional groups in drug design, to our surprise diazomethane sulfonamides **1** remain a rather unexplored type of diazo reagents. Therefore, we decided to synthesize diazomethane sulfonamides and investigate their chemical transformations.

Acetyl derivatives **2** were used as precursors of diazomethane sulfonamides **1**. Under weakly basic conditions, compounds **2** were easily deacylated to form the target compounds. Unfortunately, *α*-diazomethane sulfonamides were obtained from only *N,N*-disubstituted diazo ketosulfonamides (Figure 1) [1].

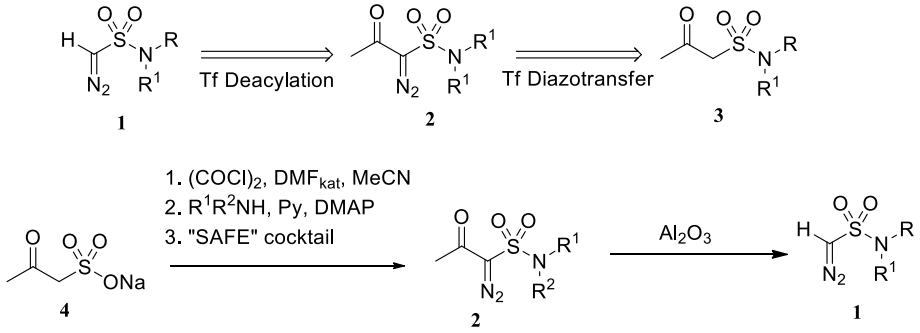

Figure 1. Retrosynthetic analysis of target molecules and their synthesis.

The study of the reactivity of diazomethane sulfonamides was mainly concerned with the consideration of various cycloaddition reactions. Diazomethane sulfonamides have been involved in a wide range of transformations with various unsaturated compounds:

1. with acetylenes to form pyrazoles **5**, this reaction can also be carried out in an intramolecular format;
2. with arendiazonium salts to form tetrazoles **6**;
3. in three-component reaction with aldehyde and amine to form triazolines **7**.

The mentioned triazolines can be introduced into subsequent oxidation affording 1,2,3-triazoles **8** (Figure 2) [2,3].

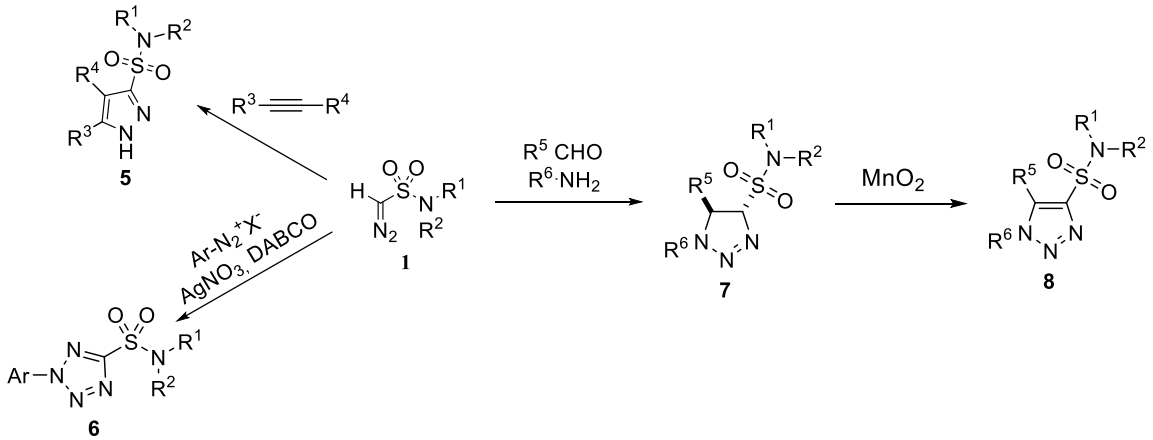

Figure 2. Some chemical transformation of diazomethane sulfonamide.

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PHOTOCHEMICAL SYNTHESIS OF AZAHETEROCYCLIC COMPOUNDS FROM ARYL NITRENES

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The development of photochemical synthesis of azaheterocyclic compounds from aromatic azides is interesting due to the simplicity of the synthesis. At the first stage of the reaction the photochemical decomposition of aryl azides **1** initiates cascade of reversible structural rearrangements of aryl nitrenes **A** to 1,2-didehydroazepines **B** and **B'**.

The reactions of these intermediates with different nucleophiles form the wide variety of products. It was found that the nature of the solvents determines the direction and efficiency of the formation of various azepine-containing heterocyclic compounds.

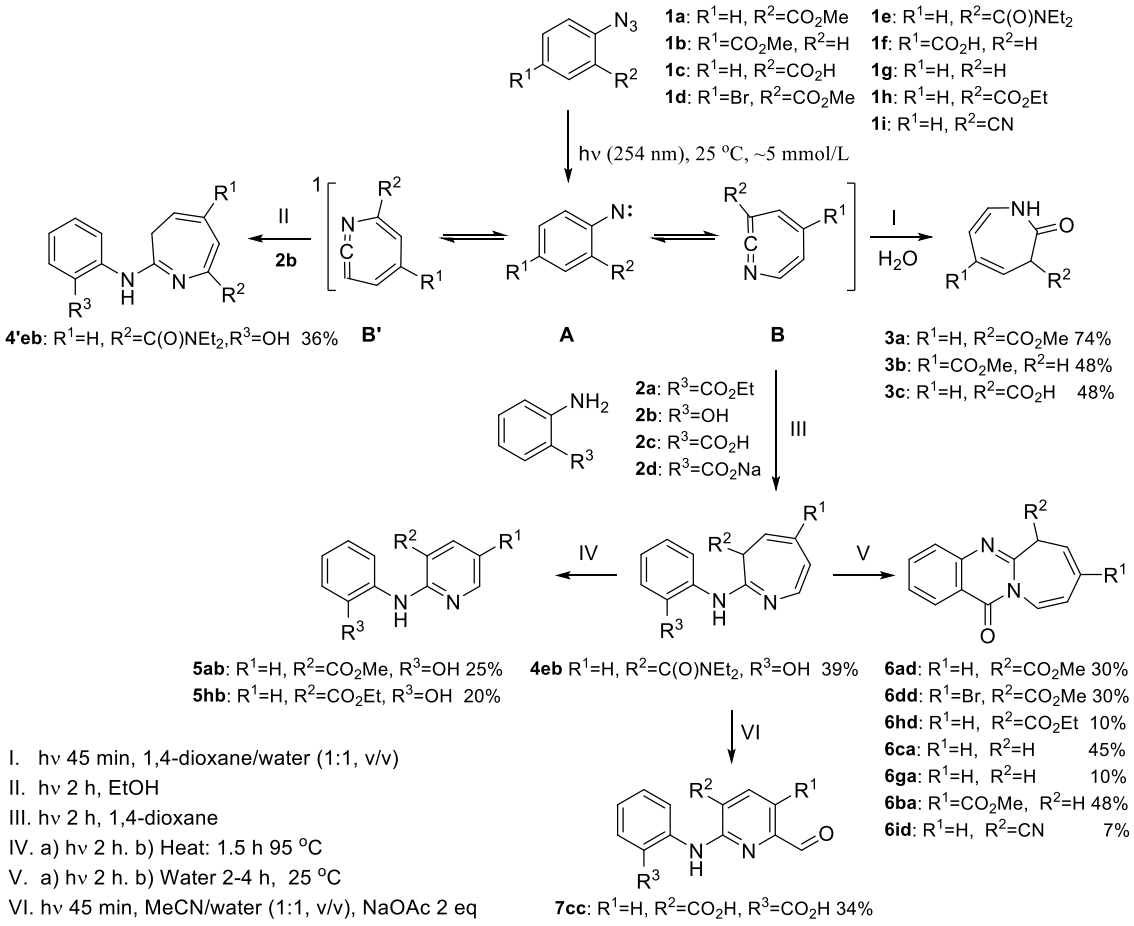

Figure 1.

The structures of the isolated compounds were determined by NMR spectroscopy and MS EI (70 eV), the structures of compounds **3a**, **5ab** and **6ad** were confirmed by X-ray structural analysis (carried out by G.K.Fukin, Institute of Organometallic Chemistry, RAS).

For example, azepino[2,1-*b*]quinosolines **6** can be obtained by cyclocondensation of 2-anthranilo-3H-azepines in an organo-aqueous solvents, compounds **5** can be obtained by heating of 2-anilino-3H-azepine-3-carboxylates in MeCN or in aqueous MeCN.

Thus, the wide variety of heterocycles can be obtained by varying the nucleophile added to cyclic ketenimine **B/B'**, using different solvents and synthesizing at different temperatures.

[2+2+1] GOLD-CATALYZED SYNTHESIS OF FULLY SUBSTITUTED 1,3-OXAZOLES FROM ALKYNYLSULFONES

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Gold-catalyzed reactions of alkynes found the wide application in the synthesis of various carbo- and heterocyclic structures [1]. In particular, the oxidative transformations of gold *α*-oxo carbenes generated from alkynes are of special interest due to the possibility of a facile growth of the molecular complexity using relatively small building blocks [2]. While the plethora of such reactions of propiolate alkyne substrates are known, only a few cases of the use of related alkynylsulfones has been described to the date [3,4].

1,3-Oxazole derivatives attracts a great attention due to their numerous valuable biological activities [5]. Therefore, the development of new effective synthetic strategies for assembly of highly substituted 1,3-oxazole framework is in the high demand. Recently, in our group the [2+2+1] gold(I)-catalyzed oxidative heterocyclization of propiolates to furnish 4-acylsubstituted oxazoles was developed [6]. Based on this, we suggested that alkynylsulfones can act as an alternative to propiolates in this process. Here we report on [2+2+1] gold(I)-catalyzed synthesis of fully substituted 1,3-oxazoles from alkynylsulfones (Figure 1). This highly selective annulation proceeds smoothly under mild conditions ($Ph_3PAuNTf_2$ 5 mol %, 60 °C, 3 h, the reacting nitriles serve as solvents) and exhibits a high functional group tolerance and the yields up to 85%).

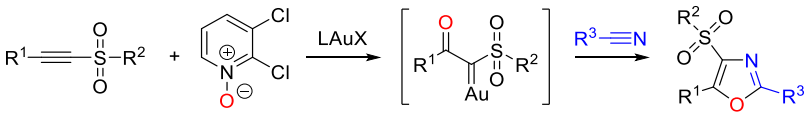

Figure 1. [2+2+1] Gold-catalyzed synthesis of fully substituted 1,3-oxazoles from alkynylsulfones.

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SYNTHESIS AND PROPERTIES OF HETEROCYCLOALKYNES FUSED TO A HETEROCYCLIC CORE

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Cyclic alkynes are unique strained organic molecules which are of great interest for both chemists and biologists [1]. Cycloalkynes have found a broad application as reagents for biorthogonal bioconjugation due to their selective high reactivity towards different «alkynophiles» (azides [2], diazo compounds [3]). These reactions can be carried out either with modified biopolymeric molecules or with metabollicaly labeled cells and even organisms.

Despite the fact, that numerous cycloalkyne-based reagents have been synthesized and are in use [4], the search for new cycloalkynes with improved synthetic accessibility, stability and some additional properties such fluorescence is in great demand.

In our research we combined two well-known strategies [5] to creation new cycloalkyne molecules – annulation with an additional ring and introduction of a σ-acceptor into the cycle to the propargylic carbon atom. The general synthetic approach to all target structures is based on the electrophile-promoted cyclization and the Sonogashira coupling for the formation of a heterocycle with essential functional groups followed by the Nicholas reaction for the closure of a strained alkyne cycle. Following this way we were able to synthesize stable heterocyclonynes, while their 8-membered homologs were kinetically unstable.

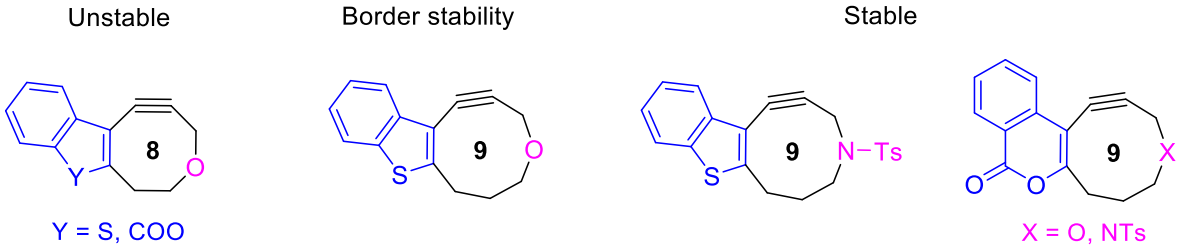

Figure 1. Heterocyclononynes fused to benzothiophene and isocoumarin.

Using experimental and theoretical studies the similar reactivity of stable cyclononynes and unstable cyclooctynes towards organic azides was discovered with the crucial influence of both structural parameters into the close reactivity. The most reactive towards azides azacyclononyne fused to a benzothiophene, was also reactive in cycloaddition with diazocarbonyl compounds and diazosulfonamides.

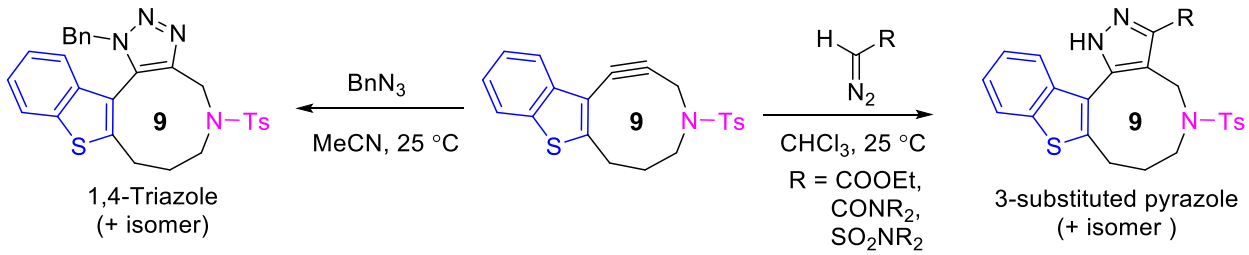

Figure 2. Cycloaddition of azaxyxlononyne with benzyl azide and diazo compounds.

The details of cyclononynes synthesis, reactivity with azides and diazo compounds, and the applicability of these reactions for bioconjugation will be discussed.

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A 'SULFONYL-AZIDE-FREE' DIAZO TRANSFER REACTION IN AQUEOUS MEDIA FOR PARALLEL AND DIVERSITY-ORIENTED SYNTHESIS

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Until now, diazo transfer remains one of the most popular methods for the preparation of diazocarbonyl compounds, however, in its classical performance, it is not devoid of some drawbacks. Recently, we have developed 'sulfonyl-azide-free' (SAFE) protocol for diazo transfer in an aqueous medium.[1-3] The generation of a water-soluble diazo transfer agent *in situ* allows one to avoid working with an explosive sulfonyl azide and to isolate the target diazo compounds by conventional extraction without the use of chromatography.

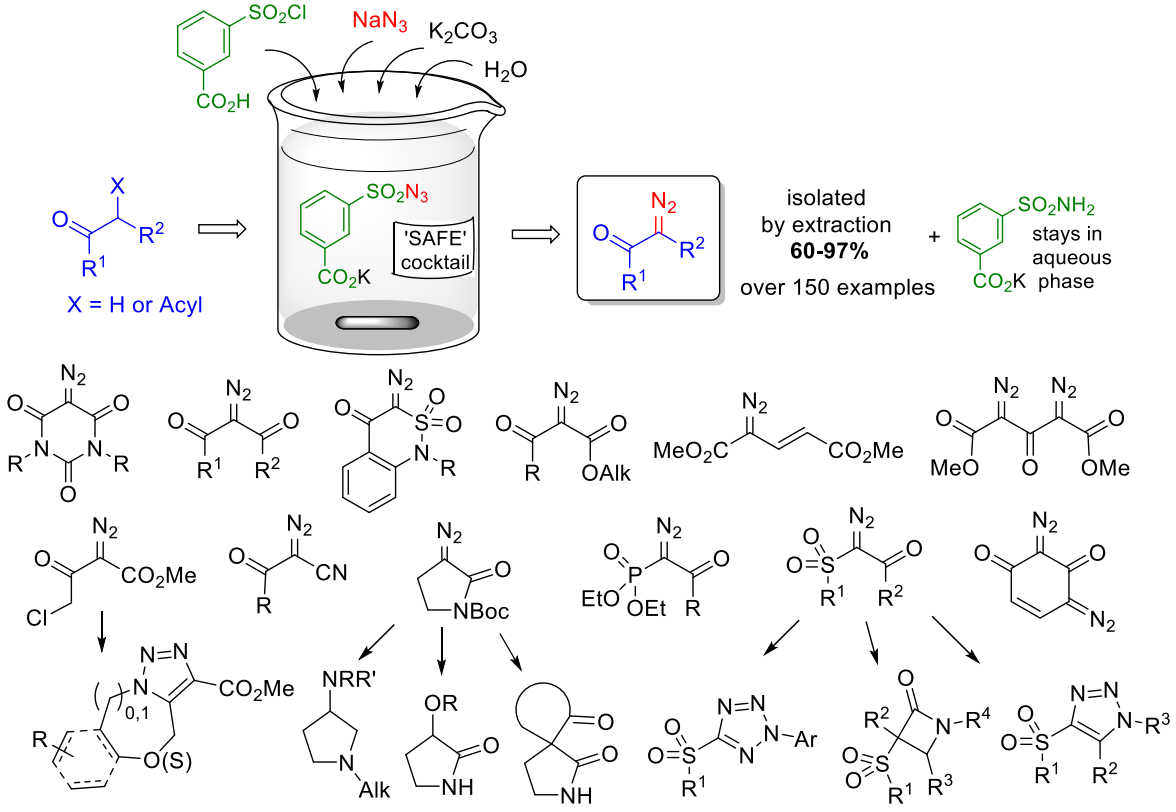

Figure 1. 'Sulfonyl-azide-free' (SAFE) protocol for diazo transfer in an aqueous medium and some transformations of the obtained diazo compounds.

The method has been found workable for a wide range of structurally diverse, active-methylene substrates and produced the respective diazo compounds in high product yields and purities. It is applicable to producing diazo compounds in an array format as well as in multigram scale. The range of chemistries applied to the evolution of the diazo compound scaffold can be expanded so as to enable diversity-oriented synthesis of skeletally unique compounds.

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GOLD-CATALYZED ANNULATION OF *N*-ALLYLYNAMIDES WITH BENZOFUROXANS VIA CYCLOPROPANATION OF ALFA-IMINO GOLD CARBENES

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In the last decade, an extraordinary progress was achieved in transformations involving gold carbene species [1]. Benzofuroxan has been recently proposed as an effective reagent for the gold-catalyzed generation of 2-amino-7-nitroindoles from ynamides (Figure 1, A) [2]. The key step of this reaction is the CH-insertion of gold α-imino carbene into the nitrophenyl substituent; the latter is generated via the ring-opening of the furoxan. Inspired by this work, we hypothesized that benzofuroxans could also serve as a source of gold α-imino carbenes for intramolecular cyclopropanations [3]. Indeed, the gold-catalyzed reaction between *N*-allylynamides and benzofuroxans leads to 3-azabicyclo[3.1.0]hexan-2-imines (Figure 1, B). This highly selective annulation proceeds smoothly under mild conditions (Ph_3AuNTf_2 5 mol %, PhCl, 60 °C) and exhibits a high functional group tolerance (up to 96%, 20 examples). The obtained cyclopropanated products represent a useful synthetic platform with easily modulated substitution pattern as was demonstrated by post-functionalizations.

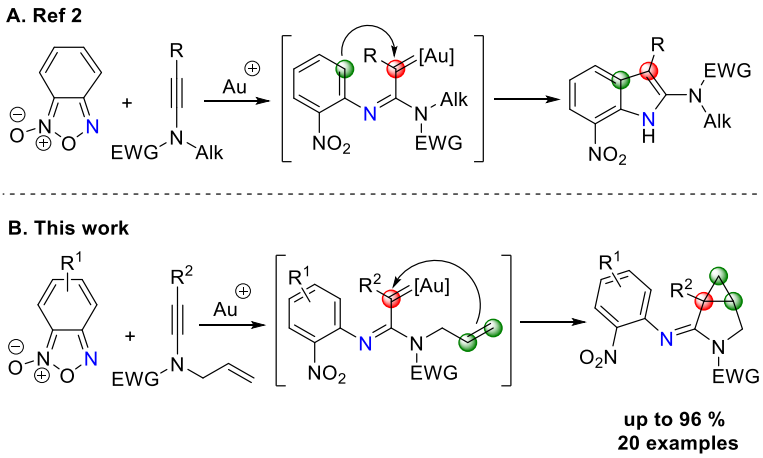

Figure 1. Gold-catalyzed annulations of ynamides with benzofuroxans.

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HOW DO DIAZONIUM SALTS BEHAVE IN DEEP EUTECTIC SOLVENTS?

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In recent years, deep eutectic solvents (DESs) attracted intensive attentions as less expensive, easily synthetically accessible, nontoxic and benign solvents turning to be a good and *green* alternative to volatile organic solvents. [1]

Despite the increasing use of DESs in organic synthesis, they have scarcely used as solvents in the reactions of diazonium salts. [2]

Following our previous research, which was directed towards developing the synthetic potential of arenediazonium salts in Cu catalyzed reactions [3], we decided to test arenediazonium tetrafluoroborates **1** in Ullmann reactions via copper-catalyzed coupling [4] and we resolved to employ DES formed by KF as hydrogen bond acceptor (HBA) and glycerol as hydrogen bond donor (HBD) as reaction media. In absence of Cu as catalyst a controlled reduction of diazonium salts took place. We proposed a plausible mechanism where a relatively fast (strictly depending on the electronic effects of the substituents bound to the aromatic ring) reduction reaction occurs initiated by the formation of a glycerolate-like species. On the contrary, in the presence of Cu as catalyst, the homo-coupling products **3** were obtained in good yields. In order to explain this different behavior in the presence of Cu, in-depth mechanistic studies are underway. It must be emphasized that the literature shows only one relatively recent example of Ullmann homo-coupling of diazonium salts [5].

Interestingly, the behavior of salts in DES formed by glycerol (HBD) and KBr or tetrabutyl ammonium bromide (HBA) was completely different. In fact, brominated adduct **4** formed, in fairly good yields. To the best of our knowledge, this is the first example of a bromodediazotation of salts **1** carried out under *green* conditions in the absence of Cu as a catalyst.

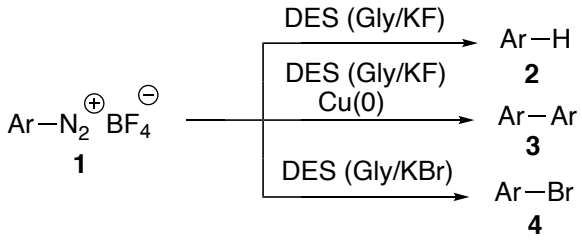

Figure 1. Diazonium salts in DESs.

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DESIGN, SYNTHESIS AND INVESTIGATION OF PHOTOPHYSICAL PROPERTIES OF NEW 5-ARYL-4-ARYLETHYNYL-1*H*-1,2,3-TRIAZOLES

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Last years, 1*H*-1,2,3-Triazoles are of increasing interest as one of the most promising classes of heterocyclic compounds for different purposes of bioconjugation, design of new catalysts, supramolecular ensembles, and polymeric materials. Today, a new field of application of triazoles as dyes and fluorophores is rapidly developing [1]. In the same time, 4-ethynyl-1*H*-1,2,3-triazole moiety were not previously used as linker for fluorophores. One of the most promising classes of triazole derivatives are 5-Iodo-1*H*-1,2,3-triazoles due to the possibility of involving in a wide range of C-I functionalization reactions [2]. In particular, the possibility to carried out 1-iodobuta-1,3-diynes in CuAAC and modification of obtaining compounds in cross-coupling reactions were shown by our research group [3].

The aim of this work was design, synthesis and investigation of photophysical properties of new 5-aryl-4-arylethynyl-1*H*-1,2,3-triazoles. The cycloaddition reactions of 1-iodobuta-1,3-diynes **1** with azide **2** were carried out in solvent-free conditions as it was described for previous examples. The cycloadditions proceeds proceed with high regioselectivity giving products **3** with from average to good yields. The Suzuki-Miyaura reaction was carried out using $Pd(PPh_3)_4$ as a catalyst and K_3PO_4 as a base and gave from average to high yields. (Figure 1)

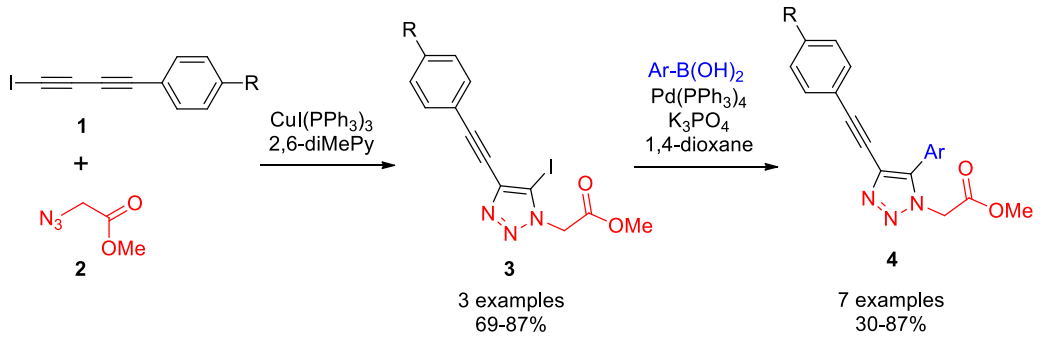

Figure 1. Synthesis of 5-aryl-4-arylethynyl-1*H*-1,2,3-triazoles.

Next, we investigated fluorescent properties and solvatochromic effects for synthesized compounds. The promising photophysical properties were demonstrate for all compounds **4** (Φ_F up to 64.5%, Stokes shifts up to 15815 cm^{-1}). The effects of the solvent on fluorescent parameters were demonstrate for two the most perspective compounds. [4]

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

THE USE OF A-DIAZO-Г-BUTYROLACTAMS IN THE SYNTHESIS OF NOVEL SPIROCYCLIC HETEROCYCLES

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Spirocyclic scaffolds represent a high value to produce biologically active compounds due to their inherent three-dimensional structure and limited conformational lability [1]. In addition, the frequent appearance of spirocyclic motifs in natural products generates interest in synthetic approaches aimed at the formation of such structures.

The Büchner-Curtius-Schlotterbeck reaction provides broad opportunities towards the synthesis of spirocyclic compounds. The result of this reaction is the insertion of the diazo compound backbone into the C–C bond of various cyclic ketones, which leads to ring expansion. The only cyclic α-diazocarbonyl compound employed in the insertion on C-C bond of cyclic ketones to date was α-diazo-γ-butyrolactone [2]. In continuation of the study of the synthetic potential of *N*-substituted α-diazobutyrolactams [3], our research was aimed at the possibility of obtaining on their basis of new spiro heterocycles.

