

**ACADEMICIAN N. N. VOROZHTSOV SCIENTIFIC HERITAGE AT
THE CONTEMPORARY DEVELOPMENT STAGE OF RESEARCHES
OF NOVOSIBIRSK ORGANIC CHEMISTRY INSTITUTE OF
SIBERIAN BRANCH OF RAS**

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The work of Academician N. N. Vorozhtsov has its deserved place in the history of Russian science. It had adsorb in itself all the greatness of Russian organic chemistry traditions and enriched it with discovery and development of new research fields. Scientific interests of Academician N. N. Vorozhtsov realized in his work heritage became that "seed" from which all the directions of reseraches of a school created by him had grown and gained their development in Novosibirsk Organic Chemistry Insitute of Siberian Branch fo RAS.

Aromatic nucleophilic substuituion had been of N. N. Vorozhtsov's great interest of during all his life as one of the main ways of moving from base arenes to their functional derivatives. The results obtained at that were of fundamental significance for forming of up-to-date views on mechanism of metal complex catalysis at aromatic nucleophilic substitution. The system of patterns of relationship, discovered by N. N. Vorozhtsov and his co-workers during studying of aromatic nucleophilic substuituion reations and experimental approaches worked at that created a powerful potential for fluoroaromatic copounds break-through into chemistry.

The brightest period of scientific work of N. N. Vorozhtsov is an extensive research cycle in the field of fluoroaromatic compounds carried out together with his students. Due to it N. N. Vorozhtsov had become a part of the history of science as a founder of this scientific direction in our country.

Realizing the importance of isomerization of aromatic compounds, giving the opportunities of transfer from isomers initially formed in the reactions of electrophilic substitution to less available N. N. Vorozhtsov had carried out a thorough study of the processes of organic compounds isomerization. The works of N. N. Vorozhtsov and his co-workers regarding the isomerization of aromatic compounds were devoted to finding the main patterns of relationship of passing and of a delicate mechanism of the substituent migration process. They had consisted one of the main directions in his work.

One of the side effects obtained together with V. A. Koptug became a starting point for development of the scientific direction, connected with the synthesis based on α -hydroxylaminoxymes derivatives of imidacol ans stable nitroxyl radicals.

On the assumption of the fact that the flora of Siberia is the richest source for biologically active compounds N. N. Vorozhtsov laid the foundations for the powerful development of direction regarding dendrochemistry and chemistry of biologically active compounds for the further coming years.

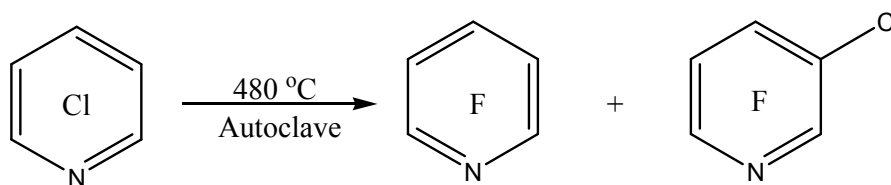
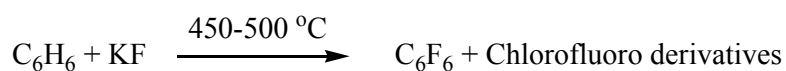
PL-2

FLUOROAROMATIC CHEMISTRY AND MICROREACTORS

R.D. Chambers

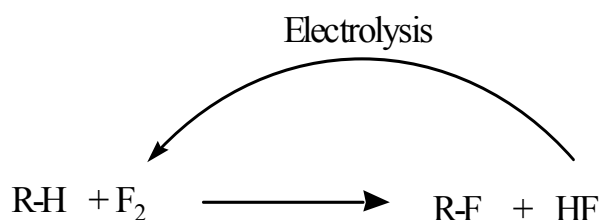
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Foundations for the synthesis of highly fluorinated aromatic compounds were laid many years ago by the pioneering work of Professor N.N. Vorozhtsov and his group who developed a highly successful synthesis of hexafluorobenzene, by heating hexachlorobenzene with potassium fluoride at high temperature, in the absence of a solvent.¹ This development had a considerable influence on our own work which includes a continuing interest in the synthesis and chemistry of highly fluorinated N-heterocyclic aromatic compounds.²



Synthesis of partly fluorinated aromatic compounds continues to be an important topic. Direct selective fluorination by replacement of hydrogen by fluorine is an attractive approach because, in principle, it is an environmentally friendly process with recovery of hydrogen fluoride, the by-product, being possible.

The design of microreactors³ and their application to this and other problems will be outlined.



[1] N.N.Vorozhtsov, V.E.Platonov, and G.G. Yakobson, Bull. Acad. Sci., U.S.S.R, **1963**.

[2] R.D.Chambers, 'Fluorine in Organic Chemistry', Blackwell, **2004**.

[3] R.D.Chambers and R.C.H.Spink, J.Chem.Soc.,Chem.Comm., **1999**, 883; R.D.Chambers, D.Holling, R.C.H.Spink, and G.Sandford, Lab on a Chip, **2001**, 1, 132.

FLUORINE CONTAINING HETEROCYCLES: SYNTHESIS, STRUCTURE PARTICULARITIES, CHARACTERISTICS

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Fluorine containing heterocycles practically can't be find in a wild nature, but for more 50 years of history of fluorine chemistry development they had become such a significant class of compounds, that it would be difficult to imagine a contemporary arsenal of medicines without them.

In the report the synthesis methods, structure particularities and properties of a wide range of nitrogen-, sulphur- and oxygen containing heterocycles (pyridines, pyridazines, pyrimidines, pyriazines and triazines, furanes, pyrrols, thiazoles, thia- and oxazines, dioxines, thiadiazines etc.) are being considered and also their benzene analogues (quinoline and isoquinoline, acridines, quinazolines, quinoxalines and 1,24-benzotriazines, benzoxazines, benzoxadiazines and benzothiadiazines, indoles, benzimidazoles, furazanes and benztriazoles, chromones and cumarines etc.) carrying one, two or three or more fluorine atoms are discussed here too. The information on X-ray analysis and spectral methods (IR, ¹H, ¹³C и ¹⁹F ЯМР) are being discussed as well, they refer to the particularities of the structure of fluorine containing azoles and azines and their oxa-, thia- and benzene analogues. We also consider here the movability of fluorine atoms in the systems under consideration and also the influence of fluorine atoms on the reactivity, complexing and other properties of fluorine containing heterocycles.

