ПОДСЕКЦИЯ «АНГЛИЙСКИЙ ЯЗЫК»

The synthesis of 8-methyl-γ-carboline by the Graebe-Ullmann reaction

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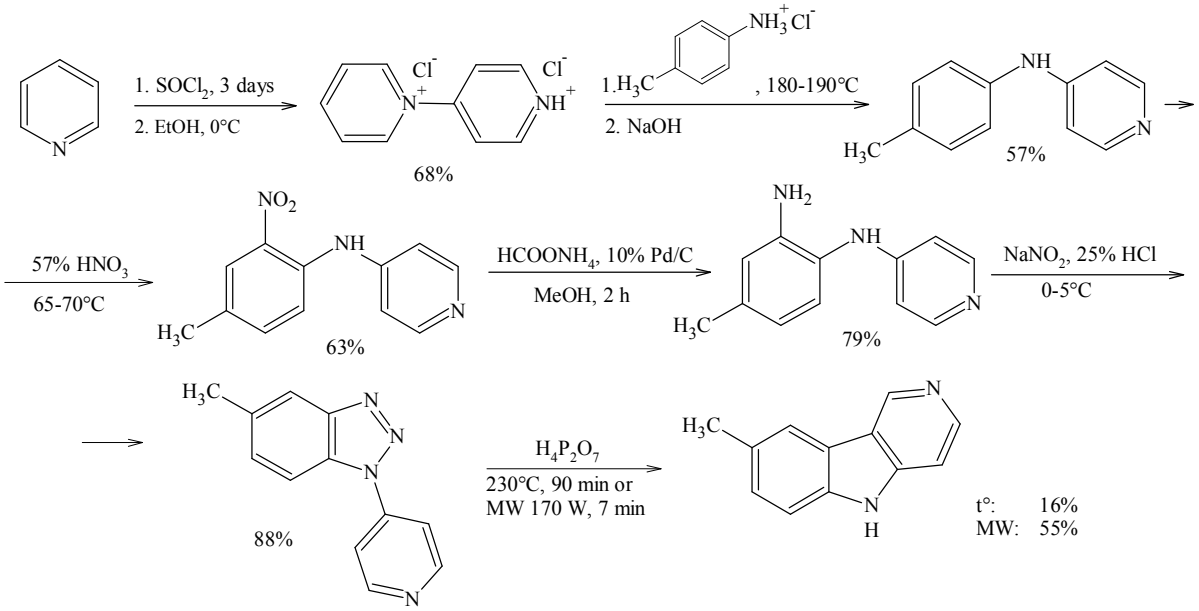
8-Methyl-γ-carboline synthesized for the first time in 1964 from 2-benzyl-8-methyl-1,2,3,4-tetrahydro-γ-carboline by heating in the presence of metallic palladium [1] is highly useful in medicinal chemistry. It is of great synthetic value as the building block in the syntheses of various physiologically active compounds, including «Dimebone»® – the original domestically produced medicine which possesses antihistamine and neuroprotective activity.

One of the possible synthetic approaches for this substance to obtain is the Graebe-Ullmann reaction, which was offered to produce carbazoles at first [2]. This method implies formation of γ-carbolines by decomposition of appropriate 1-(4-pyridil)benzotriazoles [3] or pyridil[3,4-d]-vic-triazoles [4]. The key stage in the synthesis of required 8-methyl-γ-carboline is the production of 5-methyl-1-(4-pyridil)benzotriazole that can be obtained from corresponding N-(4-pyridil)-2-amino-4-methylaniline by the diazotization reaction. It is a special case in the synthesis of 1-substituted benzotriazoles possessing substituents with asymmetric arrangement in benzene fragment.

We suggested the following original synthetic scheme for 8-methyl-γ-carboline to obtain via the Graebe-Ullmann reaction:



It should be noted that 8-methyl-γ-carboline was synthesized for the first time by the application of our original procedure described above.