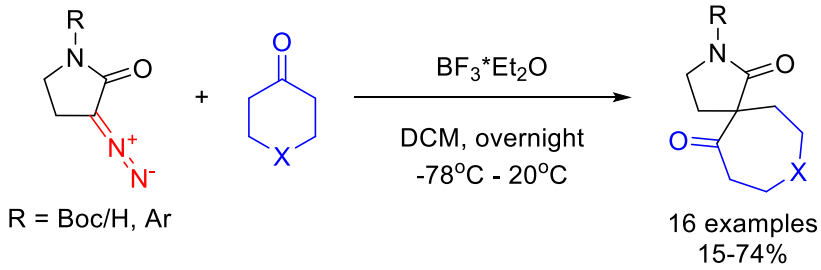

Figure 1. Büchner–Curtius–Schlotterbeck reaction of α-diazo-γ-butyrolactams

In this work we have described a novel approach to spirocyclic 2-pyrrolidones via the Büchner–Curtius–Schlotterbeck reaction of N-(hetero)aryl-, N-alkyl-, and N-Boc-protected 3-diazo-2-pyrrolidones. The best results were obtained using one equivalent of $BF_3 \times Et_2O$ and performing the reaction at –78°C. In total, we synthesized 16 spiro-pyrrolidones in 15–74% yields.

These findings substantially enhance the possibilities offered by cyclic α-diazocarbonyl compounds in constructing privileged spirocyclic scaffolds for drug design.

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AROMATIC AND HETEROAROMATIC DIAZONIUM TRIFLUOROMETHANESULFONATES: SYNTHESIS AND INVESTIGATION OF PROPETIES

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Aromatic and heteroaromatic diazonium tetrafluoroborates, sulfates and chlorides are widely used in organic synthesis [1]. In the last 20 years, diazonium sulfonate salts (tosylates, triflates, silicate sulfates, camphor sulfonates, etc.), which are characterized by stability, high solubility and reactivity, have been of greater interest in comparison with classical diazonium salts [2].

In our work, we investigated the reactions of diazotization of anilines, aminopyridines, and aminotriazoles in the presence of trifluoromethanesulfonic acid.

Anilines under these conditions are diazotized to form stable arendiazonium trifluoromethanesulfonates. These diazonium salts have high stability, reactivity, and good solubility in both polar and low-polar media [3].

2 - and 4-aminopyridines under these conditions are diazotized to form valuable pyridyltrifluoromethanesulfonates, and 3-aminopyridine forms a relatively stable disaonium salt, which can be converted to other valuable derivatives [4].

Aminotriazoles, which is characteristic of π-excess aminoheterocycles, are diazotized to form a stable diazonium salt. Such a diazonium salt enters into the typical reactions for diazonium salts more difficult than arendiazonium salts. But as a rule, it forms target products with high yields.

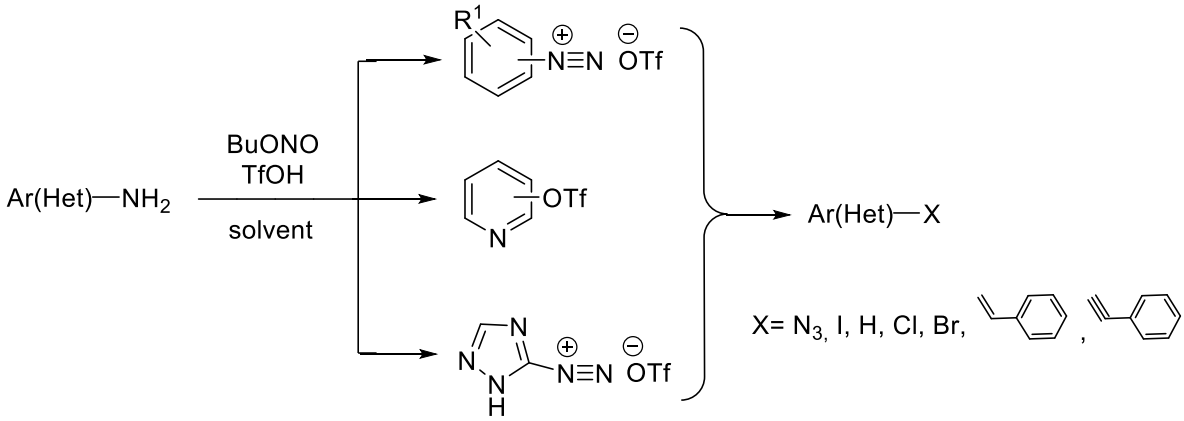

Figure 1. Diazotization of aromatic and heteroaromatic amines.

Thus, diazotization of aniline and aminoheterocycles in the presence of trifluoromethanesulfonic acid makes it possible to obtain aromatic and heteroaromatic diazonium salts with high stability, reactivity and good solubility, which distinguishes them from classical diazonium salts

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SYNTHETIC POTENTIAL OF 1,2,5-OXADIAZOLYL DIAZONIUM SALTS

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In a series of nitrogen heterocycles, 1,2,5-oxadiazoles (furazans) and their *N*-oxides (furoxans) became emergent scaffolds with strong application potential in various areas. Furazans possess a number of useful properties to be part of organic solar cells and exhibit various pharmacological activities [1]. On the other hand, furoxans correspond to an important subclass of heterocyclic pharmaceutical ingredients capable of exogenous release of nitric oxide (NO) [2]. In addition, furazan and furoxan subunits became essential structural motifs in modern energetic materials with excellent performance and a high level of environmental compatibility [3].

Despite numerous application patterns of 1,2,5-oxadiazoles, methods for their chemoselective functionalization are far less explored. In this presentation, we provide an overview of our recent investigations on an introduction of 1,2,5-oxadiazolyl diazonium salts in organic synthesis as useful precursors to promising organic materials and pharmacologically oriented compounds. It was found that stable 1,2,5-oxadiazolyl diazonium tetrafluoroborates **1** can be synthesized and isolated upon diazotization of the corresponding amino-1,2,5-oxadiazoles **2** with $NOBF_4$ [4]. Salts **1** are highly reactive and undergo azo coupling with electron-donating arenes resulting in a formation of (*E*)-arylazo-1,2,5-oxadiazoles **3** which are capable of visible light-induced photoisomerization to (*Z*)-arylazo-1,2,5-oxadiazoles **3'**, which are of interest in photopharmacology [5]. Azo coupling of diazonium salts **1** with potassium nitroformate in acidic media proceeds further with an assembly of the azasydnone ring. Both (furazanyl)- and (furoxanyl)azasydnones **4** exhibited high NO-donor properties since azasydnone motif is also able to release NO under physiological conditions [6]. Chemoselective reduction of the diazonium moiety in **1** results in a generation of 1,2,5-oxadiazolylhydrazines which are unstable upon isolation but can be trapped with aldehydes to afford a series of the corresponding hydrazones **5** [7].

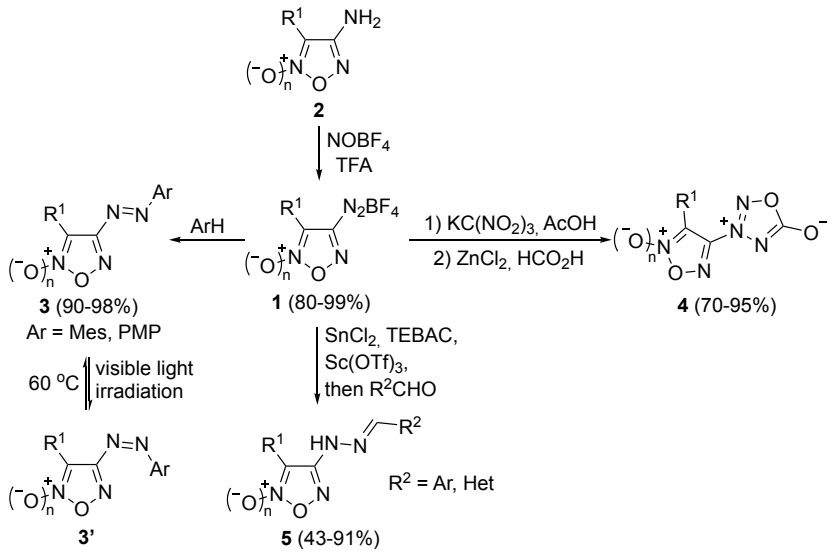

Figure 1. Synthetic potential of 1,2,5-oxadiazolyl diazonium tetrafluoroborates.

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ARENE (HETEROARENE) DIAZONIUM SULFONATES: SYNTHESIS, STABILITY, STRUCTURE, REACTIVITY

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Methods of preparation, stability, and properties of arene (heteroarene) diazonium sulfonates (ADS) Ar (Het) N_2^+ RSO_3^- (RSO_3^- = TfO, TsO, camphorsulfonate; Het = pyridines and pyridines-N-oxides) are discussed. It was found by DSC and isothermal flow calorimetry that ADS is more stable in dry storage than arendiazonium tetrafluoroborates. It is shown that ADS, in contrast to traditional diazonium salts, are soluble in non-polar solvents and under these conditions show some new for diazonium chemistry properties.

Quantitative relationships have been established between the structure of diazonium salts, including the nature of aryl (heteroaryl radicals) and counterions, calculated quantum chemical indices, on the one hand, and reactivity in de-diazonation and azo-coupling reactions, on the other hand, which makes it possible to predict the activity of ADS in the most important reactions of diazonium compounds.

A “method for tracing the molecular orbitals” (MTMOs) has been proposed, which allows, when scanning the C-N_2^+ bond length and quantum-chemical calculations, to estimate the contribution of each MO to the binding of a diazonium group to an aromatic radical, which gives a new look at the nature of the Ar-N_2^+ bond in diazonium compounds.

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[4+1] FORMAL ANNULATION OF 2-ALKYL-2*H*-AZIRINES WITH DIAZO COMPOUNDS FOR THE SYNTHESIS OF FUNCTIONALIZED 1-PYRROLINES

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A 1-pyrroline is one of the most important and widely studied pyrrole derivatives. Compounds, containing the structural unit of 1-pyrroline, are attractive target compounds of medicinal chemistry due to their various biological activities. In particular, some 1-pyrroline derivatives exhibit antidiabetic, antiviral, and antibacterial activities. A wide range of effective and inexpensive approaches to the synthesis of 1-pyrrolines have been developed. However, only some of them could be used for introduction of substituents in 3 and 4 positions of the pyrroline ring. Moreover, some of these methods require a high loading (up to 15 mol%) of expensive catalysts based on platinum group metals, which is their significant disadvantage [1].

In this work, we have developed a novel one-pot approach to the synthesis of 1-pyrroline derivatives **4** via the base-catalyzed anionic 1,5-cyclization of 4-alkyl-2-azabuta-1,3-dienes **3**. Such 2-azabutadienes **3** can be obtained by the Rh(II)-catalyzed reaction of diazo compound **1** with 2-alkyl-2*H*-azirine **2** [2] (Fig.1). It is remarkable that anionic 1,5-electrocyclizations are very rare [3], and the proposed method is the first example of 1-pyrroline synthesis via electrocyclization. This one-pot route makes it possible to obtain 1-pyrrolines **4** containing aryl, alkyl, and ester groups at positions 2–4 of the pyrroline system in good and excellent yields. The highest yields were obtained for pyrrolines **4** containing two ester groups at the C1 and substituents R2 and R3, differed from hydrogen. Importantly, 3,4-disubstituted pyrrolines **4** were obtained only as a 3,4-*trans*-pyrrolines (Figure1). An additional advantage of the developed method is an opportunity of using 5-alkoxy-4-alkylisoxazoles **5** as precursors of some 2*H*-azirine-2-carboxylates **4** [4].

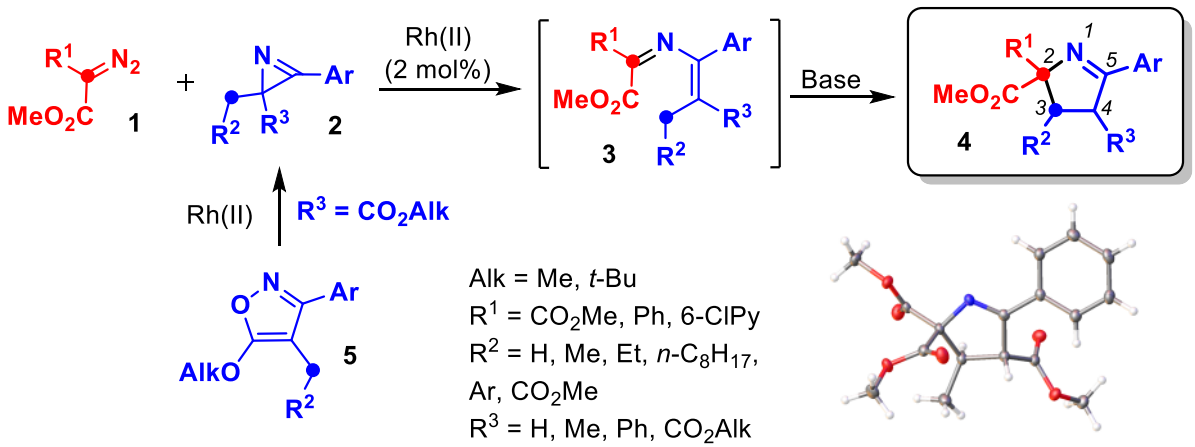

Figure 1. One-pot synthesis of 1-pyrroline derivatives

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PRODUCT SELECTIVITY OF THERMAL BUCHNER REACTION OF METHYL 2-(3-ARYLISOXAZOL-5-YL)-2-DIAZOACETATES WITH BENZENE, NAPHTHALENE AND MESITYLENE, AND RING-OPENING/CLOSING REACTION OF PRODUCTS

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Methyl 2-(3-arylisoxazol-5-yl)-2-diazoacetates **1** were synthesized and the product selectivity of their thermal Buchner reaction with benzene, naphthalene and mesitylene was studied. The reaction of the isoxazolyl-substituted diazoacetates with benzene gave a mixture of cycloheptatriene/norcaradiene isomeric adducts **6**, which are in a rapid equilibrium. Heating the same diazo compounds with naphthalene led exclusively to stable norcaradiene adducts **2**. In contrast, their thermal reaction with mesitylene gave only the products of carbene insertion into C–H bond of mesitylene **5**. According to DFT calculations, such a difference in the product selectivity of the thermal Buchner reaction of the diazoacetates with benzene, naphthalene and mesitylene is associated with the fact that the first two reactions proceed under kinetic control, and the last one under thermodynamic control.

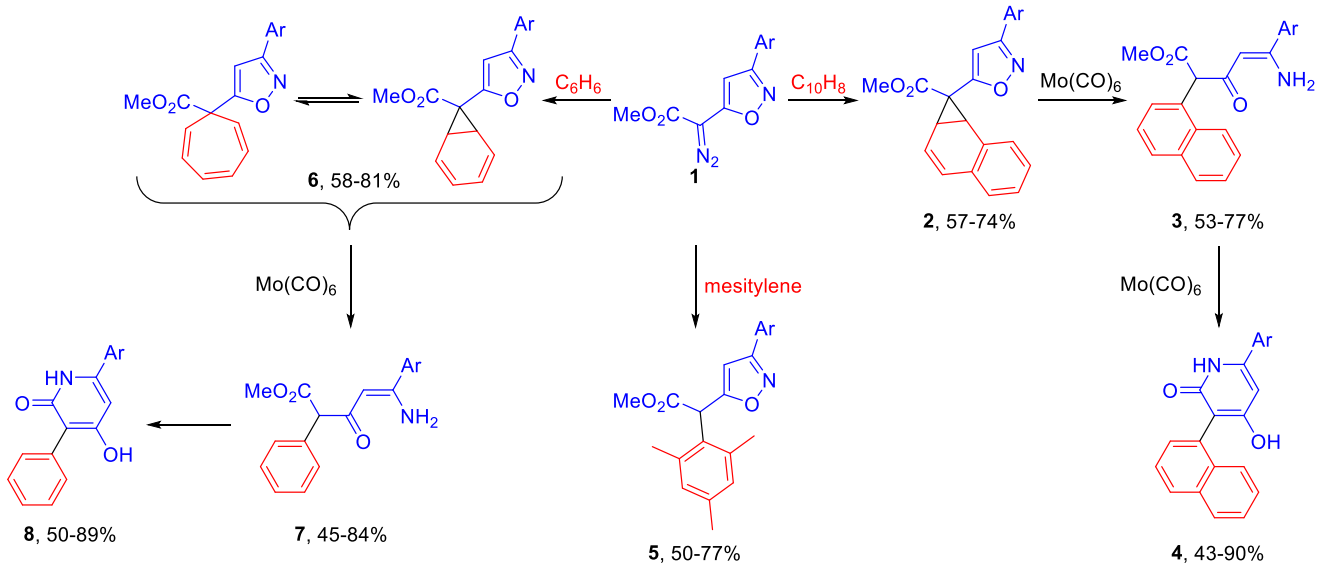

Figure 1.

Isoxazoles **2**, **5** and **6** synthesized were converted to a new family of functionalized enaminones, (*Z*)-methyl 5-amino-2,5-diaryl-3-oxo-2-arylpent-4-enoates **3** and **7** by reaction with $Mo(CO)_6/H_2O$ hydrogenative reagent, wherein $Mo(CO)_6$ catalyzes also the *retro*-Buchner reactions of the norcaradiene moiety of the starting compounds. The obtained enaminones **3** and **7** are convenient precursors of 3,6-diaryl-4-hydroxy-3-phenylpyridin-2(1*H*)-ones **4** and **8**, which were prepared from them under thermal conditions in good to high yields.

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Acknowledgements. This work was supported by the Russian Science Foundation (project No 19-13-00039).

INFLUENCE OF WATER ON PHOTOINITIATED FORMATION OF 2-AMINO-SUBSTITUTED 3H-AZEPINES FROM ARYL AZIDES

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Photoinitiated reaction of aryl azides **1** with nucleophilic substances **2**, were received corresponding 3H-azepines **3** (**aa** - N,N-diethyl-2-((2-hydroxyphenyl)amino)-3H-azepine-3-carboxyamide, **aa'** - N,N-diethyl-2-((2-hydroxyphenyl)amino)-3H-azepine-7-carboxyamide, **ab** - N,N-diethyl-2-phenylamino-3H-azepine-3-carboxyamide, **bb** - N,N-diethyl-2-phenylamino-3H-azepine-5-carboxyamide, **bc** - N,N-diethyl-2-((4-hydroxyphenyl)amino)-3H-azepine-5-carboxyamide). All compounds were isolated by preparative column chromatography and were characterized by mass spectrometry and NMR spectroscopy.

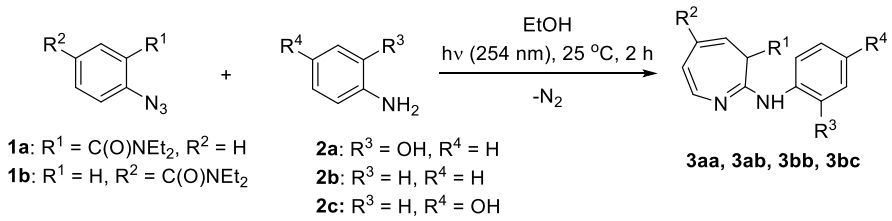

Figure 1. Reaction between aryl azides **1** and nucleophilic substances **2**

Photolyzed solutions of azide **1a** and amine **2a** in 1,4-dioxane gave only azepine **3a**. Though carrying out the same reaction in the ethanol gave two azepines **3aa** and **3aa'**.

It was found that even a small amount of water in the reaction mixture leads to an increase in the yield of compound **3aa'** and decrease of compound **3aa** at the same time. Thus, the ratio of the yields of products **3aa** and **3aa'** in 1,4-dioxane was 13: 1, in the 1,4-dioxane azeotrope (12% water) - 5:1, in a 1,4-dioxane-water mixture (56% water) - 4: 1, in a mixture of 1,4-dioxane-water (71% water) - 3: 1, in water - 2: 1. The influence of water on the yields can be explained by the difference in the rate of the reaction of the addition of the nucleophilic substance to the intermediates **C** and **C'**, which are in equilibrium. The similar pattern is observed with using aniline as a nucleophile.

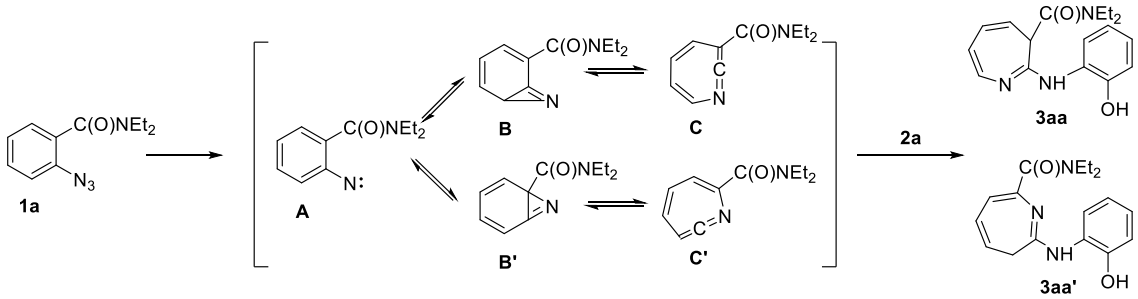

Figure 2. Presumed reaction mechanism

This assumption is also confirmed by the fact that the formation of the second 3H-azepine is not observed during the photoinitiated reaction between azide **1b** and amines (**2a** or **2b**).

The DFT/B3LYP/cc-pvtz method was used to calculate the geometric structure and vibration frequencies of intermediates **A**, **B**, and **C**, as well as the transition states between them. The search for transient states was carried out using the QST2 method. It was found that the transition from A to B occurs almost immediately, and the barrier to the transition from **B** to **C** is only 3.4 kcal/mol. Thus, the **A↔B↔C** process proceeds with a significant gain in energy ΔE = 20.44 kcal/mol and low activation barriers. This confirms the assumption of equilibrium between intermediates **C** and **C'**.

Rh(I)-CATALYZED TRANSFORMATIONS OF 1,2,3-THIADIAZOLYLIDENES

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One of the most synthetically attractive routes to preparing a variety of heterocycles from a common intermediate is the inter- and intramolecular reaction of metal carbenes, which are traditionally prepared by denitrogenative decomposition of diazo compounds [1–3]. In contrast to the α-diazo-carbonyl compounds and 1,2,3-triazoles widely used as precursors to metal carbenes, the synthetic potential of 1,2,3-thiadiazoles and the corresponding α-thiavinylcarbenes is relatively unexplored. Recently reported Rh(I)-catalyzed denitrogenative transformations of 1,2,3-thiadiazole derivatives demonstrated that α-thiavinylcarbenes are useful intermediates in the synthesis of sulphur-containing heterocycles [4–7]. To further explore the potential of 1,2,3-thiadiazoles in heterocycle synthesis, here we report some new Rh(I)-catalyzed transformations of 1,2,3-thiadiazolylidenes (Figure 1).

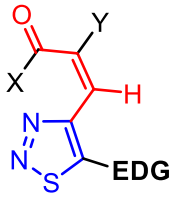

Figure 1. General structure of the 1,2,3-thiadiazolylidenes investigated in this study

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2-AZIDO-2*H*-AZIRINES: PREPARATION, ISOLATION AND USE IN CUAAC REACTIONS

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2-Haloazirine-2-carboxylic acids derivatives are synthetically available compounds that are increasingly used in the synthesis of various nitrogen-containing heterocycles [1]. Unique feature of 2-halogenazirines is their ability to exchange a halogen atom for N- or O-nucleophiles without destroying an azirine system [2,3]. In this work, we report a method for the substitution of a halogen atom in the azirine ring with an azido group to afford 2-azidoazirines, practically unexplored class of azirine derivatives.

2-Azido-2*H*-azirine-2-carboxylates/2-thiocarboxylates **2** were prepared from the corresponding 2-bromo-2*H*-azirine-2-carboxylic acid derivatives **1** in the system trimethylsilyl azide/triethylamine/DCM at room temperature. Using this protocol, we succeeded to obtain the first stable crystalline 2-azido-2*H*-azirine **2**. It was characterized by NMR and HRMS methods, its structure was confirmed by XRD analysis. The multi-stage catalytic mechanism of the formation of azidoazirines **2** from bromides **1** as well as the "structure – stability" relationship for these compounds is discussed in the report. Most of synthesized 2-azidoazirine-2-carboxylates are stable in solution at room temperature and can be successfully applied for the preparation of 2-(1,2,3-triazol-1-yl)-2*H*-azirine-2-carboxylates **3** via the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction. The one-pot protocol includes the synthesis of the 2-azidoazirines from 2-bromazirines **1** using the $TMSN_3/Et_3N$ system and the subsequent CuAAC reaction catalyzed by the CuTC/CuI/AcOH system. This method allows the installation of a variety of substituents including those with a functional group in both azirine and triazole parts of the triazolylazirinecarboxylates **3**.

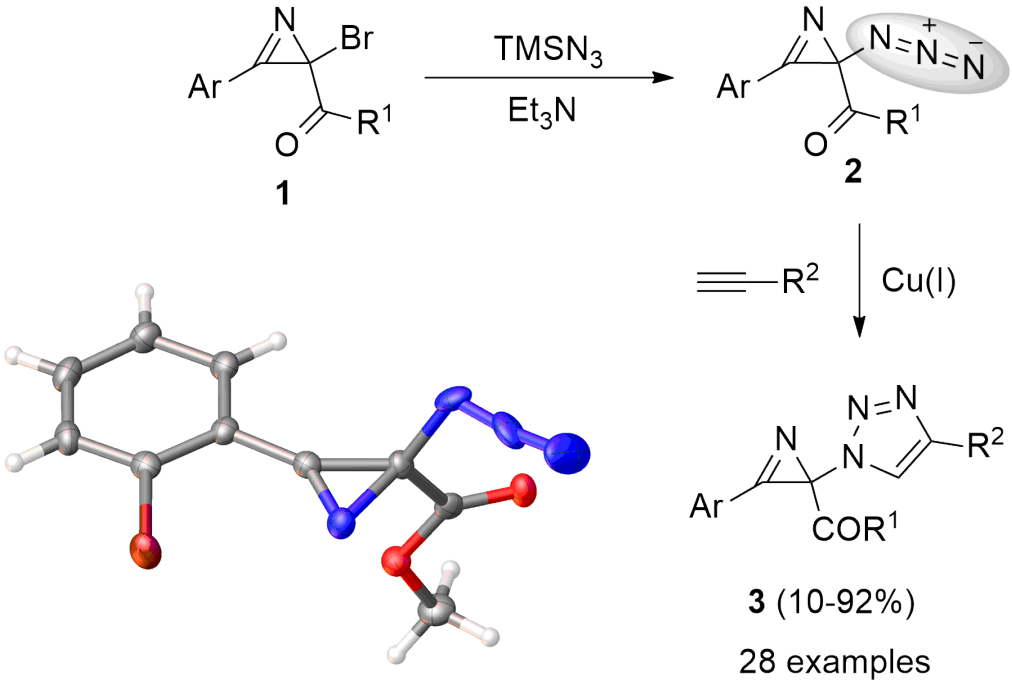

Figure 1. Synthesis of 2-azidoazirines and their derivatives.