The work had been accomplished under the financial support of the state support programme for the leading scientific schools (grant # № 9178.2006.3).

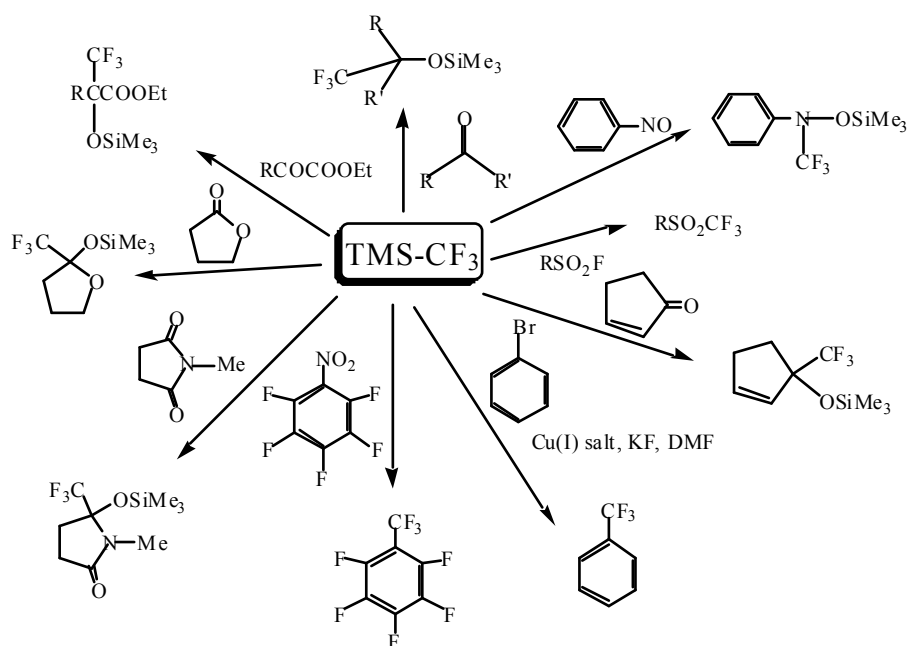
NEW FLUOROALKYLATION METHODS

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The development of methods for the efficient synthesis of fluorinated molecules is blooming because of fluorine's ability (high electronegativity and its relatively close size to hydrogen) to exert special properties on organic molecules. Last decades have also witnessed the profound use of fluorinated compounds in material science, agrochemistry and pharmaceutical industry. Although methods for selective mono and perfluorinations are well developed, similar approaches were not compatible for preparation of the corresponding trifluoromethylated compounds. We have discovered that trimethylsilyltrifluoromethane, TMS-CF₃, as an efficient trifluoromethylating agent for a variety of electrophiles under catalytic and autocatalytic conditions (using nucleophiles). Recent studies in this area will be elaborated.



Furthermore, our recent studies in the area of fluoroalkylations include not only silicon-based compounds but also sulfur containing reagents.

VINYL FLUORIDES IN SYNTHESIS

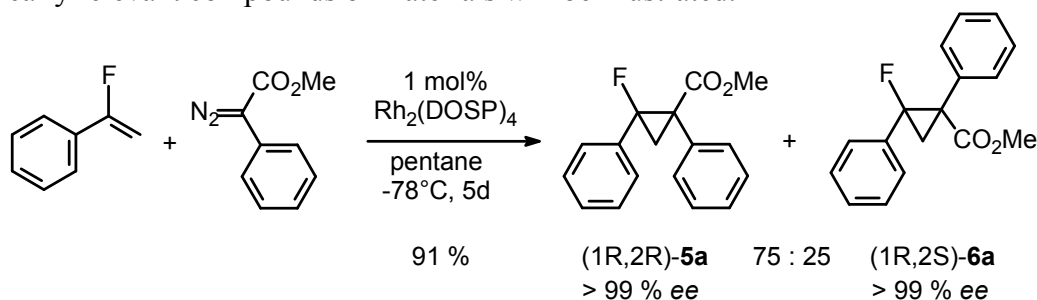
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One of the simplest ways to synthesize the title compounds is bromo-fluorination of alkenes and subsequent HBr elimination from the thus-formed vicinal bromofluoroalkanes.

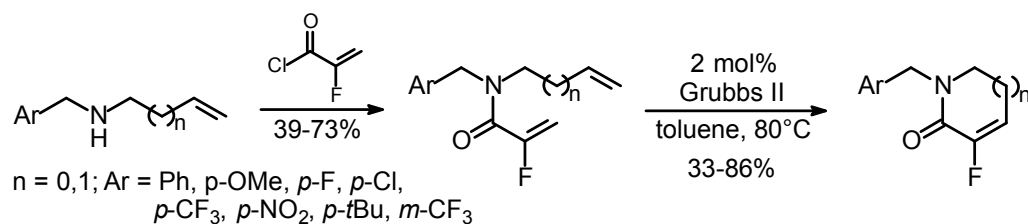
Simple vinyl fluorides have been shown to be more electron rich compared to the corresponding non-fluorinated alkenes. Consequently, these compounds are less reactive dienophiles in Diels-Alder reactions. On the other hand, fluoroalkenes are more reactive in electrophilic reactions such as carbene additions.

2-Fluoroalkenes will be shown to be excellent building blocks toward fluorinated cyclopropanes. Two methods for enantioselective cyclopropanation of vinyl fluorides, i.e. copper-catalyzed reaction with diazoacetates and rhodium-catalyzed reactions with diazomalonates and phenyldiazoacetates will be discussed and its applications in synthesis of biologically relevant compounds or materials will be illustrated.