We also investigated the decomposition conditions of 5-methyl-1-(4-pyridil)benzotriazole and their effect on the final product yield. The yield of γ-carboline proved about 16% under the thermal decomposition (230°C, 90 min), but it was over 55% under the microwave irradiation (170 W, 7 min) [5]. These results provide clear evidence of high efficacy of microwave irradiation for such aim.

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THE INVESTIGATION OF CHARGE DENSITY DISTRIBUTION IN *П*-COMPLEXES VIA HIGH-RESOLUTION XRD

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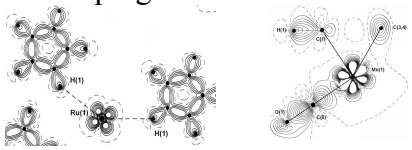
The current work is devoted to the investigation of peculiarities of charge density distribution in crystals of ruthenocene and cymantrene via the AIM [1] topological analysis of charge density distribution function $\rho(r)$ reconstructed from the X-ray diffraction data.

The investigation of ruthenocene [2] crystal allowed us to study chemical bonding in the molecule and to calculate the population of *d*-orbitals of metal atom. We showed that the empirical Espinosa correlation can be used not only for quantitative estimation of energy of closed-shell type interactions, but also for the semi-quantitative estimation of the energy of intermediate bonds like Ru-C ones. It was shown that weak intermolecular Ru…H contacts are responsible for the ordering of structure in contrast to monoclinic ferrocene.

The charge density distribution in cymantrene was analyzed to study the mutual influence of CO and Cp ligands and the reason of C-C bond lengths and atomic charge variation in Cp ring.



A B

Fig. The DED map of A. area of Ru…H contacts in Cp_2Ru; B. vertical section in $CpMn(CO)_3$.

The authors are grateful for financial support RFBR 06-03-32557

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Modeling of Proton Transport in the Gramicidin A Channel

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Finding mechanisms of chemical reactions is one of the main tasks of modern quantum chemistry. With recent developments in high performance computing the increasing attention is drawn to the research of such big molecular systems as proteins, polypeptides and membranes. The use of methods of molecular dynamics together with non empirical methods for calculation of forces is promising for the description of such systems. This allows quantitative description of bond breaking and formation processes as well as the ability to compute free energy profiles for chemical reactions in these systems.

In this work we present the results of modeling of a proton transport process in the gramicidin A channel. We use *ab initio* methods of quantum chemistry for the description of the system in question. Original software package is used for computational studies. Free energy profiles for various stages of the given process are calculated. The use of a method of umbrella sampling made it possible to run calculations of free energy profiles with high parallel efficiency on modern supercomputers. The solution of so computationally demanding problems would not be possible without such methods. In the present work we compare various quantum chemistry methods for the description of the system under study. We also characterize relative accuracy of these methods.

We modeled three distinct stages of the process of a proton transport. That is the direct transport of a proton (the Grotthus mechanism), the transport of an ionic defect, and the reorientation of a single file water chain. Free energy profiles for each of these stages have been computed. From our calculations we conclude that the most energetically advantageous is the stage of the direct proton transfer and the rate limiting stage is the reorientation of a water chain inside the channel which was investigated more thoroughly. We used combined methods of quantum and molecular mechanics for additional studies which made it possible to obtain free energy profiles using a much higher level of theory for the description of our model system. The description of a quantum part was carried at the density functional level of theory with the use of hybrid exchange-correlation functional B3LYP. The AMBER96 force field was used for the description of a molecular mechanical part. Using this method we obtained the free energy barrier of 7.7 kcal/mol for the stage of reorientation of water wire. This result is in a good agreement with the available experimental data.

Polyelectrolyte complex {horseradish peroxidase-chitosan} as a reagent in bioanalytical techniques for determination of some bioactive compounds

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One of the vividly developing fields in modern biochemistry is regulation of stability and catalytic properties of enzymes by including them into various supramolecular structures. A promising example of the latter may be complexes between enzymes and polymers based on non-covalent (e.g. electrostatic) interactions. Natural polysaccharide chitosan is one of the suitable matrices for enzyme immobilization and was previously shown to form a highly active and stable polyelectrolyte complex with horseradish peroxidase. In the present study the reasons of the activation of horseradish peroxidase by chitosan were studied and three approaches to application of this polyelectrolyte complex in chemical analysis were demonstrated.