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[(3-NITRO-1*H*-1,2,4-TRIAZOL-1-YL)-*NNO*-AZOXY]FURAZANS: ENERGETIC MATERIALS WITH N(O)=N–N FRAGMENT

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The strategy for the synthesis of substituted [(3-nitro-1*H*-1,2,4-triazol-1-yl)-*NNO*-azoxy]furazans **1–4**, in which the distal nitrogen of the azoxy group is bonded to the nitrogen atom of the azole ring, includes the reaction of 1-amino-3-nitro-1*H*-1,2,4-triazole (**5**) with 2,2,2-trifluoro-*N*-(4-nitrosofurazan-3-yl)acetamide (**6**) in the presence of dibromisocyanuric acid (DBI) followed by removing of the trifluoroacetyl protecting group to afford aminofurazan **1**. Substituted furazans **2**-**4** were synthesized by transformations of the amino group in aminofurazan **1** [1-2].

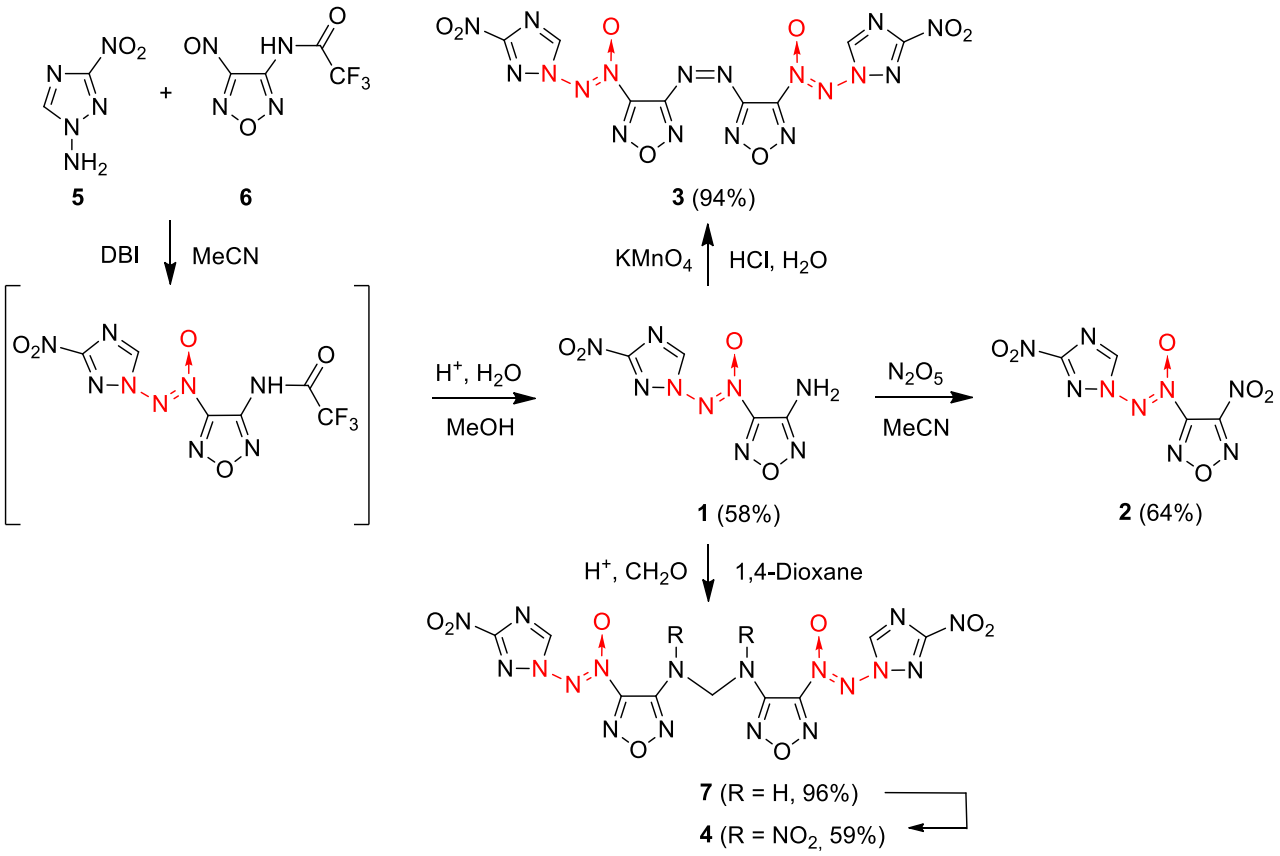

Figure 1. Synthesis of substituted [(3-nitro-1*H*-1,2,4-triazol-1-yl)-*NNO*-azoxy]furazans **1–4**.

The compounds synthesized are thermally stable (decomposition onset temperatures 147–228 °C), exhibit acceptable densities (1.77–1.80 g·cm^{-3}) and optimal oxygen balance (the oxidizer excess coefficients α = 0.42–0.71). Their standard enthalpies of formation (576–747 Kcal·kg^{-1}) were determined experimentally by combustion calorimetry and these compounds have been estimated as potential components of solid composite propellants.

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REACTION OF FRUSTRATED LEWIS PAIR WITH DIFLUOROCARBENE

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Fluorine-containing organic molecules play an important role in medicine and related. The one way to include fluorine atom in molecules is the addition of difluorocarbene to non-fluorinated compounds. The aim of this work is investigation the interaction of difluorocarbene with intramolecular frustrated Lewis pair (further *FLP*) based on *ortho*-substituted aniline

The synthesis of the investigated FLP is presented in **Fig.1**. FLP **2a-b** were obtained by the reaction of iPrOBpin with *ortho*-lithiated aniline **1a-b** (product of directed *o*-lithiation of aniline PhNR2 or halogen exchange of aryl halide with *n*-BuLi), FLP **2c-d** were generated *in situ* by the reaction aminophenols with HBpin. The next step was the reaction FLP **2a** with difluorocarbene (generated by decarboxylation of BrCF2CO2K) to form product **3a** (in DMF yield is 78%, in MeCN at 60°C yield is 94%). FLP **2b-d** in this reaction conditions formed similar products. Adducts **3a-d** was the first isolated compounds containing difluoromethylene link between nitrogen and boron atoms бора [1].

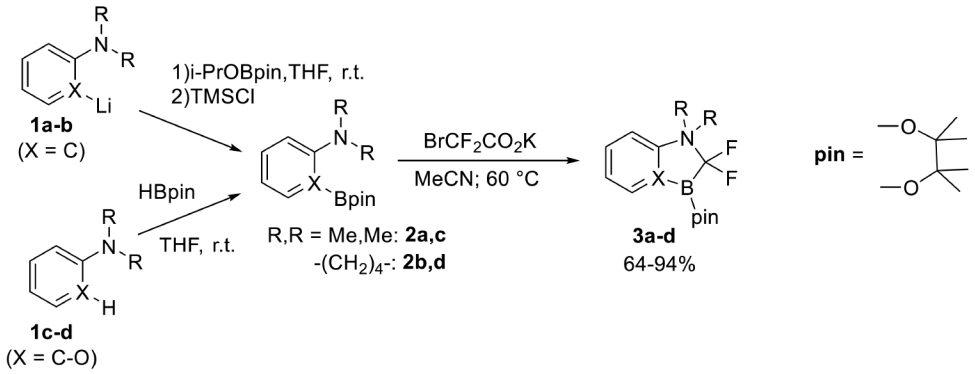
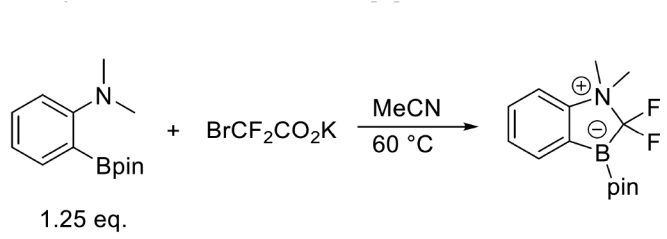


Figure 1. Synthesis of FLP and their reactions with difluorocarbene.

Compound **3a** is quite stable to heating: at least 95 % of adduct unchanged at 100°C for 2 hours in DMF or *o*-xylene. FLP **2a** captured difluorocarbene effectively in a wide concentration range (0.038– 0.77M) (**Fig. 2**). In addition, the experiment on the preparation **3a** in the presence of 1,1- diphenylethylene showed that **2a** more the two orders of magnitude more active than this standard reagent for interception of difluorocarbene [1].



concentration of $BrCF_2CO_2K$	yield **3a**
0.77 M	93%
0.26 M	89%
0.075 M	86%
0.038 M	83%

Figure 2. Effectiveness of **2a** in the reaction with difluoocarbene.

Activity **2a** in the reaction with difluorocarbene, the efficiency of this process and thermal stability of **3a** allowed us to offered **2a** as a reagent for the detection of difluorocarbene. For example, FLP **2a** made it possible to detected the participation of difluorocarbene in the difluoromethylation of O–H and N–H bonds [2], while 1,1-diphenylmethylene couldn't detect difluorocarbene as an intermediate of this process [1].

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CATALYZED REACTIONS OF HETEROCYCLIC THIOAMIDES WITH DIAZOCOMPOUNDS

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The synthesis of enaminones by the copper or ruthenium catalyzed reactions of aliphatic and aromatic thioamides with diazocompounds were initially discovered by Hussaini and co-workers [1-2]. We have studied the reaction of heterocyclic thioamides with diazoketones and diazodicarbonyl compounds for the first time. As a result of our studies, the formation of enaminones bearing a heterocyclic moiety was observed in high yields.

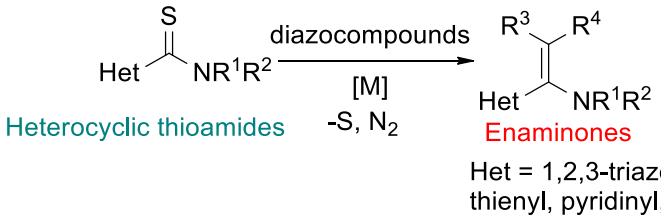

Figure 1. Reaction of heterocyclic thioamides with diazocompounds

In addition to this, a new direction for the reported reaction has been discovered. Accordingly, a range of mesoionic compounds were obtained in good yields. The optimization studies for both the reactions were comprehensively performed by using a wide range of catalysts. The scope and limitations of these reactions will also be presented.

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Acknowledgements. This work was supported by the Russian Science Foundation (project No 18-13-00161-П).

DIAZOTIZATION AND NITRATION OF 3-*TERT*-BUTYL-4-OXOPYRAZOLO[5,1-*C*][1,2,4]TRIAZINES

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Nitro-substituted azolo[1,2,4]triazines exhibit practically valuable characteristics and have been proposed as a new class of high energetic materials [1]. 2-Methylsulfanyl-6-nitro-1,2,4-triazolo[5,1-*c*][1,2,4]triazin-7(4*H*)-one (Triazavirin) is used as an effective antiviral drug [2]. However, direct nitration in the series of azolo[1,2,4]triazines is not well developed. With the aim to synthesize previously unknown 7,8-nitro(dinitro)pyrazolo[5,1-*c*][1,2,4]triazines, we have examined the diazotization and nitration reactions of 7-amino-3-*tert*-butyl-4-oxo-4,6-dihydropyrazolo[5,1-*c*][1,2,4]triazine-8-carboxylic acid (**1**, fig. 1) [3,4]. Compound **1** can be prepared from easily accessible 4-amino-6-*tert*-butyl-3-methylsulfanyl-1,2,4-triazin-5-one [3].

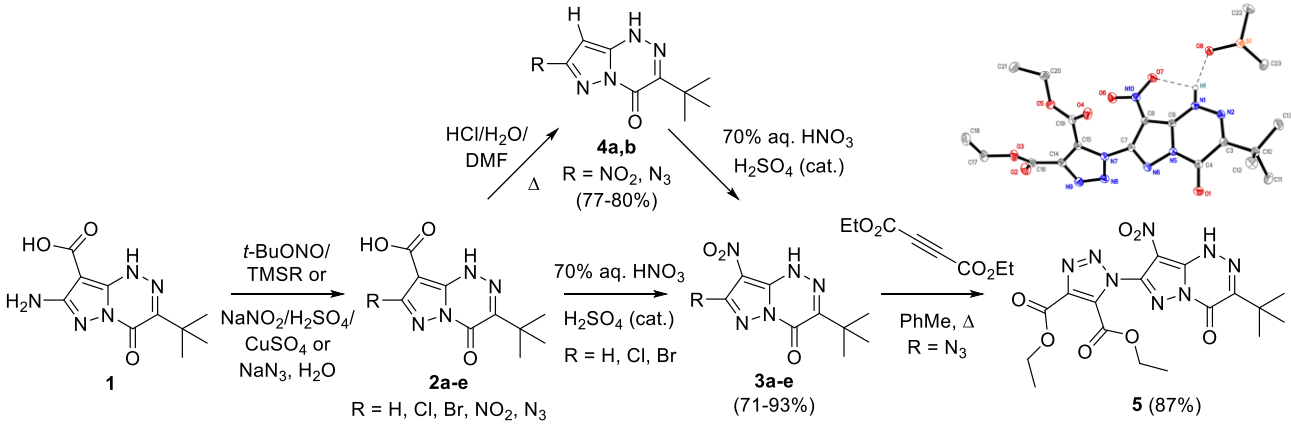

Figure 1. Transformations of 3-*tert*-butyl-4-oxopyrazolo[5,1-*c*][1,2,4]triazines

Diazotization of heterocycle **1** and further decarboxylative nitration of the formed acids **2a-c** using 70% aqueous HNO_3 in the presence of catalytic H_2SO_4 afforded a series of 7-R-3-*tert*-butyl-8-nitropyrazolo[5,1-*c*][1,2,4]triazin-4(1*H*)-ones **3a-c** (R = H, Cl, Br) in good yields. Compounds **3d,e** (R = N_3, NO_2) could not be synthesized in this way. The latter were successfully prepared by decarboxylation of acids **2d,e** in boiling HCl/DMF with further nitration of the formed compounds **4a,b** with a vacant C(8) position. Treatment of azide **3e** (R = N_3) with diethyl acetylenedicarboxylate in boiling toluene gave 1,2,3-triazole **5**. Structures of the isolated 8-nitro- and dinitropyrazolotriazines have been confirmed by spectral data and single-crystal X-ray diffraction [3,5].

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REACTIONS OF METHYL 2-DIAZO-2H-PYRROLE-4-CARBOXYLATES AND ENAMINES

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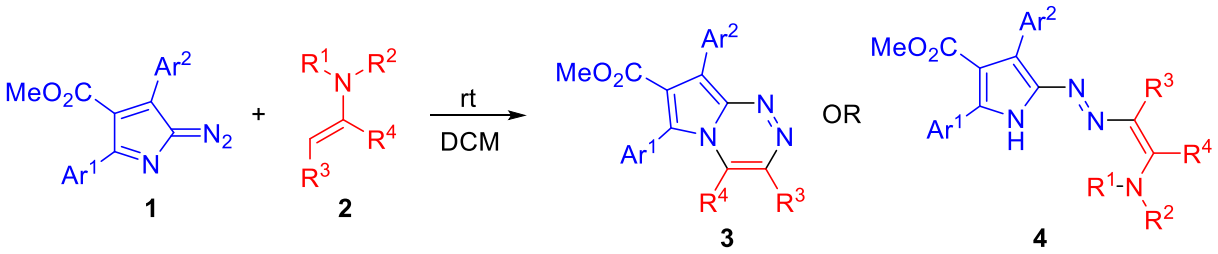
Despite the fact that there are many examples of the preparation of azole-fused 1,2,4-triazines, there is only one example of the synthesis of pyrrolotriazine [1].

So, for the first time, the reaction of α-diazopyrroles **1** [2] with a wide range of enamines **2** was investigated and it was found that, depending on the structure of enamine **2**, pyrrolotriazines **3** or N-pyrrolyl-N'-alkenyl-azo compounds **4** are obtained (Figure 1).



Ar^1 = Ph, 4-FC_6H_4; Ar^2 = 4-BrC_6H_4, 4-ClC_6H_4, 4-$MeOC_6H_4$;
R^1NR^2 = pyrrolidine, morpholine, *N*-methylpyperazine, pyperidine;
R^3=R^4 = cyclohexene, cycloheptene,1,2-dihydronaphthalene, o-bromostyrene, 2-vinylpyridine

Figure 1.

The structure of compounds **3** and **4** was confirmed by various physicochemical methods, including X-ray structural analysis (Figure 2).

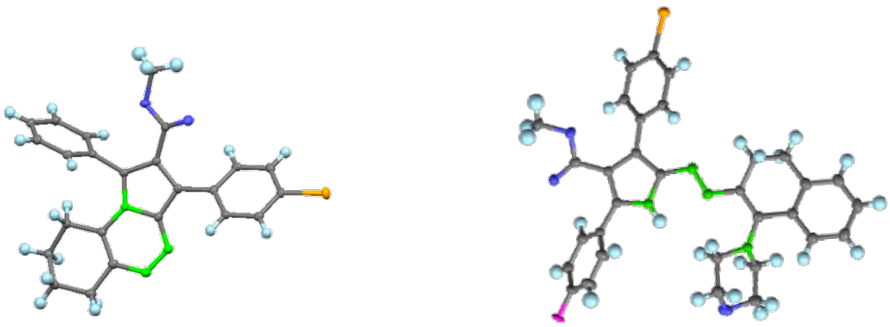


Figure 2.

To establish the reasons for the formation of diazene **4** or triazine **3** depending on the structure of the starting enamine **2** and diazopyrrole **1**, quantum-chemical calculations were carried out.

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SYNTHESIS OF NEW ALKYL PLATINUM(IV) COMPLEX WITH ACYCLIC DIAMINOCARBENES (ADCs) VIA OXIDATIVE ADDITION OF IODOMETHANE

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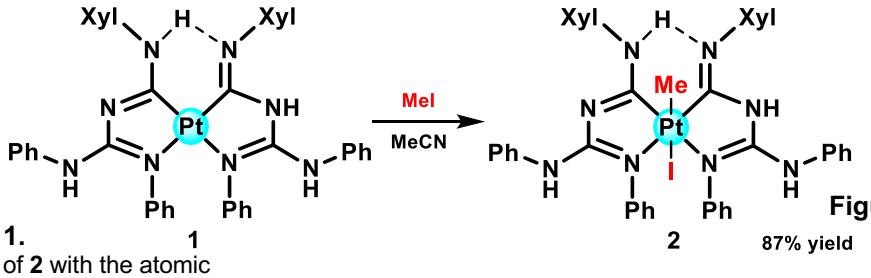
The metal complexes with ADCs ligands have attractive properties according to their chemical and thermal stability. Metal–ADCs species demonstrate outstanding performance in many organic transformations involving oxidative addition–reductive elimination steps as cross-coupling reactions [1] and hydrosilylation of alkynes [2]. In addition, they are easily obtained under mild conditions [3]. Oxidative addition of alkyl halides to a metal center is a suitable way to increase the coordination number of the complex. One of the proposed mechanisms of oxidative addition is bimolecular S_N2-type reaction where metal is considered to act like a nucleophile. It is now clear that the mechanism adopted depends on the metal substrate, the reaction conditions and the alkyl halide. In this case platinum(II) ADCs complexes stabilized by cyclometalation are good substrate for oxidative addition reactions of iodomethane due to the presence of strong σ bonds which increase the electron density at the metal center [4]. Obtained species combine the properties of ligands and platinum(IV) center that allows to get new potentially useful antitumor agents [5]. There is considerable interest in oxidative addition reactions on platinum(II) complexes with ADCs ligands since this topic of platinum transformations is still being unexplored.

In this work alkyl platinum(IV) complex *trans*-[PtI(Me){C(N(H)Xyl)(NC(N(H)Ph)N(Ph)}$_2$] **2** (Figure 2, Xyl = C_6H_3(2,6-Me_2)) was prepared via a reaction of oxidative addition of iodomethane (MeI) to platinum(II) ADC complex *trans*[Pt{C(N(H)Xyl)(NC(N(H)Ph)N(Ph)}$_2$] **1** in MeCN (Figure 1) with 87% yield.



1 **2** 87% yield

Figure 1. of **2** with the atomic

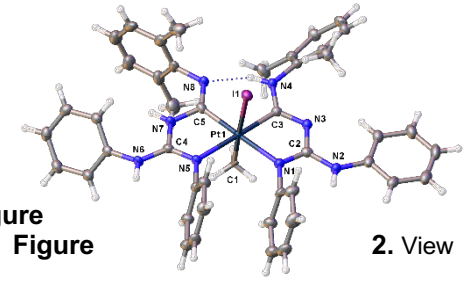


Figure 2. View numbering schemes. Thermal ellipsoids are drawn with the 50% probability.

The obtained complex **2** was isolated and characterized by HRESI$^+$-MS, IR, 1D (^{1}H,^{13}C{^{1}H}, ^{195}Pt) and 2D (^{1}H,^{1}H-COSY, ^{1}H,^{1}H-NOESY, ^{1}H,^{13}C-HMBC, ^{1}H,^{13}C-HSQC, ^{1}H,^{15}N-HSQC) NMR spectroscopies, and by X-ray diffraction.

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UNEXPECTED FORMATION OF 3-OXO-1,3-DIHYDROISOBENZOFURAN-1-CARBOXAMIDES FROM HOMOPHTHALIC ANHYDRIDE UNDER DIAZO TRANSFER CONDITIONS.

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At the moment, the synthesis of diazoanhydrides was practically not presented in the literature. There is only one example of the synthesis of acyclic diazoanhydride; the method for the synthesis of cyclic anhydrides is still unknown. Therefore, we decided to develop an approach to such compounds. First of all, we obvious to obtain diazohomophthalic anhydride **2** using the diazo transfer reaction, however, the addition of a base to the mixture of sulfonyl azide and homophthalic anhydride **1** led to active gas evolution and unexpected formation of compound **3a**.

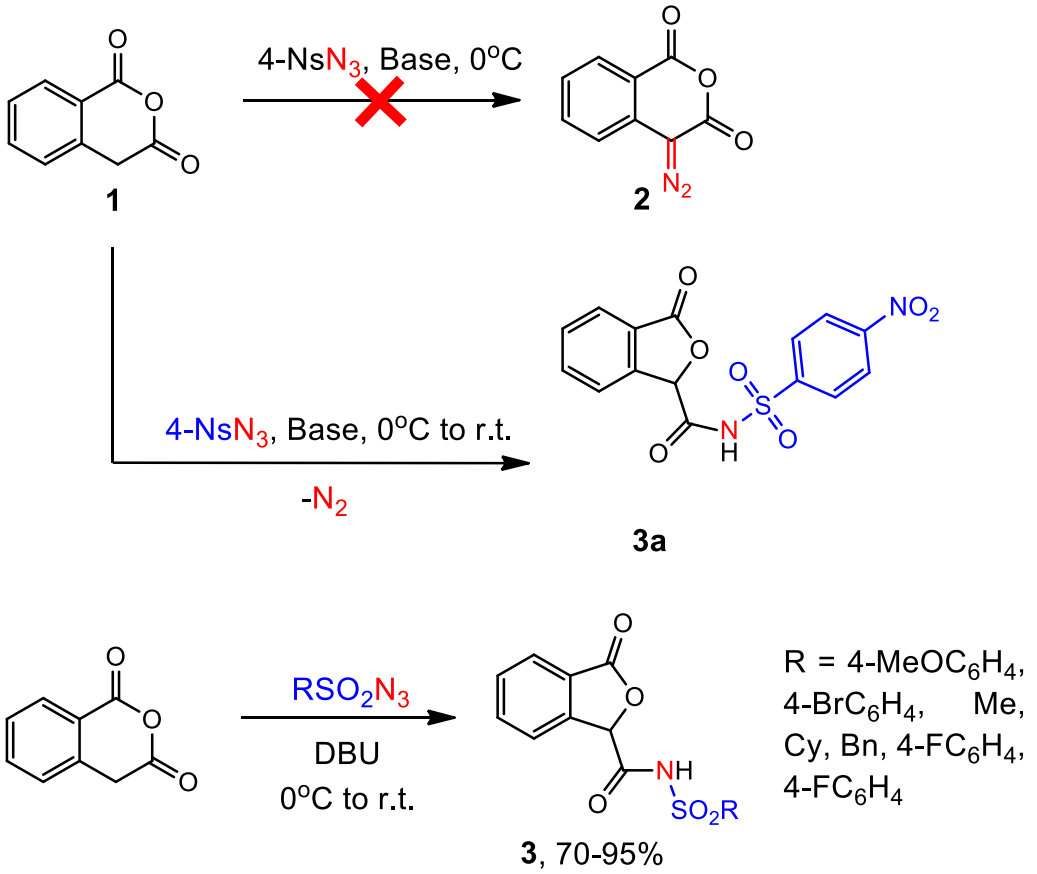

Figure 1. Synthesis of 3-oxo-1,3-dihydroisobenzofuran-1-carboxamides from homophthalic anhydride under diazo transfer conditions.

Inspired by this unusual finding we decided to continue the study using various sulfonyl azides. Screening of alkyl and arylsubstituted substrates proved the general character of discovered reaction, which resulted in isolation of a series of *N*-sulfonylcarboxamides **3**. Currently the reaction mechanism is being studied. The developed novels methodology opens facile access to synthetically challenging lactones promising for medicinal chemistry applications.

Acknowledgements. We thank the Research Center for Magnetic Resonance, the Center for Chemical Analysis and Materials Research and the Center for X-ray Diffraction Methods of Saint Petersburg State University Research Park for obtaining the analytical data.

COPPER-CATALYZED AZIDE-ALKYNE CYCLOADDITION IN THE SYNTHESIS OF A TRIAZOLE-ANNULATED CYCLONONYNE

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Bioorthogonal chemical click-reactions are becoming more and more important nowadays. It is known that azido group is the excellent choice for bioorthogonal bioconjugation either through Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC) [1,2] or Strain-Promoted Azide-Alkyne Cycloaddition (SPAAC) [3], because neither azides nor alkynes present in natural biopolymers (glycans, proteins, nucleic acids).

SPAAC has several advantages over CuAAC "click" transformation, i.e. faster kinetics and avoiding of toxic affection of Cu(I) ion to cells and organisms [3]. However, CuAAC is known as the most convenient way for the synthesis of triazoles because of its superior regioselectivity and tolerance in the presence of many functional groups [2].