Moreover, a vinylic fluorine substituent activates also the neighboring position for allylic hydroxylation using a modified Sharpless procedure. The thus formed 2-fluoroallylic alcohols on different ways provide δ -substituted esters, which in the presence of bases undergo Ireland-Claisen rearrangements to yield 4-fluoroalk-4-enoic acids bearing substituents in the 2-position. Chirality transfer from the 3-position of the allylic system to the 2-position of the substituted carboxylic acid is observed after lipase-catalyzed (*Candida antarctica* lipase-B) kinetic resolution of the allylic alcohols and subsequent [3,3]-sigmatropic rearrangement of fluoroallylic propionates and glycines.

Finally, α,β -dienes bearing one vinylic fluorine and a hetero function (N or O) in the chain will be demonstrated to be versatile starting materials to synthesize lactams or lactones, respectively, containing a fluorovinyl moiety.



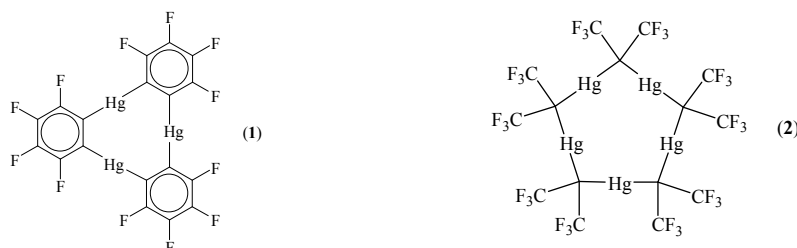
PERFLUORINATED MERCURIAL ANTIKRAUNS, COMPLEXING PROPERTIES, APPLICATION FOR ORGANIC SYNTHESIS AND CATALYSIS

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The report is devoted to coordination and catalytic chemistry of perfluorinated polymercuramacrocycles, which are a new type of reagents having prospects for the fields of molecular scattering ionic transportation and catalysis. These unique compounds contain several Lewis acidic centers in macrocyclic chain and therefore may be considered as distinctive antipodes of kraun-ethers and their thia- and aza- analogues.

In the first part of the report the information on complexing properties of perfluorinated polymercuramacrocycles namely cyclic trimeric perfluoro-*o*-phenylenemercury (*o*-C₆F₄Hg)₃ (**1**) and cyclic pentameric perfluoroisopropylidenmercury [(CF₃)₂CHg]₅ (**2**), containing three and five mercury atoms in flat nine and ten-term cycles respectively will be presented. It was determined, that the reactions of these macrocycles with different anions (Cl⁻, Br⁻, I⁻, SCN⁻, NO₃⁻, SO₄²⁻, BH₄⁻, BF₄⁻, κ1030-[B₁₀H₁₀]²⁻, [Fe(CN)₆]³⁻ and others.) and neutral Lewis bases (nitriles, thiakrauns, ferrocene, azylene, fulvene and others) result in forming of unusual complexes, in which main Lewis particle is cooperatively coordinated by all Lewis acidic centres of antikraun. That wonderful peculiar feature of perfluorinated polymercuramacrocycles reminds the behaviour of kraun-ethers and their analogues in the binding of cations and metals.



In the second part of the report you will learn about the results, obtained at using the mentioned above mercurial antikrauns for the inter-phase catalysis of electrophilic reactions such as azo coupling, chloromethylation, aromatic nitration using diluted nitric acid, nitration using nitrous acid etc. It was proved, that in the most of cases the addition of macrocycle led to sharp increase of the process velocity/rapidity and to initial substrate quantitative conversion into the end products. Also the data regarding the acceleration of Dilse-Alder's reaction and the inter-phase transfer of proton by mercurial antikrauns and their application to shift the keto-enol balances.

The work had been accomplished due to the financial support of the Russian Fund of Fundamental Researches (project # 05-03-32891) and of the Russian Science Assistance Fund (K.H.T.).

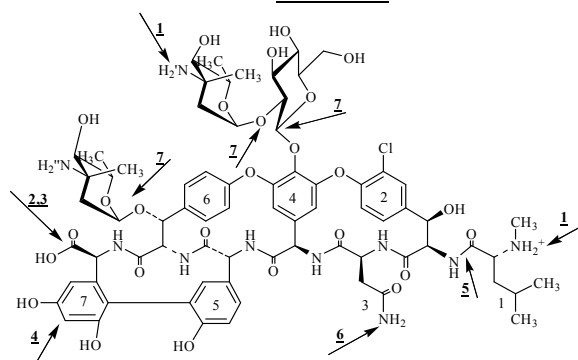
CHEMISTRY AND BIOLOGY OF ANTIBACTERIAL GLYCOPEPTIDE ANTIBIOTICS

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Glycopeptide antibiotics (Vancomycin and others.) are important chemotherapeutical medicals, which are used for treatment of dangerous bacterial infections caused by gram-positive bacteria. Studying of hydrophobic derivatives of these antibiotics resulted in discovering of the compounds active towards vancomycin-resistant staphylococcus and enterococcus. The derivatives of glycopeptides active towards vancomycin-resistant pathogens and possessing better pharmacokinetic properties than vancomycin were obtained. The antibacterial, cytotoxic and antiviral properties of more than 500 derivatives of natural glycopeptides antibiotics and their aglycones and compounds with damaged peptides were obtained and studied. The medicals which are highly effective *in vivo* for infections caused by polyresistant strains of enterococcus, staphylococcus and anthrax (*Bacillus anthracis*) were selected. The mechanism of action of hydrophobic derivatives of glycopeptides was studied as well.

The directions of selective modification of eremomycin antibiotic are as follows::



Eremomycin antibiotic modification

1. Alkylation or acylation of amino-groups
2. Carboxylic group esterification
3. Carboxylic group amidation
4. Aminomethylation
5. Degradation of antibiotic or aglycon
6. Selective asparaginamide hydrolysis
7. O-glycoside hydrolysis

It was found (During joint studies with Prof. Balsarini in the Pera Institute of Catholic University of Leven, Belgium), that some derivatives of semi-synthetic antibiotics and of their aglycones are active towards HIV at low millimolar inhibitory concentrations ($IC_{50} \sim 1 - 3 \mu M$). Antibiotics derivatives suppress effectively the resistant lines of HIV-1 virus. Preliminary investigations showed, that the derivatives of antibiotics prevent the virus from entering the cell.