In order to investigate the nature of activation of horseradish peroxidase by chitosan the influence of chitosan concentration on pKa of ionogenic groups of the enzyme and substrate employed in the peroxidation of o-dianisidine (which is one of the most well-studied peroxidase substrates) was studied. The pKa which is 5.7 for native enzyme (and thus seems to correspond to His42 group in the active centre of the enzyme) was found to increase with the growth of chitosan concentration in the system along with a significant increase of the reaction rate. Consequently, it may be local pH change in the presence of chitosan that facilitates electron transfer by His42 in the active center of the enzyme which finally results in the reaction rate increase.

The next step of the work was to show possible analytical applications of the polyelectrolyte complex {peroxidase-chitosan}. For this reason three approaches applying different types of experimental techniques were used: firstly, a conventionally designed spectrophotometric kinetic determination of chlorpromazine (a component of some drugs), secondly, an electrochemical sensor for determination of hydroquinone and, thirdly, an optical sensor for determination of hydroquinone.

The conventionally designed spectrophotometric kinetic determination of chlorpromazine was based on the effect of substrate-substrate activation of chlorpromazine on o-dianisidine peroxidation. The analytical signal was o-dianisidine peroxidation rate which was measured at 460 nm. The use of polyelectrolyte complex provided significant enhancement of the analytical signal as compared with a similar technique employing native peroxidase. The developed technique provides linear range for concentrations of analyte 1- 50 μM with c_{min} 0.5 μM.

In the case of electrochemical biosensor silver nanoparticles were used in order to structure peroxidase-chitosan film on the surface of a screen-printed electrode and improve its electroconductivity. The obtained biosensor had linear range for concentrations of analyte 15 – 520 μM with c_{min} 5μM.

The development of an optical biosensor for hydroquinone determination was based on transparency of chitosan films and its ability to react with oxidation products of some phenolic compounds. To fabricate an optical sensor a mixture of chitosan and peroxidase solutions was dried on a surface of glass slides (1.4 × 3.8 cm). The analytical signal (light absorbance of the film at 345 nm which evidently corresponds to chitosan-p-benzoquinone adduct) was measured with a spectrophotometer by registering the spectrum of the film after the sensor had been deposited in buffer solution containing hydroquinone and hydrogen peroxide for several hours. The biosensor obtain had linear range for concentrations of analyte 20-500 μM with c min 4 μM

The research was supported by Russian Foundation for Fundamental Research (project № 09-03-00823-a)

Modelling cis-trans isomerisation of green fluorescent protein (GFP) chromophore.

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Photochemical properties of the green fluorescent protein (GFP) [1,2]which is the final emitter in the bioluminescence reaction of the jellyfish Aequorea Victoria have motivated a number of experimental and theoretical studies. Furthermore, other recently discovered fluorescent proteins (FPs) homological to GFP reveal even more surprising properties of important practical applications. Due to that, detailed theoretical studies of FPs structure and properties as well as their chromophores in various environments (protein matix, water solution, gas phase and etc) form a wide scope of modern research. Gas phase GFP chromophore has been under investigation in quite a few theoretical studies in the passed decade, methods ranging from semiempirical to highly accurate ab initio multiconfigurational theories with perturbation theory corrections. One of the important aspects of such research is investigation of cis to trans isomerisation of the model chromophore.

As a model chromophore for gas or condenced phase studies and modelling one can use 4'-hydroxybenzylidene-2,3-dimethylimidazolinone (HBDI) which closely resembles electronic properties of denaturated GFP chromophore. He et al[3] obtained values for cis to trans isomerisation barrier along with energy difference of the isomers of HBDI in water solution by using NMR technique. The height of the barrier was found to be incredibly low compared to other systems having structural similarity. To our best knowledge no theoretical modelling results of this reaction consistent with the experiment are reported, although understanding of such processes is crucial for better comprehension of behavior of several GFP-like proteins (asFP595, Dronpa).