The main purpose of our work was to use CuAAC of iodalkynes [4] as a key step in the synthesis of new triazole-based SPAAC reagent **8**. The target triazole-fused cyclononyne **8** has two important structural features to maintain the optimal stability-reactivity balance: the fused triazole ring and the endocyclic nitrogen atom at the propargylic carbon atom.

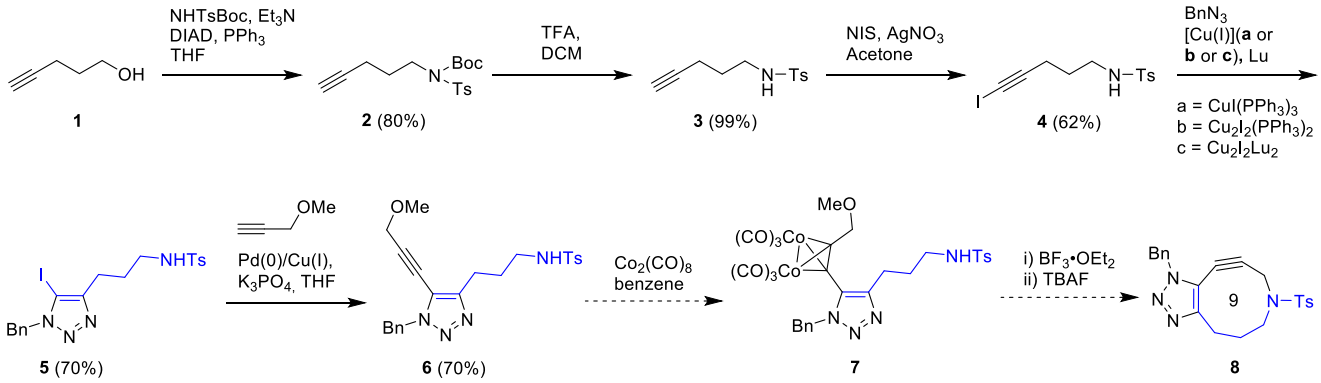

Figure 1. Supposed scheme of synthesis

The starting for CuAAC iodoalkyne **4** with the essential NHTs group was synthesized using standard chemical transformations (Fig. 1). CuAAC of iodoalkyne **4** was carried out using three different complexes of Cu(I) (**a-c**) in the presence of 2,6-lutidine (Lu) [5,6]. The highest yield of **5** was achieved using $CuI(PPh_3)_3$ catalyst. The absence of solvent and the presence of Lu was crucial; the yield of 5-iodotriazole **5** under solvent free conditions was 70%, while an attempt to carry out the reaction in THF gave only unconverted starting materials.

The next step of our research was to test whether the triazole **5** is suitable for the Sonogashira coupling. The Sonogashira reaction proceeded in high yield with the formation of desired alkyne for the further Nicholas-type cyclization, which is currently being studied.

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PREPARATION OF 1,2,3-TRIAZOLES BY THE REACTION OFAZIDE-ALKYNE CYCLOADDITION

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The interest of for metal-organic frameworks is due to the wide range of their physicochemical properties and the possibility of obtaining various multifunctional materials for catalysis [1], gas storage [2], nonlinear optics [3], and molecular recognition and separation [4]. MOFs containing 1,2,3-triazole rings in their structure play an important role in industry, agrochemistry, and pharmacy.

The main method for the synthesis of 1,2,3-triazoles is the thermal 1,3-dipolar cycloaddition of azides with alkynes, first proposed by Huisgen [5].

The aim of this study is to obtain aromatic and heteroaromatic azides based on anilines and aminopyrazoles and subsequently study their reactivity in 1,3-dipolar cycloaddition reactions with propiolic acid or methyl propyalate.

To obtain pyrazolyl azides, we proposed a procedure for diazotization-azidation of aminopyrazoles under the system BuONO / TsOH in acetonitrile. Then azidopyrazoles were introduced into the reaction of azide-alkyne cycloaddition, catalyzed by copper salts, with methyl propiolate or propiolic acid to form the target pyrazolyl-1,2,3-triazoles (Figure 1). The structure of the synthesized compounds was proved by comparing the melting temperatures with known samples, IR and NMR spectroscopy.

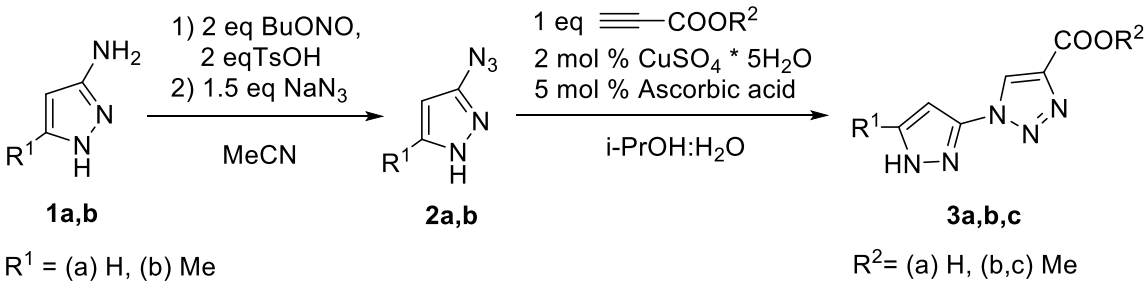

Figure 1. Reaction of azide-alkyne cycloaddition

In this work, a convenient method for the synthesis of heteroaromatic azides and triazoles from aminopyrazoles is proposed. The synthesized 1,2,3-triazoles will be used as polydentate ligands for metal-organic frameworks.

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CYCLOPENTADIENYL RHODIUM(III) CATALYSTS FOR TRANSFORMATION OF DIAZO COMPOUNDS

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Rhodium(II) carboxylates are widely used for transformation of diazo compounds. In sharp contrast, similar application of rhodium(III) catalysts is much less developed [1]. Herein we present the reactions of diazo esters in the presence of the readily available rhodium(III) complexes $[(C_5R_5)RhCl_2]_2$.

Our attention was attracted by the reactions of insertion of diazo esters in single bond heteroatom – hydrogen, where the following heteroatoms were chosen: carbon, nitrogen, silicon and boron. All processes take place in mild conditions, in the presence $[(C_5Me_5)RhCl_2]_2$, giving the target products with good yields. (fig. 1a)

Also since catalysts based on rhodium (III) are known for their activity in C–H activation reactions, we considered the interaction of diazo esters with O-pivaloylphenylhydroxamic acid. For this, catalysts containing various cyclopentadienyl ligands with different steric loading were used. As a result, target isoindolines with some enantioselectivity were obtained. (fig. 1b)

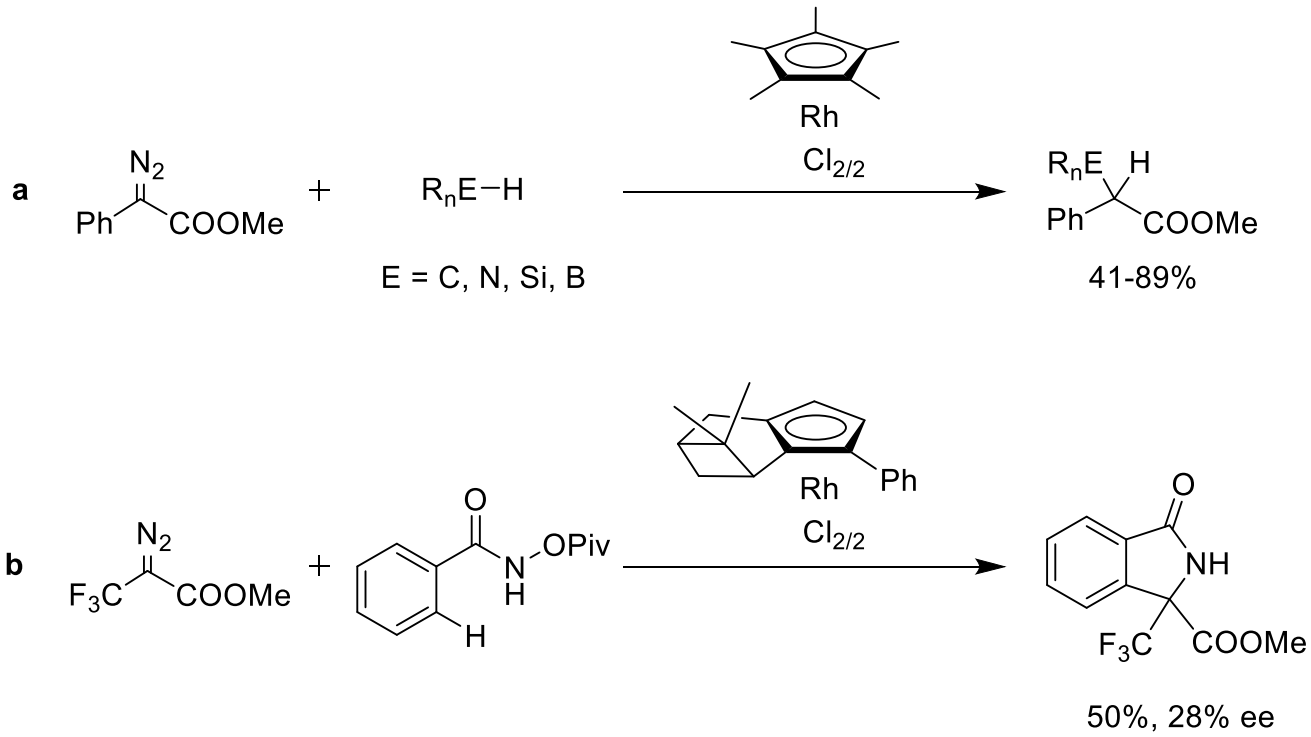

Figure 1. Insertion of diazo esters into various bond in the presence of $[(C_5R_5)RhCl_2]_2$ catalyst.

References

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APPLICATION OF DIAZO COMPOUNDS AND THEIR ANALOGS IN PREPARATION OF ARTIFICIAL LIPIDS FOR BIOLOGICAL TESTING

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A number of different types of organic compounds containing "fixed nitrogen" have found successful application in biological research.

Diazo compounds were used in the study of the Chymotrypsin protein back in 1962 [1]. High reactivity, on the one hand, and high stability, on the other, limits their application in biological research [2]. However, diazo compounds have found their niche in the synthesis of biologically useful compounds, in particular lipids.

Diazirins, the cyclic isomers of diazo compounds, have successfully taken the frontier positions in disclosing of fine interactions between biological organelles, even in living cells. Diazirins, on the one hand, are inert and biocompatible in biological objects. On the other hand, when activated by light, they generate active carbenes that can covalently bind to interacting partners. This makes it possible to discover the mechanisms of biological processes.

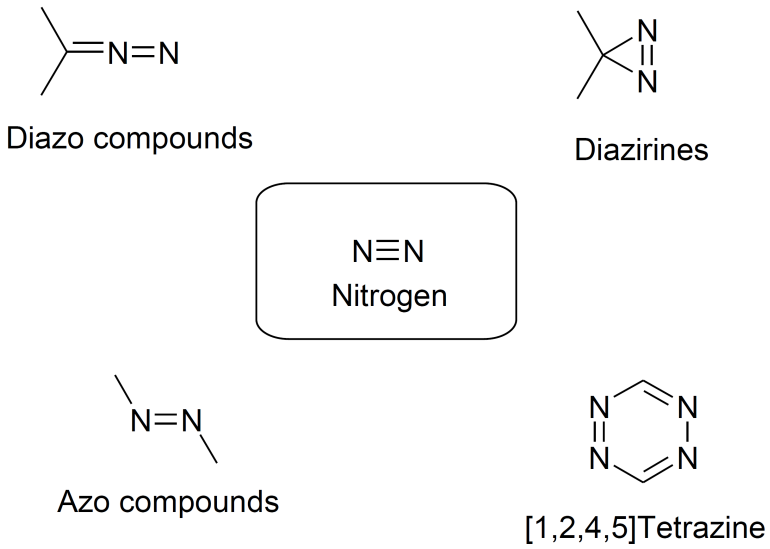

Figure 1.

Azo compounds have recently entered biological research in the form of molecular machines. The desire of researchers not only to observe, but also to be able to interfere with biological processes gave impetus to the creation of biological molecules armed with a photo isomerizable azo fragment.

Tetrazines have proven to be a successful extension of click chemistry in applications to biology. They allowing derivatization of prepared biological molecules under biocompatible conditions in a catalyst-free conditions.

Examples of the use of mentioned classes of nitrogen-containing compounds are given in this presentation.

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ANNULATION-TRIGGERED DENITROGENATIVE TRANSFORMATIONS OF 1,2,3-TRIAZOLES

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1,2,3-Triazoles are generally perceived as stable organic molecules. Nevertheless, the introduction of strong electron-withdrawing substituents at the N1 atom can be used as a tool for shifting the equilibrium from the triazole toward the corresponding tautomeric diazoimine. The interception of the latter by transition metals resulted in a booming methodology exploiting primarily *N*-sulfonyl-1,2,3-triazoles as precursors of metal-stabilized imino carbenes [1]. The similar reactivity is well-established for some fused triazoles (in particular, triazolopyridines) [2].

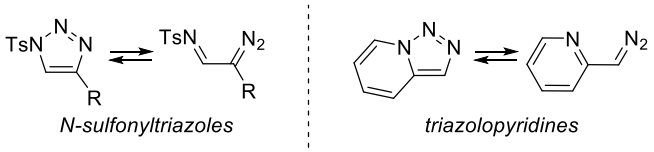

Figure 1.

Recently, we have utilized readily available 5-iodotriazoles bearing a pendant nucleophilic group as a new convenient type of diazo surrogates [3]. While these compounds are bench-stable, their heating in basic media evokes cyclization and unmasks hidden diazo functionality. Cascade trapping of the *in situ* generated diazo compounds enables straightforward assembly of functionalized azaheterocycles, such as benzoxazoles and benzoxazines. For instance, we have elaborated efficient protocols for Cu-catalyzed NH and SH insertions. Transition-metal-free conditions were employed for domino construction of benzoxazole-derived sulfonamides *via* denitrogenation of diazo intermediates upon the action of DABSO (an adduct DABCO·2SO_2) and amines.

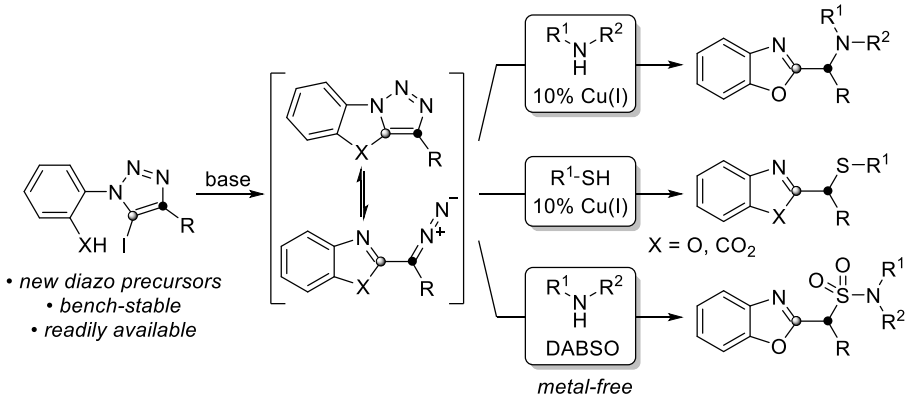

Figure 2.

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SYNTHESIS OF FUROXAN-BASED HIGH-ENERGY AZOLES WITH EXPLOSOPHORIC FUNCTIONALITIES

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Over the last few decades a search of new energetic structures has focused on high energy density materials (HEDMs), which are constructed on the basis of various nitrogen-oxygen and nitrogen-rich heterocycles like oxadiazoles, tetrazoles, triazoles etc., possessing high positive enthalpy of formation, good thermal stability and environmental greenness. [1]

The field of interest of our scientific team is focused on a search of high-energy compounds in series of furoxan derivatives. Furoxan attracts significant attention due to high positive enthalpies of formation and huge nitrogen-oxygen content presented within the core. Previously, we managed to prepare a series of energetic materials hetarylfuroxans containing explosophoric groups, which possess high density and improved properties.[2,3]

Therefore, the search for novel energetic materials with superior performances and reduced sensitivities among the bicyclic, tetracyclic structures containing the azo-bridged nitrogen-oxygen and nitrogen-rich bicyclic backbones enriched with energetic functionalities remains highly urgent.

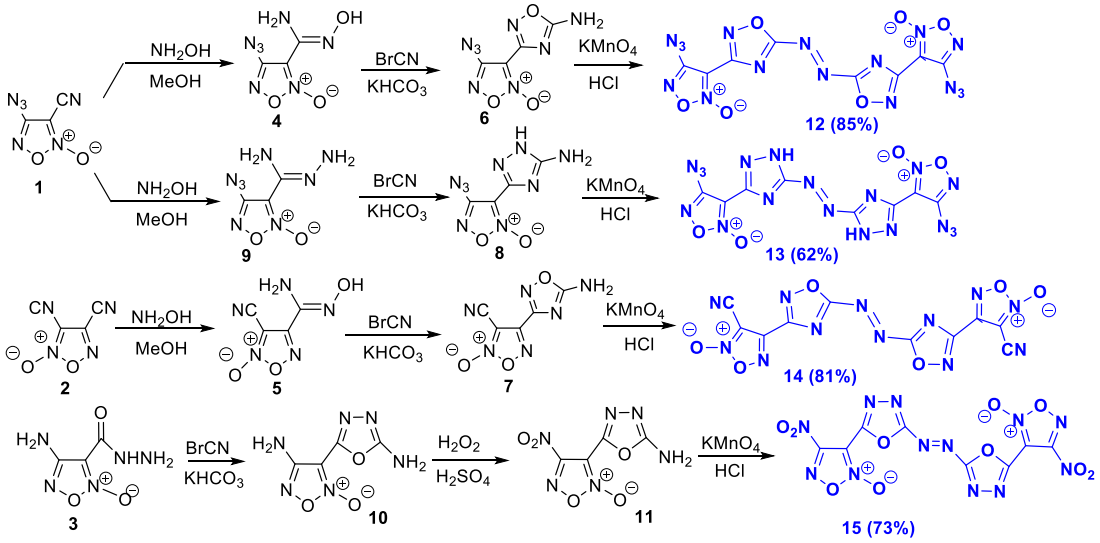

Figure 1. Synthesis of the azo-bridged bicyclic backbones.

The synthesis of the target tetracyclic azo-bridged bicyclic backbons **12-15** as well aminofuroxanylazoles **6-8,11** was based on simple transformations of lightly available cyanofuroxans **1,2** and 4-aminofuroxan-3-carboxylic acid hydrazide **3**. An interaction of CN groups in compounds **1** and **2** with hydroxylamine followed by condensation of formed amide oximes **4** and **5** with cyanogen bromide resulted in to 4-azido-3-(5-amino-1,2,4-oxadiazol-3-yl)furoxan **6** and 4-(5-amino-1,2,4-oxadiazol-3-yl)-3-cyanofuroxan **7**. 4-Azido-3-(5-amino-1,2,4-triazol-3-yl)furoxan **8** was prepared by reaction of 4-azido-3-cyanofuroxan **1** with hydrazine hydrate followed by condensation of formed amidrazone **9** with cyanogen bromide. Condensation of hydrazide **3** with cyanogen bromide allowed synthesizing diamine **10**. An oxidation of amino group, connected with furoxan ring in this compound, with 85% H_2O_2 in concentrated H_2SO_4 afforded 3-(5-amino-1,3,4-oxadiazol-2-yl)-4-nitrofuroxan **11**. The target tetracyclic azo-bridged bicyclic backbons **12-15** were synthesized via an oxidative condensation of bicyclic aminoderivatives **6-8**, **7**,**11** under the action of $KMnO_4$ in hydrochloric acid (Figure 1)

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Acknowledgements. This work was supported by the Russian Science Foundation (project No 19-73-20074).

PYRAZOLE-3(5)-DIAZONIUM SALTS AS BUILDING-BLOCKS FOR THE SYNTHESIS OF PYRAZOLE-ANNELATED HETEROCYCLIC COMPOUNDS

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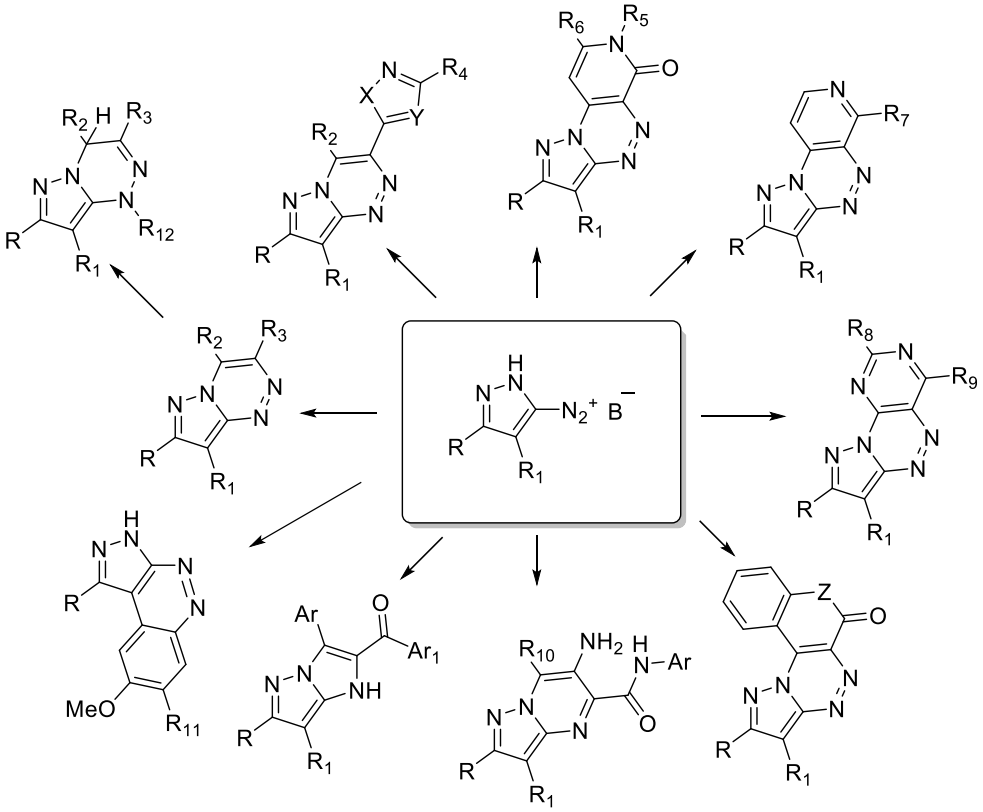
Pyrazole-3(5)-diazonium salts, like aromatic diazosalts, undergo azocoupling with CH-, CH_2-, NH- active compounds. The presence of a pyrrole-like nitrogen atom in the pyrazole ring promotes the cyclocondensation reactions of such azocoupling intermediates as azo compounds or hydrazones to give various pyrazolo[5,1-*c*][1,2,4]triazine derivatives. Pyrazole-3(5)-diazonium chlorides containing in the *o*-position to the diazo group substituent active to electrophilic attack fragments (Ar, activated multiple C–C bonds, etc.) spontaneously enter into the reaction of intramolecular azocoupling with the formation of pyrazolo[3,4-*c*]cinnolines, whereas analogous pyrazolodiazonium tetrafluoroborates in azocoupling reactions give pyrazolo[5,1-*c*][1,2,4]triazines.



B = Cl, BF_4; R = H, Alk; R_1 = H, Ar; R_2 = H, CH_3, Ar, OH, CH_2=$CH_2N(CH_3)_2$; R_3 = COMe, COAr, COOMe, COOEt, CN, Tos, Ms; R_4 = H, CH_3, OH, NH_2; R_5 = H, Alk, Ar, Het; R_6 = H, CH_3, Ar; R_7 = CH_3, NH_2, Ar; R_8 = H, OH, Ar, Het; R_9 = OH, NH_2; R_{10} = CH_3, Ar; R_{11} = H, OMe; R_{12} = H, Alk; X = CH, NH; Y = CH, S; Z = O, NH.

Figure 1. Synthetic possibilities of pyrazole-3(5)-diazonium salts

It was found that by introducing of various heterocyclic methylene active components in the reaction with pyrazole-3(5) diazonium salts, polycyclic systems containing pyrazolo-*as*-triazine fragment can be obtained. At the same time, pyrazolo[5,1-*c*][1,2,4]triazine derivatives, depending on the nature of substituents in the 3 and 4 positions of the triazine ring, can enter into substitution, addition, cyclocondensation, reduction reactions, and ANRORC-type rearrangements.

Acknowledgements. The study received financial support from the Ministry of Science and Higher Education of the Russian Federation within the framework of State Contract with universities regarding scientific research in 2020–2022, project No. FZGU-2020-0044.

SYNTHESIS OF NEW 2-NITRODIAZENE 1-*N*-OXIDES

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The first 2-nitrodiazene 1-*N*-oxides were synthesized at the N.D. Zelinsky Institute of Organic Chemistry [1]. A synthetic approach to these compounds includes the nitration of 2-(*tert*-butyl)-diazene 1-*N*-oxides. The plausible mechanism for the synthesis of 2-nitrodiazene 1-*N*-oxides involves the formation of a cationic intermediate **A** followed by elimination of the *tert*-butyl cation (Figure 1).

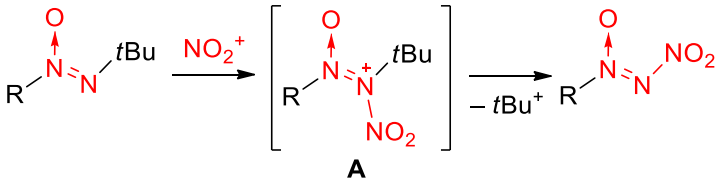

Figure 1. The plausible mechanism for the formation of nitrodiazene oxides.

The nitrodiazene oxide group has been scarcely studied and has recently attracted much attention as a novel explosophore group. There is little information available concerning thermal stability of 2-nitrodiazene 1-*N*-oxides. In order to assess the applicability of 2-nitrodiazene 1-*N*-oxides as high energy compounds, it is important to scrutinize its thermal stability.

Methods for the synthesis of novel energetic materials based on furazan cycle and nitrodiazene oxide group have been developed (Figure 2). 3-Amino-4-(*tert*-butyl-*NNO*-azoxy)furazan is a starting material for the synthesis of target compounds. The compounds obtained are relatively thermally stable. 3-Nitro-4-{[4-(nitro-*NNO*-azoxy)furazan-3-yl]-*NNO*-azoxy}furazan was found to be the most stable (T_{onset} = 115 °C). Its structure was studied by X-ray diffraction [2].