Some of the new derivatives are active towards shell viruses like HSV, VZV, CMV, and also coronavirus of SARS. The strict correlation between the inhibiting potential of compounds studied towards different viruses had not been noticed, but HIV is the most sensitive one.

PL-08

THE SYNTHETIC TRANSFORMATIONS OF HIGHER TERPENOIDS AND ALKALOIDS AS A SCIENCE BASE FOR THE DEVELOPMENT OF MEDICINAL PREPARATIONS

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Synthetical transformations of natural compounds had become one of the leading directions of medical chemistry since the middle of the last century. Nowadays the medicines obtained on the base of modificants of natural metabolites possess the leading place by the volume of sales.

The main goal of our researches devoted to the chemistry and pharmacology of phetogenous highest terpenoids and alkaloids is creating of scientific basis and commercial production technologies for medicines based on local vegetable raw materials. The goals of the fundamental plan are:

- The development of methods of selective transformations of polyfunctional compounds;
- Synthesis of new structural types;
- The nature of pharmacological influence of modificants of vegetable metabolites.

As a result of the research of one of the most available biologically active metabolites of the local flora - glycyrrhizic acid- for the first time the common approaches and methods of modification of glycosides were developed. Perspective antiviral (inhibitors of reproduction of HIV, of viral hepatitis type B, C, of herpesvirus, of Marburg, of atypical pneumonia), immunostimulating, hepatoprotective, antiphlogistic and other valued agents were disclosed. In the field of chemistry and pharmacology of triterpenoids of a lupan row the original results were obtained, they allowed to present for pre-clinical researches high effective anti HIV agents, correctors of cytostatic agents, antoulcer agents.

Based on the materials of the levopimaric and lambertian acids diterpenoids study the new conception of reactions of diene and retrodiene synthesis was advanced. New ways of synthesis of alkaloid like structures based on diterpenoids of abietanic and labdanic row were suggested. For the first time the program regarding studying the transformations of diterpenic alkaloids was carried out. The prospective of metal-complex catalysis methods was demonstrated as well. The new antiarrhythmic agents were offered for pre-clinic aprobation. High active tumor cells apoptosis inductors were revealed.

**PHYTOECDYSTEROIDS *SERRATULA CORONATA*: ISOLATIONS,
IDENTIFICATION, TRANSFORMATIONS**

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Found in 1954 firstly in the bodies of insects as hormones of ecdysis, metamorphosis and diapause, ecdysteroids were identified after 12 years period in a number of plants, at that in a significantly higher concentrations. The originality of phytoecdysteroids structure as polyhydroxylated sterines and their harmlessness for mammals and human opened the prospects for using the present class of natural compounds or their structureous analogues for medicine and agriculture.

About 200 different phytoecdysteroids are isolated and identified out of different kinds of plants. *Serratula coronata* L., which grows in the South Ural region has one of the richest sets of phytoecdysteroids. A high-performance method for isolating of phytoecdysteroids out of this plant was developed by our specialists. 18 phytoecdysteroids were isolated, identified and described as a result of that. The six out of them were isolated for the first time out of *S. coronata*, and 4 of them proved to be new phytoecdysteroids.

For the most representative *S. coronata* phytoecdysteroid – 20-hydroxyecdyzone the transformations were accomplished, mostly the ones of the non-traditional character. As a result the synthesis of a number of phyto- and zooecdysteroids of a low abundance in nature, fluorine containing analogues were developed and the analogues of ecdysteroids of a fundamentally new structure were synthesized.

PL-10

**ATTEMPTED SYNTHESIS OF 16,16,16,17,17,17-
HEXAFLUORORETINAL VIA 7,7,7,8,8,8-HEXAFLUORO- β -
CYCLOCITRAL**

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Starting from hexafluoroacetone an improved and more efficient synthesis for 7,7,7,8,8,8-hexafluoro- β -cyclocitral and new strategies for the preparation of 16,16,16,17,17,17-hexafluororetinal are described and discussed. The reactivity of the aldehyde function especially in 1,1-bis(trifluoromethyl)-5-methyl-6-formylcyclohex-3-ene, which is easy of access, was investigated.

THE CHEMISTRY OF PHATHALOCYANINES AS A BASE FOR CREATION OF FUNCTIONAL MATERIALS

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The main results obtained recently by the team of the Institute co-workers under the guidance of the authors in the field of organic and physical and organic chemistry of phthalocyanines and their analogues and also the review of new materials and technologies, which we managed to create on the base of these studies are presented in this report.

We have considered here in details:

1. The use of phthalocyanines as catalysts of ecologically pure homogeneous oxidation processes of organic substrates using oxygen, peroxides and peracides, substituting the technologies, exploiting the compounds of heavy metals as oxidizers. Pilot and small branch production of chemicals.

2. The development and implementation of chemicals based on phthalocyanines for fluorescent diagnostics and photodynamic therapy of cancer and of some non-oncological diseases into the general practice. Pre-clinical and clinical results.

3. The development of new approach for the cancer treatment – the so called catalytic therapy applying phthalocyanines as catalysts of oxidation reaction of ascorbic acid using oxygen, during which cytotoxic radicals are formed. Preclinical and clinical results.

4. Application of PcM as photosensitizer for photodynamic decontamination of drinking water, capable to replace initial chlorination for traditional purification technology. The results of pilot tests at water station.

5. The development and serial production of phthalocyanines as catalysts for oxidation of hydrogen sulphide and mercaptans for air purification, water treatment, sweetening of carbons and obtaining of important for practice disulphides.

6. Creating of system fungicides for growing and storing of potatoes based on phthalocyanines. Experimental reseraching and field tests.

PL-12

BIOLOGICALLY ACTIVE COMPOUNDS FROM THE PLANTS OF GEORGIAN FLORA

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The multiform flora of Georgia is a rich source for biologically active compounds, that can be used for medicinal purposes.