We apply modern quantum chemistry methods to modelling of HBDI both in gas phase and solution. Our focus is on modelling cis to trans isomerisation and properties of the model chromophore consistent with experimental data using modern ab initio methods. The study reveals problematic behavior of density functional theory (DFT) due to multiconfigurational character of the wave function at twisted geometry whereas complete active space self consistent field (CASSCF) yields reasonable results and explains DFT failure. Solvent effects are found to be important and can reduce activation energy by more than 10 kcal/mol. PC GAMESS[4] and GAMESS (US) [5]quantum chemistry software were used to perform the calculations. We also used original hybrid QM/MM flexible fragments technique which is based on PC GAMESS and Tinker[6] programms. We report results of CASSCF(12/11)/cc-pVDZ approximation in cluster of 49 TIP3P water molecules (first solvation shell) to be in good agreement with experimental data[3].

Authors thank SKIF-Siberia and SKIF-MSU for providing computational resources

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PREDICTION OF CATALYST LIFETIME IN ALKANES AROMATIZATION AND REFORMING PROCESSES

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Catalyst deactivation nowadays is among the most important problems of petrochemical industry. More than 6 percent of all scientific publications in heterogeneous catalysis are devoted to this issue

In industry the new catalyst charging leads to suspension of production and, as a result, to the increase of the cost of the process. Thus, it is very important to predict the catalysts lifetime in order to decrease expenses for catalyst reloading and regeneration. The lifetime of catalysts can be determined by investigation of catalyst deactivation in laboratory. But the study of several catalysts aging is difficult because of long-term catalyst lifetime.

The main idea of this work – to elaborate the new accelerated catalyst life test and to find a correlation of catalysts deactivation parameters calculated from the results of accelerated catalyst life tests with real catalyst lifetime obtained in industry, which may lead to opportunity to predict lifetime of new industrial catalysts.

The major result of the work is the new laboratory setup for accelerated catalyst life test. In new laboratory setup catalyst is placed in thermo gravimetric analyzer and catalytic process is carried out directly in it. Consequently, coke accumulation on the catalyst can be observed during a catalytic process. Products of alkane conversion are analyzed with the help of mass-spectrometer and GL-chromatograph.

The results, obtained by new laboratory setup, have demonstrated that dependence of activity and selectivity in n-heptane reforming in conventional laboratory flow reactor can be correlated with the results obtained from laboratory setup designed for accelerated catalyst life tests. Optimal conditions for accelerated n-heptane catalyst deactivation were found. They are low pressure (1-2atm), high temperature (500-540˚C) and low H2-n-heptane ratio. Also, two industrial catalysts are analyzed by new method. The results are in good correlation with their lifetimes in industry.

Synthesis of novel organic ligands for metal nanoparticles decorationand architectures based on them

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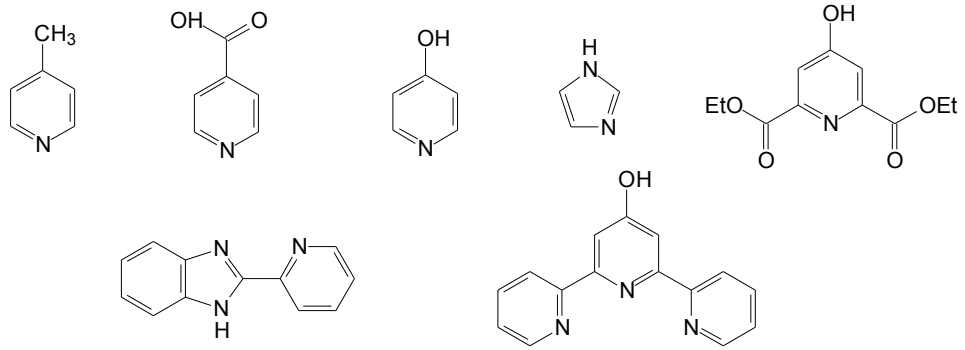
Nowadays the research on gold nanoparticles is one of the most important topics in chemistry, in life and material sciences. This is mostly due to the versatility of these systems: well-organized nanostructures often display valuable chemical, optical, catalytic, electronic and magnetic properties that are distinctly different from those of their component parts or those of larger mass. Numerous sulfur-containing compounds are widely applied for gold nanoparticles stabilization, but, unfortunately, the adsorption of organic ligands involving terminal donor groups has not been developed yet, in spite of the fact that the interaction of such nanoparticles with transition metal ions would result in obtaining new nanohybrid materials on the basis of gold nanoparticles.