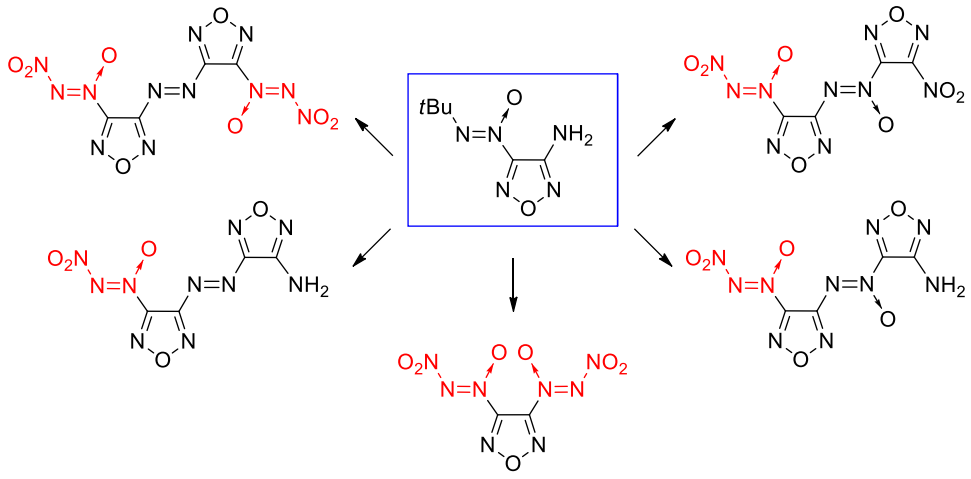

Figure 2. Novel energetic (nitro-*NNO*-azoxy)furazans.

These compounds could be considered as energetic materials.

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Acknowledgements. This work was supported by the Russian Science Foundation (project No 19-13-00276).

α-DIAZO-β-KETONITRILES IN DIASTEREOSELECTIVE CATALYST-FREE β-LACTAM SYNTHESIS VIA THERMALLY PROMOTED WOLFF REARRANGEMENT

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β-Lactams are privileged scaffolds that found broad application in drug design. Such four-membered N-heterocycles, exhibiting antibacterial activity, attract chemists to develop stereoselective synthetic methodologies for rapid assembling of polysubstituted β-lactam rings. The most common approach to β-lactam core is the Staudinger [2+2] cycloaddition of imines and ketenes, the latter being generated *in situ* via the Rh(II)-catalyzed Wolff rearrangement of α-diazocarbonyl compounds. Though this approach is well-explored, it has a main drawback such as the use of expensive Rh(II)-catalysts so as to generate carbenes. Furthermore, still there is an issue with the diversity of functional groups that can be introduced into the β-lactam ring. Recently, our research group developed a facile catalyst-free synthetic approach to various densely substituted β-lactams via the thermally initiated Wolff rearrangement of α-diazocarbonyl compounds [1-3]. Not only does this approach eliminate the need for transition metal catalysts, but also exhibits excellent diastereoselectivity and tolerance to a variety of functional groups and substituents.

In the present work, we developed the first transition metal-free diastereoselective synthesis of cyano β-lactams from imines and surprisingly insufficiently explored α-diazo-β-ketonitriles based on tandem of thermally initiated Wolff rearrangement, occurring in refluxing toluene, and Staudinger cycloaddition (Figure 1). Furthermore, the synthesis represents the first example of cyano ketenes generation from diazoketonitriles. The reaction developed tolerates substrates with various substituents, even bulky ones, and delivers exceedingly rare polysubstituted cyano β-lactams with excellent diastereoselectivity and generally high yields. The relative stereochemistry of products was assigned by the single-crystal X-ray crystallography, which confirmed cyano function and aldehyde-derived group being on the same face of the β-lactam ring. In addition, we investigated limitations of our approach and possible transformations of substituents in lactam ring.

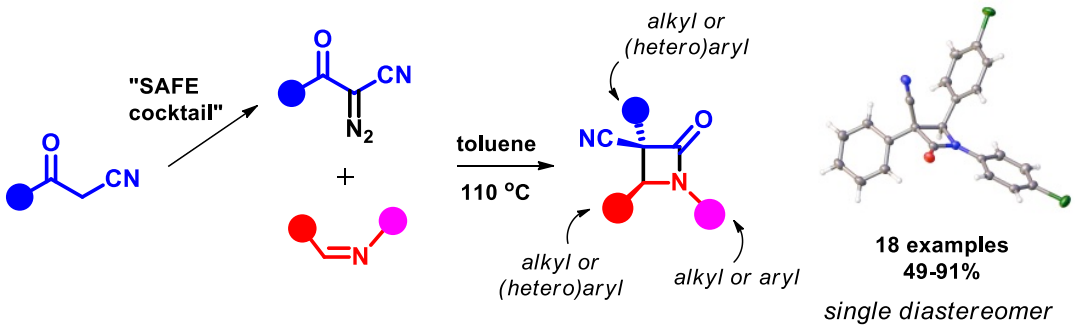

Figure 1. Synthesis of cyano β-lactams.

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SYNTHESIS OF CHROMOPHORES BASED ON THE HYDRAZINYLIDENE CYCLIC ACCEPTOR MOIETIES VIA THE REACTION OF ORGANOLITHIUM REAGENTS WITH DIAZO COMPOUNDS

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Earlier we demonstrated that donor-*π*-acceptor chromophores with a hydrazinylidene cyclic acceptor moieties are prospective donor materials within bulk heterojunction solar cells [1]. The synthesis of such chromophores was restricted by only two approaches developed. The first approach included the azo-coupling reaction between aryldiazonium salts and nucleophilic precursors of the acceptor fragments. The second one was based on the reaction of arylhydrazines with corresponding ketones [2]. The main disadvantage of these two methods was the inability to introduce a thiophene fragment into a molecule, whereas thiophenes along with their fused polycyclic derivatives are of interest as donor parts or *π*-linkers since they afford enhanced planarity in comparison with phenylene rings and advanced stability unlike in polymethyne bridges [3].

Herein we present a novel approach to the synthesis of chromophores based on various cyclic hydrazinylidene acceptor moieties via the reaction of organolithium reagents with diazo compounds [4]. This reaction is quite exceptional due to rare electrophilic reactivity of a diazo group.

The reaction of diazocyclopentadiene **1** with various organolithium reagents gave a series of hydrazones **2a-i** (**Fig. 1**). The reaction proceeded with good selectivity and moderate to high yields despite the presence of competitive reactive groups in diazo substrates. It is worth noticing that a thiophene moiety is easily introduced into a molecule due to availability of its lithiated derivative unlike in the two previous methods wherein amino and hydrazinothiophene precursors are unavailable.

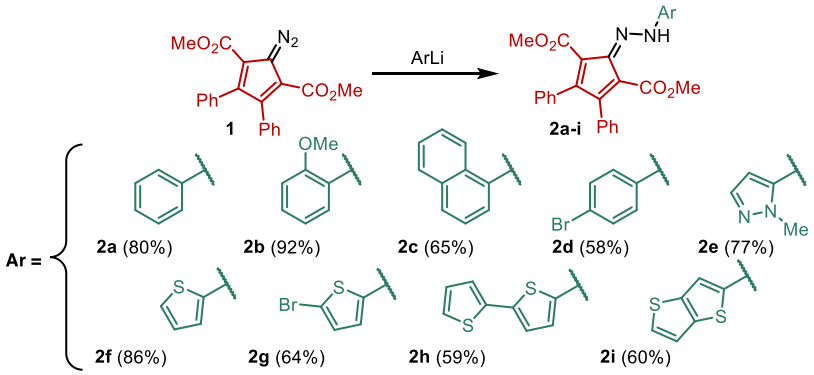

Figure 3. Reaction of diazocyclopentadiene **1** with organolithium reagents.

Furthermore, we showed that this approach affords other hydrazinylidene dyes from cyclic diazo compounds such as diazobarbituric acid, diazoindanedione and diazocyclohexadienone whose reaction with thienyllithuim gave chromophores **3a-d** (**Fig. 2**).

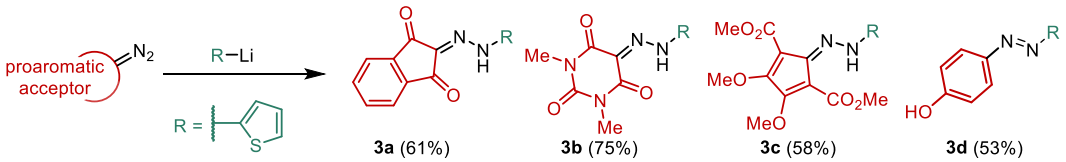

Figure 4. Reaction of thienyllithium with diazo compounds.

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SYNTHESIS OF PYRIDINES THROUGH RHODIUM-CATALYZED REARRANGEMENT OF FURYL-TETHERED TRIAZOLES

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Propensity of furans to undergo various dearomatizative transformations is extensively exploited for the synthesis of carbo- and heterocycles. Reactions of furan substrates with internal or external electrophiles often lead to unusual rearrangements, cycloadditions, or spyrocyclizations.

Intermolecular reaction of 1-sulfonyl-1,2,3-triazoles with alkylfurans in the presence of rhodium(II) source leads to transannulation to form pyrrole derivatives,[1] whereas intramolecular reaction was shown to provide only products of electrophilic heteroaromatic substitution.[2-3]

We found reaction conditions for intramolecular reaction of furans with triazole-derived azavinyl carbenoids that afforded substituted pyridines through sequential dearomatization/ring-opeingin/electrocyclization/aromatization [4] (Figure 1).

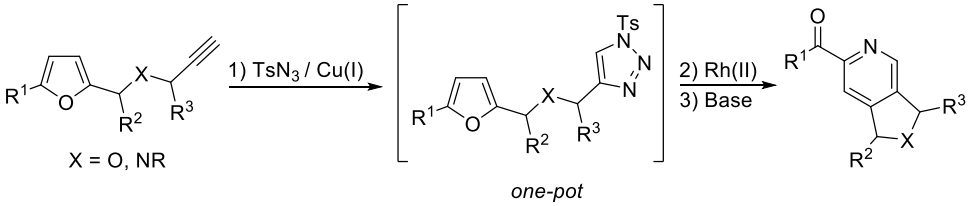

Figure 1. Synthesis of pyridines through denitrogenative decomposition of 2-furyl-tethered triazoles.

Optimization details, scope and limitations of the developed synthetic protocol toward substituted pyridines, as well as the synthetic utility of the obtained products will be discussed.

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DIAZOKETOSULFONAMIDES AS EFFECTIVE PRECURSORS FOR 1,5-DISUBSTITUTED 1,2,3-TRIAZOLES

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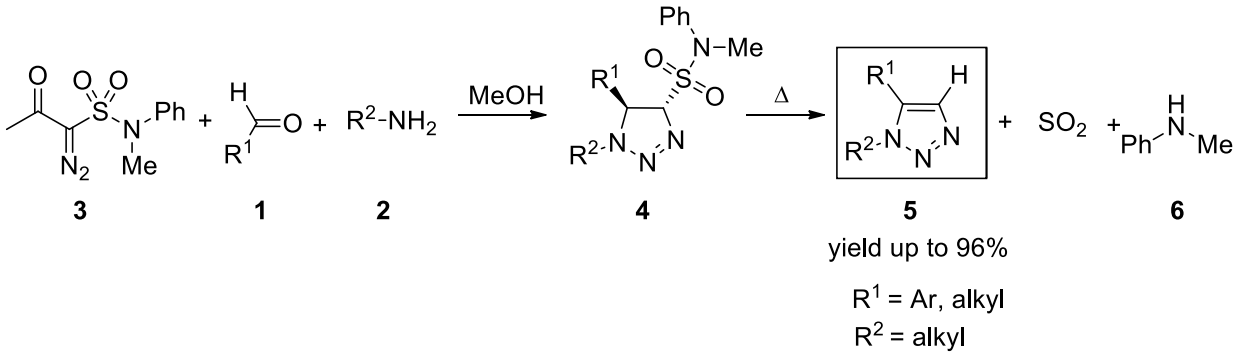
1,2,3-Triazoles are common compounds in nature. They have significant applications in medicine. The methods of disubstituted 1,2,3-triazoles generation are described in the literature. However most of them lead to the formation of 1,4-disubstituted compounds. At the same time 1,5-disubstituted structural isomers can be obtained via much smaller amount of synthetic ways. Some of them require the use of catalysts, which are often quite expensive [1]. Hard-to-get reagents are necessary for other ones [2].

The method developed by us allows to obtain isomerically pure 1,5-disubstituted 1,2,3-triazoles from available substrates: aldehydes **1** and amines **2**. Our synthetic way does not need metal-catalysts. The products were produced in good to excellent yields.

Our method is based on the three-component reaction of diazoketosulfonamide **3**, aldehyde **1** and amine **2** leading to 4-sulfonamide substituted 1,2,3-triazoline **4**. The further thermal desulfonylation reaction cause formation of target molecules **5**. By-product *N*-methylaniline **6** can be easily removed by acid extraction.



3 **1** **2** **4** **5** **6**

Figure 1. The synthetic way to 1,5-disubstituted 1,2,3-triazoles

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PHOSPHORESCENT IR(III) COMPLEXES WITH DIFFERENT N^N LIGANDS FOR OXYGEN SENSING

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Molecular oxygen is inevitable for all aerobic organisms as it plays the key role in cellular respiration. Hypoxia may be a symptom of serious pathologic processes such as cancer or cardiovascular diseases. Therefore, oximetry (measuring the concentration of oxygen) is very relevant in modern science. The PLIM (phosphorescence lifetime imaging) oximetry is gaining popularity due to its effectiveness and possibility to measure oxygenation at cellular and subcellular level. In this method, phosphorescent transition metal complexes are commonly used as molecular oxygen probes, due to its large Stokes shifts, greater lifetime values and triplet nature of excited states, which results in ability for O_2-quenching of their emission, as well as spectral and/or time-gated separation of phosphorescence from the autofluorescence of biomolecules.[1] Many octahedral Iridium (III) complexes meet such requirements for phosphorescence sensors as high sensibility for oxygen, emission in red or near-infrared (NIR) region, solubility in biological environment, biocompatibility, low cytotoxicity, redox and photobleaching stability.[2] In this work, a series of 4 new phosphorescence iridium complexes were synthesized (Figure 1).

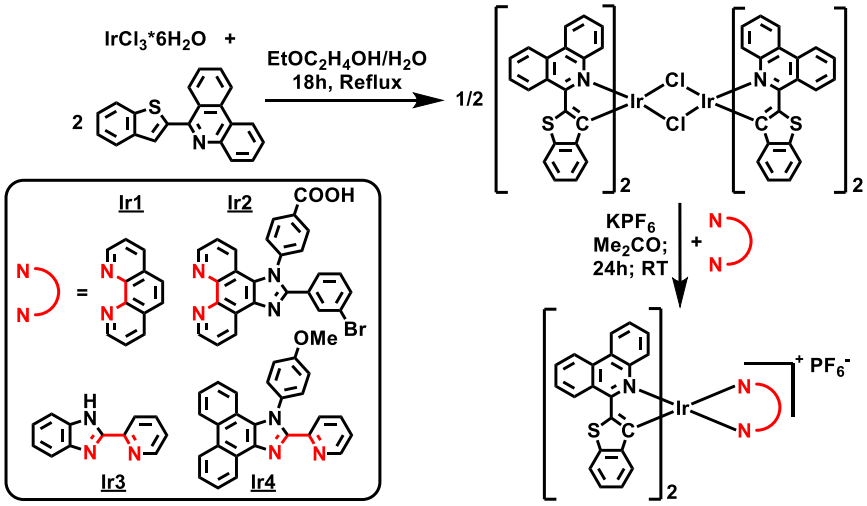

Figure 1. Synthes of Iridium complexes.

The compounds under study were fully characterized by modern methods of analysis. These complexes exhibit effective emission in NIR region with high quantum yields in solution. Study of their emission in aerated and degassed solutions made it possible to choose complex **Ir4** as most effective O_2-sensor in this series, as it showed the highest response to the presence of O_2.

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Acknowledgements. This work was supported by RSF (grant number 18-73-10021), NMR and ESI-MS analysis were performed using the equipment of the Centers for Magnetic Resonance and for Chemical Analysis and Materials Research (Research Park of St. Petersburg State University).

SYNTHESIS AND BIOLOGICAL ACTIVITY OF NEW TRIAZOLO[4,3-*a*]PYRIMIDINE DERIVATIVES

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Oncological diseases are among the most difficult to diagnose due to the various causes of their occurrence and development. Therefore, the development of new antitumor drugs is not only of practical importance, but also allows us to better study the processes at the cellular level. Since the ring system of triazolopyrimidines is isoelectronic with purine, this heterocycle has been proposed as an analog of purines that exhibit antitumor activity.

This work is devoted to the synthesis of triazolo[4,3-*a*]pyrimidine derivatives with various substituents in the aromatic ring by reducing the 2-arylhydrazone derivatives of thiazolo[3,2-*a*]pyrimidines under the conditions of a new reduction system ($NaBH_4/V_2O_5$/EtOH) [1], as well as to the assessment of the cytotoxicity of the obtained compounds. It turns out that the rearrangement is initiated by the reduction of the hydrazylidene bond C=N. After reduction, the nitrogen atom of the hydrazinyl group attacks the thiazolopyrimidine framework (C-8A) and an intermediate or transition state is formed. Desulfurization, caused by either vanadium (IV) oxide or water, results in the formation of aldehyde E, which is reduced to the intermediate compound F. The final intramolecular condensation results in 2-(hydroxymethyl)triazolo[4,3-*a*]pyrimidine structure.

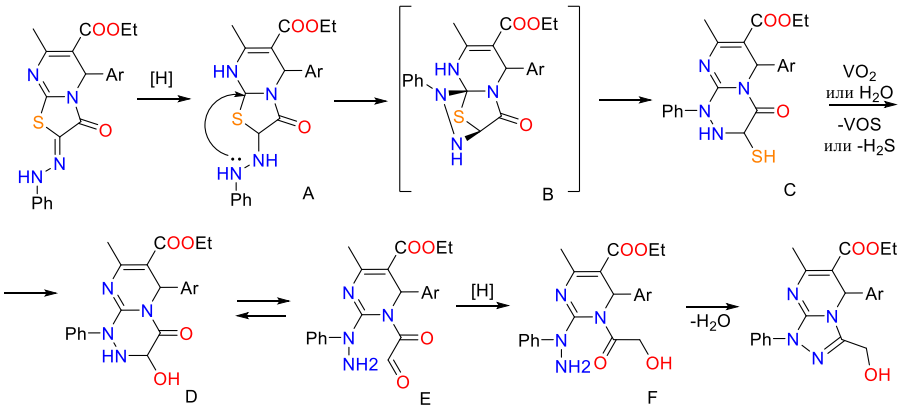

Figure 1. Suggested mechanism of formation of 2-(hydroxymethyl)triazolo[4,3-a]pyrimidine.

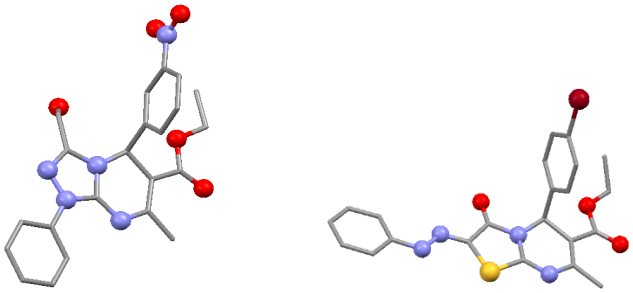

Figure 2. Crystal structure of derivatives of 2-(arylhydrazinylidene)[1,3]thiazolo[3,2-*a*]pyrimidines and 3-(hydroxymethyl)[1,2,4]triazolo[4,3-*a*]pyrimidine.

The structure of the obtained compounds was determined using mass spectrometry, X-ray diffraction analysis, IR and NMR spectroscopy

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VISIBLE LIGHT-INDUCED ACTIVATION OF 1,3,4-OXADIAZOLINES

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The chemistry of diazo compounds gives access to diverse reactive species and represents an extremely valuable branch of organic synthesis. While a number of reports on stabilized diazo compounds is constantly growing, the reactivity of non-stabilized diazoalkanes and subsequent intermediates is lacking exploration because of its problematic synthesis and hazardous nature [1-2]. In terms of safety, *in situ* generation from hydrazones, diazirines, nitrosoamides, and 1,3,4-oxadiazolines constitutes a valuable alternative [3-6].

Among others, 1,3,4-oxadiazolines have proven to serve as precursors of versatile intermediates under variable reaction modes [6]. Upon thermolysis, they generate ylides and nucleophilic carbenes, while under UV light irradiation photolysis to non-stabilized diazo compounds occurs. On the other hand, LFP conditions may lead to electrophilic carbenes.

Although oxadiazolines are stable, easily synthesized compounds, most of their synthetic applications rely on thermal activation [6]. Only within the past decade, Ley and coworkers proposed their use in UV light-induced aryl-alkyl cross-coupling and C-H functionalization reactions of aldehydes [7-8]. However, the reactivity of these heterocycles has never been investigated in the presence of visible light.

To reveal their full chemical potential, herein we explore the reactivity of 1,3,4-oxadiazolines under blue light irradiation and present formal cyclopropanation reaction of electron-deficient olefins (Figure 1). Mechanistic experiments support energy transfer process from photocatalyst and identify 1-pyrazoline as one of the reaction intermediates. The designed procedure is efficiently leading to valuable spirocyclic products within only one hour and the addition of only 0.25 mol% of a photocatalyst.

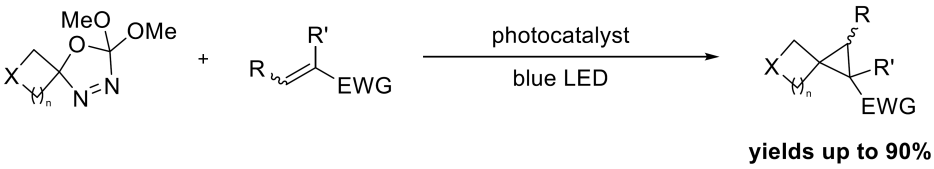

Figure 1. Photocatalyzed formation of spirocyclic compounds with 1,3,4-oxadiazolines

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ADDITION OF PHTHALIMIDONITRENE TO VINYL-SUBSTITUTED FURAN, THIOPHENE AND PYRROLE DERIVATIVES

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N-Aminophthalimide ($PhthNNH_2$) is a classic compound used for the preparation of aziridines via oxidative aminoaziridination of easily available C=C substrates [1]. Though the free phthalimidonitrene is not a relevant intermediate in this process, the resulting three-membered aziridine ring corresponds to the formal addition of a nitrene to a double carbon-carbon bond. In contrast to styrole derivatives, vinyl-substituted five-membered heterocycles (thiophene, pyrrole, furan) can accept carbenes and nitrenes not only by exocyclic double bond but by heterocyclic core itself due to its less aromaticity. Being intrigued by this idea, we have focused our attention on these substrates for aziridination.

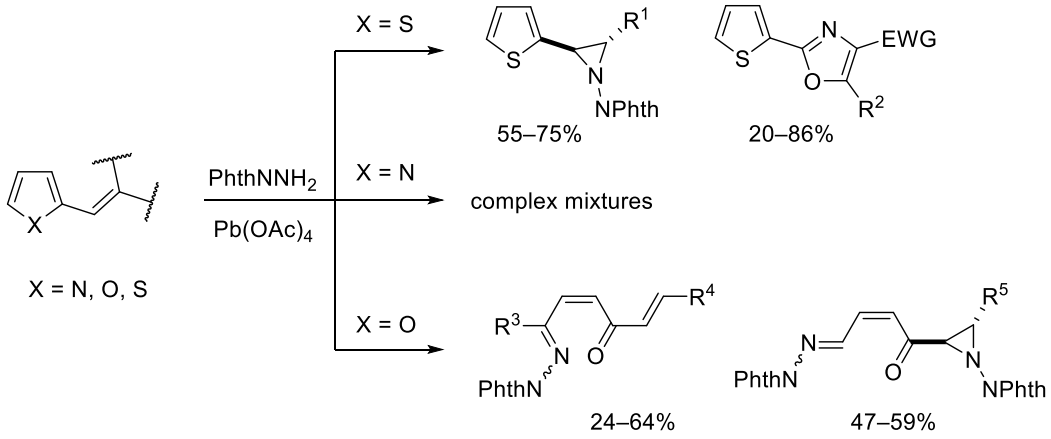

Figure 1.

Formation of fused tricyclic bisaziridines was observed for unsubstituted thiophene and selenophene [2]. A double bond attached to a thiophene ring changes the reaction pathway completely providing only thiophenyl-substituted aziridines. Such compounds with three functionalities at aziridine carbon atoms appeared to be quite unstable even at room temperature. However, the easy of ring cleavage facilitates thermal transformation of acyl-decorated substrates into thiophenyl-substituted oxazoles, and the whole sequence can serve as a direct approach to these structures.

N-Substituted pyrroles did not yiled any fused aziridines. Moreover, complex mixtures were obtained during the oxidative aminoaziridination of vinylpyrroles. Obviously, addition of phthalimidonitrene to endocyclic pyrrole bond(s) takes place but low stability and high reactivity of intermediate aziridines explain the final failure.

Oxidation of *N*-aminophthalimide in the presence of furan afforded monophthaloylhydrazone of malealdehyde [3]. Substituted 2-vinylfurans provided monophthaloylhydrazones of (2*Z*)-hexa-2,5-diene-1,4-dione derivatives by proceeding through an aziridination of the endocyclic furan C=C bond followed by a regio- and stereoselective rearrangement of the bicyclic intermediates. The formation of stable aziridines can then occur through the aziridination of the (*E*)-C=C bond of these phthaloylhydrazones.

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INSERTION OF Rh(II)-CARBENES INTO THE ANILINIC *N-H* BOND OF UNPROTECTED AMINOBENZENESULFONAMIDES IN THE SYNTHESIS OF NOVEL HUMAN CARBONIC ANHYDRASE AND HUMAN TIOREDOXIN REDUCTASE INHIBITORS

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Nowadays researchers from all over the world are trying to develop effective cancer therapy. Targeted mode of anticancer drug action is mainly based on inhibition of tumor-related proteins which are overexpressed in malignancies. One of such proteins is zinc-based metalloenzyme human carbonic anhydrase (*h*CA) that catalyzes the interconversion between carbon dioxide and bicarbonate ion ($CO_2 + H_2O \rightleftharpoons HCO_3^- + H^+$) in living organisms. The most explored class of *h*CA inhibitors are primary sulfonamides [1]. One drawback of such agents is low translation of inhibitory activity on recombinant enzymes into antiproliferation activity on cancer cell cultures. One of the ways to improving their cytotoxicity is the design of so-called dual-inhibitors with multiple modes of anticancer action [2]. Such molecules usually comprise multiple pharmacophore groups.