About one thousand plants were studied in regards with containing of such chemical classes as cardial glycoside of cardenolyde and buffadienolyde groups, steroid and triterpenoic saponins, lipids, flavonoids, toluenyenes, coumarins, tannins, anthraquinones. Several hundreds of individual compounds were isolated and described among them there are plenty new. The structures of isolated compounds were defined by state-of-the-art analytical methods.

The results of studying of the following plants biologically active compounds have been presented: *Digitalis ciliata* Trautv., *Digitalis ferruginea* L., *Helleborus abchasicus* A.Br., *Helleborus caucasicus* A.Br., *Yucca gloriosa* L., *Tribulus terrestris* L., *Ruscus ponticus* P.F.Yeo., *Hedera caucasigena* Pojark., *Hedera coclchica* L., *Hedera pastuchowii* Woron., *Cephalaria gigantea* L., *Caltha polypetala* Hochst., *Fatsia japonica* (Thunb) Decne et Phanch., *Cyclamen vernalis* Sweet., *Paliurus spina-christii* Mill., *Astragalus falcatus* L., *Rhododendron Ungernii* Trautv., *Saturea hortensis* L., *Rhamnus frangulae* L.

Cardiotonic, antiatherosclerotic, bronchospasmolytic, antirheumatic, antiphlogistic, antiviral, hepatoprotecting and cholagogic, hypoazotemic, antipsoriatic, hypoglycemic, regulating the gastrointestinal tract medicals based on the different compounds classes have been created.

Economic raw materials for synthesis of steroid hormonal preparations and also growth – promoting factor for plants have been suggested.

CHEMICAL COMPOSITION OF SIBERIAN LARCH AND GUMHAR BIOMASSES AND TECHNOLOGY FOR MEDICALS ISOLATING OUT OF WOOD AND RIND

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Более чем 20-ти летние исследования, проводимые в лаборатории химии древесины ИрИХ СО РАН, строения соединений биомассы лиственницы, как основной лесообразующей породы России, привели к выводу о том, что её биомасса может служить неисчерпаемым источником медицинских препаратов [1].

Флавоноиды древесины, представлены дигидрокверцетином (ДКВ), дигидрокемпферолом, нарингенином; коры – нарингенином, дигидрокемпферолом, дигидрокверцетином, кемпферолом, кверцетином, изорамнетином, (-)-эпиафцелехином, (+)-катехином, (-)-эпикатехином, димерными, олигомерными и полимерными флавоноидами. Впервые показано, что димеры и олигомеры представлены спироструктурами с γ -лактонным циклом (лариксинол, лариксидинол, ларизинол, трифлариксинол). Эти же структуры лежат в основе строения наиболее представительной по весу полимерной части этилацетатного экстракта коры (антиоксидантный комплекс – «Пикнолар»).

Высокая биологическая активность мажорного мономерного флавоноида древесины лиственницы сибирской и Гмелина – дигидрокверцетина, позволила создать на его основе новый медицинский препарат широкого терапевтического действия – «Диквертин» (субстанция для производства более двух десятков БАД, в том числе «Капиллар») по оригинальной технологии его промышленного производства, томскими учеными созданы новейшие медицинские препараты: «Саливертин» (ДКВ+аспирин), «Асковертин» (ДКВ+витамин С).

Для повышения биодоступности дигидрокверцетина нами совместно с Институтом твердого тела и механохимии СО РАН разработаны наноконпозиты с карбонатами: нанодиквертин – Са и Mg, наноасковертин – Mg и Са, наносаливертин – Са и Na.

Значительную часть биомассы лиственницы составляет арабиногалактан (10-25%). Лаборатория, совместно с ООО ИНПФ «Химия древесины», разрабатывает малозатратную технологию промышленного производства высокочистого АГ для медицины по междисциплинарному проекту СО РАН и ДВО РАН. На основе АГ разработан БАД «Фибролар» с иммунокорректирующими и другими свойствами.

Кроме антиоксидантного комплекса, состоящего из фенолокислот, мономерных флавоноидов и спирановых ди-, олиго- и полимерных флавоноидов, в коре лиственницы охарактеризованы воск, танины и пектин.

Целлюлоза целлолигнинового остатка после извлечения экстрактивных веществ из древесины подвергается гидролизу концентрированной серной кислотой при низких температурах с целью получения кристаллической глюкозы для медицины и глюкозных сиропов для пищевой промышленности.

[1] Бабкин В.А., Остроухова Л.А., Иванова С.З., Иванова Н.В., Медведева Е.Н., Малков Ю.Н., Трофимова Н.Н., Федорова Т.Е. Продукты глубокой химической переработки биомассы лиственницы. Технология получения и перспективы использования // Рос. хим. ж. (Ж. Рос. хим. об-ва им. Д. И. Менделеева). 2004. Т. XLVIII. №3. С. 62-69.

СИНТЕЗ И СЕНСОРНЫЕ СВОЙСТВА ФЛУОРЕСЦЕНТНЫХ ПРОИЗВОДНЫХ КУМАРИНА

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Многие производные кумарина отличаются повышенной фоточувствительностью (фотоиндуцируемые реакции [2+2]-циклоприсоединения и димеризации). Некоторые из них обладают эффективной флуоресценцией и являются промышленными лазерными красителями. 7- и 4-Гидроксикумарины подвержены, кроме того, таутомерным и изомеризационным превращениям под влиянием растворителей и облучения. Производные кумарина рассматриваются поэтому в качестве весьма перспективных соединений в создании новых сенсорных систем, пригодных для целей нанотехнологии.

В докладе систематически обсуждено строение различных производных 4- и 7-гидроксикумаринов и их превращения, инициируемые облучением и взаимодействием с растворителями. Далее перечислены отдельные группы производных кумарина и его аналогов, для которых обнаружены фото- или сольватоиницируемые превращения, сопровождаемые изменением флуоресценции:

- 1) 4- и 7-гидроксикумарины – таутомерные переходы и реакции [2+2]-циклоприсоединения;
- 2) 3-ацил-4-гидроксикумарины – гидрокси/кето - таутомерные переходы и реакции димеризации;
- 3) имины 3-ацил-4-гидроксикумаринов – (гидрокси)имино/(кето)енамино таутомерные переходы;
- 4) гидразоны 3-ацил-4-гидроксикумаринов – (гидрокси)гидразоно/(кето)ен-гидразино таутомерные переходы;
- 5) 4-гидрокси-3-пирозолинилкумарины – фотоароматизация.