We have developed several synthetic approaches to a number of new sulfur containing compounds (thiols and disulfides) on the basis of pyridine, 4-hydroxypyridine, isonicotinic acid, imidazole, pyridine-2,6-dicarboxilic acid, benzimidazole and terpyridine, which were obtained by alkylation using various dibromoalkanes. All compounds were characterized by NMR ^{1}H, ^{13}C, IR-spectroscopy, mass-spectrometry and elemental analysis data.



We managed to obtain gold nanoparticles, modified by these ligands, of different size (2-5 nm), which actually depends on the ligand's structure and experimental conditions. All nanoparticles were studied by transmission electron spectroscopy, UV-vis absorption spectroscopy, dynamic light scattering, NMR ^{1}H and IR-spectroscopy. One of the most urgent problems in nanotechnology nowadays is concerned with controlled and reversible obtaining of gold nanoparticles ensembles – dimers, trimers and polymers. We have shown unusual well-organized spherical aggregates with the average size of 100 nm to form upon interaction of pyridine containing nanoparticles with $Cu(ClO_4)_2$ (Fig.1) and large aggregates of different size to form upon interaction with $Co(ClO_4)_2$ (Fig.2). Dimer nanoparticles were obtained treating complex compound of the benzimidazole derivative and $CuCl_2$ by citrate stabilized gold nanoparticles. The average size of dimer aggregates is 25 nm, the concentration of dimers reaching 60%, which is a result of great significance at present time (Fig.2).

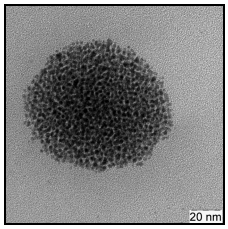


Figure 1

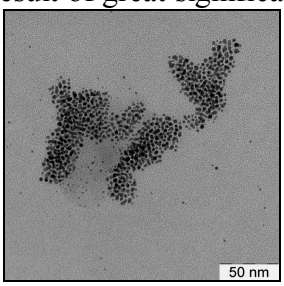


Figure 2

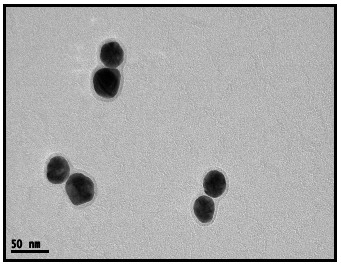


Figure 3

The comparison of analytical possibilities of atomic absorption techniques based on hollow cathode lamp and high-resolution continuous source

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The method of atomic absorption spectroscopy (AAS) remains one of the most applicable methods for the elemental analysis due to its sensitivity and selectivity. Detection limits without preconcentration achieve 10^{-5}-10^{-7}% (depending on element and atomization technique). Traditional way of realization of atomic absorption elemental analysis is based on Walsh approach. Its concept consists of using the line radiation sources (hollow cathode lamp, HCL), modulation of the radiation and the use of a selective amplifier tuned to the same modulation frequency. This concept guarantees the well-known selectivity and specificity of AAS.

At the same time conventional AAS has some disadvantages. The main of them are impossibility of realization of multielement analysis and problems concerning background correction and spectral interferences.