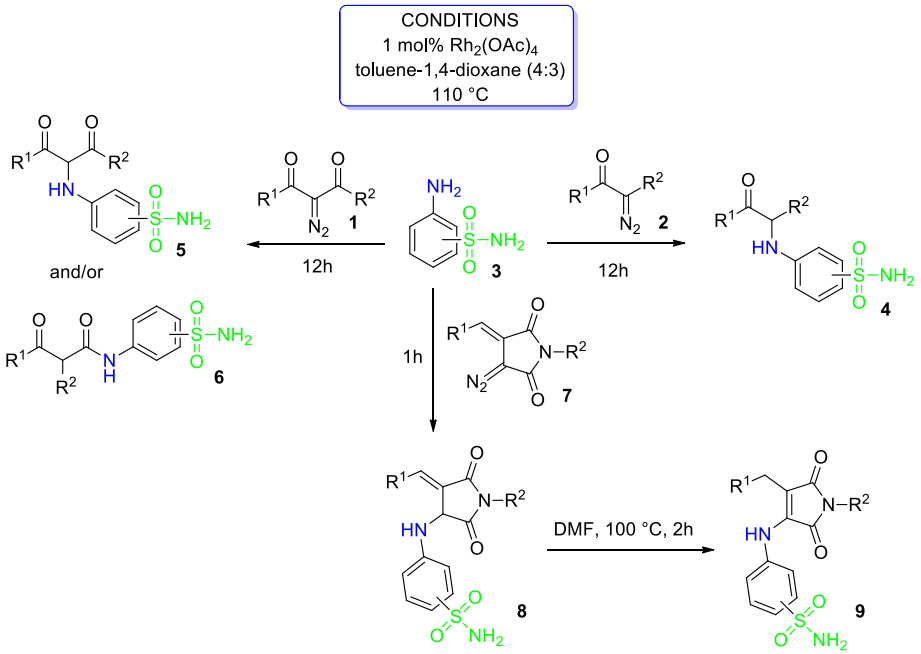

Figure 1. *NH*-insertion reactions of diazocompounds **1**, **2** and **7** into 3- and 4-aminobezenesulfonamides **3**.

In our study we synthesized a series of primary sulfonamides *via NH*-insertion reaction of *α*-diazo mono- and dicarbonyl compounds **1**,**2** into 3- and 4-aminobezenesulfonamides **3**. Despite high nanomolar activity of products **4**, **5**, **6** against IX and XII isoforms of *h*CA (validated antitumor therapeutic targets) their antiproliferative properties were found neglectable [3]. These facts encouraged us to synthesize alternative series of inhibitors which included not only primary sulfonamide group but also Michael acceptor (activated double bond) moiety. Such motif is capable of blocking another therapeutically important enzyme – thioredoxin reductase (TrxR1). To our delight, compounds **8** and their isomers **9** demonstrated enhanced antiproliferative activity against cancer cells with certain degree of selectivity over healthy human fibroblast cells used as control.

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NEW RHODIUM(I) CATALYSTS WITH CHIRAL DIENE LIGANDS FOR ENANTIOSELECTIVE INSERTION OF DIAZO COMPOUNDS INTO E−H BONDS

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Asymmetric insertion of diazo esters into B−H and Si−H bonds is an interesting reaction, which provides chiral boranes and silanes, that cannot be obtained by classical hydroboration or hydrosilylation of alkenes [1]. We have found that this reaction is effectively promoted by the rhodium(I) complexes with chiral barrelene ligands (Figure 1). The rhodium catalysts have been obtained by a new convenient procedure, which involves the separation of racemic complexes by selective capturing of one of the enantiomers with an auxiliary chiral ligand [2]. The DFT calculations have been used to predict the efficiency of the separation of enantiomers as well as the stereoselectivity of catalytic reaction.

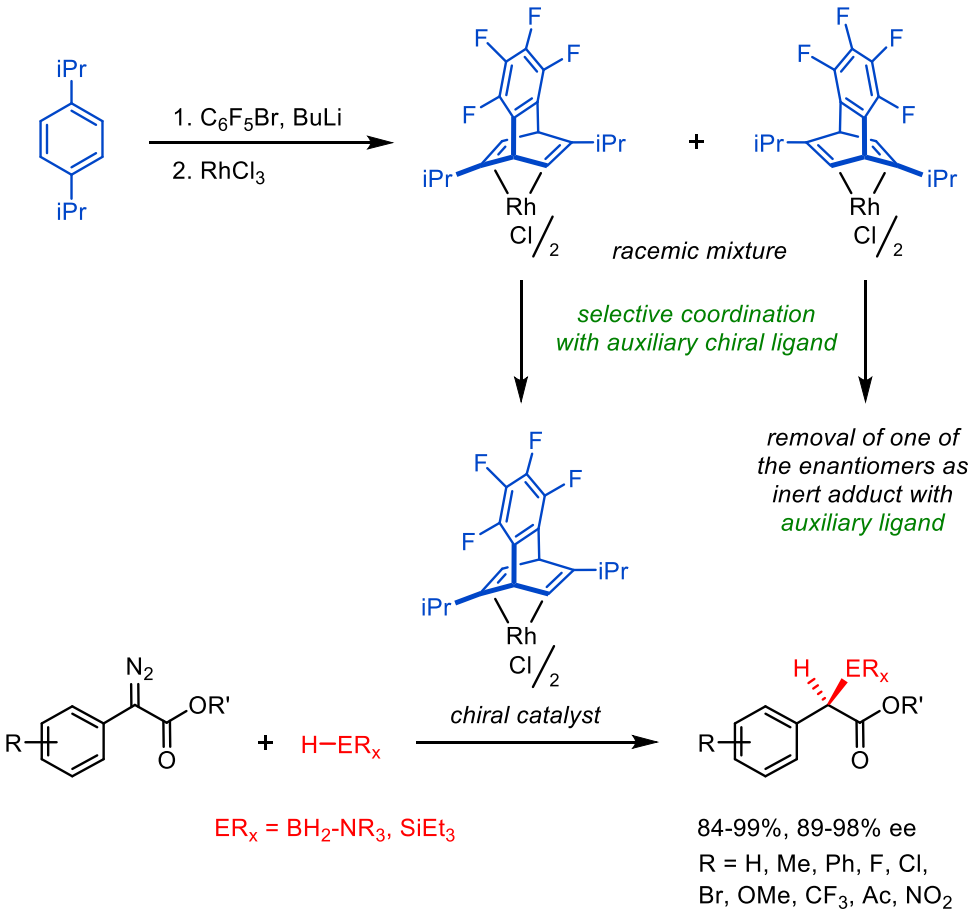

Figure 1. Synthesis of chiral rhodium catalysts and their application for reactions of diazo compounds.

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Acknowledgements. This work was supported by the Russian Science Foundation (project # 17-73-20144).

SYNTHESIS OF FUNCTIONALYZED 2- AND 3-(1,2,3-SELENADIAZOL-4-YL)FURANS

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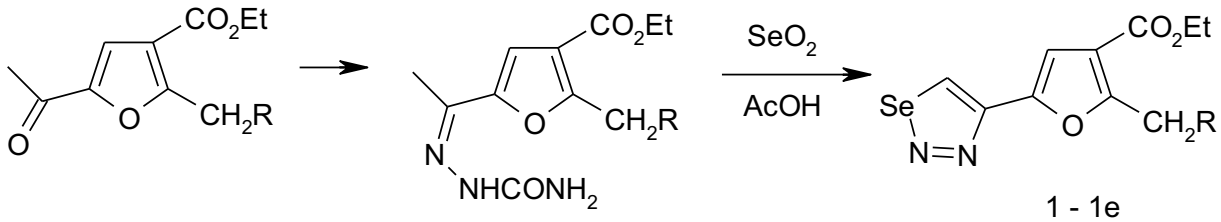
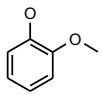
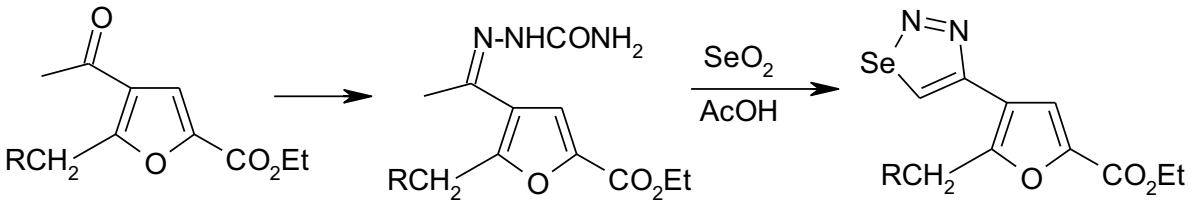
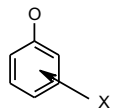
Hybride heterocyclic systems containing furan ring conjugated with 1,2,3-selenadiazole one are of great interest from the point of view of searching of new antibacterial drugs [1]. Besides, they can be regarded as the sourse of dihydrogen selenide, the main substance from which selenacystein is synthesized in living organisms by means of the reaction with serine bound to its t-RNA [2]. That means that use of specially prepared selenacystein or selenamethionine for curing of deseases arising from the deficite of selenium is not effective or even dangerous. Only some representatives of (1,2,3-selenadiazolyl)furans were prepared [1] and occurred to be thermally unstable. We have found that for stabilization of such systems introduction of electron-accepting substituent such as ester group is necessary. By this way compounds **1,2** were prepared in good yields from corresponding semicarbazones by oxidation with selenium dioxide in acetic acid. It occurred that further functionalyzation of these substances by consecutive bromination and nucleophilic substitution can not be performed because selenadiazoles **1,2** decompose under the action of NBS. That is why desired substituents must be introduced on previous stages. The main problem in synthesis of target compounds is the stability of such substituents to the action of selenium dioxide. It was found that ethers, sulfides, sulfoxides and phosphonates are stabile, while aminomethyl group is oxidized more eagerly, than semicarbazone.



R = H (1), OH (1a), OAc (1b),  (1c), S-Bu (1d), $PO(OEt)_2$ (1e)



R = H (2),  (2a), S-Bu (2b), $S\text{-}CH_2CO_2Et$ (2c), $S\text{-}CH_2\text{-}CH_2OAc$ (2d), SO_2Ar (2e)

X=OCH_3, CO_2Me, CO_2Et, $CONH_2$

Figure 1.

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Acknowledgements. This work was supported by the state project of Ministry of Science and Education of Russia no 785.00X6019

Pd^{II} AND Pt^{II}-MEDIATED COUPLING OF ARYL ISOCYANIDES WITH *N*-HETEROCYCLIC THIONES AS A WAY TO MONO- AND POLYNUCLEAR AMINOCARBENE COMPLEXES

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In recent decades, transition metal complexes with aminocarbene ligands (NHC – N-heterocyclic carbenes, ADC – acyclic diaminocarbenes) have taken a special place in coordination and organometallic chemistry due to their wide application in catalysis, material design, and medical chemistry [1]. One of the promising and facile methods for generating complexes with various types of aminocarbene ligands is the metal-mediated addition of nucleophiles to coordinated isocyanides [2].

In the present work, we have studied the Pd^{II} and Pt^{II}-mediated coupling of aryl isocyanides with *N*-heterocyclic thiones acting as ambident *S,N*-nucleophiles. The reaction of equimolar amounts of *bis*(aryl isocyanide) complexes and corresponding thione in the presence of one equivalent of base leads to the formation of mononuclear *C,S*-chelated aminocarbene complexes in which the carbene fragment is formed by the endocyclic nitrogen atom of thione and the triple CN of an isocyanide ligand (Figure 1) [3]. At the same time, the utilization of an excess of a base in the reaction with unsubstituted thiones yields the deprotonation of the formed complexes and allows obtaining polynuclear coordination macrocyclic compounds, which structure was confirmed both in a solution (by NOESY and DOSY NMR technics, mass-spectrometry) and in a solid state (by single-crystal X-ray diffraction). However, the latter compounds could be downgraded again to the mononuclear species by the addition of triphenylphosphine (PPh_3).

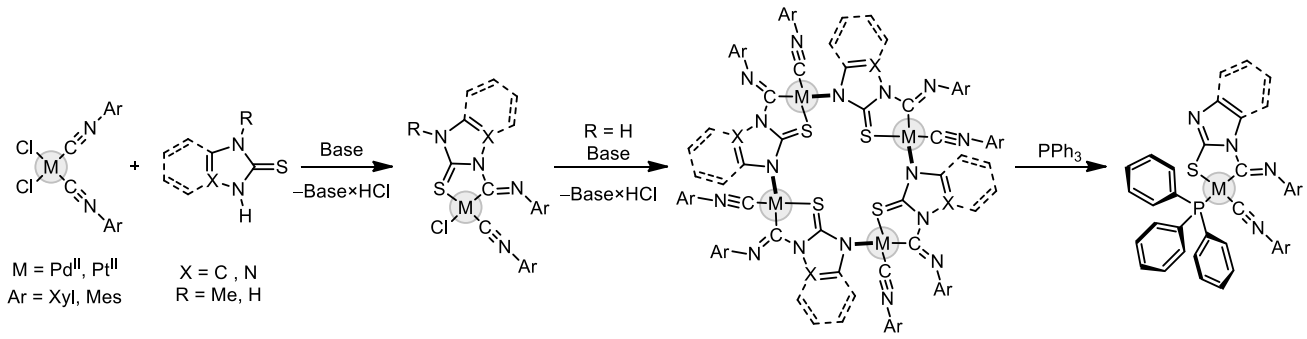

Figure 1. Coupling of *bis*-(aryl isocyanide) Pd^{II} and Pt^{II} complex with *N*-heterocyclic thiones.

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Acknowledgments. This work was supported by the Russian Science Foundation (project No 19-13-00008). Physicochemical studies were performed at the Center for Magnetic Resonance, Center for X-ray Diffraction Studies, Center for Chemical Analysis and Materials Research, and Chemistry Educational Centre (all belong to SPbU).

ADVENTURES IN DENITROGENATIVE REACTIONS OF 1,2,3-TRIAZOLES

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Denitrogenative reactions of 1,2,3-triazoles are currently an actively developing area of organic synthesis [1, 2]. In the presence of a metal catalyst, these reactions are believed to proceed via the generation of reactive metal-bound azavinyl carbenes. The unique and diverse reactivity of these species and further intermediates derived from them has made it possible to achieve significant progress in the development of new methods for the synthesis of a wide range of acyclic and heterocyclic compounds, including natural compounds.

In our research group, we are developing an approach to a straightforward one-step synthesis of complex functionalized heterocycles based on the Rh(II)-catalyzed reaction of *N*-sulfonyl-1,2,3-triazoles **1** (or pyridotriazoles **2**) with accessible *N*-heterocyclic compounds (Fig. 1). Such reactions proceed via intermediate formation of azapolyenes **3** followed by further cyclization or rearrangement. Thus, using variously substituted pyrazoles and *N*-sulfonyl-1,2,3-triazoles **1** we recently synthesized unique aza-bridged compounds **4** (route *a*) and (*Z*)-2-(2-aminovinyl)imidazoles **5** (route *b*) [3]. Novel (*Z*)-1-(2-aminovinyl)indoles **6** were prepared by the reaction of 2,2-diaryl-2*H*-azirines with *N*-sulfonyl-1,2,3-triazoles **1** [4] (route *c*). Using 3,4,5-trisubstituted isoxazoles and *N*-sulfonyl-1,2,3-triazoles **1**, a convenient method for the synthesis of 2-aroylpyrimidines **7** was developed (route d). Finally, the Rh(II)-catalyzed reaction of pyridotriazoles **2** with 2*H*-azirines afforded stable non-aromatic 4*H*-pyrido[1,2-*a*]pyrazines **8** [5] (route e). The intricate mechanisms of the reactions were studied experimentally and by DFT calculations.

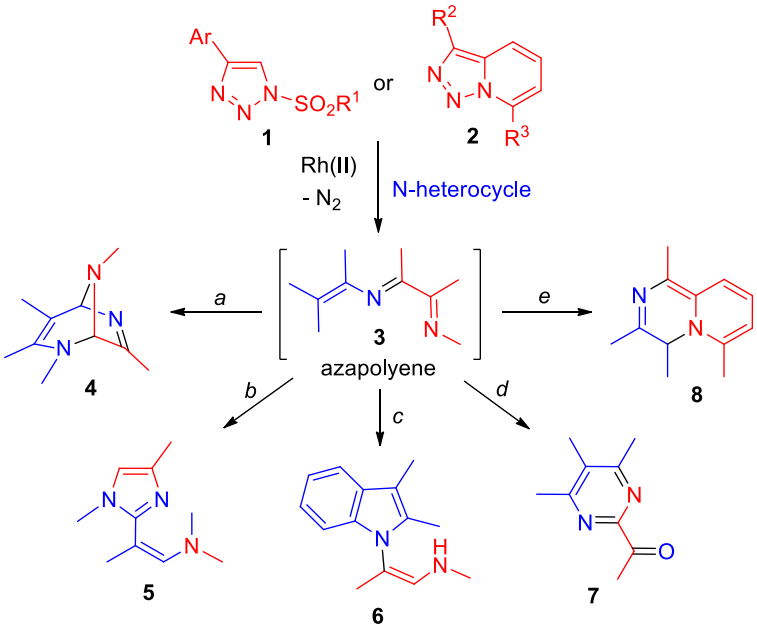

Figure 1. Rh(II)-catalyzed denitrogenative reactions of 1,2,3-triazoles with *N*-heterocycles.

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Acknowledgements. This work was supported by the Russian Science Foundation (projects 17-13-01078 and 19-73-10090). This research used resources of the Magnetic Resonance Research Centre, Chemical Analysis and Materials Research Centre and Centre for X-ray Diffraction Studies of the Research Park of St. Petersburg State University.

VISIBLE LIGHT INDUCED ALLENE FORMATION THROUGH DOYLE-KIRMSE REACTION

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Diazo compounds as a source of reactive species are considered a powerful tool in organic synthesis. Upon photolysis, thermolysis, or metal catalysis they generate carbenes in either singlet or triplet state, which then easily undergo rearrangements, insertion reactions, cycloadditions, and others [1].

Application of visible light in organic transformations, since these processes are more environmental-friendly, is of growing interest. In this line, both elimination of expensive and toxic metal catalysts and application of visible light, make such methods extremely attractive. Photochemical reactions engaging diazo compounds have been investigated over the years [2]. Although UV-light-induced carbene generation is well known in diazo chemistry, only recently it became clear that introduction of a donor group to diazoacetates shifts the absorption spectra batochromically enabling their photolysis under blue irradiation [3]. α-Diazoesters have been also utilized in visible light mediated photoredox reactions. They were distinguished as efficient alkylating reagents of carbonyl compounds [4-5] and 2-acylimidazoles which in the presence of chiral photocatalysts furnish products with high enanioselectivities [6]. Recently, Xiao and coworkers proposed blue-light mediated, metal-free gem-difluoroallylation of aryl diazoesters [7]. Despite growing interest in diazo chemistry, still little is known about reactivity of these compounds upon light irradiation.

Here, we present light induced approach toward allene synthesis (Figure 1). The plausible mechanism involves carbene and subsequent ylide formation in the presence of propargil reagent followed by [2,3] rearrangement to give desired allene product. The methodology leads to an efficient functionalization of methylenes in a fast and green way with extrusion of nitrogen as a side product.

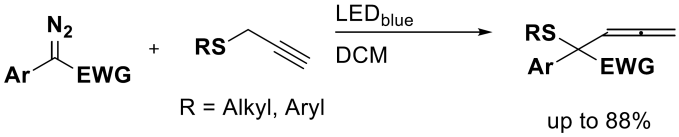

Figure 1. Visible light induced allene formation.

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REACTIONS OF 5-DIAZOAZOLES WITH 3-AZOLYL ENAMINES

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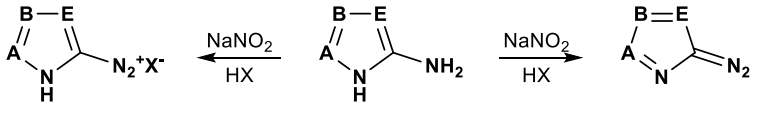
Diazotization of *N*-unsubstituted aminoazoles **1** can lead to the formation of both the corresponding heterocyclic diazonium salts **2** and diazoazoles **3** depending on the reaction conditions and the nature of the substituents in the azole ring [1, 2]. It is important to emphasize that the reactivity of diazonium salts and diazo compounds can differ significantly in the same types of reactions. However, chemists who are carried out organic synthesis very often don't take this knowledge to plane their own experiments [3].

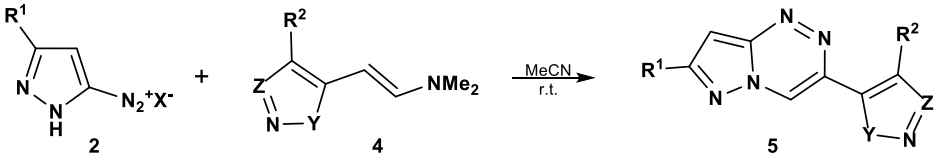


2 **1** **3**

A = N, B = E = CH/CR; A = E = CH/CR, B = N; A = B = N, E = CH/CR

Figure 1. Synthesis of azole diazonium salts **2** and diazoazoles **3**

Previously we have reported the reactions of 3-substituted pyrazole-5-diazonium salts **2** with β-azolyl enamines **4** which resulted in only 3-azolylpyrazolo[5,1-*c*][1,2,4]triazines with good yields [4].

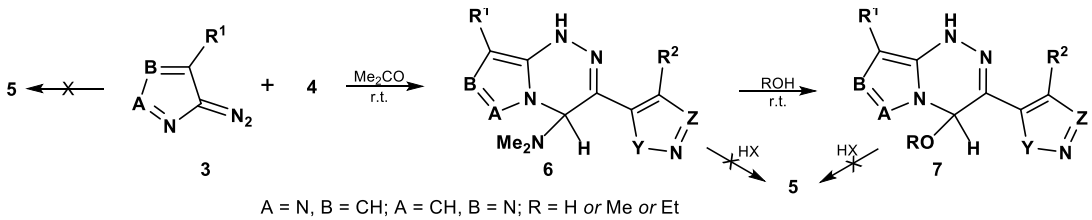


2 **4** **5**

X = HSO_4^- / BF_4^- Y = O, Z = CR; Y = S, Z = N

Figure 2. Synthesis of 3-azolylpyrazolo[5,1-*c*][1,2,4]triazines **5**

In the current research we studied the reaction of 5-diazoazoles **3**, such as ethyl 5-diazopyrazole-4-carboxylate and 4-substituted 5-diazoimidazoles, with *β*-azolyl enamines **4** containing isoxazole and thiadiazole moieties. It was found that only nonaromatic derivatives **6** are formed in these reactions, which are easily converted to compounds **7** by the action of nucleophiles (water or alcohol). It should be noted that aromatic derivatives **5** couldn't be obtained by the action of organic and mineral acids on compounds **6** and **7**.



3 **6** **5** **7**

A = N, B = CH; A = CH, B = N; R = H *or* Me *or* Et

Figure 3. Synthesis of 1,4-dihydroazolo[5,1-*c*][1,2,4]triazines **6** and 1,4-dihydroazolo[5,1-*c*][1,2,4]triazines **7**

The structures of the compounds **6** and **7** were characterized by ^{1}H and ^{13}C NMR spectroscopy, mass-spectrometry, elemental and X-ray diffraction analyses. Possible reaction mechanisms of enamines **4** with diazonium salts **2** or diazo compounds **3** will be discussed during the poster session.

The photophysical properties of compounds **6** and **7** were studied in various solvents using UV-Vis and fluorescence spectroscopy. It was found that in solutions these compounds exhibit green and yellow fluorescence with emission maxima in the region of 500–560 nm and quantum yields from 2 to 24 %.

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Rh(II)-CATALYZED COUPLING OF 1-SULFONYL-1,2,3-TRIAZOLE AND 1-ALKYL-1,2,3-TRIAZOLE

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1-Sulfonyl-1,2,3-triazoles are widely used in organic synthesis mainly due to their unique ability to undergo reversible ring opening to highly reactive α-diazo imines under relatively mild conditions. α-Diazo imine intermediates, generated from 1-sulfonyl-1,2,3-triazoles under catalysis, photolysis or thermolysis, easily react with various unsaturated and heteroatomic substrates to provide a straightforward route to hard-to-synthesize acyclic and heterocyclic nitrogen-containing compounds. Rhodium-bound azavinyl carbenes (Rh-AVC), due to their high reactivity, can react with a wide range of nucleophilic substrates, including aromatic heterocycles [1–4].

We turned our attention to *N*-alkyl-1,2,3-triazoles as potential reaction partners for Rh-AVC. As a result, we developed a method for the synthesis of 1-alkyl-3-sulfonamido-1*H*-pyrroles by the Rh(II)-catalyzed denitrogenative coupling of two different types of 1,2,3-triazoles: 1-alkyl-4-aryl- and 1-sulfonyl-4-aryl-1,2,3-triazoles. According to the DFT calculations, the reaction proceeds via the attack of the rhodium-bound azavinyl carbene, derived from the sulfonyl-1,2,3-triazole, at the N2 atom of the 1-alkyl-4-aryl-1,2,3-triazole and the successive formation of the rhodium-bound 1,2,3-triazol-3-ium ylide, metal-free 1,2,3-triazol-3-ium ylide, 1,4,5,8-tetraazaocta-1,3,5,7-tetraene, and 3-(azavinyl)-3,4-dihydro-1,2,4-triazine. The concerted denitrogenative ring contraction of the latter followed by 1,2-prototropic shift affords the 1-alkyl-3-sulfonamidopyrrole. This protocol provides 3-sulfonamidopyrroles from 1-alkyl-4-aryl-1,2,3-triazoles in 24–91% yield. In contrast to 1-alkyl-4-aryl-1,2,3-triazoles, 1,4-dialkyl-1,2,3-triazoles under the same conditions afford stable 1,2,3-triazol-3-ium ylides in 30–99% yield.

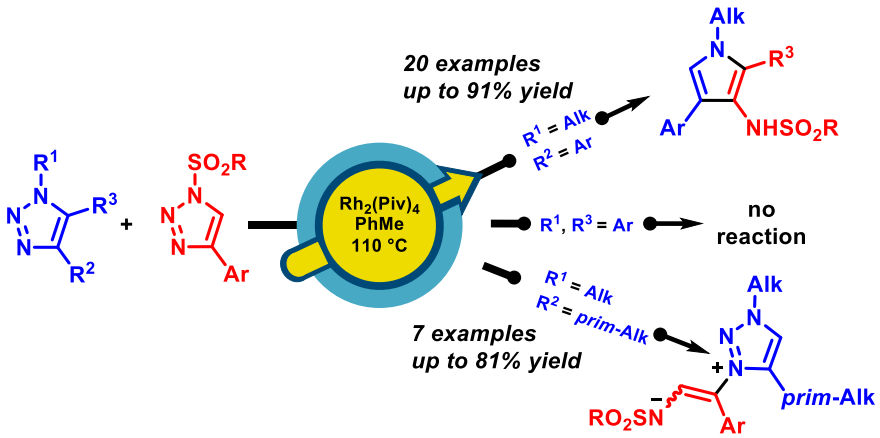

Figure 1. Rh(II)-catalyzed reaction 1-sulfonyl-1,2,3-triazole with 1-alkyl-1,2,3-triazole

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Acknowledgments. We gratefully acknowledge the financial support of the Russian Science Foundation (20-13-00044). This research used resources of the Magnetic Resonance Research Centre, Chemical Analysis and Materials Research Centre, Computing Centre, Centre for X-ray Diffraction Studies, and Chemistry Educational Centre of the Research Park of St. Petersburg State University.