Обсуждены также новые схемы синтеза и превращения 4-гидрокси-3-дiazepинилкумаринов, полиметиновых красителей – производных 3-ацетил-4-гидроксикумаринов и некоторых их аналогов – производных 2-хинолона.

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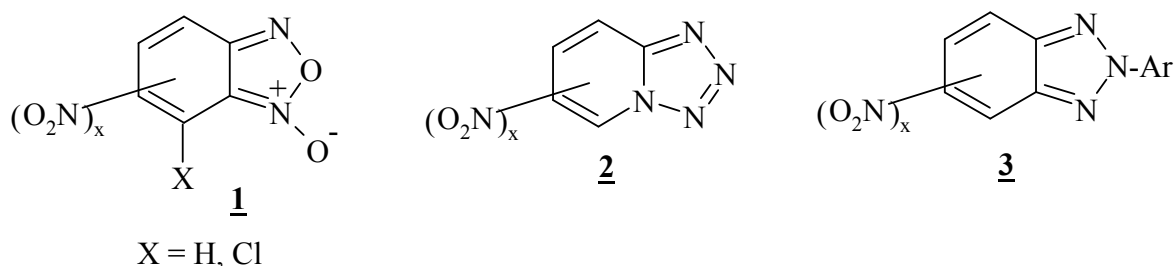
THE DUAL SUPERELECTROPHILIC AND PERICYCLIC REACTIVITY OF NITROBENZOFUROXANS AND RELATED HETEROCYCLES. FACILE S_NAR-S_EAR COUPLINGS AND POLAR DIELS-ALDER CYCLOADDITIONS.

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Going to extremely electron-deficient aromatic or heteroaromatic structures results in a large broadening of the scope of nucleophilic aromatic substitutions and related σ -complexation processes. This will be emphasized through a discussion of the ease of C-C coupling of some nitro-activated benzofuroxan, tetrazolopyridine and benzotriazole structures (**1-3**) with very weak carbon p-nucleophiles, e.g. indoles, pyrroles, anilines. Extensive kinetic studies of these reactions have revealed that the reactivity of **1-3** fits nicely the general structure-reactivity relationship recently introduced by Mayr et al to describe the rate of many nucleophile-electrophile combinations (Acc.Chem.Res.2003,36,66), allowing the positioning of these neutral reagents on the electrophilicity scale E defined for carbocationic species. Values of E for **1-3** are found to fall in the same domain of reactivity as such strongly electrophilic cations like 4-nitrobenzenediazonium or tropylium cations, making reasonable to accord superelectrophilic properties to **1-3**. These compounds can actually be used as convenient probes to detect low basicities with some interesting applications in analytical chemistry.

Of equal interest is that the superelectrophilicity of **1-3** is closely related to the low aromatic character of the six-membered ring. As a result, these heteroaromatics exhibit a high propensity to contribute to a variety of Diels-Alder reactions. Selected examples will be discussed with a particular focus on the evidence obtained that most of the cycloadditions proceed through a two-step addition-cyclization pathway, i.e. they have a very polar character. Importantly, these cycloadditions provide a promising approach to synthesis of highly functionalized heterocyclic structures.



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ELECTRON-RICH NOBLE METAL COMPLEXES OF TRIPOD PHOSPHANE LIGANDS WITH BORON OR FLUOROSILICON ACCEPTOR CENTRES

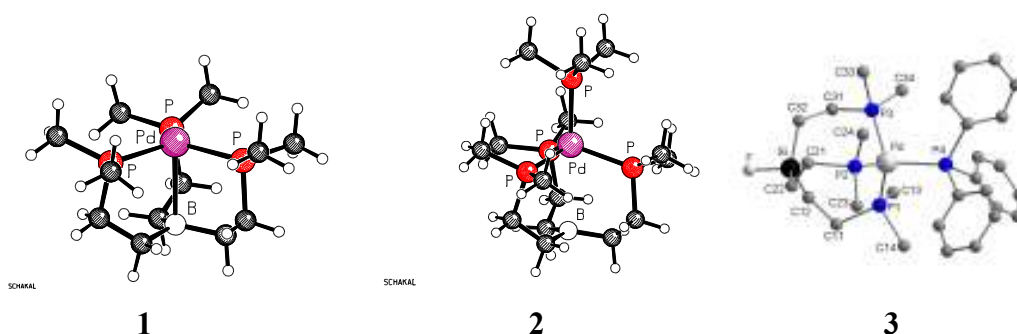
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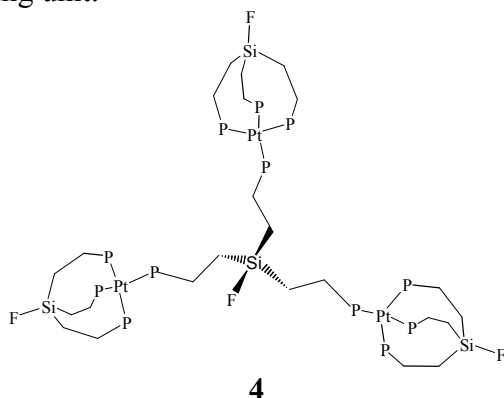
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Tripod-phosphane ligands of the type $A(\text{CH}_2\text{CH}_2\text{PMe}_2)_3$ ($A = \text{B, FSi}$) have been prepared and used for the syntheses of novel noble metal cage complexes $A(\text{CH}_2\text{CH}_2\text{PMe}_2)_3\text{M}$ (structures **1 - 3**).



Structures **1** and **2** have been deduced from NMR spectroscopic data in comparison with previously investigated nickel complexes of related tripod ligands, for which structural data were obtained by single crystal X-ray diffraction studies [1, 2]. In accord with the spectroscopic results, the observed bond lengths and angles, especially the surprisingly short Pd–Si distance of 3.875 Å, which is smaller than the Ni–Si distance in the corresponding nickel complex [3], prove the expected through-cage Pd→Si and Pd→B interactions in **1 - 3**.