One of the ways to solve the foregoing problems is using new conception based on high-resolution continuum source AAS combined with a specially developed high-resolution double monochromator. The new concept uses a specially developed xenon short-arc lamp as a continuum source with very high radiation intensity, especially in the UV range, a high-resolution double monochromator with a prism pre-monochromator and an echelle grating monochromator with active wavelength stabilization and a UV-sensitive CCD linear array detector with a few hundred pixels that make visible the entire spectral environment of the analytical line.

Since the intensity of radiation in the AAS technique has no influence on the sensitivity but does influence the noise, the detection limits with HR-CS AAS are improved by a factor of 2-5 on average. Using a linear array detector makes it possible to measure the absorbance not only in the line core but also on the line wings. As a result the dynamic working range can be extended to 5-6 orders of magnitude without any problems.

Naturally all spectral lines are fully available as well, i.e. also lines of elements for which no line sources (HCL) are available. An absolutely novel feature is also the possibility of using absorption lines of di-atomic molecules such as PO or CS for element determining (such as phosphorous or sulfur).

Our contribution is devoted to comparison of analytical possibilities of atomic absorption techniques based on hollow cathode lamp and high-resolution continuous source. The estimation of detection limits and other metrological characteristics for both techniques has been made. The results obtained will be presented and discussed in detail.

Extraction and determination of polycyclic aromatic hydrocarbons in soils

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Environmental pollution is an urgent problem in industrial countries, with polycyclic aromatic hydrocarbons (PAHs) being one of the most hazardous pollutants. PAHs are a group of hydrocarbon compounds containing fused aromatic rings in their structures. They are formed during incomplete combustion of fossil fuels, waste incineration, and some industrial processes. Motor vehicle emissions also contribute to the PAH input to the environment. Entering the environment mainly as air pollutants, PAHs are transported over time to water, soil, sediment, and biota. PAHs are known to be human carcinogens and mutagens; thus, it is important to monitor their amount in the environment. Sixteen PAHs have been designated by the United States Environmental Protection Agency as priority pollutants. Six of them have been selected by the European Union for monitoring. In Russia, only benzo[a]pyrene is used as an indicator of PAH pollution.

For the determination of PAHs in solid matrices a careful sample preparation including extraction, concentration, and extract cleanup and the use of a powerful analytical method such as high-performance liquid chromatography (HPLC) are necessary. There are numerous but sometimes contradictory data in the literature concerning PAH analysis in soils; therefore, developing the methods of extraction and determination of PAHs in soils is still an actual task.

In the present study, several methods were used to extract PAHs from naturally contaminated soil samples before analysis by HPLC with time-programmed fluorescence detection. The influence of extraction time and solvent composition on PAH recovery after mechanical shaking, ultrasonication, and Soxhlet extraction was examined. The efficiencies of these methods were compared with the efficiency of microwave-assisted and supercritical fluid extraction. Soxhlet extraction with a mixture of hexane and acetone (1:1) was found to be the most suitable procedure.

A new approach to chromatographic method development in which optimization of stationary phase was the main goal was tested. After a rough first choice of mobile phase, only the stationary phase needed to be optimized. Technically this was realized by using a segmented column system. First retention times were determined with isocratic chromatographic runs of PAHs on five different stationary phases using the same mobile phase. The stationary phases were bonded silica gels (phenyl, cyanopropyl, C_{18}, C_{18} with enhanced polar selectivity, and C_{30}). The obtained individual retention times then were used for the calculation of the best combination of column segments performed by the optimization software. The separation of the sixteen priority PAHs on the segmented column under isocratic conditions was compared with the separation obtained using usual reversed phase column Zorbax SB C18 and a column YMC-PAH specially designed for the analysis of PAH mixtures in gradient elution mode.