DIAZOTIZATION OF AMINOPYRIDINE-1-OXIDES IN THE PRESENCE OF SULFONIC ACIDS

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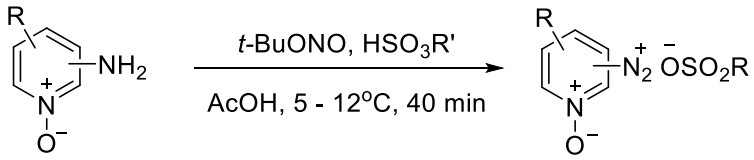
Aromatic diazonium salts are important intermediates in modern organic synthesis. It is known that diazotization of aromatic amines in the presence of such sulfonic acids as *p*-toluenesulfonic acid (*p*-TsOH) [1], trifluoromethanesulfonic acid (TfOH) [2], camphorsulfonic acid ($CamphSO_3H$) [3] provides relatively stable arendiazonium sulfonates $ArN_2^+RSO_3^-$. In contrast, the diazotization of aminopyridines under these conditions leads to the formation of the corresponding pyridyl sulfonates – $PyOSO_2R$ [4,5], which is explained by the instability of diazonium salts of pyridine structure. Recently, it was shown that aminopyridine-1-oxides are successfully diazotized in the presence of *p*-TsOH with the formation of the corresponding diazonium salts, which easily enter into the iododeamination reaction [6].

The aim of this work was to study the diazotization reaction of aminopyridine N-oxides in the presence of sulfonic acids (*p*-TsOH, TfOH, $CamphSO_3H$). It was shown for the first time that aminopyridine-1-oxides in a solution of acetic acid in the presence of sulfonic acids (*p*-TsOH, TfOH, $CamphSO_3H$) are diazotized by the action of *t*-BuONO with the formation of 1-oxidopyridine diazonium sulfonates (tosylates, triflates, camphorsulfonates). In all cases, diazotization takes place within 1 hour. The molecular structure of the obtained diazonium salts was proved using IR-, NMR-spectroscopy, mass spectrometry with electrospray ionization.



HSO_3R' = p-TsOH, TfOH, $CamphSO_3H$

Figure 1. Diazotization of aminopyridine-1-oxides.

It was found that 1-oxide-2-pyridinediazonium sulfonates can exist in two tautomeric forms: cyclic and non-cyclic, which is due to the nature of the substituent in the pyridine ring.

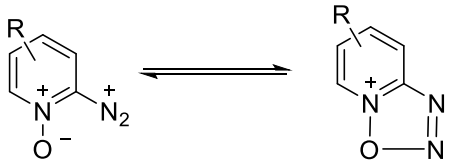


Figure 2. Tautomeric forms of 2-diazopyridine-1-oxides.

1-Oxidopyridinediazonium sulfonates are soluble both in water and in organic solvents of various polarities. They are able to enter into reactions of iodo- and azidodeamination typical of diazonium salts, interact with 2-naphthol, as well as with amines, forming pyridine triazenes.

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CYANINE DYES WITH SUBSTITUTED AMINO GROUP AT THE *MESO*-POSITION OF THE POLYMETHINE CHAIN

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Cyanine dyes have a number of favorable properties: tunable positions of the absorption and fluorescence maxima, very high extinction coefficients, fairly good photostability (especially in the presence of stabilizers and "blinking" buffers), bright emission, and the flexibility in synthesis which allows to decorate cyanines with various reactive and polar groups. The length of the polyene chain in cyanine dyes, and the nature of the aromatic "side groups" allow control and predictably change the luminescent properties of the chromophore, such as absorption wavelength and extinction coefficient, photostability and emission properties [1]. The versatile and easy access to *meso*-functionalized cyanine dyes would greatly improve their structural diversity and usefulness, and expand the applicability. At present, this kind of functionalization was impossible for Cy3 dyes, and very limited for Cy5 dyes, due to low yields, limited variability of the building blocks related to the central structural units, as well as undesirable elimination reactions at later synthesis steps.

In this work we introduced a substituted amino group to *meso*-position of the polymethine chain in Cy3 and Cy5 dyes. In particular, an amino group linked with a diazoketone residue was introduced. The spectral properties, and Wolff rearrangement of these compounds were studied. The photoconvertible cyanines undergoing transitions between non-fluorescent and fluorescent states upon irradiation with UV and visible light are candidates for the use in fluorescence microscopy, and in particular, MINFLUX nanoscopy [2].

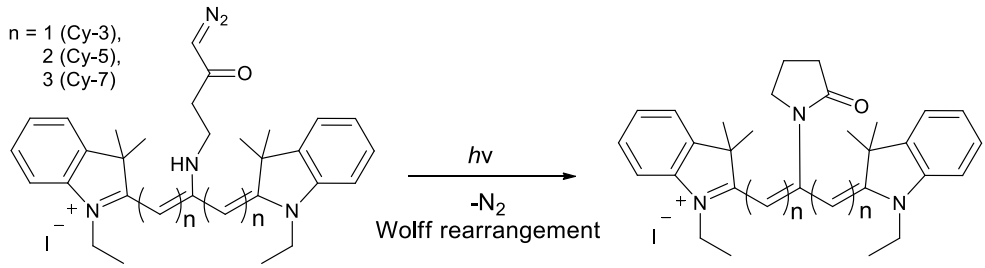

Figure 1. Photoconversion of cyanine dyes to lactam structures in the course of the photochemically induced Wollf rearrangement.

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SYNTHESIS OF 5-CYCLOPROPYL-1,3-OXAZOLES VIA THERMAL RECYCLIZATION OF *N*-PHTHALIMIDOAZIRIDINES

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Oxazole-based compounds are widely used in drugs production as pharmaceutically active ingredients. Oxazole derivatives reveal numerous biological activities, namely antibacterial, antiviral, antitubercular, anticancer, anti-inflammatory, antidiabetic, antioxidative properties etc. [1]. Herein we report the synthesis of 5-cyclopropyl-1,3-oxazoles via thermal transformation of *N*-phthalimidoaziridines.

The synthetic sequence includes several steps. At first, 1-cyclopropyl-3-arylprop-2-en-1-ones were obtained in good yields by base-catalyzed condensation of aromatic aldehydes and cyclopropyl methyl ketone. The reaction successfully occurred at room temperature in aqueous ethanol. Subsequently, corresponding *N*-phthalimidoaziridines were prepared by oxidation of *N*-aminophthalimide with lead tetraacetate in the presence of 1-cyclopropyl-3-arylprop-2-en-1-ones. The reaction was performed at –10 °C in CH_2Cl_2 as a solvent. Relative spatial position of substituents was preserved in this stereospecific reaction.

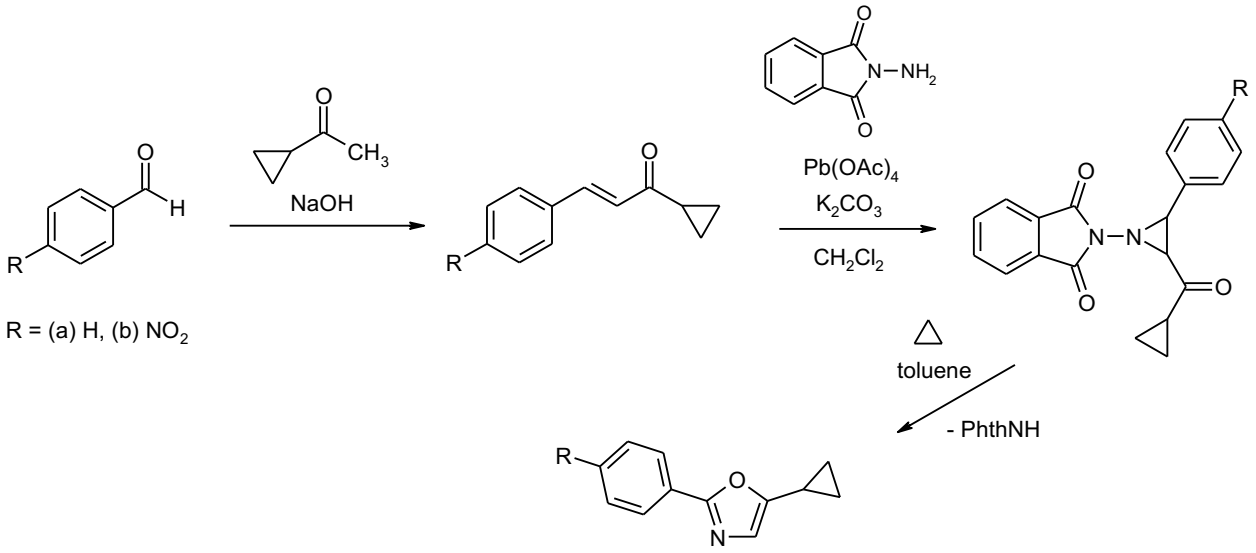

Figure 1. Synthesis of 5-cyclopropyl-1,3-oxazoles.

On the final step, *N*-phthalimidoaziridines were heated in toluene at 160 °C for 10 hours to give 5-cyclopropyl-1,3-oxazoles in good yields. The reaction is believed to proceed through thermal C–C cleavage of an aziridine ring to form azomethine ylide which is able to 1,5-electrocyclization accompanied by elimination of a phthalimide molecule [2]

The structures of synthesized compounds were confirmed by their IR, ^{1}H and ^{13}C NMR spectra.

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Acknowledgements. NMR spectroscopy studies were performed at the Saint Petersburg State University Center for Magnetic Resonance.

SYNTHESIS OF NEW PALLADIUM(II) ACYCLIC DIAMINOCARBENE COMPLEXES AND THEIR CATALYTIC ACTIVITY IN THE SUZUKI REACTION

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Palladium(II) acyclic diaminocarbene complexes have been successfully applied as catalysts in cross-coupling reactions (e.g. Suzuki–Miyaura, Mizoroki-Heck, Sonogashira) over the last few decades [1]. Acyclic aminocarbenes possess similar electronic stabilization as nonaromatic N-heterocyclic carbenes (NHCs), but their wider range of net electron-donor properties and steric flexibility as compared to NHCs allow greater control of both donor and steric properties [2].

In the present work, the reactions of 3,4-diaryl-1*H*-pyrrol-2,5-diimines with bisisocyanide palladium(II) complexes bearing aromatic isocyanides were studied.

Depending on the isocyanide substituents, the reaction proceeds via two alternative routes A and B (Figure 1). In all cases, only one coordinated isocyanide is subjected to nucleophilic addition attack. The unreacted isocyanide ligand either remains coordinated to the metallocenter (route A, 2,6-dimethylphenyl isocyanide), or is replaced with chloride anion (route B, 2-pivaloyloxyphenyl isocyanide). The primary reason for such behavior is the steric properties of isocyanide substituents.

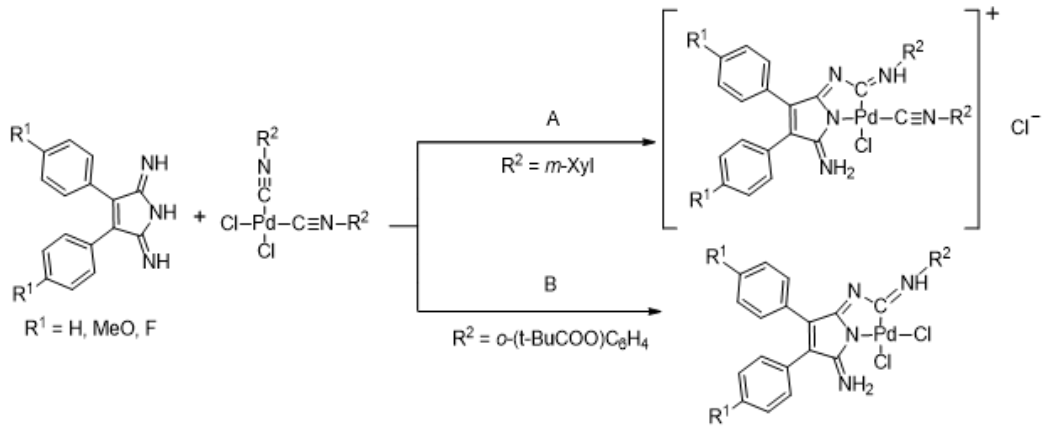

Figure 1. Two routes of reactions between 3,4-diaryl-1*H*-pyrrol-2,5-diimines and *cis*-[$PdCl_2(CN\text{-}R^2)_2$]

The catalytic potential of the complexes has been preliminarily assessed in the model Suzuki reaction between *p*-bromoanisole and phenylboronic acid, where these complexes display promising activity. Comparison of their catalytic activities in the Suzuki reaction revealed that the complexes with electron-donor substituents are the best catalysts.

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SYNTHESIS OF *B*-SUBSTITUTED ARYLAZO DERIVATIVES OF *ORTHO*-CARBORANE

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Icosahedral carboranes $C_2B_{10}H_{12}$ and their derivatives are of interest for a variety of applications, from medical chemistry to the development of new materials [1]. This requires the development of new convenient methods for their synthesis. Due to the different reactivity of the CH and BH groups in carboranes, different methods are used for synthesis of their *C*- and *B*-substituted derivatives. Earlier, a series of *C*-substituted arylazo derivatives of carboranes were prepared by direct [2-5] or decarboxylative [6-8] azo-coupling reactions using aryldiazonium salts. Recently we described synthesis a series of *B*-substituted arylazo derivatives of *ortho*-carborane 3-XC_6H_4-N=N-1,2-$C_2B_{10}H_{11}$ by the reaction of its diazonium derivative [3-N≡N-1,2-$C_2B_{10}H_{11}$][BF_4] with aryl Grignard reagents (Figure 1 and 2) [9]. Complexation reactions of arylazo derivatives of carboranes with various transition metals will be discussed.

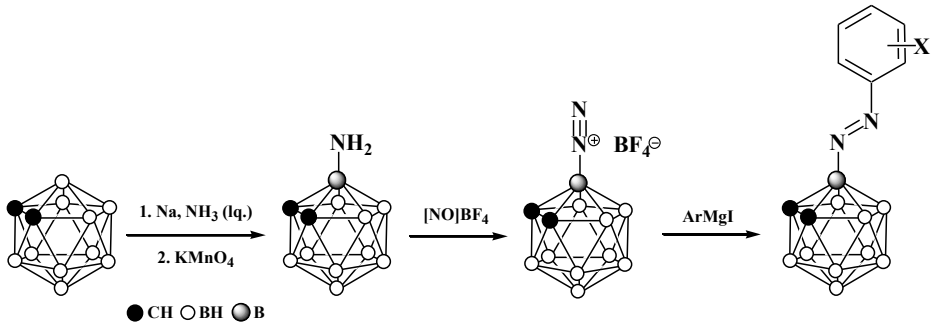

Figure 1. Synthesis of *B*-substituted arylazo derivatives of *ortho*-carborane 3-XC_6H_4-N=N-1,2-$C_2B_{10}H_{11}$.

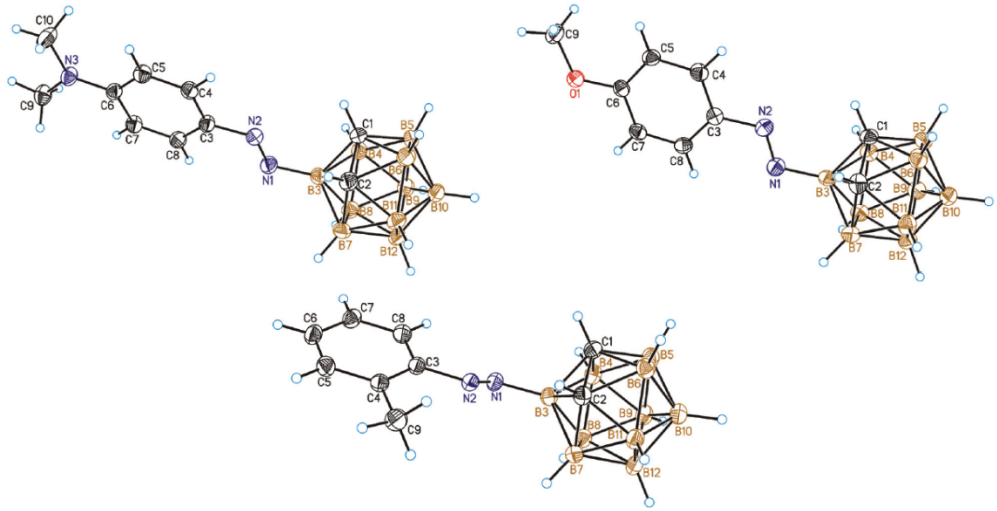

Figure 2. Crystal molecular structures of 3-arylazo derivatives of *ortho*-carborane 3-(XC_6H_4)-N=N-1,2-$C_2B_{10}H_{11}$ (X = 4'-NMe_2 (top left), 4'-OMe (top right) and 2'-Me (bottom)).

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1,3-DIPOLAR CYCLOADDITION OF DIAZO COMPOUNDS TO ACTIVATED ENYNES

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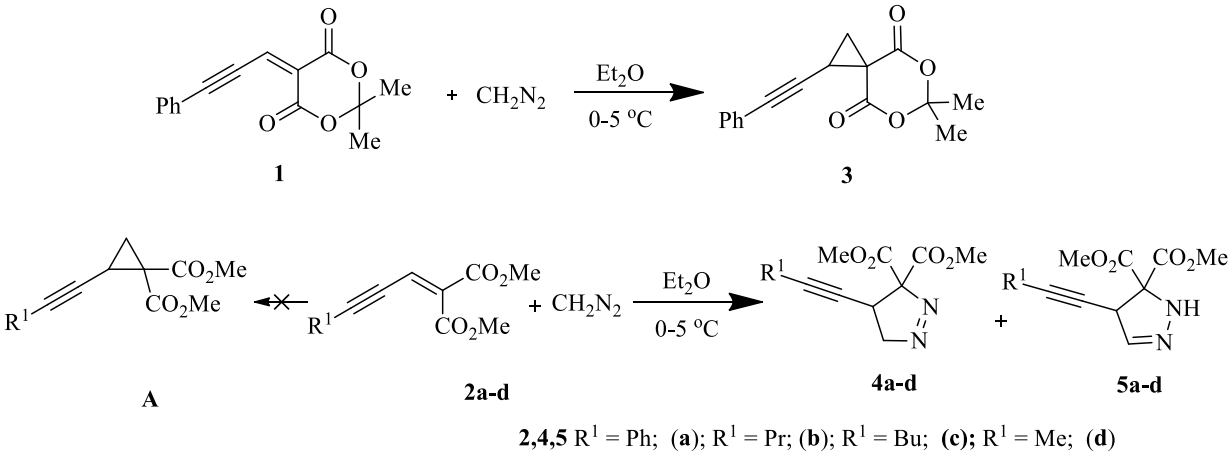
The reactions of 1,3-dipolar cycloaddition of diazo compounds to unsaturated compounds is a well-studied topic presented in many works [1-2]. Reactions of diazomethane with polycentric molecules, such as enynones cause great interest. As shown earlier, such interaction in the presence of catalysts can lead to the formation of furan derivatives [3]. The interaction of activated enyne structures is poorly studied. We have studied the 1,3-dipolar cycloaddition of diazomethane to the enyne derivatives of Meldrum acid **1** and dimethylmalonate **2 (**fig. 1**)**.

It was shown that compounds **1** and **2**, due to the polarization effect of CO groups, easily react with diazo compounds, specifically at double C=C bonds. In the case of the Meldrum acid derivative **1**, the reaction with an ether solution of diazomethane gives the cyclopropane derivative **3** with a yield of 80%. This can be explained by the significant steric loading of carbon atoms at the double bond in the starting enyne.

The reaction of compounds **2** with an ether solution of diazomethane proceeds with the formation of pyrazolines **4** and **5** in high yields (>95%). Structures 5 are minor isomers, the content of which does not exceed 10%. It should be noted that for products **4** and **5**, it is not possible to register high-resolution mass spectra, since under electrospray conditions they decompose with the evolution of nitrogen; in this case, a peak corresponding to the molecular ion of cyclopropane is recorded. Nevertheless, the composition of these products is reliably confirmed by quantitative elemental microanalysis for carbon and hydrogen. The structure was confirmed by NMR spectroscopy. The formation of cyclopropane derivatives **A**, similar in structure **3**, does not occur.



2,4,5 R^1 = Ph; (**a**); R^1 = Pr; (**b**); R^1 = Bu; **(c);** R^1 = Me; (**d**)

Figure 1. Reaction of enynes with diazomethane solution.

Thus, we have shown that electron-deficient 1,3-enynes containing in the first position, one or two electron-withdrawing groups, react with diazomethane on a double carbon-carbon bond in the absence of a catalyst. The data obtained can further serve as the basis for the development of methods for the synthesis of polyfunctional compounds containing structural elements of nitrogen-containing heterocycles and cyclopropane.

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O-H CARBENE INSERTION – CYCLIZATION SEQUENCE AS SYNTHETICAL APPROACH TOWARDS NOVEL 3,4-DIHYDRO-1,4-OXAZINE SULFONAMIDES AND SULFONES

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A short and practically convenient, modular approach to hitherto unknown dehydromorpholine sulfones and sulfonamides from α-acyl-α-diazomethane sulfones and sulfonamides, respectively, has been developed. It involves Rh(II) carbene insertion into the O-H bond of 2-bromoethanol followed by thermally promoted tandem S_N2 displacement of the bromine atom by a primary amine and cyclodehydration.

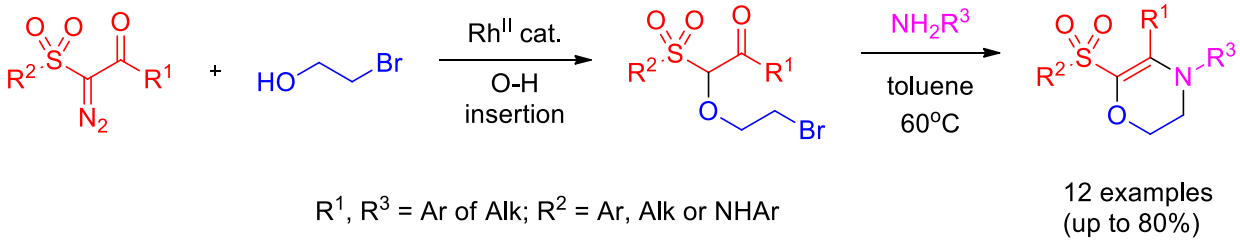

Figure 1. Preparation of dehydromorpholine sulfones and sulfonamides.

The newly synthesized versions of dehydromorpholine represent a valuable addition to the potentially bioactive compounds that are based on the privileged morpholine core.

Acknowledgements. This work was supported by the Russian Foundation for Basic Research (project grant 19-33-90018).

HYDRAZO COUPLING – THE EFFICIENT TRANSITION-METAL-FREE C–H FUNCTIONALIZATION OF 8-HYDROXYQUINOLINE AND PHENOL THROUGH BASE CATALYSIS

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Azodicarboxylate esters are common reagents in organic synthesis laboratories due to their utility in the Mitsunobu reaction. They can also be regarded as possible starting compounds for C–H functionalization, which was up till now mainly achieved by the transition-metal-catalyzed reactions. During our latest studies in the synthesis of the potential antiviral and antibacterial compounds we have developed a novel reaction of quantitative addition of azodicarboxylate esters to 8-hydroxyquinoline or phenol/naphthols without transition metal catalysis. The functionalization proceeds under mild base-catalyzed conditions selectively, and either ortho-position of 8-hydroxyquinolines or para-position of the phenolic substrates can be involved in the reaction. Herein, we discuss a plausible mechanism of this catalyzed substitution, backing our findings by deuterium NMR experiments and by varying starting compounds and bases.

This type of transformation can be considered as “hydrazo coupling” (by analogy with azo coupling). Using Boc-N=N-Boc as a substrate, we have developed the convenient and efficient synthesis of (8-hydroxyquinolin-7-yl)hydrazines, as well as demonstrated a new stereoselective route for the synthesis of important in medicinal chemistry 4-hydroxyphenylhydrazine that almost doubles the yield of the common industrial process and reduces the number of synthetic steps. 4-Hydroxyphenylhydrazine is a precursor of the well-known non-steroidal anti-inflammatory drug Indometacin and a key intermediate compound in the synthesis of new but still expensive drug – bazedoxifene – the latest generation selective estrogen receptor modulator. Nowdays, 4-hydroxyphenylhydrazine is prepared only in 59% yield in industry, thus, being the lowest-yield product of the total synthesis. We have proposed an efficient gram-scale protocol that eliminates two steps of synthesis with harsh reagents and doubles the overall yield, making it perfect for laboratory needs and screening in medicinal chemistry.

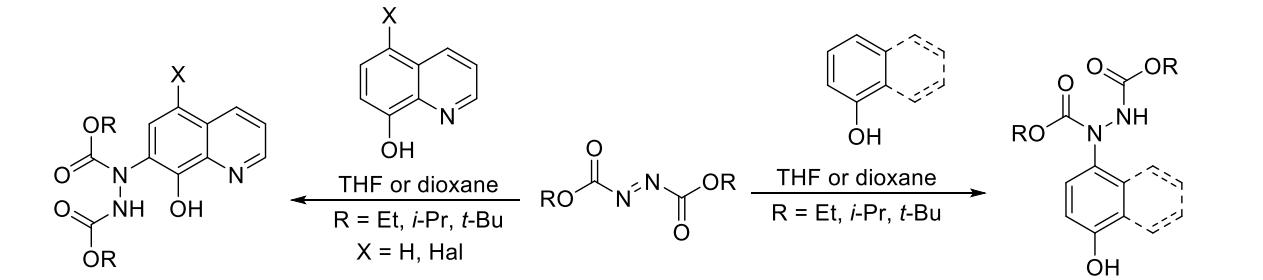

Figure 1. Hydrazo coupling.

We have synthesized a series of aromatic hydrazone derivatives based on 7-hydrazino-8-hydroxyquinoline *via* a new “one-pot” procedure and tested their cytotoxicity and biological activity towards viral proteins (HIV reverse transcriptase, HIV integrase), human Ku70 protein, and some bacteria.