The preparation of the analogous platinum complex from various precursors and the tripod ligand $\text{FSi}(\text{CH}_2\text{CH}_2\text{PMe}_2)_3$ was unsuccessful, but surprisingly led to the trinuclear complex $[\text{FSi}(\text{CH}_2\text{CH}_2\text{PMe}_2)_3\text{Pt}]_3(\text{PMe}_2\text{CH}_2\text{CH}_2)_3\text{SiF}$ (**4**) containing three cages of type **1** with FSi instead of boron in the bridge-head position and an additional tripod ligand as bridging unit.



Quantum chemical calculations have been carried out to elucidate the coordination geometry expected for cages **1 - 3** and the corresponding platinum cage in **4**. The calculations support the structures within the expected limitations of the experimental and theoretical methods and – in spite of the extremely soft coordination sphere – are in accord with the spectroscopic results.

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CONSTRUCTION OF BICYCLE AND CAGE COMPOUNDS USING ALLYLIC BORON DERIVATIVES

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S.Yu. Erdyakov, G.D. Kolomnikova, T.V. Potapova (Moscow, Russia)

The report will discuss the principles of reactions of allylboranes(types of the reactions) and their application for building various heterocycles. The main attention will be given to three fundamental reactions:

- allylboron-acetylen condensation (ABAC)
- reductive trans- α,α' - diallylation of nitrogen aromatic compounds and
- $-\alpha,\alpha'$ -diallylation of lactams

These reactions run regio- and stereoselectively to form one or several new C-C and B-C bonds. On the basis of ABAC there were synthesized optically active 3-borabicyclo[3.3.1]non-6-enes, their O-, S- and NR analogues, as well as 1-bora- and 1-azaadamantanes. Bridged and spiro-joint azabicycles were obtained by combination of diallylation of pyridines, pyrrole and lactams and intramolecular metathesis. Diallylation of lactams was applied in full synthesis of cephalotaxine, which esters posses anti leukemic and antimalarial activity.



The work has been supported by RF President's grants (NSh 2878.2006.03), RFFI (05-03-32953, 05-03-33268) as well as by RAS Presidium (Tartakovsky V.A. and Grigor'ev A.I.) (programs ##1,10).

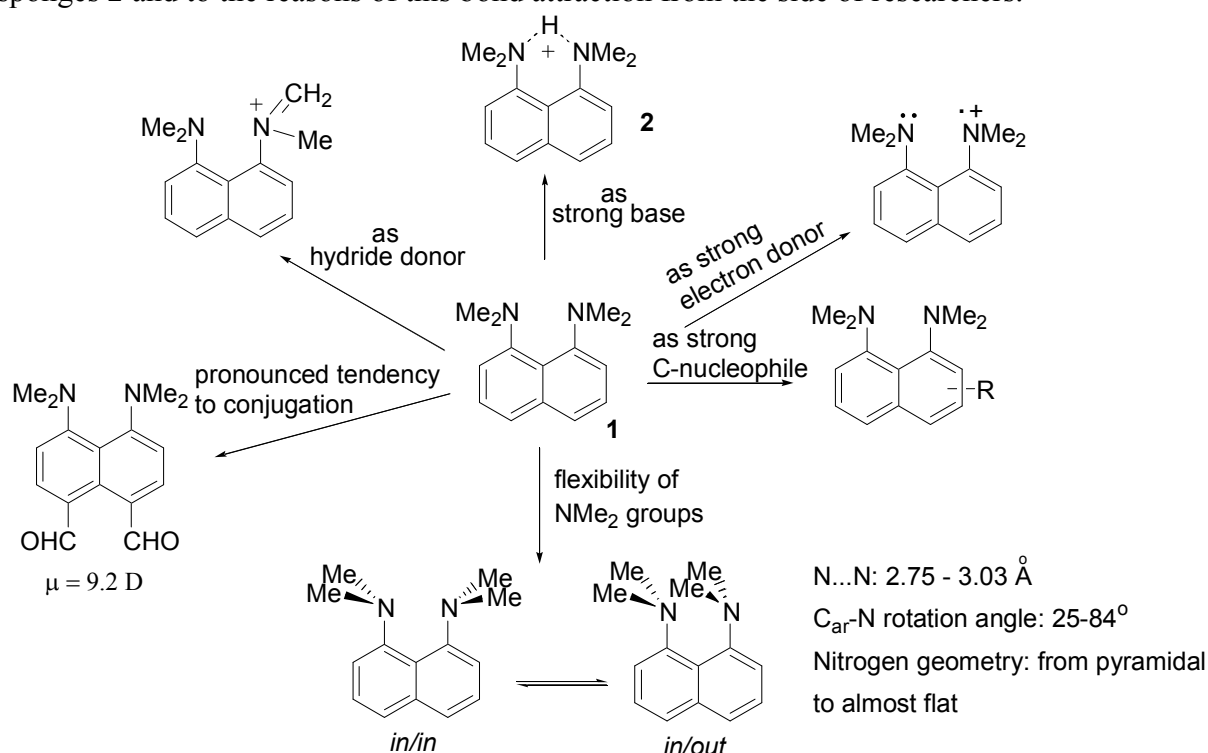
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PROTON SPONGES: MAIN TRENDS

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Proton sponges is a variety of neutral organic bases, which extraordinary high basicity is combined with drastically reduced nucleophilicity. The parent compound of the whole family of these compounds is 1,8-bis(dimethylamino) naphthalene **1**, the most studied representative of them. The field is strongly developing both from fundamental and from applied problems of view. The report, along with general issues such as the history of invention and classification of proton sponges, concerns problems of their practical application, structural, physical and chemical characteristics as well as basicity and the most fundamental aspects of reactivity. It will be shown that the proton sponges are not only strong bases but also very strong C-nucleophiles, donors of electrons and hydride ion. A special attention is given to the nature of intermolecular hydrogen bond in the cations of proton sponges **2** and to the reasons of this bond attraction from the side of researchers.