Reactions of donor-acceptor cyclopropanes with furan derivatives

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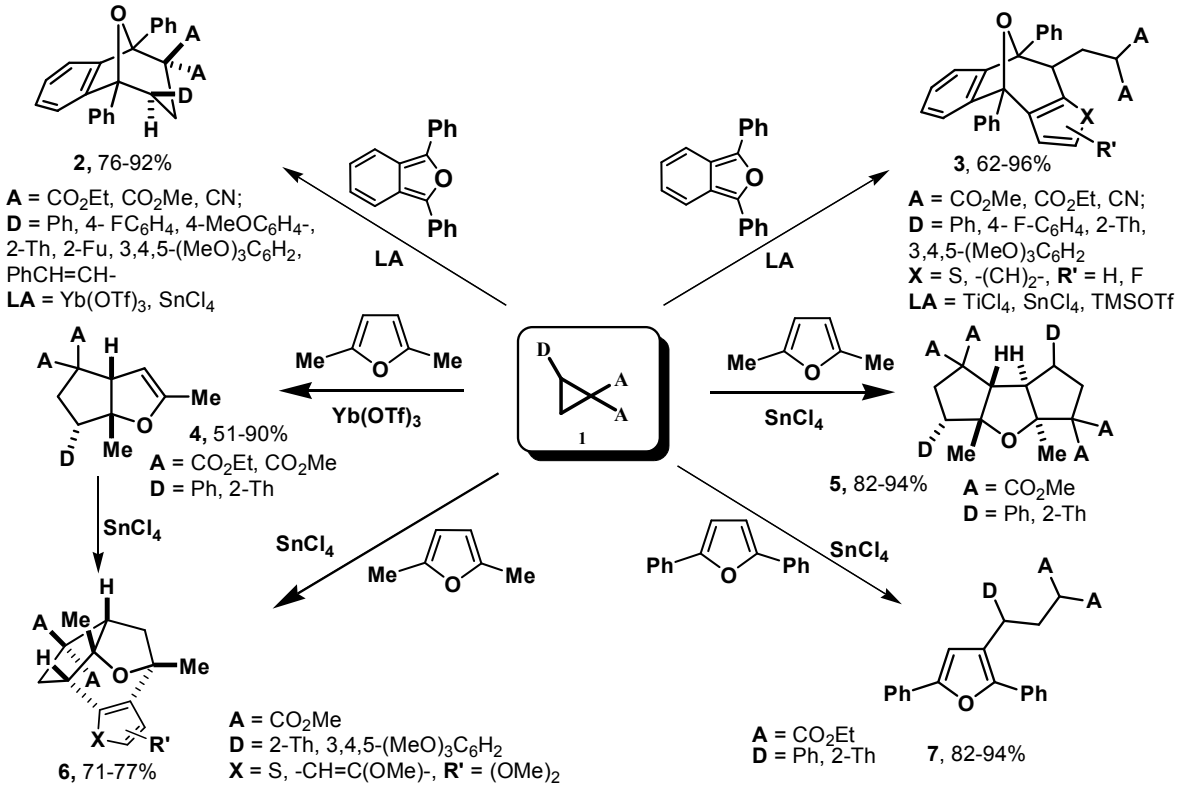
Donor-acceptor cyclopropanes attract significant attention of chemists due to the broad scope of their reactivity. Besides the reactions with electrophiles and nucleophiles donor-acceptor cyclopropanes can enter [3+2] and [3+3]-cycloaddition reactions with various unsaturated compounds. Such reactions afford five- and six-membered carbo- and heterocycles and might be applied for construction of complex natural compounds.

Recently we have demonstrated for the first time a possibility of Lewis acid-mediated [4+3]-cycloaddition of donor-acceptor cyclopropanes to 1,3-diphenylisobenzofuran [1]. This process affords a seven-membered cycle and might be regardered as an analogue of the Diels-Alder reaction.

Further to our research we decided to carefully investigate the reactions between various furan derivatives and donor-acceptor cyclopropanes aiming to determine the preferable mode of their interaction and the influence of reaction's conditions on the course of the reaction. We have obtained products of electophilic substitution, [3+2] and [4+3]-cycloaddition. Thus reaction's pathway depends greatly on the properties of the initial substrates and Lewis acid applied.



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