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INTER- AND INTRAMOLECULAR ELECTROPHILIC AMINATION OF ARENES BY AMINODIAZONIUM CATIONS

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Aromatic amines are a sought-after functionality encountered in biologically active compounds, drug molecules, materials, agrochemicals, etc. Among the preparation methods available, direct electrophilic amination represents the most straightforward approach to the desired anilines [1]. Although highly attractive, this reaction faces serious limitations including the use of hydrazoic acid, necessity of harsh acidic conditions and limited substrate scope. A lack of understanding the underlying mechanisms makes it difficult to circumvent these disadvantages. Herein, we decipher the mechanisms of both inter- and intramolecular electrophilic amination of arenes by aminodiazonium cations using quantum chemical calculations (B3LYP/aug-cc-pVDZ and MP2/aug-cc-pVTZ) and provide experimental examples of mild amination routes that utilize new diazonium salt - aminodiazonium triflate as aminating reagent (inter-) or previously unknown amino-dealkenylation reaction (intramolecular variant).

Our study of intermolecular direct electrophilic amination of arenes by hydrazoic acid demonstrated that this reaction follows classical S_{EAr} mechanism with aminodiazonium cation $H_2N_3^+$ as electrophile. The reaction is characterized by an early transition state where nitrogen elimination and electrophilic attack occur at the same time [1]. We discovered that aminodiazonium cation can be trapped by a triflate anion resulting in new diazonium salt - aminodiazonium triflate **2** that is capable to aminate benzene **1** in organic solvents such as CCl_4 producing aniline **3a** in 15% yield (Figure 1).

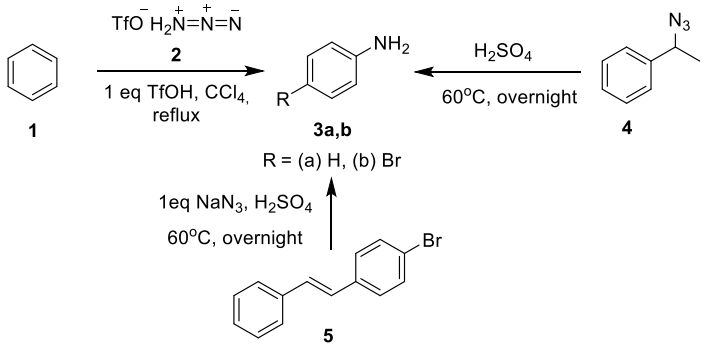

Figure 1. Inter- and intramolecular electrophilic amination of arenes by aminodiazonium cations.

We demonstrated that acid-catalyzed intramolecular rearrangement of azides could serve as a potent synthetic route to amines including preparation of synthetically challenging heterocyclic ones. In this reaction, protonated azide moiety can be considered as substituted aminodiazonium cation that rearranges via a concerted transition state with nitrogen elimination and alkyl/aryl migration occurring at the same time. Experiment showed that H_2SO_4-promoted rearrangement of (1-azidoethyl)benzene **4** followed by the hydrolysis yields in 50% of aniline **3a**. We have found that this reaction can be conducted in a cascade fashion using stilbenes as a starting material (amino-dealkenylation). For example, rearrangement of 4-bromostilbene **5** in H_2SO_4 in the presence of NaN_3 results in anilines **3a** and **3b** with 22% and 10% yield, respectively (Figure 1).

Our studies allow drawing important analogies between aminodiazonium $[RNH\text{-}N{\equiv}N]^+$ and aromatic diazonium cations $[Ar\text{-}N{\equiv}N]^+$. The key structural parameters of these two compound classes are very close, moreover, the reactions in both cases are accompanied by nitrogen elimination (dediazotization). Therefore, aminodiazonium cations can be seen as members of diazonium family, and their transformations - as part of the chemistry of diazo compounds.

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SYNTHESIS OF POLYFUNCTIONAL O- AND S-CONTAINING HETEROCYCLIC COMPOUNDS BASED ON CHEMICAL TRANSFORMATION OF ETHYL 2-DIAZO-3-OXOBUTANOATE

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Diazo carbonyl compounds are widely used in the synthesis of polyfunctional heterocycles [1-2], which have complexing properties, biological activity and can be used as ligands to obtain highly efficient and selective catalysts [3-5].

This work presents the results on the synthesis of heterocycles, including macrocyclic compounds, oxo esters, and benzofurans based on the interaction of cyclic acetals, alcohols, phenols with ethyl 2-diazo-3-oxobutanoate in the presence of complex catalysts based on copper and rhodium [6-10].

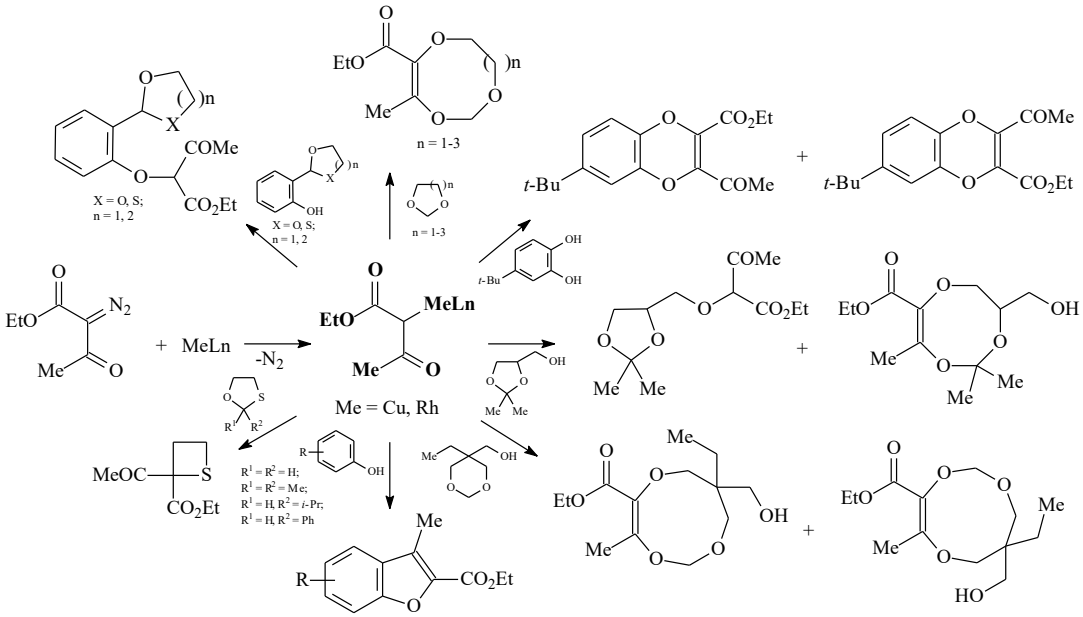

Figure 1. The report presents the regio- and stereoselectivity data of the reaction and the yields of the main products.

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CHEMOSELECTIVE REACTIONS OF 2*H*-AZIRINE-2-CARBOXYLIC ACIDS WITH DIAZO COMPOUNDS

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For many years, diazo compounds have been used as convenient precursors of carbenes, which are used both in modification and functionalization of various compounds and in the synthesis of new carbo- and heterocyclic structures [1, 2]. When several reaction centers are present in a molecule, the main problem is to select conditions for their chemoselective transformation.

Recently, our research group has developed a method for the preparation of 2*H*-azirine-2-carboxylic acids, which have two reaction centers that can interact with carbenes: azirine nitrogen atom and carboxylic group [3]. The aim of this work is to study the reactions of 2*H*-azirine-2-carboxylic acids with diazo compounds under photolysis and metal catalysis conditions. It was found that the blue light-induced reaction of acids **1** with aryldiazoacetates **2** makes it possible to selectively obtain the O-H insertion product, azirine **3** in diastereomeric ratio 1:1, while catalysis with rhodium acetate leads to the formation of 1,3-oxazin-6-ones **4** (Fig. 1).

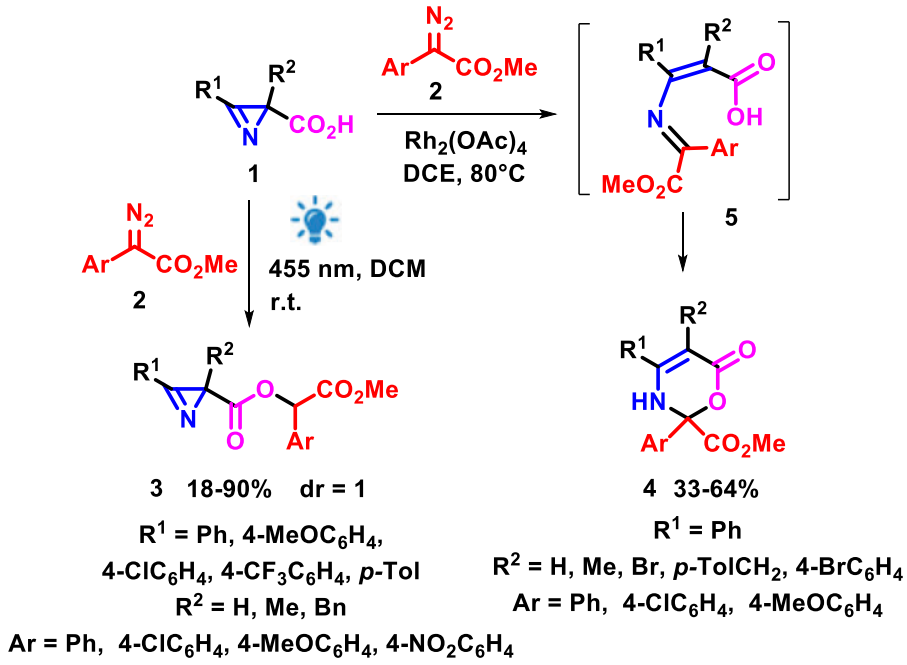

Figure 1. Reactions of 2*H*-azirine-2-carboxylic acids with diazo compounds

The formation of **4** probably proceeds through the 2-azadiene intermediate **5** followed by its cyclization. Two isomeric 2-azadienes, differing in the configuration of the C=C bond, can be formed in the reaction. It is noteworthy that in the case of $R^2 \neq H$, the yield of the final product **4** increases significantly, which is likely due to the predominance of isomer **5** required for the cyclization. In the near future, it is planned to expand the scope of the reactions with respect to diazo compounds and acids.

We gratefully acknowledge the financial support of the Russian Science Foundation (grant no. 19-73-10090). This research used resources of “Magnetic Resonance Research Centre” and “Chemical Analysis and Materials Research Centre” of St. Petersburg State University.

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VITAMIN B_{12} AS THE CATALYST IN ORGANIC REACTIONS

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Cobalt catalysis perfectly fits in the present trend in organic synthesis focusing on using cheap, earth-abundant, non-toxic first row transition metal catalysts [1]. The best evidence for environmentally friendly properties of cobalt is its occurrence in the living organisms in the active centre of vitamin B_{12} – a cofactor of several enzymes. Inspired by nature, scientists transferred natural functions of cobalamin to organic synthesis, harnessing it to catalyze reactions such as methylation, isomerisation and dehalogenation. In the course of subsequent studies, it appeared that the catalytic potential of vitamin B_{12} is far greater [2].

The unique abilities of cobalamin rely on the redox properties of the central Co(III) cation. In the reducing conditions vitamin B_{12} can take two forms characterized by different modes of action –radical Co(II) or 'supernucleophilic' Co(I) form. Both of them are able to form Co-C bonds which can be cleaved by electrolysis or light irradiation. Thus, created reagents are partners for the reactions with a variety of carbon species.

We showed that vitamin B_{12} offers exceedingly wide range of possibilities when applied as the catalyst in organic synthesis. With the use of cobalamin and its derivatives we were able to generate alkyl radicals furnishing electron-rich olefins [3] and acyl radicals reacting with electron-deficient olefins [4]. Moreover, we developed vitamin B_{12}-based method for deprotection of (allyloxy)arenes [5]. Lately, we harnessed cobalamin derivative to generate radicals from the strained bicyclo[1.1.0]butanes which could then react with SOMOphiles and electrophiles [6]. These examples clearly indicate versatility of vitamin B_{12} as the catalyst and suggest that many of its possibilities still remain to discover.

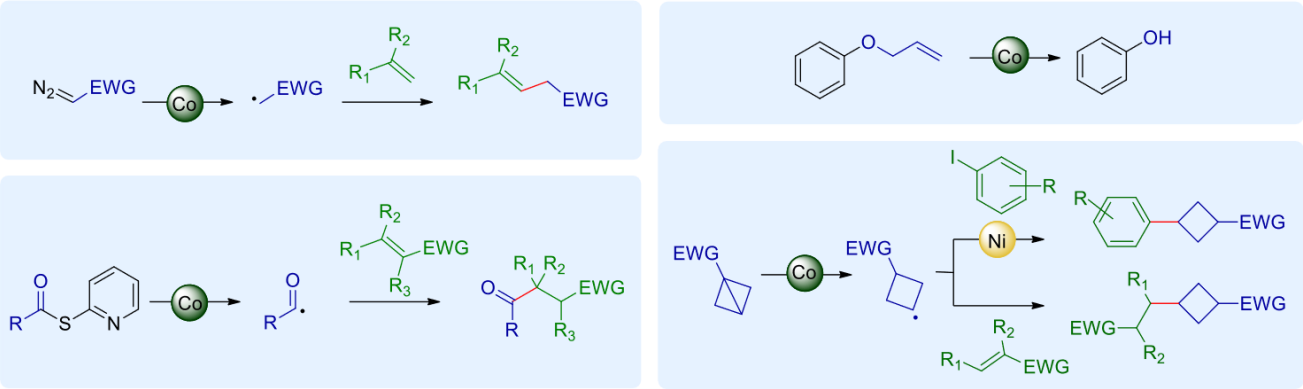

Figure 1. Reactions catalyzed by Vitamin B_{12}.

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[5+2] CYCLOADDITION OF SUBSTITUTED VINYL DIAZO SUCCINIMIDES TO KETONES. SYNTHESIS OF FUSED OXEPINES

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New convenient approach to the synthesis of substituted vinyl diazo succinimides (**1**) [1a] was proposed in our scientific group. Chemistry of these compounds was poorly studied until recently. During the past year diazo imides **1** were shown to may be involved both in well-known reactions of diazo compounds (X-H insertion reactions [1b] and formation of oxiranes from aldehydes [2]) and in uncommon for diazocarbonyl compounds reaction of formal insertion into C-O bond of ethers [1c].

Interaction between substituted vinyl diazo succinimides and ketones under Rh(II)-catalysis was investigated in the present work. As main reaction products benzo-annelated oxepines **3** were isolated in high yields (68-98%). They are probably resulted from cyclization of initially formed carbonyl ylide **2**. In certain cases, the target reaction was accompanied by the formation of byproducts **4** or **5**.

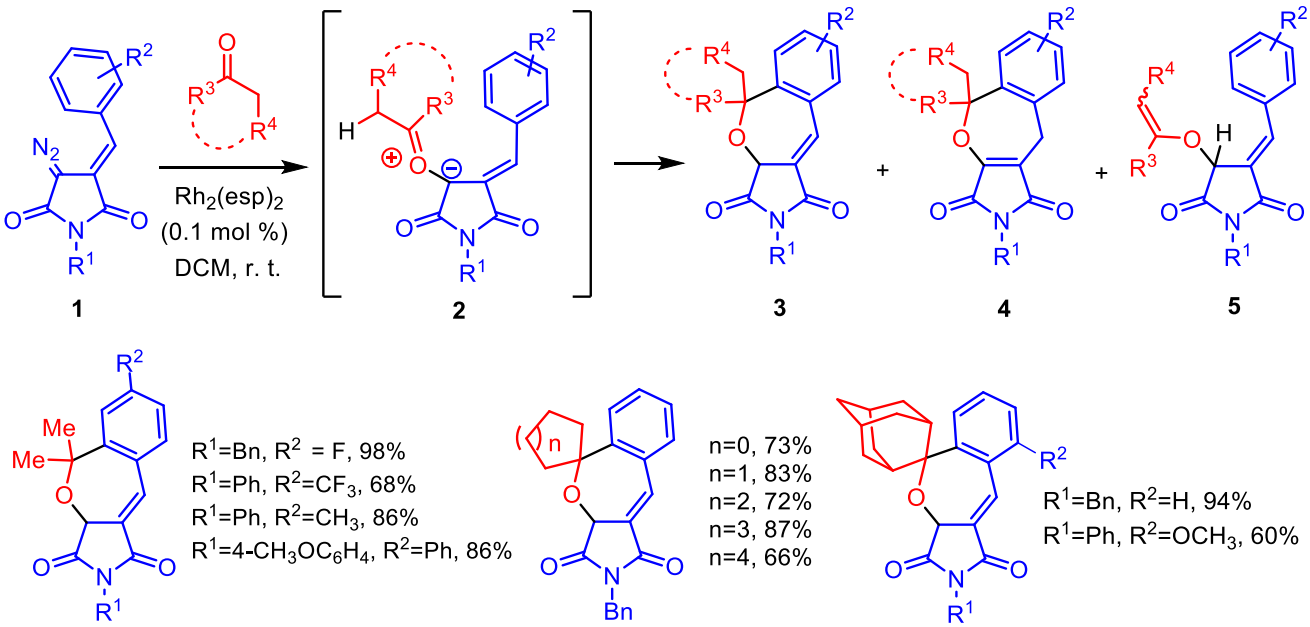

Figure 1. Studied reaction and isolated fused oxepines

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"CLICK"-SYNTHESIS OF 1-BENZYL-4-PHENYL-1*H*-1,2,3-TRIAZOLES FACILITATED BY COPPER(I) COMPLEX OF 1,2-BIS(2-*TERT*-BUTYLTETRAZOL-5-YL)DIAZENE

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1,2,3-Triazoles are basically five-membered nitrogen heterocyclic compounds. They have tremendous application in various research fields, including synthetic organic chemistry, medicinal chemistry and pharmaceutical synthesis [1]. It should be noted that the investigation of pathways of synthesis 1,2,3-triazoles are important, because they demonstrated a wide range of biological activities: antitumor, antiviral, antihistamic and fungicidal, thus gaining a lot of attention from medicinal chemists as the source for new potential therapeutic agents [2]. To date, many catalytic systems have been proposed for Huisgen [3+2] cycloaddition reaction, however most of them are quite expensive.

Taking into account these circumstances, herein we focused our attention on the catalytic synthesis of model 1-benzyl-4-phenyl-1*H*-1,2,3-triazole from phenyl acetylene and benzyl azide using copper(I) complex of 1,2-bis(2-*tert*-butyltetrazol-5-yl)diazene as a catalyst (Fig. 1). The catalyst was obtained *via* redox reaction between $CuCl_2$ and 1,2-bis(2-*tert*-butyltetrazol-5-yl)hydrazine and characterized by elemental analyses, HR ESI(+) mass-spectrometry, IR-spectroscopy, DSC/TG and powder X-ray diffraction. It demonstrated valuable catalytic features such as: a) high catalytic activity; b) low catalytic loading; c) cheapness. By using this catalyst, Huisgen [3+2] cycloaddition reaction proceeds under aerobic conditions at 80ºC in acetonitrile in relatively short reaction time with excellent yield of the product of up to 96%.

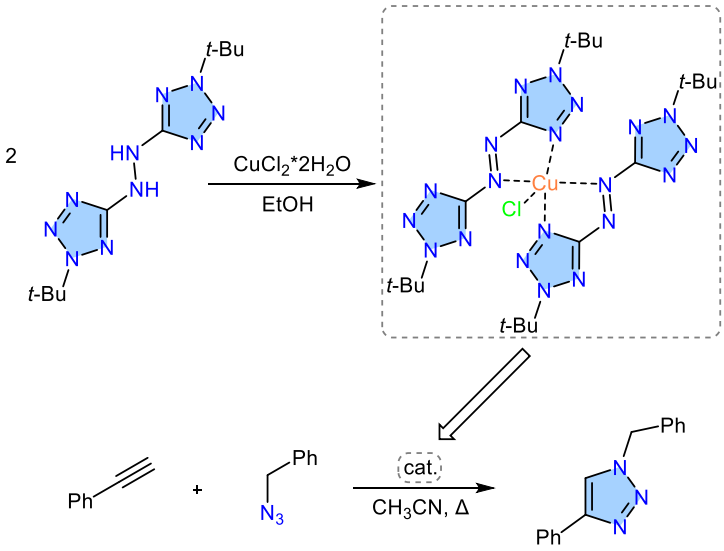

Figure 1. Schemes of the copper(I) complex of 1,2-bis(2-*tert*-butyltetrazol-5-yl)diazene synthesis and "click-synthesis of model 1-benzyl-4-phenyl-1*H*-1,2,3-triazole

The structure of the synthesized 1-benzyl-4-phenyl-1*H*-1,2,3-triazole was confirmed by ^{1}H and ^{13}C NMR spectroscopy.

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RHODIUM(III)-CATALYZED TRIFLUOROMETHYL-CARBENOID FUNCTIONALIZATION OF HETEROAROMATIC COMPOUNDS

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The development of new methods for the synthesis of heteroaromatic compounds is an ever-expanding area in bioorganic and medicinal chemistry. At the same time, the significant impact of fluorine functionalities on the modern drug discovery process is well recognized and has been the subject of numerous publications [1]. Therefore, the development of new effective methods for the selective introduction of fluorine and fluorinated groups in (hetero)arenes has a great current interest.

On the other hand, in the past decade the transition-metal-catalyzed functionalization of the C–H bond has emerged as one of the most efficient synthetic methods in terms atom-economy to construct diverse organic molecules from simple starting materials [2]. We have recently elaborated an efficient approach for direct CF_3-carbenoid C-H functionalization of functionalized benzenes, indoles, indolines and purines under chelation-controlled Rh(III)-catalysis using readily available methyl-3,3,3-trifluoro-2-diazopropionate as a cross-coupling partner [3].

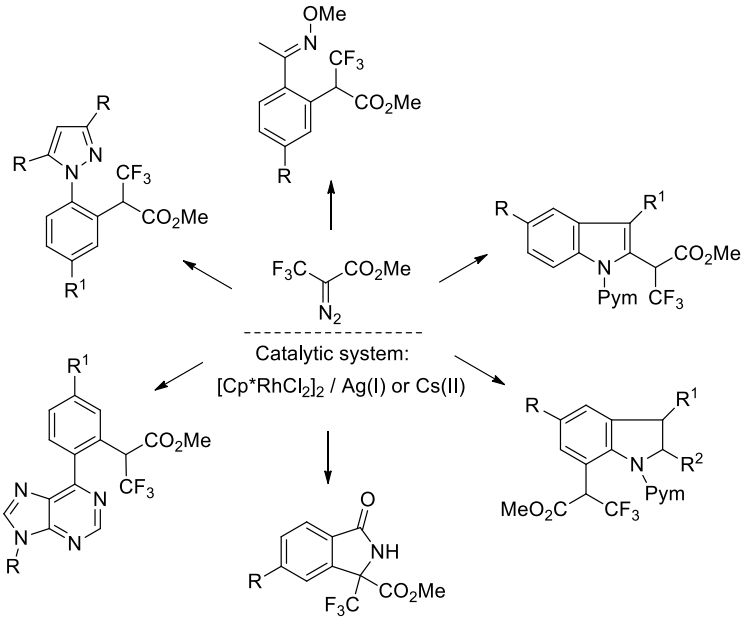

Figure 1. Rh-catalysed CF_3-carbenoid C-H functionalization of heteroaromatic compounds.

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A NEW THERMAL CYCLIZATION OF 4-AZIDO-3-TRIAZENO-1,2,5-OXADIAZOLE

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A previously unknown thermal cyclization in the 1,2,5-oxadiazole series involving an intramolecular reaction of the triazene group and the azido group is presented (Figure 1). The reaction results in 1,2,5-oxadiazole annulated with 1,2,3-triazole ring bearing an amino group at the N-2 atom. This new structure includes a Y-shaped nitrogen moiety with a specific type of charge distribution in which the central nitrogen atom is surrounded by three other nitrogen atoms.

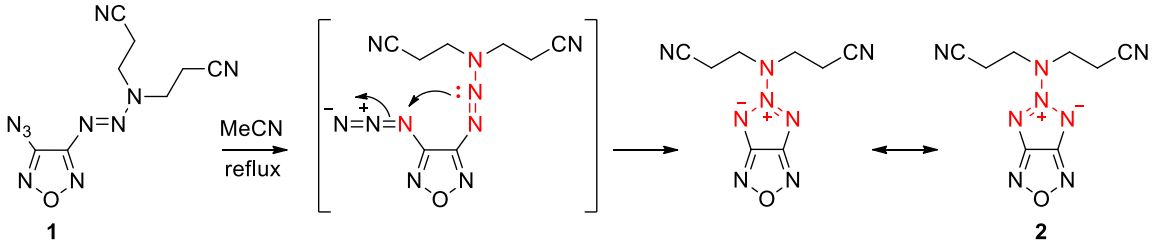

Figure 1. Thermal cyclization of azidotriazene **1**.

Starting azidotriazene **1** was obtained by the reaction of bis(2-cyanoethyl)amine with previously unknown diazonium salt **3** in CH_2Cl_2 at –35 °C. The latter was synthesized by a modified method [1] involving the reaction of 3-amino-4-azido-1,2,5-oxadiazole with $NOBF_4$ in TFA at 0–5 °C followed by solvent removal at this temperature.

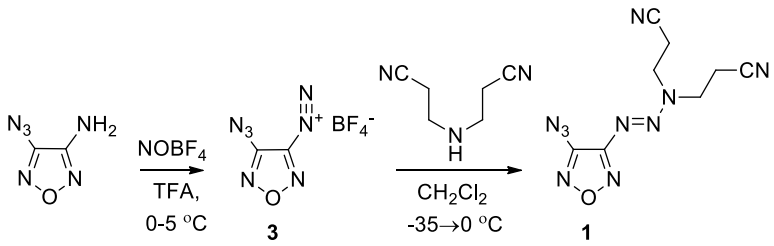

Figure 2. Synthesis of azidotriazene **1**.

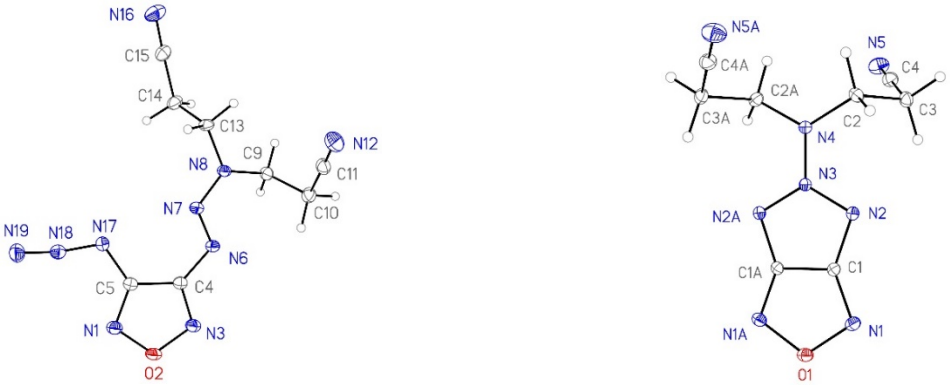

Figure 3. General view of molecules **1** and **2** as determined by single crystal X-ray diffraction.

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