CATALYTIC SYNTHESIS OF 3H-BENZO[E]- AND 1H-BENZO[G]INDOLES

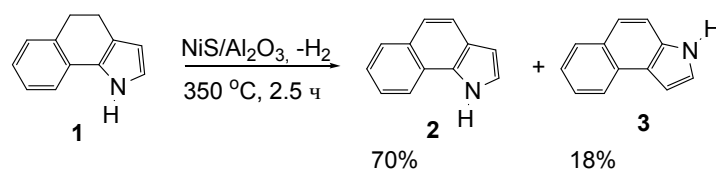
A.I. Mikhaleva, A.V. Ivanov, A.M. Vasil'tsov, E.Yu. Schmidt, B.A. Trofimov

A.E. Favorsky Irkutsk institute of chemistry SB RAS

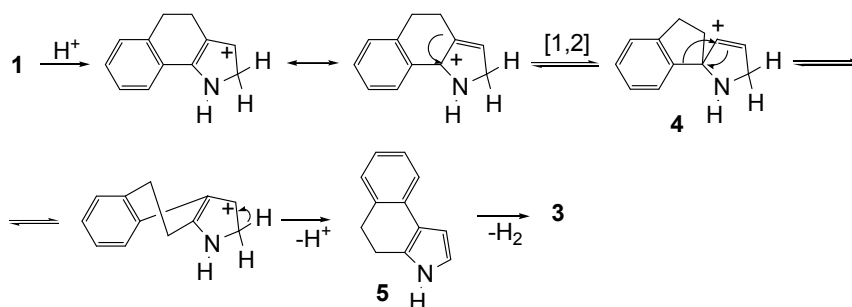
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The chemistry of benzoindoles is strongly studied due to the invention of indole antibiotics (CC-1065 and duocarmicines) which are strong cytotoxines and potential anticancer drugs. Among them, benzoindole analogues are the most stable and pharmacologically active. Meanwhile, the known syntheses of benzoindoles run in several stages and are based on the raw difficult of access.

We have found that 3H-benzo[g]- (2) and 1H-benzo[e]indoles (3) can be obtained by catalytic dehydrogenation of available 4,5-dihydrobenzoindole (1) produced in one preparative stage from 1-tetralonoxime (or from 1-tetralone and hydroxylamine) and acetylene according to Trofimov reaction [1-3].



The rearrangement resulting in [e]-isomer runs, obviously, through spiro intermediate 4 with the substituent migration to form 4,5-dihydro-3H-benzo[e]indole 5 followed by its dehydrogenation to indole 3.



The work has been fulfilled by financial support of Federal agency on science and innovations (contract № 02.445.11.7296)

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PL-20

S_N^H REACTIONS FOR THE SYNTHESIS OF MACROCYCLES
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The report is dedicated to the main mechanisms and synthetic methods to realize reactions of nucleophilic aromatic replacement of hydrogen (S_N^H).

The use of this methodology was demonstrated by an example of construction and modification of macrocycles by means of p-deficient heterocycles. Benzo crown ethers, podands, kalixarenes, porphyrins are involved in these conversions. There were studied structural features of some new macrocycles, their ability to bind ions of metals and amino acids.

TRADITIONS AND MODERN TENDENCIES IN SCIENTIFIC INVESTIGATIONS OF N.N. VOROZHTSOV'S LABORATORY OF ORGANIC DYES AND INTERMEDIATE PRODUCTS

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The department of chemical technology of organic dyes and intermediates was established in 1923y by professor N.N.Vorozhtsov Senior and was governed by N.N.Vorozhtsov-younger, an academician to be, since 1946 till 1961y. The main works of his disciples were devoted to investigation of mechanisms of electrophilic and nucleophilic substitution in aromatic series, to development of synthesis methods to obtain new aromatic and heteroaromatic substances and further they were developed by Novosibirsk institute of organic chemistry of USSR AS. N.M. Przhiyalgovskaya (1953)studied isomerization of fluoro-, chloro- and bromonaphtalenes in gas phase on Al₂O₃ in the presence of halogenated hydrocarbons that opened a way to isomers difficult of access. N.I.Karandasheva (1956) determined features of sulfonation of 2-chloronaphthalene. S.I.Kutkevichus carried out an investigation of products of interaction of epichlorohydrin with aromatic amines and synthesized azo-components of interest for disperse dyes. A series of works by V.A.Koptyug (1957-1960) using radioactive tracers allowed to determine the mechanisms of isomerization of 1-chloronaphthalene, 1-methylnaphthalene and aromatic sulfones as well as naphthalene monosulfo acids. G.G.Yakobson (1958) studied interaction of aromatic halogenated nitro compounds with metal fluorides that became the basis for chemistry of various organofluoric compounds.

Since 1961 till 1989y the department was headed by B.I.Stepanov. Within this period there were completed the works in the field of nucleophilic substitution of a halogen in nitrogen-containing compounds of aromatic series (B.I.Stepanov, 1963y), in aromatic o-halogen carbonic acids in the presence of copper complexes (V.N.Lisitsyn, 1974y.).Fundamental investigations were held in the field of color theory of organic compounds and there were synthesized numerous sulfur- (V.Ya.Rodionov, A.Ya.Zheltoy), phosphorus-(A.I.Bokanov), silicon-(V.F.Traven), boron-containing (G.V.Avramenko) compounds with various inclusions of elements into chromophore systems. As a result, the development of new unique laser triarylmethane dyes was awarded the USSR State prize (B.I.Stepanov, N.N.Bychkov, 1987y). Active connections of the department with branch institutes (VNIIMethanolproject, VNIIOPIK, VNIIMonocrystals) made possible investigations on the basis of 3(5)-methylpyrazole. As a result, there was studied the reactivity of pyrazole substituents and various organic dyes and luminophores were synthesized (Perevalov V.P.,1988).

Nowadays the department activity is directed to the works in the field of combinatorial and supramolecular chemistry. On the basis of disubstituted chlorobenzoic acids there were synthesized multifunctional derivatives of benzimidazole, potential color stabilizers of benzotriazole series. Syntheses of new photo- and cationsensitive compounds on the basis of chromenes and crown ethers including compounds of rotoxane series were carried out as well.